Original research

Exosomes derived from *Fusobacterium nucleatum*-infected colorectal cancer cells facilitate tumour metastasis by selectively carrying miR-1246/92b-3p/27a-3p and CXCL16

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ABSTRACT

Objective Exosomes released from tumour cells are packed with unique RNA and protein cargo, and they are emerging as an important mediator in the communication network that promotes tumour progression. The facultative intracellular bacterium *Fusobacterium nucleatum* (Fn) is an important colorectal cancer (CRC)-associated bacterium. To date, the function of exosomes from Fn-infected CRC cells has not been explored.

Design Exosomes were isolated by sequential differential centrifugation and verified by transmission electron microscopy, NanoSight analysis and Western blotting. Given that exosomes have been shown to transport miRNAs and proteins to alter cellular functions, we performed miRNA sequencing and proteome analysis of exosomes from Fn-infected and non-infected cells. The biological role and mechanism of exosomes from Fn-infected cells in CRC tumour growth and liver metastasis were determined in vitro and in vivo.

Results We demonstrated that exosomes delivered miR-1246/92b-3p/27a-3p and CXCL16/RhoA/IL-8 from Fn-infected cells into non-infected cells to increase cell migration ability in vitro and promote tumour metastasis in vivo. Finally, both circulating exosomal miR-1246/92b-3p/27a-3p and CXCL16 levels were closely associated with Fn abundance and tumour stage in patients with CRC.

Conclusion This study suggests that Fn infection may stimulate tumour cells to generate miR-1246/92b-3p/27a-3p-rich and CXCL16/RhoA/IL-8 exosomes that are delivered to uninfected cells to promote prometastatic behaviours.

Significance of this study

What is already known on this subject?

- *Fusobacterium nucleatum* (Fn) is the most important microbe-related risk factor in the initiation and progression of colorectal cancer (CRC).
- Fn is a facultative intracellular bacterium.
- Tumour-derived exosomes (TEXs) carry cargo reflecting genetic or signalling alterations in the cancer cells of origin and serve in the communication network of tumours.

What are the new findings?

- Fn infection increases the secretion of exosomes from CRC cells.
- Fn infection stimulates tumour cells to generate miR-1246/92b-3p/27a-3p-enriched and CXCL16/RhoA/IL-8-enriched exosomes.
- Exosomes secreted from Fn-infected cells promote CRC metastasis.
- Patients with CRC had significantly higher levels of circulating exosomal miR-1246/92b-3p/27a-3p and CXCL16 than healthy subjects.

How might it impact on clinical practice in the foreseeable future?

- As exosomes from Fn-infected CRC cells function as an oncogenic factor promoting CRC development and metastasis, it may be a promising therapeutic strategy to eradicate Fn infection to treat CRC.

INTRODUCTION

Exosomes are extracellular vesicles (EVs) produced by various cell types via endocytosis and released into the extracellular milieu.[1] Exosomes contain a wide range of functional lipids, proteins, RNA and DNA that can be transferred horizontally to recipient cells.[2] Tumour-derived exosomes (TEXs) carry cargo reflecting the genetic or signalling alterations in the cancer cells of origin and they serve in the communication network of the tumour.[3 4] TEXs have been recently implicated in the tumour metastatic process via the transfer of miRNA and proteins to normal tissues.[5] Specific proteins present in TEXs have been reported to be promoters of metastatic pathways and to determine organ-specific metastasis.[6] TEXs were also shown to target non-transformed cells in premetastatic organs and to modulate premetastatic organ cells predominantly through transferred miRNAs.[7] These dysregulated miRNAs and proteins, which can be delivered to local and distal cells by exosomes play a critical role in tumour metastasis.

Chronic inflammation and infection are the most important epigenetic and environmental factors contributing to tumourigenesis and tumour progression. During viral, bacterial, parasitic and fungal infections, pathogens secrete exosomes to spread infection and avoid the host immune system and also stimulate exosomes production in host cells to regulate host immune responses.[8] Host-derived vesicles carry specific RNA and protein from both pathogens and hosts. Several studies have reported that *Mycobacterium*-miRNA can repattern host metabolism machinery to favour its intracellular survival.[9] Exosomes derived from CagA-positive *H. pylori* infection were reported to promote macrophage-derived foam cell formation.[10]

Fusobacterium nucleatum (Fn) is an obligate anaerobic oncogenic bacterium that is the most important microbe-related risk factor in the initiation and progression of colorectal cancer (CRC).[11 12] The elucidated mechanisms of Fn involved in colorectal carcinogenesis include immune modulation (increasing myeloid-derived suppressor cells and inhibitory receptors of natural killer cells), virulence factors (FadA and Fap2), microRNAs (miR-21) and bacterial metabolism.[13–15] Our previous study indicated that Fn is a facultative intracellular bacterium that can survive in macrophages.[16] However, whether specific exosomes can be derived from Fn-infected cells and what affects exosome-mediated communication between Fn-infected cells and recipient cells have not been investigated.

In the present study, we investigated the exosomal microRNA and protein profiles during Fn infection and described the role of exosomes secreted from Fn-infected cells on CRC progression and development.

MATERIALS AND METHODS

Patients and specimen collection

The serum and stool samples from 82 patients with primary CRC were selected from an archive of blood samples at the Cancer Center of Sun Yat-sen University (SYSUCC) as previously described.[17 18] In addition, healthy blood samples were obtained from 102 subjects without any malignancy. Background grouping of the study cohorts is shown in online supplemental figure S1.

Exosome isolation, characterisation and nanoparticle tracking analysis

Exosomes were isolated by differential centrifugation. The exosome size and number were measured by a nanoparticle tracking analysis (NTA) using a Zetasizer Nano S90 system (Malvern Instruments, England) equipped with a blue laser (405 nm). Purified exosomes were observed with a JEM1400 transmission electron microscope (TEM) operated at 120 kV (JEOL, Japan).

RNA isolation and quantitative RT-PCR

Total RNA from exosomes was extracted using a total exosome RNA and protein isolation kit (Thermo Fisher Scientific, USA) according to the instructions of the manufacturer. Quantification of miRNA expression was performed using a Mir-X miRNA RT-qPCR TB Green Kit (TaKaRa, Japan) on a Light Cycler 480 II (Roche, Applied Science). The primers were used as shown in online supplemental table S1.

Cell transfection with miRNA mimics or inhibitors

Cells were transfected with miR-1246/27a-3p/92a-3p mimics, inhibitors or negative control (NC) chemical synthesis oligonucleotides (Gene Pharma, China) using Lipofectamine 3000 reagent (Invitrogen, USA) at the indicated concentrations according to the supplier's instructions. The sequences were used as shown in online supplemental table S2.

Mass spectrometry analysis of exosome proteins

Total protein from exosomes was digested by Pierce Trypsin/Lys-C Protease Mix, MS-Grade (Thermo Fisher Scientific, USA) and then protein digestion was conducted by using Nano-LC-MS/MS analyses (Thermo Fisher Scientific, USA).

Experimental mouse techniques

To establish a human CRC xenograft model, 6-week-old BALB/c nude mice were subcutaneously inoculated with 2×10^6 HCT116 cells. To establish a mouse CRC homograft model, 6-week-old BALB/c mice were inoculated with 2×10^6 CT26 cells by tail vein injection. After tumour transplantation, phosphate buffer saline (PBS), si-Ex, Ex or Fn-Ex was injected intratumourally or intravenously every other day. The mice were sacrificed 2 weeks after the treatment began, and the tumours were surgically removed and counted. All of the animal studies were conducted in accordance with protocols approved by the Institutional Animal Care and Research Advisory Committee.

Statistical analyses

Statistical analyses were performed using GraphPad 6.0. Significance was considered $p<0.05$.

The detailed methodology can be found in online supplemental information.

RESULTS

Fn infection increases the secretion of exosomes from CRC cells

To study the specific Fn-infection associated exosomes from CRC cells, HCT116 cells were infected with live Fn at an MOI of 10:1 (bacteria:cells) and then were cultured for 48 hours. Then, exosomes from the supernatant of Fn-infected HCT116 cells (Fn-Ex) were isolated, and exosomes from uninfected HCT116 cells (Ex) and exosomes from *E. coli*-infected HCT116 cells (Ec-Ex) were used as controls. TEM analysis showed that these purified vesicles samples were oval and globular (figure 1A, online supplemental figure S2A). The NTA revealed that Fn-Ex has a slightly bigger size and higher number than Ex (average 117.4 ± 35.5 vs 90.2 ± 40.6 nm; 6.18 ± 1.69 vs 4.59 ± 1.52 10^8 particles/10^7 cells, both $p<0.05$) (figure 1B), while Ex and Ec-Ex are similar in size and number (online supplemental figure S2B). Furthermore, the presence of exosome biomarkers (CD9 and CD63) were verified by Western blotting in Fn-Ex, Ex and Ec-Ex (figure 1C, online supplemental figure S2C). Fn infection markedly increased the secretion of exosomes which were collected from the same volume culture supernatant by Western blotting analysis (figure 1D). Then, 1×10^5 HCT116 cells were incubated with 10 µg of PKH26-stained Fn-Ex for 0, 6 and 12 hours. Confocal imaging showed that Fn-Ex was indeed taken up by HCT16 cells at 6-hour postincubation (figure 1E,F).

These data indicate that Fn infection is able to increase the secretion of exosomes from CRC cells and that the infected cells can secrete slightly larger exosomes.

Exosomes derived from Fn-infected cells promote the migration of CRC cells

To determine the effect of exosomes released by Fn-infected cells on recipient cells, we incubated Fn-Ex, Ex and Ec-Ex with HCT116 and SW480 cells, respectively. CCK8 assays showed that HCT116 and SW480 cells exhibited a significant toxicity following Ec-Ex treatment ($p<0.05$), while a slight but not significant toxicity following Fn-Ex or Ex treatment (figure 2A). Interestingly, both Fn-Ex treated HCT116 and SW480 cells

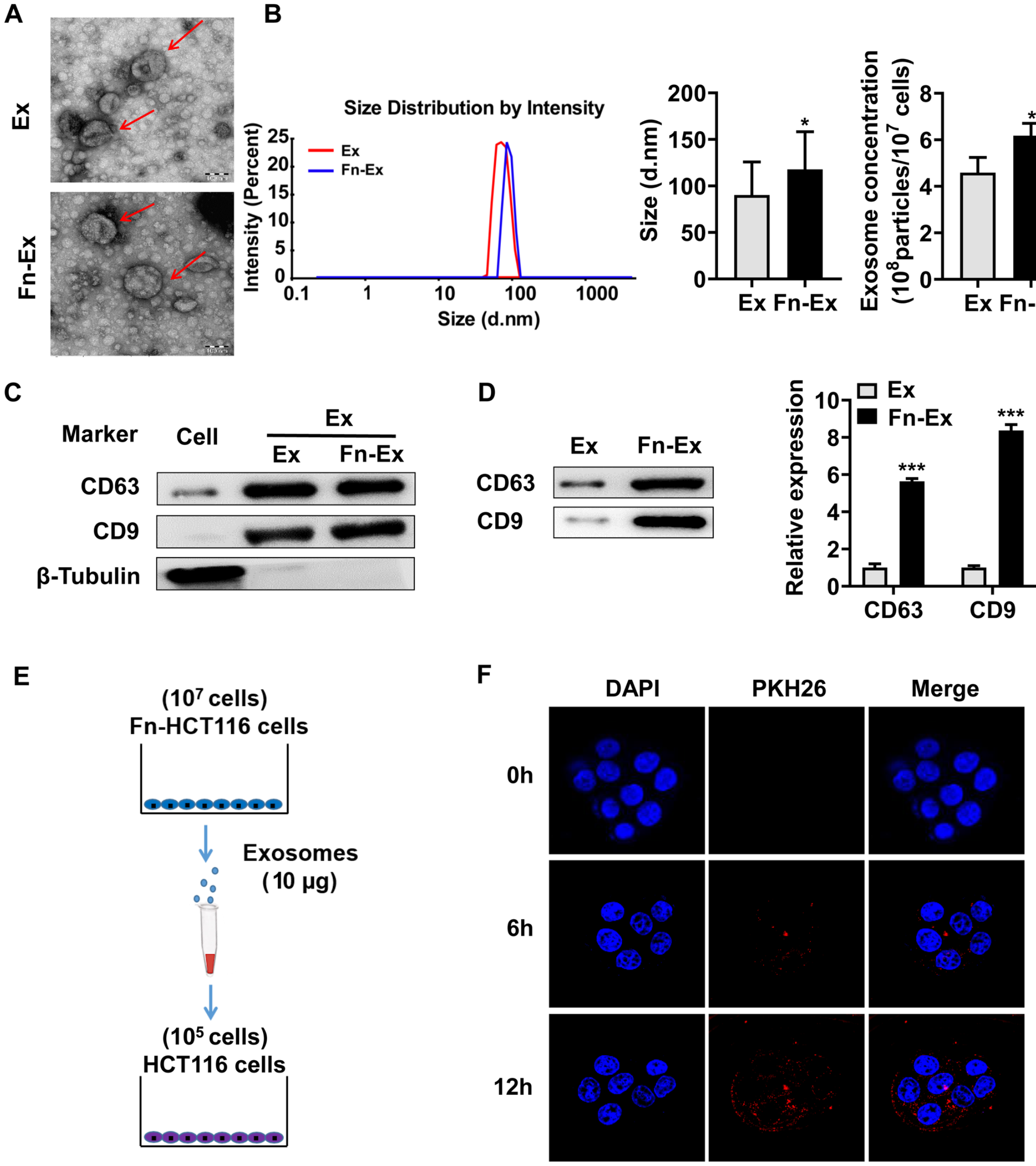

Figure 1 Identification of exosomes derived from HCT116 cells (Ex) and Fn-infected HCT116 cells (Fn-Ex). (A) TEM images of purified Ex and Fn-Ex. Scale bar=100 nm. (B) NTA of number and size distribution in Ex and Fn-Ex (n=3). (C) Western blot analysis of markers (CD63 and CD9) in exosomal protein purified from HCT116 cells and Fn-infected HCT116 cells supernatants, tubulin served as an internal control in whole-cell lysates. (D) Western blot analysis (left) of Ex and Fn-Ex proteins (CD63 and CD9) collected from the same volume HCT116 cells culture supernatant and quantitative analysis (right). (E) Schematic description of the experimental design. Fn-Ex were isolated and then 1×10^5 HCT116 cells were incubated with 10 µg of PKH26-stained Fn-Ex for the indicated time. (F) Confocal microscopy image of the internalisation of fluorescently labelled exosomes in HCT116 cells for the indicated times. Scale bars=50 mm; Error bars, SD: *$p<0.05$; ***$p<0.001$. CRC, colorectal cancer; NTA, nanoparticle tracking analysis.

exhibited obvious morphological changes into spindle shapes, which was different from that of the Ex-treated or Ec-Ex-treated cells (figure 2B).

Furthermore, Transwell migration assays showed that Fn-Ex treatment significantly promoted HCT116 cells migration to levels that were not observed in the Ex and Ec-Ex treatment (2.9 fold, $p<0.001$; 3.9 fold, $p<0.001$). A similar trend was also observed when SW480 cells were recipient cells (2.3 fold, $p<0.001$; 3.4 fold, $p<0.001$) (figure 2C). Additionally, scratch wounding assays further showed that Fn-Ex treatment significantly accelerated wound closure in both HCT116 and SW480 cells compared with Ex and Ec-Ex treatment (average 65.8% vs 10.3% and 10.1%, $p<0.001$; 76.9% vs 16.3% and 6.7%, $p<0.001$, respectively) (figure 2D).

These results showed that exosomes derived from Fn-infected cells change the cell morphology and promote the migration of CRC cells, suggesting that recipient cells may be remodelled by exosomes from Fn-infected cells.

Specific miRNAs are enriched in exosomes secreted by Fn-infected CRC cells

Next, the differential microRNA expression profile of Fn-Ex and Ex was investigated by miRNA-seq analysis. Online supplementary table S3 shows the reads identified for the small RNA and unannotated RNA categories. The percentages of miRNAs in the total RNA isolated from Fn-Ex and Ex were 16.55% and 13.26%, respectively (figure 3A). A total of 277 and 211 types

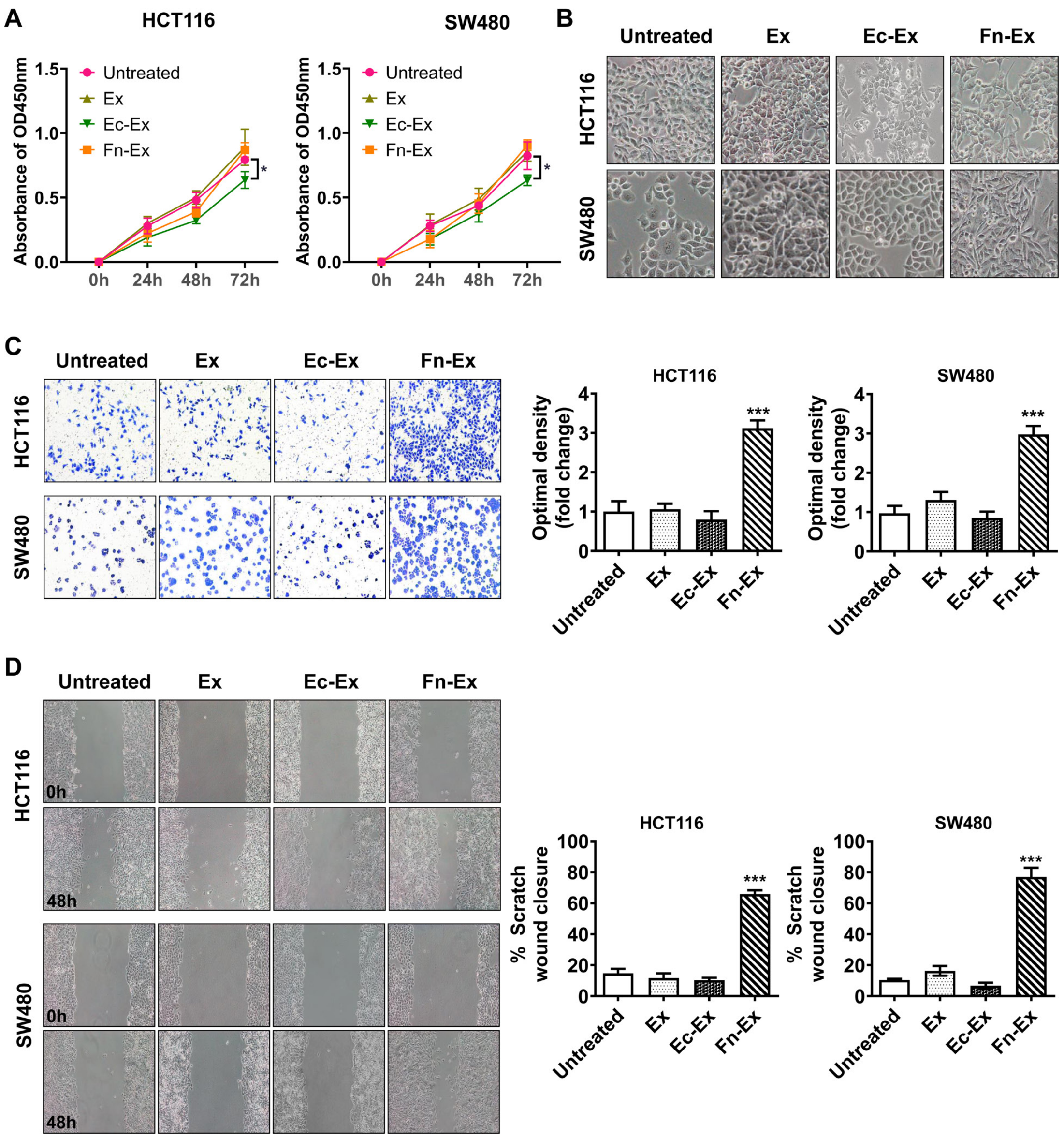

Figure 2 Fn-Ex promotes the migration of CRC cells. (A) CCK8 assays were used to detect the effects of Ex, Ec-Ex or Fn-Ex on cell proliferation at 24, 48 and 72 hours in HCT116 and SW480 cells. (B) Morphological changes in HCT116 and SW480 cells were observed following treatment with Ex, Ec-Ex or Fn-Ex for 48 hours. (C) The migration of Ex, Ec-Ex or Fn-Ex-treated CRC cells was assessed using Transwell migration assays. Representative images of the assay (right). (D) Analysis of CRC cells migration by in vitro scratch assays. Images were acquired at 0 and 48 hours. Quantitative analysis of scratch wound closure (right). Data represent at least three experiments performed in triplicate. Scale bar=200 µm; error bars, SD: *p<0.05; ***p<0.001. CRC, colorectal cancer.

of known miRNAs in Fn-Ex and Ex, respectively, were identified (online supplemental table S4). In addition, 282 miRNAs were simultaneously identified in both groups. The number of overlapping and unique miRNAs between the two groups is shown in figure 3B.

We next compared the expression levels of miRNAs in Fn-Ex and Ex. We found that 91 miRNAs were significantly different between the two groups ($p<0.05$) (figure 3C; online supplemental table S5). There were 23 miRNAs upregulated and 1 miRNA downregulated in Fn-Ex compared with Ex (normalised value ≥2; $p<0.05$) (figure 3D). Furthermore, the top 10 most highly expressed miRNAs were chosen for validation by RT-qPCR in Fn-Ex, Ex, Ec-Ex and K-Fn-Ex (exosomes from heat-killed Fn-infected HCT116 cells). Five miRNAs (miR-27a-3p, miR-21–5 p, miR-7704, miR-92b-3p and miR-1246) were confirmed to be significantly increased in Fn-Ex (all, $p<0.01$). In particular, Fn infection dramatically increased the expression levels of three miRNAs, miR-1246/92b-3p/27a-3p (miR-1246, miR-92b-3p and miR-27a-3p), as observed when comparing Fn-Ex with Ex, Ec-Ex and K-Fn-Ex (all, $p<0.001$) (figure 3E, online supplemental figure S3).

These data indicated that live Fn infection altered exosomal miRNA profile of CRC cells, which was accompanied with increased expression of miR-1246/92b-3p/27a-3p.

Exosomal miR-1246/92b-3p/27a-3p promotes CRC cells migration by targeting GSK3β and activating the Wnt/β-catenin pathway

To explore the underlying biological functions of *exosomal* miRNAs during Fn infection, we chose the three miR-1246/92b-3p/27a-3p generated overexpressing (mimics) and knocked

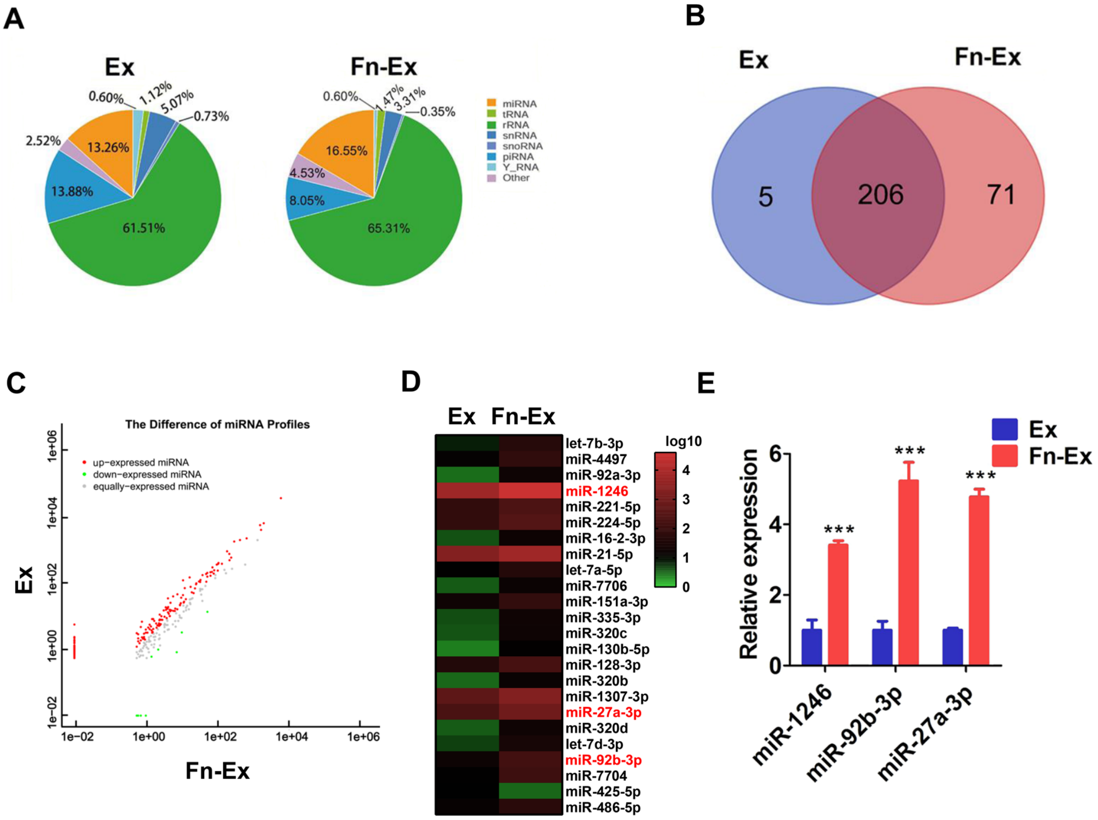

Figure 3 miR-1246/92b-3p/27a-3p upregulated in Fn-Ex. (A) The percentage of small RNA categories in all reads mapped to non-coding RNA databases. (B) Venn diagram showing the unique and overlapping miRNAs between HCT116 cells and Fn-infected HCT116 cells-derived exosomes (Ex and Fn-Ex). (C) Differentially expressed miRNAs between the Ex and Fn-Ex groups. Red, increased expression; green, decreased expression; and grey, no difference. p<0.05 and fold change >2 were considered significant. (D) Heatmap diagram of differential miRNA expression between Ex and Fn-Ex. (E) Quantitative real-time PCR validated the increase of miR-1246, miR-92b-3p and miR-27a-3p in Fn-Ex. Error bars, SD: ***p<0.001.

down (inhibitors) miRNAs. Transwell migration assays showed that miR-1246/92b-3p/27a-3p mimics greatly promoted migration in HCT116 cells, compared with that of the negative control (NC), while the combination of three miRNA inhibitors partially abolished Fn-Ex-mediated migration. Similar trends were also observed in SW480 cells (figure 4A). In addition, a scratch wounding assays showed that miR-1246/92b-3p/27a-3p mimics obviously promoted wound closure, compared with that of the control in HCT116 cells and SW480 cells, while the combination of three inhibitors partly rescued the Fn-Ex-mediated wound closure rate (figure 4B).

Next, based on the predictive results of the bioinformatics analysis, we found that miR-1246/92b-3p/27a-3p can directly target the 3’-UTR of GSK3β mRNA, and the association is highly conserved among species (online supplemental table S6). We further generated luciferase reporter plasmids that harboured either wild-type (WT) or mutated-type miR-1246/92b-3p/27a-3p binding sites within the 3’-untranslated region (UTR) of GSK3β (figure 5A–C). As shown in figure 5D–F, miR-1246/92b-3p/27a-3p mimics and Fn-Ex or inhibitors significantly suppressed or increased luciferase activity of the reporter genes containing the WT 3’-UTR of GSK3β (all, p<0.05), but no inhibitory effects were observed in mutated cell lines. Moreover, we found that GSK3β was consistently downregulated in miR-1246/92b-3p/27a-3p overexpressing cells while upregulated in miR-1246/92b-3p/27a-3p inhibited cells, suggesting that GSK3β was a putative target gene of miR-1246/92b-3p/27a-3p (figure 5G). Furthermore, Transwell migration and wound-healing scratch assays displayed that GSK3β overexpression markedly retarded and GSK3β knockdown slightly promoted miR-1246/92b-3p/27a-3p mimics-mediated and Fn-Ex-mediated migration in both CRC cell lines (online supplemental figure S4).

Next, the expression of GSK3β and the Wnt/β-catenin pathway was examined by Western blot. As shown in figure 6, GSK3β levels were significantly decreased in Fn-Ex treated HCT116 and SW480 cells compared with that of Ex-treated cells, while β-Catenin levels were increased in both Fn-Ex treated cell types. Moreover, decreased expression of the epithelial marker E-cadherin and increased expression of the mesenchymal marker Vimentin were observed after Fn-Ex treatment. The expression of the proto-oncogenes Cyclin D1 and C-Myc were increased in Fn-Ex treatment. Similar results were also observed in three miR-1246/92b-3p/27a-3p mimics. Collectively, these results indicated that during Fn infection, miR-1246/92b-3p/27a-3p-enriched exosomes induce CRC cells migration *via* targeting GSK3β and activating the Wnt/β-catenin pathway.

Identification of exosome proteins and functional categorisation in Fn-infected CRC cells

To screen the specific proteins carried by Fn-Ex, the differentiated protein expression profiles of Fn-Ex and Ex were investigated by proteomic analysis. A total of 384 and 550 proteins were detected by Nano-LC–MS/MS analysis in Fn-Ex and Ex, respectively (online supplemental table S7). Venn diagram analyses revealed 197 proteins overlapping between the two groups. Fn-Ex carried 187 unique proteins, including 85 Fn proteins and 102 cell proteins (figure 7A). Among 102 unique Fn-Ex cell

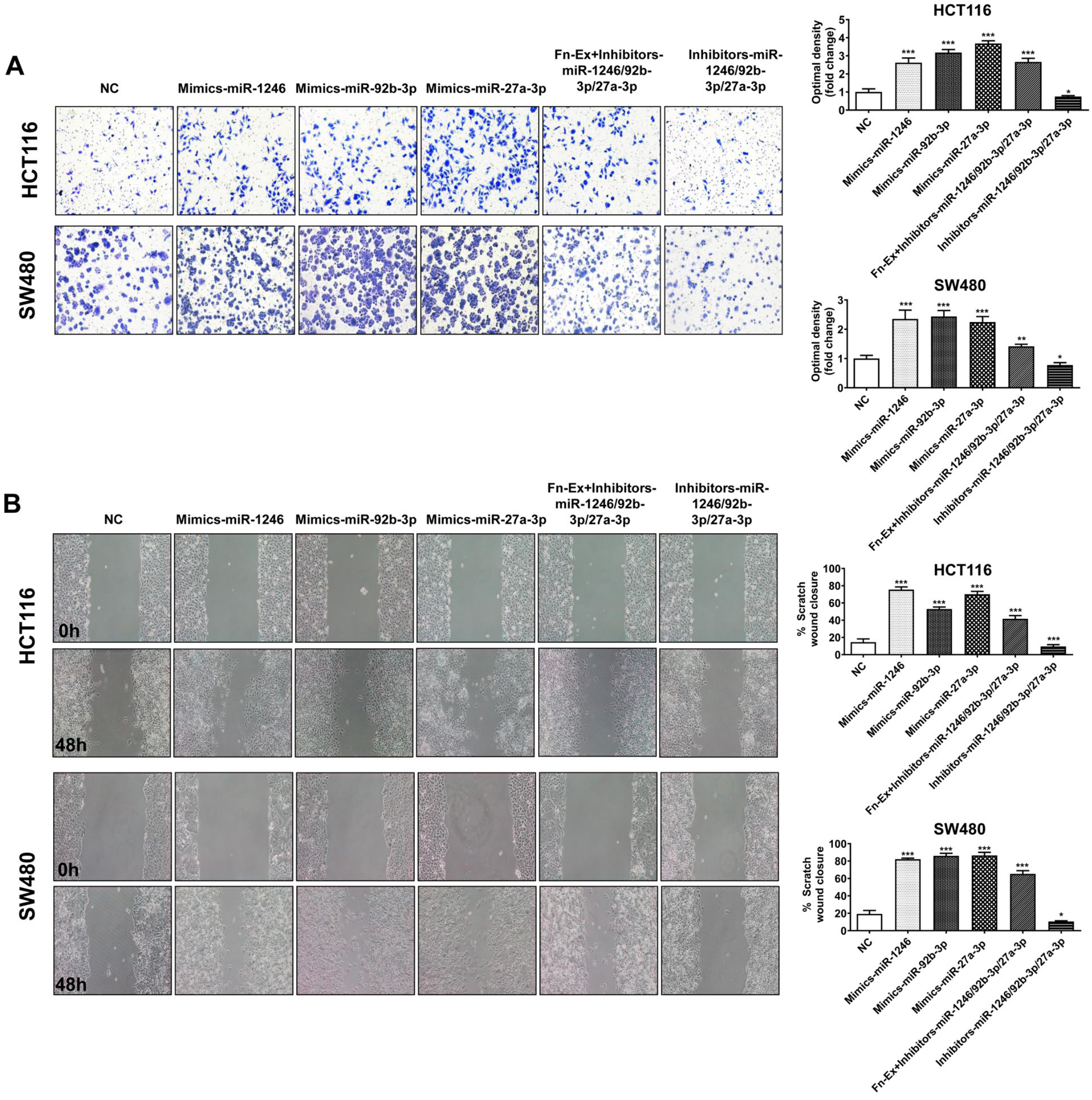

Figure 4 Exosomal miR-1246/92b-3p/27a-3p promotes the migration of CRC cells. (A) The migration of CRC cells was assessed using a Transwell migration assays. Representative images of the assay (right). (B) Analysis of CRC cells migration by in vitro scratch assays. Images were acquired at 0 and 48 hours. Right, quantitative analysis of scratch wound closure. Data represent at least three experiments performed in triplicate. Scale bar=200 µm; error bars, SD: $^{*}p<0.05$; $^{**}p<0.01$; $^{***}p<0.001$. CRC, colorectal cancer.

proteins, the most significantly enriched GO terms were structural molecule activity and molecular transducer activity (online supplemental figure S5). KEGG pathway analysis showed that the ribosome, chemokine signalling pathway and mTOR signalling pathway were enriched among these proteins (figure 7B; online supplemental table S8). It is well known that chemokine signalling pathways are involved in tumour metastasis. We further selected three proteins with chemokine signalling pathways for validation by immunoblotting. As shown in figure 7C, interleukin-8 (IL-8), C-X-C motif chemokine 16 (CXCL16) and Ras homolog family member A (RhoA) were more enriched in Fn-Ex than in Ex. Interestingly, CXCL16 exhibited the strongest abundance in Fn-Ex compared with Ex. In addition, Western blot analysis revealed that the expression of CXCL16 was increased in Fn infected HCT116 cells (figure 7D).

In addition, Transwell migration assays showed that Fn-Ex promoted migration (2.2-fold, $p<0.01$; 3.7 fold, $p<0.001$) and that treatment with CXCR6 protein largely abrogated Fn-Ex-mediated migration (1.6 fold, $p<0.05$; 1.7-fold, $p<0.05$) in both HCT116 and SW480 cells, respectively (figure 7E). Migration was also blocked by treatment with CXCR6 in the wound-healing scratch assays (average 57.9% vs 29.9%, $p<0.01$; 81.6% vs 31.5%, $p<0.001$) (figure 7F). These data suggest that Fn infection could increase the expression of the metastasis-associated protein CXCL16 in CRC cells, and CXCL16 was further selectively packaged and enriched in Fn-Ex, promoting tumour cell migration via the CXCL16/CXCR6 axis.

Exosome secreted from Fn-infected cells promote CRC metastasis

To evaluate the potential contribution of Fn-infected exosomes to tumour metastasis in vivo, Fn-Ex activity was evaluated in two mouse colorectal tumour models. Exosomes from HCT116 cells which were transfected with miR-1246/27a-3p/92a-3p inhibitors and siRNA-CXCL16 were used as control for Fn-Ex group (si-Ex). HCT116 cells were injected subcutaneously (into BALB/c nude mice to develop a human CRC xenograft model. Ex, Fn-Ex or si-Ex was administered intratumourally every other day once the tumour volume reached 50 mm^3 (figure 8A).

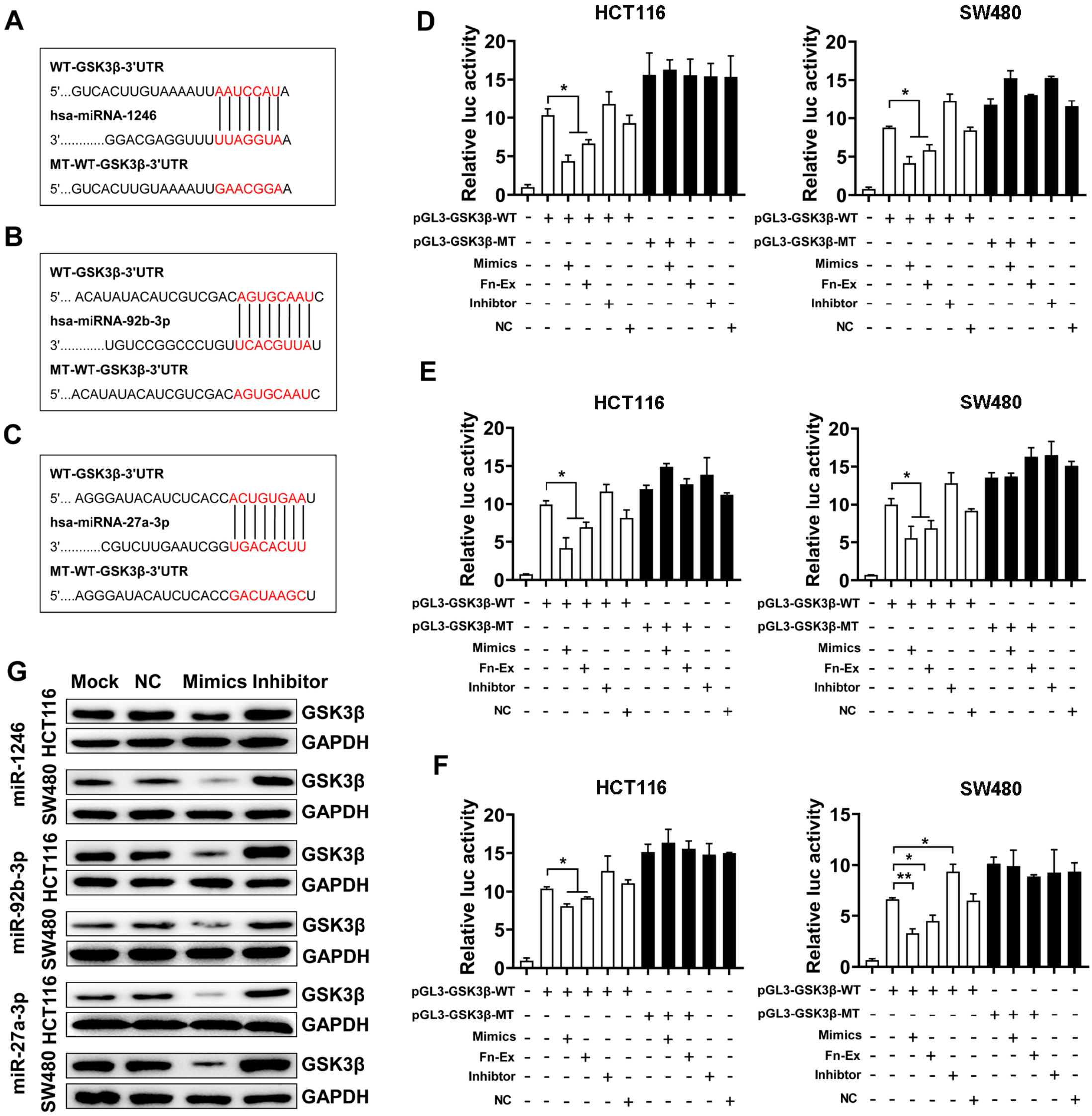

Figure 5 Identification of GSK3β as a direct target of miR-1246/92b-3p/27a-3p. Luciferase reporter plasmids that harbour either WT or MT miR-1246 (A), miR-92b-3p (B) and miR-27a-3p (C) binding sites in the 3′-UTR of GSK3β. HCT116 and SW480 cells were transiently transfected with luciferase constructs along with miR-1246 (D), miR-92b-3p (E) and miR-27a-3p (F) mimics, Fn-Ex (10 µg/mL), inhibitors or negative controls. After 48 hours, the luciferase activity was measured. (G) Representative Western blot images showing that overexpression or inhibition of miR-1246, miR-92b-3p and miR-27a-3p downregulated or upregulated GSK3β expression, respectively, in HCT116 cell and SW480 cells. Data represent at least three experiments performed in triplicate. Error bars, SD: $^{*}p<0.05$; $^{**}p<0.01$. MT, mutated type; UTR, untranslated region; WT, wild type.

Twenty-one days later, the tumours were harvested by surgical removal (figure 8B). The results showed that mice treated with Fn-Ex did not show differences in tumour diameter, tumour volume or body weight loss from the Ex, si-Ex or PBS groups (online supplemental figure S6). However, H&E stained liver sections showed obvious intrahepatic metastasis around blood vessels in the Fn-Ex groups, while the other three groups showed few signs of metastasis (figure 8C,D). Moreover, the expression of GSK3β was decreased in tumour tissues of the Fn-Ex administered group by both immunohistochemical and Western blotting analyses, whereas si-Ex significantly reversed the expression of GSK3β (figure 8E,F).

Additionally, we also investigated whether Fn-Ex could enhance tumour metastasis in mice with CT26 lung homografts. Ex, Fn-Ex, si-Ex or PBS control was administered intravenously (figure 8G). All four groups developed obvious tumour nodules on the pulmonary surface, and the Fn-Ex treated group presented the highest number of nodules, compared with the other three groups ($p<0.001$) (figure 8H,I). H&E stained lung sections showed the largest area and highest number of cancer nests inside damaged lung tissues in Fn-Ex group (figure 8J). Moreover, the expression of GSK3β was decreased in lung tissues of the Fn-Ex administered group (figure 8K,L).

Collectively, these results suggest that exosomes from Fn-infected cells significantly facilitate tumour metastasis by carrying the cargo of Fn infection-specific miRNA and protein in vivo.

Association of miR-1246/92b-3p/27a-3p and CXCL16 with clinical characteristics of patients with CRC

We further isolated and characterised exosomes from the serum of patients with CRC and from HS. Western blots showed that these exosomes were highly enriched for the exosome-associated proteins CD63 and CD9 (figure 9A). Total RNA was further extracted from circulating exosomes. We compared the three mean values of miR-1246/92b-3p/27a-3p between samples from

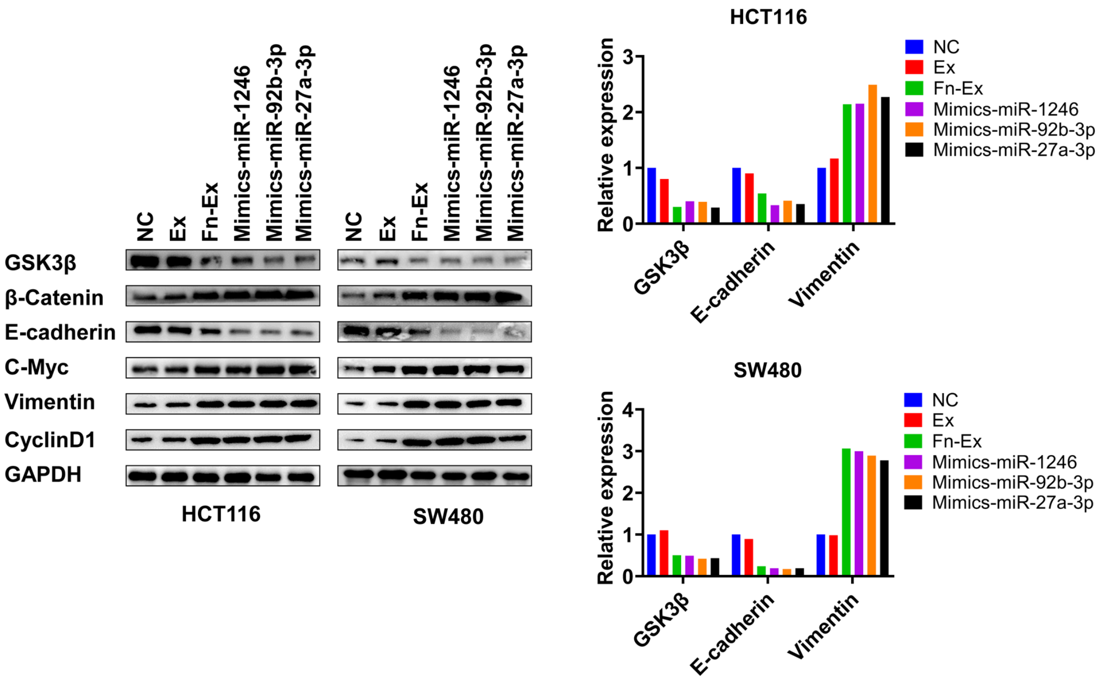

Figure 6 miR-1246/92b-3p/27a-3p inactivates the Wnt/β-catenin pathway by directly targeting GSK3β. Western blot images show the expression pattern of Wnt/β-catenin-related proteins in CRC cells after HCT116 cells and Fn-infected HCT116 cells-derived exosomes (Ex and Fn-Ex) and miR-1246/92b-3p/27a-3p mimics transfection. Right, quantitative analysis of Wnt/β-catenin related protein expression. CRC, colorectal cancer.

each patient. Patients with CRC (n=40) had significantly higher levels of circulating exosomal miR-1246/92b-3p/27a-3p than the HS (n=40) (all, $p<0.001$) (figure 9B).

Furthermore, the carriage of Fn was investigated in faecal samples (n=82) by qPCR. Pearson's correlation coefficient and linear regression analysis were applied to analyse the correlation between the levels of Fn and circulating exosomal miR-1246/92b-3p/27a-3p. Abundance of Fn showed a positive correlation with miR-1246 (r=0.232, p=0.04) and miR-27a-3p (r=0.370, p=0.001) levels, but there was no correlation with miR-92b-3p (r=0.018, p=0.870) (figure 9C).

In addition, circulating exosomal CXCL16 levels were significantly upregulated in patients with CRC compared with HS ($p<0.001$) (figure 9D). More importantly, circulating exosomal CXCL16 was positively correlated with the abundance of Fn in patients with CRC (r=0.319, p=0.03) (figure 9E).

Next, the correlation between circulating exosomal miR-1246/92b-3p/27a-3p, CXCL16 and clinicopathological parameters was analysed (online supplemental table S9). Circulating exosomal miR-1246 and miR-92b-3p were not obviously correlated with CRC age, sex, gender, tumour location, histological differentiation, T classification, N classification, metastasis or expression of tumour markers CEA, CA19-9 or gFOBT. However, there was a significant association between miR-27a-3p levels and clinical stage (p=0.04). Further, circulating exosomal CXCL16 levels were significantly associated with metastasis (p=0.006).

These results indicate that the levels of circulating exosomal miR-1246, miR-27a-3p and CXCL16 were elevated and exhibit a positive correlation with gut Fn abundance in the patients with CRC, suggesting that excessive Fn levels might contribute to tumour progression through the release of Fn-associated exosomes.

DISCUSSION

Here, we found that exosomes from Fn-infected CRC cells carried both bacteria and host components that were internalised by uninfected cells. We further observed an increased size and enhanced release of exosomes from Fn-infected cells, which is in line with the features of EV from other bacterial infections such as *Mycobacterial* and *Legionella pneumophila*,[19 20] indicating that Fn stimulated the production of exosomes during infection.

Currently, numerous studies have reported that exosomes isolated from cells infected with various intracellular pathogens contain microbial components.[21 22] However, almost all of these studies have focused on the role of exosomes in infection and immunity, which few have focused on the role of cancer progression. It has been well recognised that Fn is a powerful driving force for CRC progression.[15] Moreover, as an important intratumour bacterium, Fn participates in tumour progression and mediates tumour resistance to chemotherapeutic drugs.[23] Most *excitingly,* our study reveals that exosomes from Fn-infected cells play a newly identified role promoting cancer progression.

miRNAs have recently emerged as major players in the interactions between host cells and bacterial pathogens. Substantial evidence confirms that infections with pathogenic organisms lead to significant changes in exosomal miRNA. Our study found Fn infection alters exosomal miRNA profiles of CRC cells. Usually, bacteria modify host miRNA expression for their own benefit, promoting survival, replication and persistence.[24] Similarly, exosome-mediated transfer of miRNA to neighbouring cancer cells might help Fn to survival inside tumour tissues.

Furthermore, many studies have demonstrated that miRNAs play pathogenic role in the development of colitis-associated colon cancer. Some data have highlighted that specific miRNAs contribute to colorectal carcinogenesis, and several such miRNAs can serve as biomarkers for diagnosis, prognosis, and metastasis prediction in patients with CRC.[25] We confirmed that metastasis-related miRNAs, including

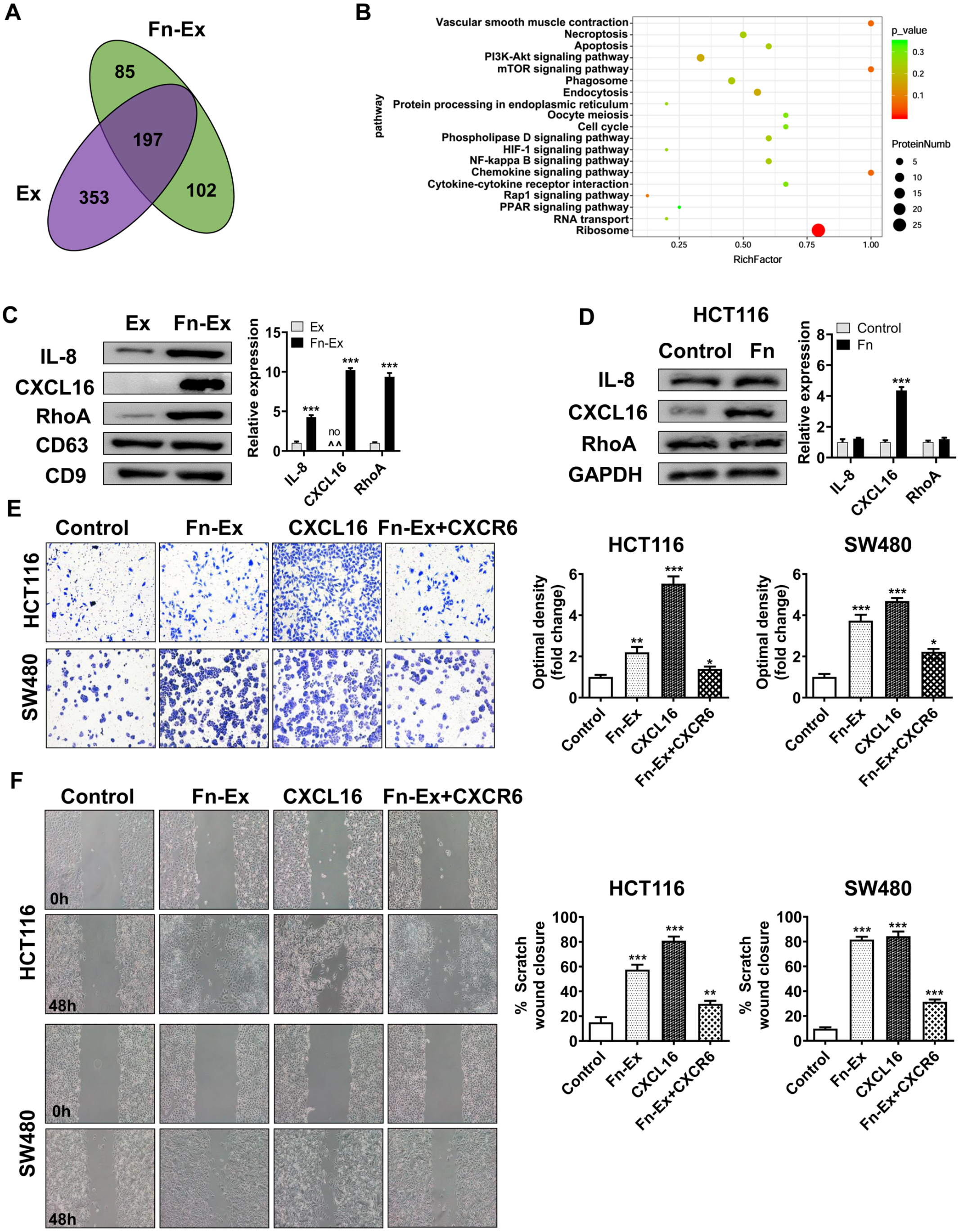

Figure 7 CXCL16 of Fn-Ex to promote CRC cells migration in vivo. (A) Venn diagram showing the unique and overlapping proteins between HCT116 cells and Fn-infected HCT116 cells-derived exosomes (Ex and Fn-Ex). (B) KEGG pathway analysis of Fn-infected HCT116 cells-derived exosome (Fn-Ex) unique cell proteins. (C) The protein levels of IL-8, CXCL16 and RhoA were detected by Western blot in HCT116 cells and Fn-infected HCT116 cells-derived exosomes (Ex and Fn-Ex). Right, quantitatively analysed. (D) The protein levels of IL-8, CXCL16 and RhoA were detected by Western blot in HCT116 cells. On the right, the quantitatively analysis. Migration of HCT116 cells and SW480 cells that were untreated, or treated with Fn-Ex, CXCL16 or Fn-Ex +CXCR6, as detected by Transwell migration assays (E) and wound healing assays (F). Data represent at least three experiments performed in triplicate. Scale bar=200 μm; error bars, SD: *p<0.05; **p<0.01; ***p<0.001. CRC, colorectal cancer.

miR-1246, miR-92b-3p and miR-27a-3p, were selectively secreted in Fn-Ex and enhanced CRC migration. Consistent with our research, CRC cells-derived exosomes containing miR-1246 were reported to promote angiogenesis.[26] Moreover, both miR-92b-3p and miR-27a-3p were reported to promote CRC cells proliferation, invasion and migration,[27–29] and the serum exosomal levels of miR-1246 and miR-27a-3p were validated as biomarkers of colon cancer.[30 31]

An increasing number of studies have identified specific miRNAs (eg, miR-21, miR-155 and miR-103a) that lead to

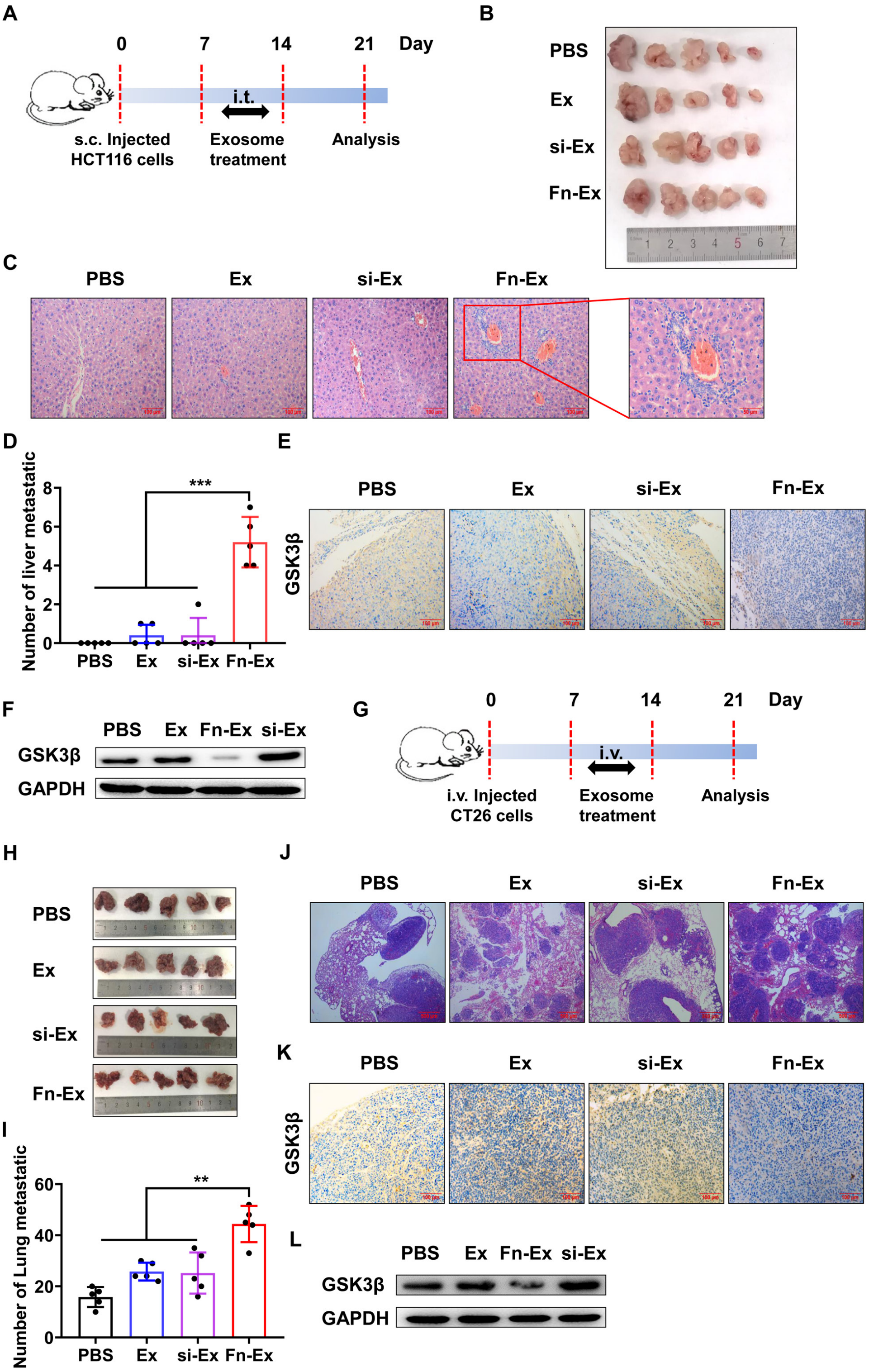

Figure 8 In vivo verification shows that Fn-Ex promotes migration. (A,B) A flowchart depicting the in vivo experimental design and morphology. (C) Histopathological examination of the liver tissue sections (n=5) and (D) the number of liver tumours were quantitatively analysed. (E) Immunohistochemical analysis of the paraffin-embedded tumour tissues using a GSK3β antibody (n=5). (F) GSK3β expression in implanted tumours (n=5). (G) A flowchart depicting the in vivo experimental design. (H) Photograph of the harvested lungs showing regions with multiple nodules (n=5) and (I) quantitative analysis. (J) Histopathological examination of the lung tissue sections (n=5). (K) Immunohistochemical analysis of the paraffin-embedded lung tissues using a GSK3β antibody (n=5). (L) GSK3β expression in implanted tumours (n=5). Error bars, SD: **p<0.01; ***p<0.001.

alteration of Wnt/β-catenin signalling in CRC.[32] Moreover, recent evidence has suggested that premetastatic niches in the liver could be promoted by miR-21 in exosomes from CRC cells through the miR-21-TLR7-IL6 axis.[33] Significantly increased levels of serum exosomal miR-6803–5 p, miR-17–5 p and miR-92a-3p[34 35] and decreased levels of miR-548c-5p and miR-638 have been recently associated with poor survival and liver metastasis in patients with CRC.[36 37] In line with these studies,

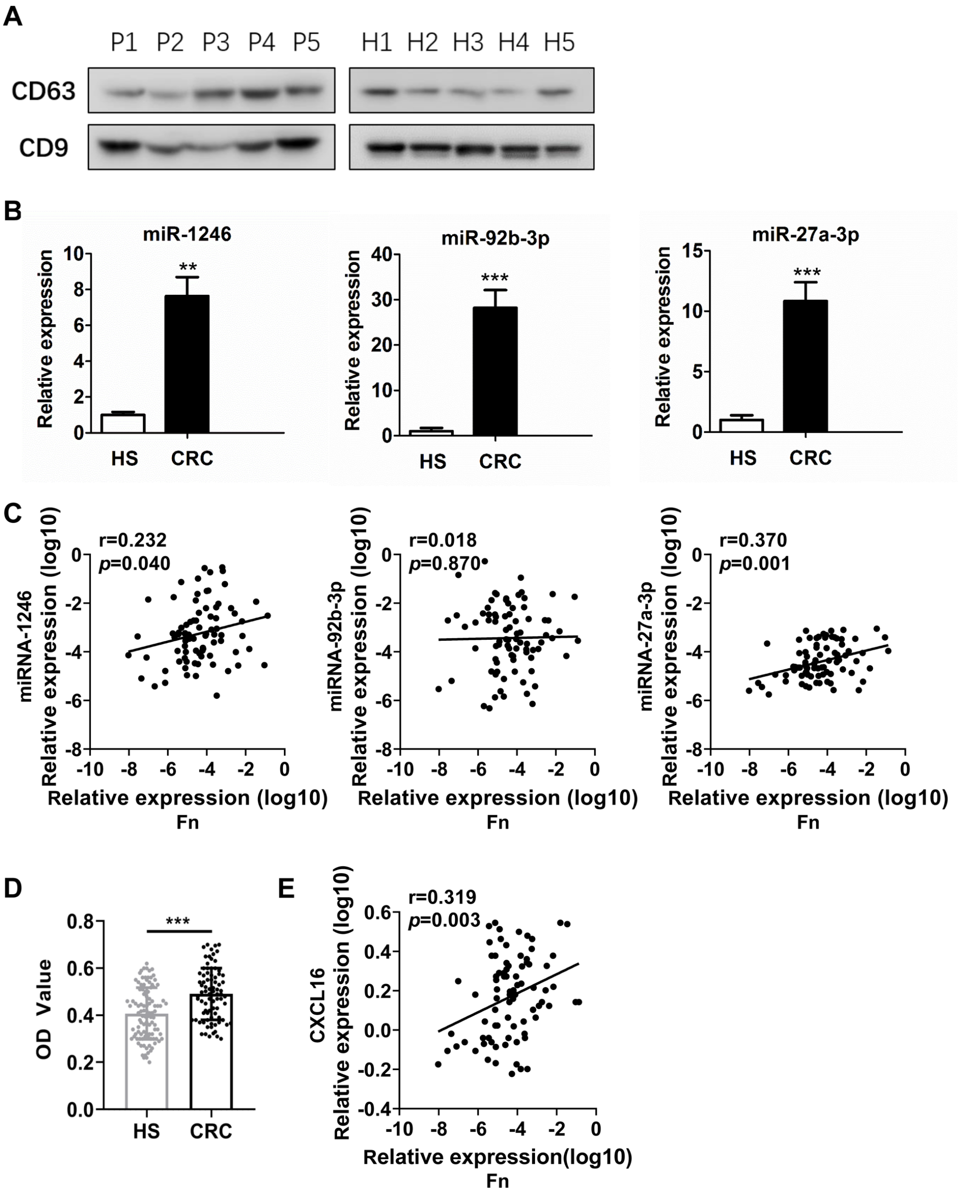

Figure 9 Circulating exosomal miR-1246/92b-3p/27a-3p and CXCL16 levels correlate with Fn in patients with CRC. (A) Western blot analysis of the expression of markers (CD63 and CD9) in serum exosomal protein purified from healthy subjects (H1–H5) and patients with CRC (P1–P5). (B) Exosome miR-1246, miR-92b-3p and miR-27a-3p levels were measured by RT-qPCR in the serum of patients with CRC and HS. (C) Correlation between the abundance of Fn in the faeces of patients with CRC and the levels of miR-1246, miR-92b-3p and miR-27a-3p in exosomes from the serum of patients with CRC. Patients were analysed by Pearson's correlation coefficient and linear regression. (D) Exosome CXCL16 levels were measured by ELISA in the serum of patients with CRC and HS. (E) Correlation between the abundance of Fn in faeces and the levels of CXCL16 in circulating exosomes from patients with CRC. Error bars, SD: $^{**}p<0.01$; $^{***}p<0.001$. CRC, colorectal cancer; HS, healthy subjects.

we identified that metastasis-related exosomes can be transported from Fn-infected CRC cells to non-infected cells. These miR-1246$^+$miR-92b-3p$^+$miR-27a-3p$^+$ exosomes modulated the bioactivity of uninfected cells by activating Wnt/β-catenin signalling and downregulating GSK3β.

Usually, exosomes from bacteria-infected hosts can induce the biosynthesis of various cytokines in recipient cells.[38] Exosomes from *Salmonella*-infected macrophages increased TNF-α production by human monocytes.[38] Exosomes from *Mycoplasma*-infected cells induce a mixed cytokine response, including the production of both IFN-γ and IL-10 from B cells. Exosomes from *Mycobacterial*-infected cells secreted TNF-α and IFN-γ. These cytokines promote both recruitment and activation of immune cells and may play a role in promoting the innate immune response on bacterial infection.

Interestingly, in contrast to these inflammatory bacteria, we found that the cancer-causing bacterium Fn stimulated the production of the chemokines CXCL16. It is well known that chemokines and their receptors selective mediators of leucocyte migration to inflammatory sites. They also play a critical role in tumour initiation, promotion and progression.[39] Numerous studies have proposed an important role for the CXCL16/CXCR6 chemokine axis in the metastasis of different tumours including prostate, liver, ovarian cancers, lung and breast cancers as well as meningioma and hepatocellular carcinoma.[40–43] Specifically, elevated levels of CXCL16 were reported in the serum, tumour tissues and lymph

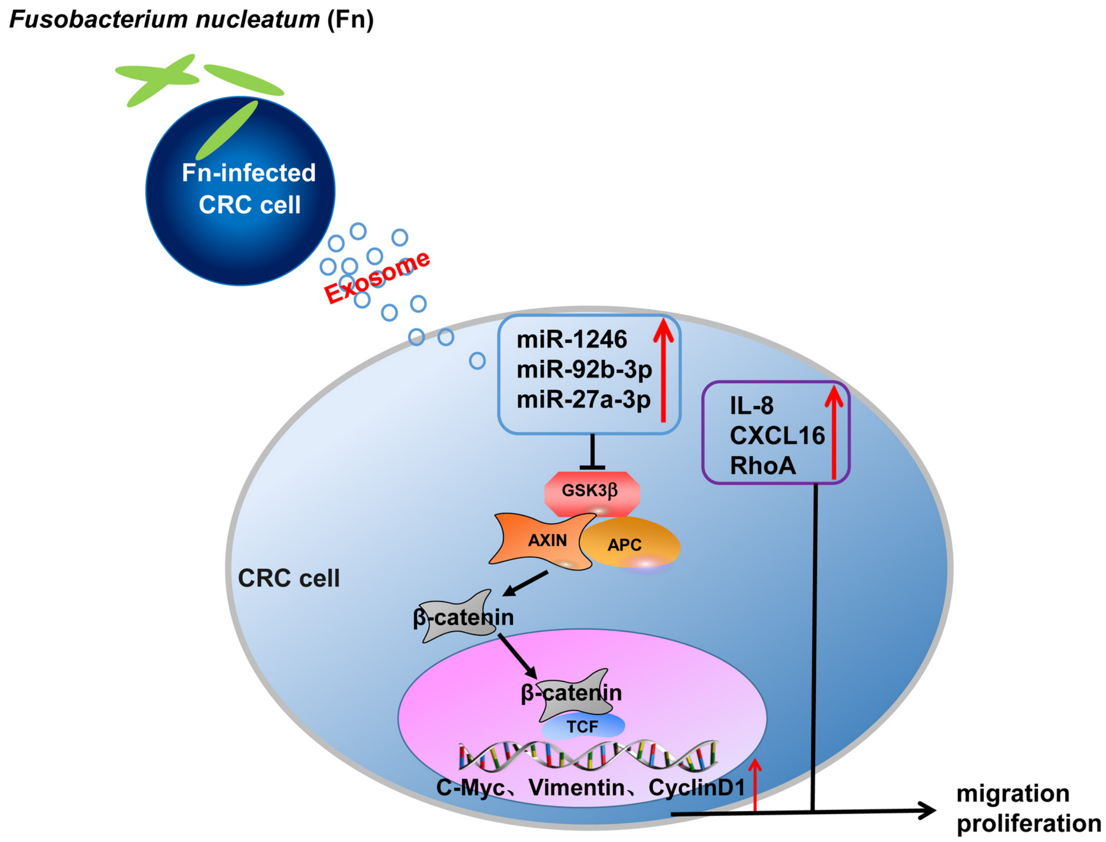

Figure 10 A schematic model of Fn-Ex functions in tumour metastasis.

nodes of patients with CRC and indicate a sign of a poor prognosis in CRC.[44–46] These observations raise the possibility that CXCL16/CXCR6 interactions may be important for CRC invasion and metastasis.[46]

Intriguingly, several groups indicated that CXCL16/CXCR6 signalling correlates with liver-specific homing and lung-specific homing during inflammatory events.[47 48] CXCR6$^+$ natural killer T cells are highly enriched in the human liver and are specifically recruited by liver sinusoidal endothelial cells, which are the major source of CXCL16. CCR6 has been previously associated with colorectal liver metastasis in patients with CRC.[49] In our study, Fn infection induced the expression of CXCL16 in CRC cells and also promoted the release of CXCL16 loaded exosomes from these infected cells. These CXCL16$^+$ Fn-Ex facilitate the homing of non-infected recipient CRC cells to hepatic vessels by the CXCL16/CXCR6 axis. In light of the evidence that CXCL16 plays a role in angiogenesis, intrahepatic metastatic nests were observed to locate around blood vessels in our study. Recently, a study reported that *Clostridium* species modified bile acids to signal liver sinusoidal endothelial cells to produce CXCL16.[50] These results that some intestinal anaerobes have the ability to stimulate the production of CXCLl6 the homing of cells to the liver.

Moreover, our proteomic analysis rapidly identified the presence of CXCL16, IL-8 and RhoA in Fn-Ex, clearly indicating their involvement in tumour invasion. Interestingly, the CXCL16/CXCR6 axis has been reported to enhance the activity of the ERK1/2 pathway, which activates RhoA to promote tumour progression.[41] Plasma levels of IL-8 have been shown to be significantly and persistently elevated after minimally invasive colorectal resection.[51] Elevated CXCL16, IL-8 and RhoA were also observed in Fn-Ex in our study, suggesting that the CXCL16$^+$RhoA$^+$IL-8$^+$ exosome paly role facilitating metastasis.

TEXs are an important component of the tumour microenvironment and are currently considered to be one of the main contributors to tumour metastasis by transporting specific proteins and RNA. The specific molecules present in TEXs have been reported to determine organ-specific metastasis and the survival of patients with cancer.[52] Previous data exploring the characteristics of the metastatic pattern of CRC have revealed that the liver is the main metastatic site of CRC, while lungs, bones and the brain are less common.[53] Consistent with these studies, our results confirmed that Fn infection further accelerated liver metastasis by the combination of enhanced cytokines, chemokines and miRNAs via exosome release.

In summary, we elucidated a schematic model of Fn-Ex functions in tumour metastasis (figure 10). This figure depicts that Fn-infected CRC cells release exosomes carrying metastasis-related miRNAs and proteins. These Fn exosomes are internalised and drive uninfected recipient cells towards a prometastatic phenotype. We therefore conclude that TEXs released from Fn-infected tumour cells may function as messengers to promote CRC cell metastasis. Exploring the mechanism and function of Fn infected-derived exosomes may prove beneficial for preventing metastasis, and eliminating Fn infection may be a valuable therapy.

Correction notice This article has been corrected since it published Onine First. The first affiliations has been updated and a sentence within the 'Identification of exosome proteins and functional categorisation in Fn-infected CRC cells' paragraph has been amended.

Contributors SG, WLL, QZ and GZ: acquisition of data, analysis and interpretation of data, statistical analysis and drafting of the manuscript. SG, JC and FC: technical and material support. WLL and GZ: study concept and design, analysis and interpretation of data, drafting of the manuscript, obtained funding and study supervision. All authors read and approved the final manuscript.

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Correction: *Exosomes derived from Fusobacterium nucleatum-infected colorectal cancer cells facilitate tumour metastasis by selectively carrying miR-1246/92b-3p/27a-3p and CXCL16*

Guo S, Chen J, Chen F, *et al*. Exosomes derived from Fusobacterium nucleatum-infected colorectal cancer cells facilitate tumour metastasis by selectively carrying miR-1246/92b-3p/27a-3p and CXCL16. *Gut* 2021;70:1507–19. doi: 10.1136/gutjnl-2020-321187

The representative image of Ex SW480 cells in Figure 2D, the representative images of mimics-miR-27a-3p SW480 cells in Figure 4A, and Figure 8F, L were incorrect.

The correct figures 2, 4 and 8 are shown below:

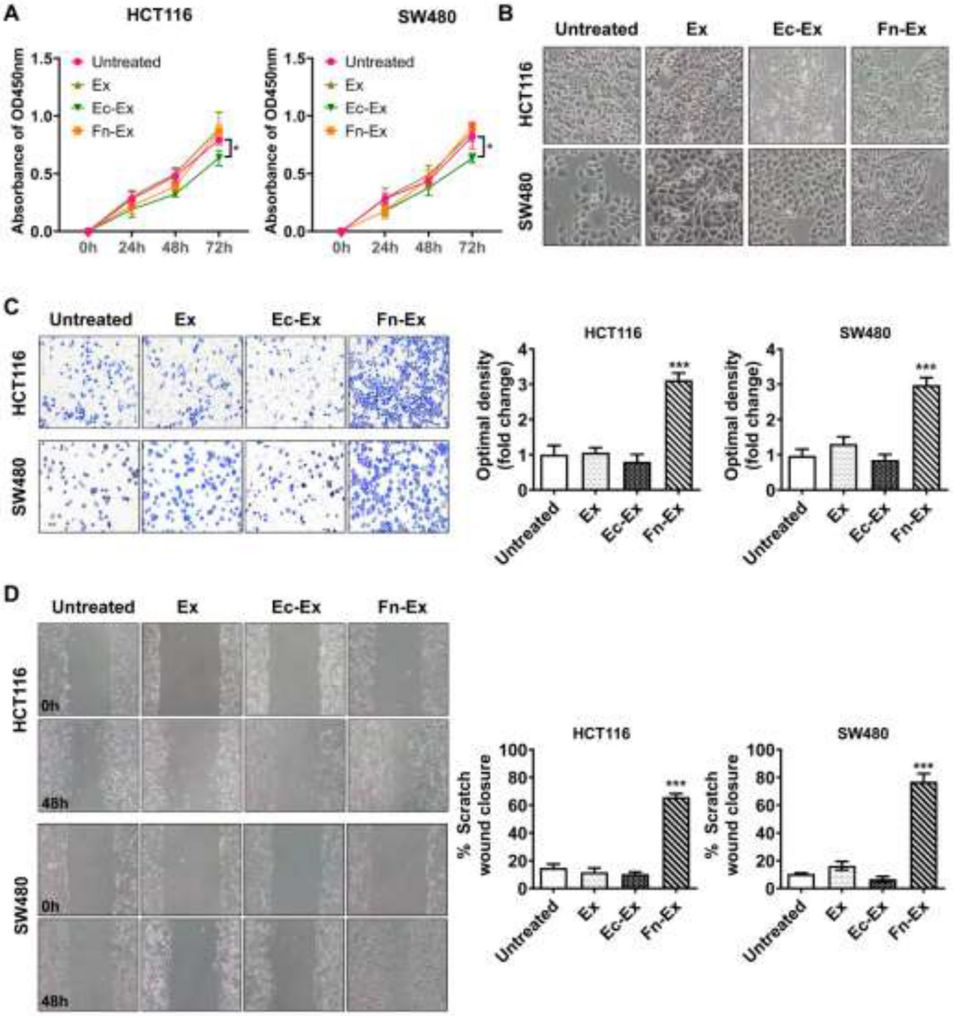
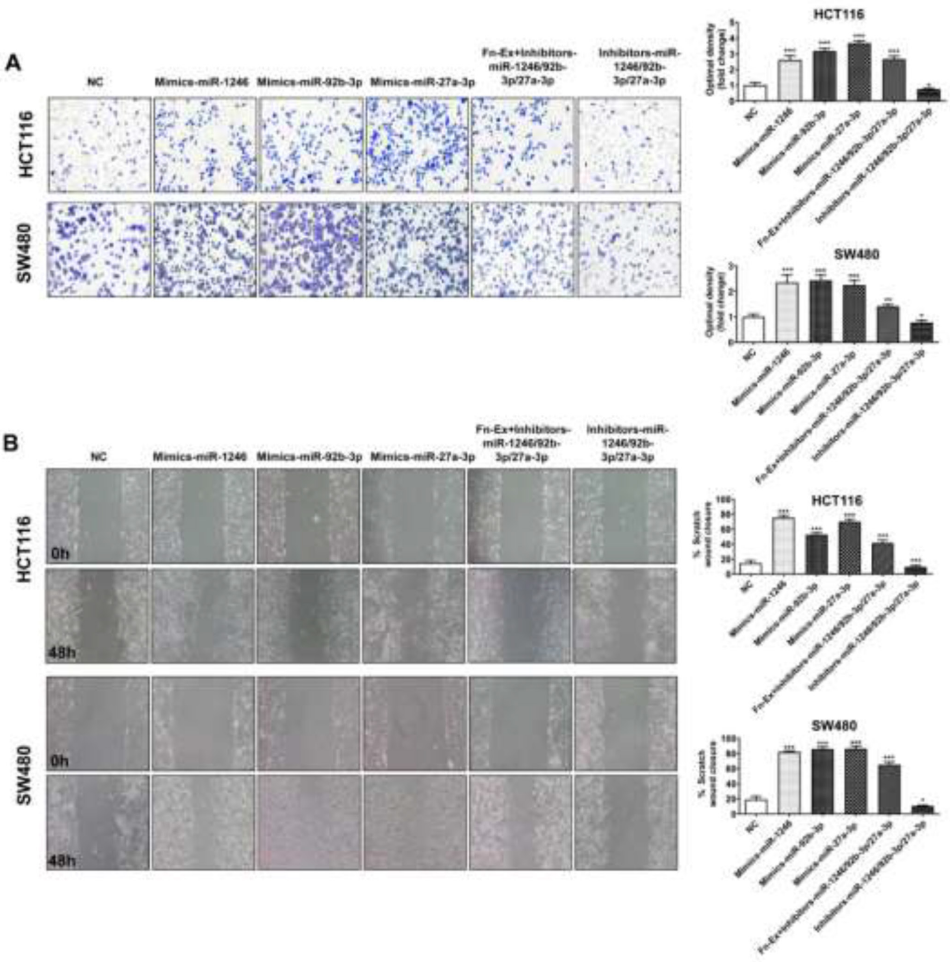


Figure 2


A
NC
Mimics-miR-1246
Mimics-miR-92b-3p
Mimics-miR-27a-3p
Fn-Ex+Inhibitors-miR-1246/92b-3p/27a-3p
Inhibitors-miR-1246/92b-3p/27a-3p
HCT116
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Optimal density (fold change)
0
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Figure 4

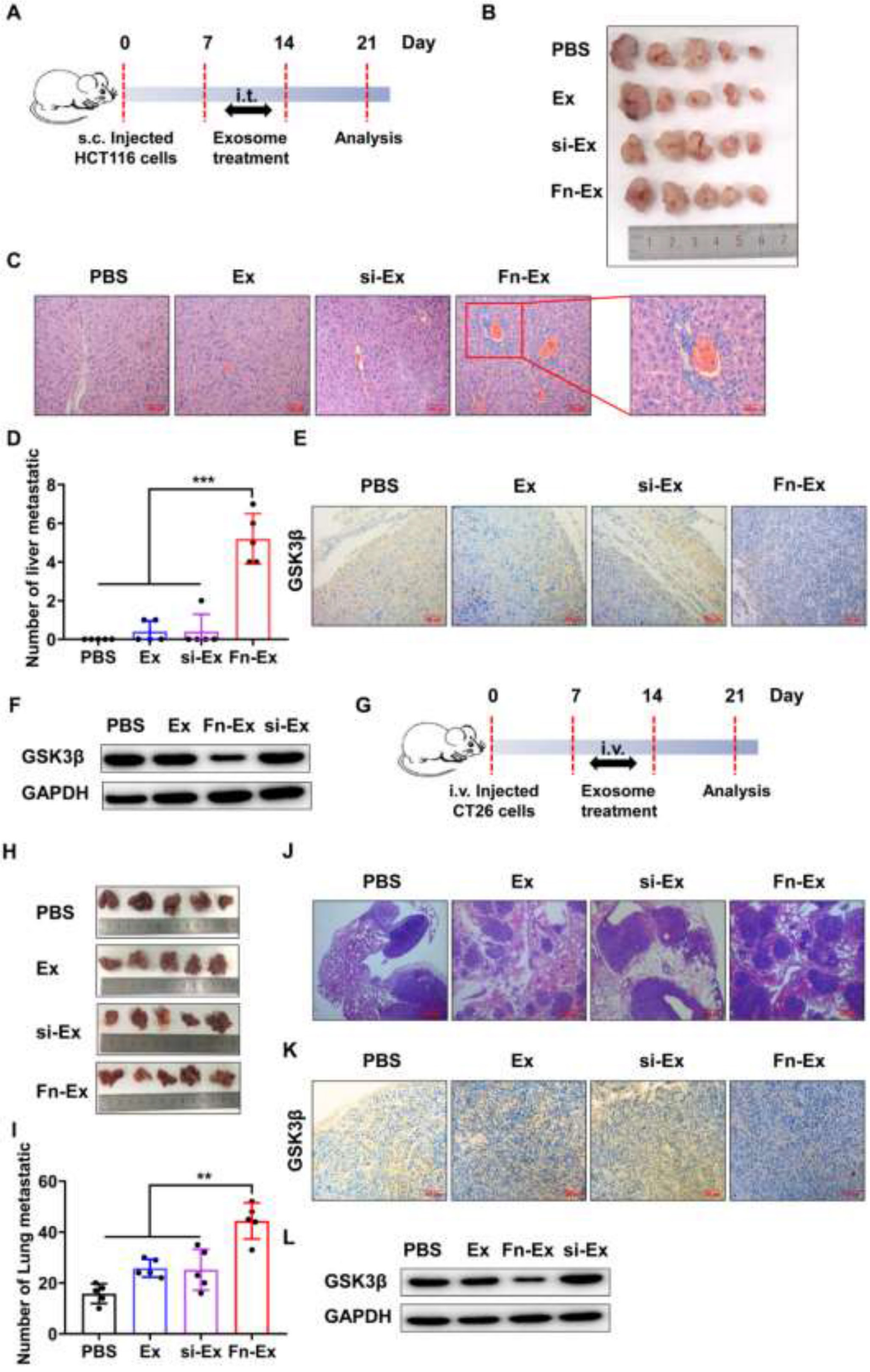


Figure 8

Gut 2022;**71**:e1. doi:10.1136/gutjnl-2020-321187corr1

Exosomes derived from *Fusobacterium nucleatum*-infected colorectal cancer cells facilitate tumor metastasis by selectively carrying miR-1246/92b-3p/27a-3p and CXCL16

Songhe Guo, Jun Chen, Fangfang Chen, Qiuyao Zeng, Wanli Liu, Ge Zhang

Supplementary Information

Materials and Methods

Patients and samples

The serum and stool samples from 82 patients with primary CRC were selected from an archive of blood samples at the Cancer Center of Sun Yat-sen University (SYSUCC). Ethics approval was granted by the Ethics Committee of SYSUCC. In addition, healthy blood samples were obtained from 102 subjects without any malignancy. All experiments were carried out in accordance with the approved guidelines and related regulations.

Bacterial culture

Fn ATCC 25586 was purchased from the Institute of Microbiology of Chinese Academy of Sciences. Fn was grown anaerobically at 37 °C for 48 h in brain heart infusion broth (BHI, Oxoid, UK). Heat-killed (dead) Fn was made by heating at 100 °C for 10 min. *E. coli* (DH5α; Tiangen, China) was cultured aerobically at 37°C for 24 h in an LB agar plate. Bacteria were centrifuged and then suspended to a concentration of 1×10^8 colony-forming units (CFUs)/ml with RPMI 1640 (Gibco, USA) for the infection experiment.

Cell culture

The human CRC cell lines HCT116 and SW480 and the mouse CRC cell line CT26 were cultured in the recommended medium supplemented with 10% fetal bovine serum (FBS, Gibco, USA) in a humidified incubator at 37°C with 5% CO_2.

Exosome isolation, characterization and nanoparticle tracking analysis

Exosomes were isolated by differential centrifugation. Briefly, the cell supernatant was centrifuged at 16,500 g for 20 min and then passed through a 0.22 μm filter. Then, the filtered supernatant was subjected to ultracentrifugation at 120,000 g for 70 min at 4°C and the exosomal pellet was resuspended in PBS to produce exosome-enriched fractions. Serum samples (2 ml) from CRC patients and healthy subjects (HS) were collected from the same volume serum as a quantitative indicator of exosome and diluted eight-fold with PBS and the exosome-enriched fractions were prepared as described above. The exosome size and number were measured by a nanoparticle tracking analysis (NTA) using a Zetasizer Nano S90 system (Malvern Instruments, England) equipped with a blue laser (405 nm). The movement under Brownian motion was recorded in 9 s sample videos which were analyzed with NTA analytical software (version 2.2). Purified exosomes were observed with a JEM1400 transmission electron microscope (TEM) operated at 120 kV (JEOL, Japan) and photographs were captured with a Canon A650 digital camera.

PKH26 staining for exosomes

Exosomes were labeled using PKH26 red fluorescent cell linker kits (Sigma, USA) according to the manufacturer’s instructions. Briefly, exosomes were resuspended in 100 μl of Diluent C. Then, 5 μM PKH26 dye was added, which was followed by 15 min of incubation at room temperature in the dark. The staining was stopped by adding 200 μl of bovine serum and incubating for 1 min. The stained exosomes were evaluated by CLSM (OLYMPUS-FV3000, Japan).

miRNA library construction and sequencing

Total RNA from exosomes was used for miRNA library preparation and sequencing. Library preparation and sequencing were conducted by Guangzhou RiboBio Co., Ltd. Briefly, total RNA samples were separated on a 15% Tris-borate-EDTA (TBE) polyacrylamide gel (Invitrogen, USA) and small RNAs ranging between 18 and 30 nucleotides (nt) were used for library preparation. Small RNAs were reverse transcribed and amplified by PCR. The PCR products were sequenced using an Illumina HiSeq 2500 platform (Illumina, USA).

RNA isolation and quantitative RT-PCR

Total RNA from exosomes was extracted using a total exosome RNA and protein isolation kit (Thermo Fisher Scientific, USA) according to the instructions of the manufacturer. cDNA was synthesized using PrimeScript™ RT Master Mix (TaKaRa, Japan). Quantification of miRNA expression was performed using a Mir-X™ miRNA RT-qPCR TB Green™ Kit (TaKaRa, Japan) on a Light Cycler® 480 II (Roche, Applied Science). The data were normalized to U6 small nuclear RNA expression and was calculated as $2^{-\triangle\triangle CT}$ expression.

Cell proliferation assay

Cells were seeded into 96-well plates at a density of 3,000 cells/well and cocultured with PBS, Ex，Ec-Ex or Fn-Ex at a concentration of 10 μg/ml. Cells were incubated at

37 ˚C in an incubator supplied with 5% CO_2 for 0, 24, 48 and 72 h. Cell Counting kit-8 (CCK8; Sigma) assays were performed according to the manufacturer's protocol. Finally, the absorbance of each sample was detected at a wavelength of 450 nm using a plate reader (Bio-Rad, USA).

miRNA transfection

Cells were transfected with miR-1246/27a-3p/92a-3p mimics, inhibitors, or negative control (NC) chemical synthesis oligonucleotides (Gene Pharma, China) at a final concentration of 50 nM using Lipofectamine 3000 reagent (Invitrogen, USA) at the indicated concentrations according to the supplier's instructions.

Stool sample DNA extraction and bacterial quantification

DNA was extracted using a TIANamp Stool DNA Kit (Tiangen, China) according to the manufacturer's instructions and was stored at -20 °C prior to amplification steps. The quantification of Fn was performed as described previously.[1]

miRNA target prediction and luciferase activity assay

miRNA target prediction and analysis were performed with the algorithms from TargetScan (http://www.targetscan.org/vert_72/), PicTar (https://pictar.mdc-berlin.de/), and miRanda (http://miranda.org.uk/). Wild-type GSK3β-3′untranslated regions (UTRs) or GSK3β-3′UTRs with various miRNA-binding site mutations were placed in a pmirGLO vector (Gene Pharma, China).

Luciferase reporter assays were performed using a dual-specific luciferase assay kit (Promega, USA) according to the manufacturer's protocol. The reporters were transfected into cells using Lipofectamine 3000 (Invitrogen, USA). The relative expression of firefly luciferase activity was normalized to Renilla luciferase activity.

GSK3β overexpression and knockdown

To generate GSK3β overexpression cells, cells were transfected with pcDNA3.1-GSK3β or pcDNA3.1 vector control using Lipofectamine 3000 reagent (Invitrogen, USA). For GSK3β knockdown, cells were transfected with si-GSK3β RNA (si-GSK3β, sense: 5’-CCACTCAAGAACTGTCAAGTA-3’; anti-sense: 5’-UUCUCCGAACGUGUCACGUTT-3’, GenePharma, China) at a working concentration of 50 nM using Lipofectamine 3000 reagent (Invitrogen, USA).

Wound healing assay

Cells were seeded in 60-mm dishes to create a confluent monolayer. The cell monolayer was then scraped with a p200 pipette tip in a straight line to create a "scratch". After the first image of the scratch was acquired, cells were cocultured with Ex (10 μg/ml)，Ec-Ex (10 μg/ml)，Fn-Ex (10 μg/ml)，CXCL16 (20 ng/ml, Sinobiological, China)，or Fn-Ex (10 μg/ml) and CXCR6 (10 ng/ml, Sinobiological, China) for 48 h prior to acquisition of the second image. The percent wound closure (%) = migrated cell surface area/total surface area ×100.

Transwell migration assay

The effect of exosomes on the migration of cancer cells was determined by using Transwell 24-well plates (8-μm pores; Corning). Ex (10 μg/ml), Ec-Ex (10 μg/ml)，Fn-Ex (10 μg/ml), CXCL16 (20 ng/ml, Sinobiological, China), or Fn-Ex (10 μg/ml) and CXCR6 (10 ng/ml, Sinobiological, China) were added to the bottom chambers to act as chemoattractants. Cells across pores were fixed with 4% paraformaldehyde and stained with 1% crystal violet solution. For each chamber, three fields were randomly chosen and cells were counted.

Western blotting

Cellular and exosomal proteins were separated by 12% SDS-PAGE, transferred to polyvinylidene difluoride membranes, and probed with antibodies against GSK3β and IL8 (1:1,000, BOSTER), CXCL16 and RhoA (1:2,000, BOSTER), β-Catenin and E-cadherin (1:2,000, Abcam), C-Myc, Vimentin and CyclinD1 (1:1,000, CST). Horseradish peroxidase (HRP)-conjugated anti-rabbit or anti-mouse antibodies (1:1,000, BOSTER) were used as secondary antibodies. GAPDH/β-Tubulin protein levels were determined by using the specific antibodies (1:5,000, BOSTER), and their levels were used as a loading control for samples, CD9 and CD63 (1:1,000, Abcam) antibodies were used as markers for exosomes.

Protein analysis

a. Sample preparation for proteomic analysis

Exosome-protein pellets were re-suspended in digestion buffer (8 M urea, 100 mM Tris-HCl; pH 8.5). The mixture was brought to 5 mM Tris [2-carboxyethyl] phosphine (TCEP) and incubated at room temperature (RT) for 15 min. Iodoacetamide was then added to a final concentration of 10 mM and the resultant mixture was incubated at RT for 20 min in the dark, when Lys-C was added at 1:50 (enzyme to substrate ratio) followed by incubation at 37 °C for 4 h. The digest was then diluted to achieve a final concentration of 2 M urea with 100 mM Tris-HCl; pH 8.5 and trypsin digestion (1:50 protease to protein ratio) was carried out at 37 °C overnight. Protein digestion was stopped by the addition of formic acid at 4% final concentration.

b. Nano-LC–MS/MS analysis of proteins

Analysis by Nano LC-Q Exactive Plus (Thermo Fisher). The injection volume was 10µl, and the flow rate was 500 nl/min. The mobile phases consisted of 0.5% acetic acid (A) and 0.5% acetic acid and 80% acetonitrile (B). A three-step linear gradient of 5–10% B in 5 min, 10–40% B in 60 min, 40–100% B in 5 min, and 100% B for 10 min was used. A spray voltage of 2400 V was applied *via* the metal connector. The MS was operated in data-dependent MS/MS mode in which each full MS scan was collected in the orbitrap, precursor ion range of 300–1600 m/z (R = 6000 @ 400 m/z), followed by up to eight MS/MS scans performed in the linear ion trap where the most abundant peptide molecular ions were selected for collision-induced dissociation (CID), using a normalized collision energy of 35%.

c. Database searches

Data from the first set of samples was searched against the human proteome (Uniprot) with no enzyme constraint, methionine oxidation as variable modification, using average mass with a peptide tolerance of 1.4 Da and a MS/MS tolerance of 0.5 Da using Mascot (v2.4.0, Matrix Science Ltd.). Filtering the data was performed using Scaffold (version 4.2.0, Proteome Software Inc., Portland, OR). Peptide identifications were accepted if they could be established at greater than 95.0% probability by the Scaffold Local FDR algorithm. Protein identifications were accepted if they could be established at greater than 99.0% probability.

ELISA

The quantification of serum exosome cytokines was determined using a Quantibody Human CXCL16 Array 1 Kit (MEIMIAN, China) following the manufacturers' protocol. Briefly, 0.5 µg of serum exosomes or a standard was added to a 96-well ELISA plate and then reacted with their cognate primary antibodies and HRP-conjugated secondary antibodies. 3, 3′, 5, 5′-Tetramethylbenzidine (TMB) was used as the substrate, and the absorbance was measured at 450 nm with a microplate reader (Bio-Rad, USA)

CXCL16 knockdown

Cells were cultured in 6-well plates with a 5×10^5/ml density. The cells were then transfected with 50 nM siCXCL16 RNA (si-CXCL16, sense: 5'-CAAAGAAUGUGGACAUGCU-3' ;anti-sense:

5’-AGCAUGUCCACAUUCUUU-3’; GenePharma, China) using the Lipofectamine 3000 reagent (Invitrogen，USA) for 48 h. The scrambled siRNA (GenePharma, China) was used as a negative control. The efficiency of knockdown was examined by RT-qPCR. The expression of target gene CXCL16 was detected by RT-qPCR and Western blot.

Experimental mouse techniques

Mice were obtained from the Model Animal Center of Nanjing University (Nanjing, China) and were raised under pathogen-free conditions in Sun Yat-sen University Animal Center (Guangzhou, China). All of the animal studies were conducted in accordance with protocols approved by the Institutional Animal Care and Research Advisory Committee.

To establish a human CRC xenograft model, six-week-old BALB/c nude mice were subcutaneously (*s.c.*) inoculated with 2×10^6 HCT116 cell. To establish a mouse CRC homograft model, six-week-old BALB/c mice were inoculated with 2×10^6 CT26 cells by tail vein injection. After tumor transplantation, Fn-Ex, si-Ex or Ex (10 μg) were injected intratumorally (*i.t.*) or intravenously (*i.v.*) every other day. PBS were injected as a control. Tumor growth and body weight were monitored every 2 days. Xenograft tumor growth was measured in three dimensions twice a week with a caliper. Tumor volume was calculated using the following formula: $(\text{length}\times\text{width}^2)/2$. The mice were sacrificed two weeks after the treatment began, and the tumors were surgically removed and counted.

Histology

Tissues were fixed in 10% buffered formalin for 24 h, processed, and embedded in paraffin for sectioning according to the conventional methods. The paraffin-embedded tissues were cut into 5-μm-thick sections. The sections were dewaxed, rehydrated and rinsed.

The tumor cell density in H&E stained sections was calculated by scanning the tissue sections under a microscope at ×40-power and counting the number of nuclei in each histological image in ten different, randomly selected fields. Data were averaged over the ten fields for statistical analysis.

Histology immunohistochemical assays

Tissue sections were incubated with a primary antibody GSK3β (1:50, BOSTER) at 4°C overnight. After washing with PBST, the sections were incubated with an HRP-conjugated anti-mouse or anti-rabbit secondary antibody (1:5000, BOSTER) at room temperature for 2 h. The sections were developed with 3-diaminobenzidine tetrahydrochloride for 10 s, which was followed by counterstaining with 10% Mayer's haematoxylin.

Statistical analyses

The data represent the mean ± SD unless otherwise indicated. Data were analyzed by two-tailed unpaired Student's t-test between two groups and by One-Way ANOVA followed by Bonferroni test for multiple comparisons. Significance was considered $P < 0.05$. Statistical analyses were performed using GraphPad 6.0.

References

1 Guo S, Li L, Xu B*, et al.* A Simple and Novel Fecal Biomarker for Colorectal Cancer: Ratio of Fusobacterium Nucleatum to Probiotics Populations, Based on Their Antagonistic Effect. Clin Chem 2018;**64**:1327-37.

Supplementary Table

Table S1 Sequence of primer.

miRNA	Primer (5’-3’)
hsa-miR-1246	AATGGATTTTTGGAGCAGGAA
hsa-miR-92b-3p	GCACTCGTCCCGGCCTCC
hsa-miR-27a-3p	TCACAGTGGCTAAGTTCCGC
hsa-miR-128-3p	TCACAGTGAACCGGTCTCTTT
hsa-miR-7704	GGGTCGGCGGCGACGTG
hsa-miR-3195	CGCGCCGGGCCCGGGTT
hsa-miR-224-5p	CAAGTCACTAGTGGTTCCGTT
hsa-miR-151a-3p	CTAGACTGAAGCTCCTTGAG
hsa-miR-1307-3p	GCGTGGCGTCGGTCGTG
hsa-miR-21-5p	TAGCTTATCAGACTGATGTTGA
U6	F: CTCGCTTCGGCAGCACA
	R: AACGCTTCACGAATTTGCGT

Table S2 Sequences for microRNA mimics and inhibitors.

Name	Sequence (5'-3')
miR-1246 mimics	AAUGGAUUUUUGGAGCAGG
miR-1246 inhibitor	CCUGCUCCAAAAAUCCAUU
miR-92b-3p mimics	GCACUCGUCCCGGCCUCC
miR-92b-3p inhibitor	GGAGGCCGGGACGAGUGC
miR-27a-3p mimics	UCACAGUGGCUAAGUUCCGC
miR-27a-3p inhibitor	GCGGAACUUAGCCACUGTGA
negative control (NC)	ACUAGUCGAUCUAUGUGUGAUATT

Table S3 Summary of small RNA sequencing of Fn-infected and non-infected exosomes (Fn-Ex and Ex).

Categories	**Ex**		**Fn-Ex**	
	Clean Reads	**percent**	**Clean Reads**	**percent**
All	18170471	100%	18668313	100%
miRNA	2408579	13.26%	3089284	16.55%
tRNA	202727	1.12%	274875	1.47%
rRNA	11175946	61.51%	12192919	65.31%
snRNA	920965	5.07%	584985	3.13%
snoRNA	132751	0.73%	65536	0.35%
piRNA	2522604	13.88%	1502548	8.05%
Y_RNA	348825	1.92%	112815	0.60%
Others	458074	2.52%	845351	4.53%

Table S4 Number of miRNA identified in each sample.

Ex		
miRNA_ID	**Total_Count**	**Normalized_Value**
hsa-let-7a-3p	44	2.4215
hsa-let-7a-5p	7718	424.7551
hsa-let-7b-3p	130	7.154
hsa-let-7b-5p	1891	104.0699
hsa-let-7c-5p	871	47.9349
hsa-let-7d-3p	88	4.843
hsa-let-7d-5p	455	25.0406
hsa-let-7e-5p	305	16.7855
hsa-let-7f-1-3p	16	0.8805
hsa-let-7f-5p	28025	1542.3376
hsa-let-7g-5p	4376	240.8303
hsa-let-7i-5p	29850	1642.7752
hsa-miR-100-5p	11846	651.9369
hsa-miR-101-3p	210	11.5572
hsa-miR-103a-3p	591	32.5253
hsa-miR-105-5p	60	3.3021
hsa-miR-106a-5p	43	2.3665
hsa-miR-106b-3p	587	32.3052
hsa-miR-106b-5p	17	0.9356
hsa-miR-107	12	0.6604
hsa-miR-10a-5p	3929	216.2299
hsa-miR-10b-5p	832	45.7886
hsa-miR-1180-3p	52	2.8618
hsa-miR-122-5p	122	6.7142
hsa-miR-1246	107246	5902.2135
hsa-miR-1248	131	7.2095
hsa-miR-1255a	19	1.0457
hsa-miR-125a-5p	389	21.4084
hsa-miR-125b-1-3	18	0.9906
hsa-miR-125b-2-3	10	0.5503
hsa-miR-125b-5p	170	9.3558
hsa-miR-126-3p	315	17.3358
hsa-miR-1273g-3p	30	1.651
hsa-miR-127-3p	13	0.7154
hsa-miR-1283	36	1.9812
hsa-miR-128-3p	691	38.0287
hsa-miR-1290	10	0.5503
hsa-miR-1291	40	2.2014
hsa-miR-129-5p	69	3.7974
hsa-miR-1301-3p	15	0.8255
hsa-miR-1304-3p	23	1.2658
hsa-miR-1307-3p	196	10.7867
hsa-miR-130a-3p	16	0.8805
hsa-miR-130b-5p	44	2.4215
hsa-miR-132-3p	79	4.3477
hsa-miR-132-5p	20	1.1007
hsa-miR-139-5p	16	0.8805
hsa-miR-1-3p	44	2.4215
hsa-miR-140-3p	256	14.0888
hsa-miR-140-5p	18	0.9906
hsa-miR-143-3p	684	37.6435
hsa-miR-145-5p	10	0.5503
hsa-miR-146a-5p	19	1.0457
hsa-miR-146b-5p	102	5.6135
hsa-miR-148a-3p	3879	213.4782
hsa-miR-148b-3p	682	37.5334
hsa-miR-149-5p	42	2.3114
hsa-miR-151a-3p	3365	185.1906
hsa-miR-152-3p	175	9.631
hsa-miR-15b-3p	32	1.7611
hsa-miR-15b-5p	27	1.4859
hsa-miR-16-2-3p	73	4.0175
hsa-miR-16-5p	67	3.6873
hsa-miR-17-5p	205	11.282
hsa-miR-181a-2-3	13	0.7154

Fn-Ex		
miRNA_ID	**Total_Count**	**Normalized_Value**
hsa-miR-16-5p	99	5.3031
hsa-miR-92a-3p	31	16.957612
hsa-miR-221-5p	26	1.3927
hsa-miR-182-5p	4814	257.8701
hsa-miR-320a	2528	135.4166
hsa-miR-361-3p	222	11.8918
hsa-miR-20a-5p	1172	62.7802
hsa-miR-152-3p	650	34.8184
hsa-miR-516a-5p	32	1.7141
hsa-let-7i-5p	70993	3802.861
hsa-let-7g-5p	10444	559.4507
hsa-let-7f-5p	98404	5271.178
hsa-let-7a-5p	35131	1881.8519
hsa-miR-222-3p	464	24.855
hsa-miR-4497	1264	67.7083
hsa-miR-584-5p	131	7.0172
hsa-miR-574-3p	98	5.2495
hsa-miR-582-3p	1240	66.4227
hsa-miR-4746-5p	34	1.8213
hsa-miR-30b-5p	23	1.232
hsa-miR-10a-5p	8727	467.4766
hsa-miR-423-3p	2218	118.8109
hsa-miR-24-2-5p	107	5.7316
hsa-miR-203a-3p	273	14.6237
hsa-miR-1246	638174	34184.8779
hsa-miR-7706	282	15.1058
hsa-miR-3934-5p	36	1.9284
hsa-miR-98-5p	1049	56.1915
hsa-miR-15b-3p	35	1.8748
hsa-miR-335-5p	20	1.0713
hsa-miR-335-3p	340	18.2127
hsa-miR-1307-3p	778	41.6749
hsa-miR-425-5p	59	3.1604
hsa-miR-194-5p	25	1.3392
hsa-miR-1304-3p	74	3.9639
hsa-miR-7704	2167	116.079
hsa-miR-17-5p	251	13.4452
hsa-miR-3656	85	4.5532
hsa-miR-5701	142	7.6065
hsa-miR-31-5p	28	1.4999
hsa-miR-1273g-3p	43	2.3034
hsa-miR-95-3p	397	21.266
hsa-miR-1255a	31	1.6606
hsa-miR-548o-3p	99	5.3031
hsa-miR-365b-3p	192	10.2848
hsa-miR-1301-3p	38	2.0355
hsa-miR-378d	32	1.7141
hsa-miR-374a-3p	99	5.3031
hsa-miR-26b-5p	600	32.14
hsa-miR-378g	35	1.8748
hsa-miR-30e-3p	1998	107.0263
hsa-miR-331-3p	20	1.0713
hsa-miR-19a-3p	37	1.982
hsa-miR-486-5p	246	13.1774
hsa-miR-941	7223	386.9123
hsa-miR-106b-3p	1981	106.1156
hsa-miR-501-3p	89	4.7674
hsa-miR-26a-5p	6808	364.6821
hsa-miR-140-3p	371	19.8732
hsa-miR-193a-5p	72	3.8568
hsa-miR-1283	56	2.9997
hsa-miR-129-5p	160	8.5707
hsa-miR-1180-3p	141	7.5529
hsa-let-7d-3p	457	24.48
hsa-miR-93-5p	293	15.695

hsa-miR-181a-5p	119	6.5491
hsa-miR-181b-5p	86	4.733
hsa-miR-181d-5p	29	1.596
hsa-miR-182-5p	4624	254.4788
hsa-miR-183-5p	1846	101.5934
hsa-miR-185-5p	345	18.9868
hsa-miR-186-5p	201	11.0619
hsa-miR-191-5p	636	35.0018
hsa-miR-192-5p	1419	78.0937
hsa-miR-193a-5p	18	0.9906
hsa-miR-193b-3p	29	1.596
hsa-miR-194-5p	26	1.4309
hsa-miR-196a-5p	1586	87.2845
hsa-miR-196b-5p	161	8.8605
hsa-miR-197-3p	75	4.1276
hsa-miR-199a-3p	21	1.1557
hsa-miR-199b-3p	21	1.1557
hsa-miR-19a-3p	42	2.3114
hsa-miR-19b-3p	45	2.4765
hsa-miR-200b-3p	42	2.3114
hsa-miR-200c-3p	36	1.9812
hsa-miR-203a-3p	92	5.0632
hsa-miR-20a-5p	618	34.0112
hsa-miR-210-3p	60	3.3021
hsa-miR-212-5p	43	2.3665
hsa-miR-215-5p	28	1.541
hsa-miR-21-5p	35446	1950.7475
hsa-miR-218-5p	15	0.8255
hsa-miR-221-3p	362	19.9224
hsa-miR-221-5p	31	1.7061
hsa-miR-222-3p	205	11.282
hsa-miR-22-3p	72	3.9625
hsa-miR-224-5p	1310	72.095
hsa-miR-23a-3p	596	32.8005
hsa-miR-23b-3p	307	16.8955
hsa-miR-24-2-5p	61	3.3571
hsa-miR-24-3p	942	51.8424
hsa-miR-25-3p	1729	95.1544
hsa-miR-26a-5p	2410	132.6328
hsa-miR-26b-5p	338	18.6016
hsa-miR-27a-3p	321	17.666
hsa-miR-27b-3p	1157	63.6747
hsa-miR-27b-5p	10	0.5503
hsa-miR-28-3p	463	25.4809
hsa-miR-28-5p	14	0.7705
hsa-miR-29a-3p	162	8.9156
hsa-miR-29b-3p	13	0.7154
hsa-miR-3065-5p	12	0.6604
hsa-miR-30a-3p	1149	63.2345
hsa-miR-30a-5p	3126	172.0374
hsa-miR-30b-5p	16	0.8805
hsa-miR-30c-2-3p	84	4.6229
hsa-miR-30c-5p	881	48.4853
hsa-miR-30d-5p	2837	156.1324
hsa-miR-30e-3p	550	30.2689
hsa-miR-30e-5p	74	4.0725
hsa-miR-3135b	24	1.3208
hsa-miR-3195	14	0.7705
hsa-miR-3196	22	1.2108
hsa-miR-320a	1569	86.3489
hsa-miR-320b	57	3.137
hsa-miR-320c	71	3.9074
hsa-miR-320d	65	3.5772
hsa-miR-32-5p	30	1.651
hsa-miR-328-3p	13	0.7154
hsa-miR-330-3p	177	9.7411
hsa-miR-331-3p	15	0.8255
hsa-miR-335-3p	76	4.1826

hsa-miR-320b	271	14.5166
hsa-miR-132-3p	214	11.4633
hsa-miR-132-5p	58	3.1069
hsa-miR-148a-3p	13493	722.7755
hsa-miR-30d-5p	4467	239.2825
hsa-miR-125a-5p	894	47.8886
hsa-miR-125b-5p	444	23.7836
hsa-miR-30c-5p	1967	105.3657
hsa-miR-99b-5p	3626	194.2329
hsa-miR-345-5p	34	1.8213
hsa-miR-125b-1-3p	58	3.1069
hsa-miR-32-5p	54	2.8926
hsa-miR-183-5p	4247	227.4978
hsa-miR-320c	321	17.1949
hsa-miR-105-5p	175	9.3742
hsa-let-7f-1-3p	39	2.0891
hsa-miR-1-3p	39	2.0891
hsa-miR-200b-3p	95	5.0888
hsa-miR-424-3p	102	5.4638
hsa-miR-149-5p	93	4.9817
hsa-miR-193b-3p	75	4.0175
hsa-miR-197-3p	237	12.6953
hsa-miR-532-5p	1930	103.3837
hsa-miR-4516	130	6.9637
hsa-miR-340-5p	96	5.1424
hsa-miR-338-5p	56	2.9997
hsa-miR-21-5p	112217	6011.0948
hsa-miR-130a-3p	29	1.5534
hsa-miR-185-5p	945	50.6205
hsa-miR-30e-5p	71	3.8032
hsa-miR-23b-3p	455	24.3729
hsa-miR-4508	149	7.9814
hsa-miR-30a-5p	3542	189.7333
hsa-let-7d-5p	1647	88.2244
hsa-miR-1290	71	3.81395
hsa-miR-342-3p	131	7.0172
hsa-miR-27b-3p	2975	159.3609
hsa-miR-99a-5p	4345	232.7473
hsa-miR-25-3p	6441	345.0231
hsa-miR-181a-2-3p	82	4.40854
hsa-miR-191-5p	806	43.1748
hsa-let-7c-5p	3362	180.0913
hsa-miR-1261	21	1.1249
hsa-miR-23a-3p	1184	63.423
hsa-miR-340-3p	28	1.4999
hsa-miR-320d	335	17.9448
hsa-miR-140-5p	25	1.3392
hsa-miR-450a-5p	23	1.232
hsa-miR-196a-5p	3116	166.9139
hsa-let-7b-5p	6766	362.4323
hsa-miR-3135b	32	1.7141
hsa-miR-130b-5p	203	10.874
hsa-miR-92b-3p	2646	141.7375
hsa-miR-7-5p	6443	345.1303
hsa-miR-103a-3p	1193	63.9051
hsa-miR-330-3p	161	8.6242
hsa-miR-21-3p	43	2.3034
hsa-miR-451a	28	1.4999
hsa-miR-760	40	2.1427
hsa-miR-378a-3p	3876	207.6245
hsa-miR-744-5p	110	5.8923
hsa-let-7a-3p	144	7.7136
hsa-miR-22-3p	132	7.0708
hsa-miR-210-3p	62	3.3211
hsa-miR-19b-3p	24	1.2856
hsa-miR-186-5p	377	20.1946
hsa-miR-502-3p	29	1.5534
hsa-miR-629-5p	181	9.6956

hsa-miR-338-5p	29	1.596
hsa-miR-340-5p	38	2.0913
hsa-miR-342-3p	145	7.98
hsa-miR-345-5p	13	0.7154
hsa-miR-34a-5p	11	0.6054
hsa-miR-361-3p	126	6.9343
hsa-miR-3615	27	1.4859
hsa-miR-361-5p	16	0.8805
hsa-miR-3656	60	3.3021
hsa-miR-365a-3p	157	8.6404
hsa-miR-365b-3p	157	8.6404
hsa-miR-374a-3p	59	3.247
hsa-miR-374a-5p	22	1.2108
hsa-miR-374b-5p	79	4.3477
hsa-miR-378a-3p	1268	69.7836
hsa-miR-378f	14	0.7705
hsa-miR-3934-5p	17	0.9356
hsa-miR-3960	12	0.6604
hsa-miR-421	19	1.0457
hsa-miR-423-3p	605	33.2958
hsa-miR-423-5p	236	12.9881
hsa-miR-425-5p	182	10.0163
hsa-miR-4488	116	6.384
hsa-miR-4492	21	1.1557
hsa-miR-4497	220	12.1076
hsa-miR-4508	29	1.596
hsa-miR-450b-5p	42	2.3114
hsa-miR-4516	119	6.5491
hsa-miR-451a	12	0.6604
hsa-miR-452-5p	238	13.0982
hsa-miR-454-3p	30	1.651
hsa-miR-455-3p	11	0.6054
hsa-miR-455-5p	47	2.5866
hsa-miR-4634	10	0.5503
hsa-miR-4664-3p	26	1.4309
hsa-miR-484	105	5.7786
hsa-miR-486-5p	947	52.1175
hsa-miR-500a-3p	42	2.3114
hsa-miR-501-3p	25	1.3759
hsa-miR-505-3p	11	0.6054
hsa-miR-516a-5p	11	0.6054
hsa-miR-522-3p	70	3.8524
hsa-miR-532-5p	593	32.6354
hsa-miR-548e-3p	10	0.5503
hsa-miR-548o-3p	73	4.0175
hsa-miR-5701	48	2.6416
hsa-miR-574-3p	45	2.4765
hsa-miR-576-3p	33	1.8161
hsa-miR-582-3p	425	23.3896
hsa-miR-584-5p	31	1.7061
hsa-miR-589-5p	136	7.4847
hsa-miR-615-3p	8	0.41276
hsa-miR-619-5p	18	0.9906
hsa-miR-625-3p	11	0.6054
hsa-miR-629-5p	49	2.6967
hsa-miR-641	12	0.6604
hsa-miR-651-5p	22	1.2108
hsa-miR-6516-3p	25	1.3759
hsa-miR-664a-3p	26	1.4309
hsa-miR-671-3p	23	1.2658
hsa-miR-744-5p	35	1.9262
hsa-miR-7-5p	10799	594.3159
hsa-miR-7641	23832	1311.5785
hsa-miR-767-5p	25	1.3759
hsa-miR-769-5p	39	2.1463
hsa-miR-7704	197	10.8418
hsa-miR-7706	66	3.6323
hsa-miR-92a-3p	53	2.928378

hsa-miR-15b-5p	58	3.1069
hsa-miR-200c-3p	82	4.3925
hsa-miR-589-5p	294	15.7486
hsa-miR-6130	24	1.2856
hsa-miR-18a-3p	22	1.1785
hsa-miR-96-5p	275	14.7308
hsa-miR-181d-5p	55	2.9462
hsa-miR-3196	31	1.6606
hsa-miR-3195	124	6.6423
hsa-miR-181a-5p	308	16.4985
hsa-miR-16-2-3p	305	16.3378
hsa-miR-450b-5p	111	5.9459
hsa-miR-374a-5p	42	2.2498
hsa-miR-30c-2-3p	183	9.8027
hsa-miR-192-5p	3458	185.2337
hsa-miR-106b-5p	27	1.4463
hsa-miR-151a-5p	32	1.7141
hsa-miR-1281	23	1.232
hsa-miR-651-5p	36	1.9284
hsa-miR-28-3p	1758	94.1703
hsa-miR-143-3p	521	27.9083
hsa-miR-29a-3p	385	20.6232
hsa-miR-4488	261	13.9809
hsa-miR-455-3p	39	2.0891
hsa-miR-101-3p	493	26.4084
hsa-miR-125b-2-3p	56	2.9997
hsa-let-7b-3p	860	46.067
hsa-miR-484	263	14.088
hsa-miR-330-5p	23	1.232
hsa-let-7e-5p	575	30.8009
hsa-miR-215-5p	61	3.2676
hsa-miR-421	21	1.1249
hsa-miR-146b-5p	103	5.5174
hsa-miR-199b-3p	19	1.0178
hsa-miR-625-3p	52	2.7855
hsa-miR-181b-5p	256	13.7131
hsa-miR-128-3p	3116	166.9139
hsa-miR-122-5p	88	4.7139
hsa-miR-106a-5p	50	2.6783
hsa-miR-22-5p	21	1.1249
hsa-miR-27b-5p	22	1.1785
hsa-miR-522-3p	143	7.66
hsa-miR-10b-5p	1470	78.7431
hsa-miR-199a-3p	19	1.0178
hsa-miR-3615	149	7.9814
hsa-miR-455-5p	105	5.6245
hsa-miR-671-3p	101	5.4102
hsa-miR-374b-5p	73	3.9104
hsa-miR-148b-3p	1168	62.5659
hsa-miR-4664-3p	68	3.6425
hsa-miR-99b-3p	284	15.2129
hsa-miR-196b-5p	166	8.8921
hsa-miR-542-3p	34	1.8213
hsa-miR-454-3p	21	1.1249
hsa-miR-500a-3p	105	5.6245
hsa-miR-135b-5p	23	1.232
hsa-miR-4448	41	2.1962
hsa-miR-576-3p	44	2.3569
hsa-miR-361-5p	54	2.8926
hsa-miR-139-5p	43	2.3034
hsa-miR-769-5p	73	3.9104
hsa-miR-7641	34912	1870.1208
hsa-miR-100-5p	39358	2108.2783
hsa-miR-767-5p	46	2.4641
hsa-miR-4492	83	4.446
hsa-miR-126-3p	417	22.3373
hsa-miR-212-5p	137	7.3386
hsa-miR-151a-3p	16153	865.263

hsa-miR-92b-3p	301	16.5653
hsa-miR-93-5p	286	15.7398
hsa-miR-941	1932	106.3264
hsa-miR-95-3p	162	8.9156
hsa-miR-96-5p	239	13.1532
hsa-miR-98-3p	22	1.2108
hsa-miR-98-5p	591	32.5253
hsa-miR-99a-5p	1466	80.6804
hsa-miR-99b-3p	84	4.6229
hsa-miR-99b-5p	940	51.7323

hsa-miR-221-3p	628	33.6399
hsa-miR-615-3p	62	3.32114
hsa-miR-224-5p	5314	284.6535
hsa-miR-452-5p	329	17.6234
hsa-miR-423-5p	588	31.4972
hsa-miR-28-5p	42	2.2498
hsa-miR-27a-3p	1378	73.8149
hsa-miR-30a-3p	3788	202.9107
hsa-miR-365a-3p	192	10.2848
hsa-miR-24-3p	2800	149.9868
hsa-miR-148b-5p	19	1.0178
hsa-miR-29b-3p	18	0.9642
hsa-miR-219a-1-3p	18	0.9642
hsa-miR-125a-3p	18	0.9642
hsa-miR-576-5p	18	0.9642
hsa-miR-454-5p	18	0.9642
hsa-miR-1291	18	0.9642
hsa-miR-664a-5p	18	0.9642
hsa-miR-92b-5p	17	0.9106
hsa-miR-1254	17	0.9106
hsa-miR-93-3p	16	0.8571
hsa-miR-107	16	0.8571
hsa-miR-519c-5p	16	0.8571
hsa-miR-519b-5p	16	0.8571
hsa-miR-523-5p	16	0.8571
hsa-miR-518e-5p	16	0.8571
hsa-miR-522-5p	16	0.8571
hsa-miR-519a-5p	16	0.8571
hsa-miR-942-5p	16	0.8571
hsa-miR-378f	16	0.8571
hsa-miR-4791	16	0.8571
hsa-miR-6747-3p	16	0.8571
hsa-miR-98-3p	15	0.8035
hsa-miR-422a	15	0.8035
hsa-miR-548e-3p	15	0.8035
hsa-miR-1248	15	0.8035
hsa-miR-2110	15	0.8035
hsa-miR-3622a-5p	15	0.8035
hsa-miR-331-5p	14	0.7499
hsa-miR-652-3p	14	0.7499
hsa-miR-1303	14	0.7499
hsa-miR-4485-3p	14	0.7499
hsa-miR-23b-5p	13	0.6964
hsa-miR-339-3p	13	0.6964
hsa-miR-505-3p	13	0.6964
hsa-miR-3690	13	0.6964
hsa-miR-378e	13	0.6964
hsa-miR-4677-3p	13	0.6964
hsa-miR-218-5p	12	0.6428
hsa-miR-126-5p	12	0.6428
hsa-miR-328-3p	12	0.6428
hsa-miR-1827	12	0.6428
hsa-miR-548aq-3p	12	0.6428
hsa-miR-6720-3p	12	0.6428
hsa-miR-9-5p	11	0.5892
hsa-miR-185-3p	11	0.5892
hsa-miR-324-3p	11	0.5892
hsa-miR-532-3p	11	0.5892
hsa-miR-641	11	0.5892
hsa-miR-1250-5p	11	0.5892
hsa-miR-664a-3p	11	0.5892
hsa-miR-3065-5p	11	0.5892
hsa-miR-3960	11	0.5892
hsa-miR-4661-5p	11	0.5892
hsa-miR-30d-3p	10	0.5357
hsa-miR-10a-3p	10	0.5357
hsa-miR-146a-5p	10	0.5357
hsa-miR-130b-3p	10	0.5357

hsa-miR-338-3p	10	0.5357
hsa-miR-409-3p	10	0.5357
hsa-miR-675-3p	10	0.5357
hsa-miR-320e	10	0.5357
hsa-miR-4326	10	0.5357
hsa-miR-3928-3p	10	0.5357
hsa-miR-548ah-3p	10	0.5357
hsa-miR-4634	10	0.5357

Table S5 miRNA with significantly different expression levels between Ex and Fn-Ex.

miRNA_ID	Ex (normalized value)	Fn-Ex(normalized value)	up/down	log2(foldchange)	P-value
hsa-miR-1248	7.2095	0.8035	down	-3.1655	1.91E-07
hsa-miR-6516-3p	1.3759	0	down	-7.1042	9.48E-06
hsa-miR-619-5p	0.9906	0	down	-6.6302	7.45E-05
hsa-miR-425-5p	10.0163	3.1604	down	-1.6642	0.000154
hsa-miR-127-3p	0.7154	0	down	-6.1607	0.00053
hsa-miR-34a-5p	0.6054	0	down	-5.9198	0.001409
hsa-miR-145-5p	0.5503	0	down	-5.7821	0.001996
hsa-miR-1291	2.2014	0.9642	down	-1.191	0.003964
hsa-miR-664a-3p	1.4309	0.5892	down	-1.2801	0.008158
hsa-miR-486-5p	13.1774	52.1175	up	1.9837	1.47E-05
hsa-miR-424-3p	0	5.4638	up	9.0938	3.19E-07
hsa-miR-21-3p	0	2.3034	up	7.8476	0.000157
hsa-miR-760	0	2.1427	up	7.7433	0.000244
hsa-miR-4448	0	2.1962	up	7.7789	0.000244
hsa-miR-542-3p	0	1.8213	up	7.5088	0.000622
hsa-miR-378g	0	1.8748	up	7.5506	0.000622
hsa-miR-4746-5p	0	1.8213	up	7.5088	0.000622
hsa-miR-7704	10.8418	116.079	up	3.4204	0.000857
hsa-miR-450a-5p	0	1.232	up	6.9449	0.001006
hsa-miR-330-5p	0	1.232	up	6.9449	0.001006
hsa-miR-135b-5p	0	1.232	up	6.9449	0.001006
hsa-miR-1281	0	1.232	up	6.9449	0.001006
hsa-miR-151a-5p	0	1.7141	up	7.4213	0.001028
hsa-miR-378d	0	1.7141	up	7.4213	0.001028
hsa-miR-18a-3p	0	1.1785	up	6.8808	0.001409
hsa-miR-1261	0	1.1249	up	6.8137	0.001409
hsa-miR-22-5p	0	1.1249	up	6.8137	0.001409
hsa-miR-31-5p	0	1.4999	up	7.2287	0.001744
hsa-miR-340-3p	0	1.4999	up	7.2287	0.001744
hsa-miR-502-3p	0	1.5534	up	7.2793	0.001744
hsa-miR-335-5p	0	1.0713	up	6.7432	0.001996
hsa-miR-125a-3p	0	0.9642	up	6.5913	0.002864
hsa-miR-576-5p	0	0.9642	up	6.5913	0.002864
hsa-miR-454-5p	0	0.9642	up	6.5913	0.002864
hsa-miR-148b-5p	0	1.0178	up	6.6693	0.002864
hsa-miR-664a-5p	0	0.9642	up	6.5913	0.002864
hsa-miR-219a-1-3p	0	0.9642	up	6.5913	0.002864
hsa-miR-92b-3p	16.5653	141.7375	up	3.097	0.003633
hsa-miR-6130	0	1.2856	up	7.0063	0.004066
hsa-miR-92b-5p	0	0.9106	up	6.5087	0.004166
hsa-miR-519a-5p	0	0.8571	up	6.4214	0.006149
hsa-miR-422a	0	0.8035	up	6.3282	0.006149
hsa-miR-6747-3p	0	0.8571	up	6.4214	0.006149
hsa-miR-518e-5p	0	0.8571	up	6.4214	0.006149
hsa-miR-615-3p	0.41276	3.2114	up	3.0083	0.006575
hsa-miR-3615	1.4859	7.9814	up	2.4253	0.007351
hsa-let-7d-3p	4.843	24.48	up	2.3376	0.007357
hsa-miR-320d	3.5772	17.9448	up	2.3267	0.008072
hsa-miR-4485-3p	0	0.7499	up	6.2286	0.009224
hsa-miR-1303	0	0.7499	up	6.2286	0.009224
hsa-miR-652-3p	0	0.7499	up	6.2286	0.009224
hsa-miR-331-5p	0	0.7499	up	6.2286	0.009224
hsa-miR-27a-3p	185.1906	865.263	up	2.2241	0.00923
hsa-miR-4508	1.596	7.9814	up	2.3222	0.009773
hsa-miR-3195	0.7705	6.6423	up	3.1078	0.011498
hsa-miR-1307-3p	424.7551	1881.8519	up	2.1474	0.011623
hsa-miR-320b	3.137	14.5166	up	2.2102	0.011661
hsa-miR-128-3p	38.0287	166.9139	up	2.1339	0.012266
hsa-miR-125b-2-3p	0.5503	2.9997	up	2.4465	0.01307
hsa-miR-130b-5p	2.4215	10.874	up	2.1669	0.013488
hsa-miR-320c	3.9074	17.1949	up	2.1377	0.013557
hsa-miR-4677-3p	0	0.6964	up	6.1218	0.014079
hsa-miR-339-3p	0	0.6964	up	6.1218	0.014079
hsa-miR-3690	0	0.6964	up	6.1218	0.014079
hsa-miR-378e	0	0.6964	up	6.1218	0.014079
hsa-miR-23b-5p	0	0.6964	up	6.1218	0.014079

hsa-miR-335-3p	4.1826	18.2127	up	2.1225	0.014249
hsa-miR-151a-3p	17.666	73.8149	up	2.0629	0.015305
hsa-miR-7706	3.6323	15.1058	up	2.0561	0.017318
hsa-miR-1290	0.5503	3.81395	up	2.7363	0.017994
hsa-let-7a-5p	10.7867	41.6749	up	1.9499	0.018158
hsa-miR-21-5p	1950.7475	6011.0948	up	1.6236	0.018331
hsa-miR-16-2-3p	4.0175	16.3378	up	2.0238	0.018517
hsa-miR-224-5p	72.095	284.6535	up	1.9812	0.018688
hsa-miR-221-5p	69.7836	207.6245	up	1.573	0.019129
hsa-miR-671-3p	1.2658	5.4102	up	2.0956	0.01997
hsa-miR-185-3p	0	0.5892	up	5.8807	0.0219
hsa-miR-1250-5p	0	0.5892	up	5.8807	0.0219
hsa-miR-9-5p	0	0.5892	up	5.8807	0.0219
hsa-miR-548aq-3p	0	0.6428	up	6.0063	0.0219
hsa-miR-1246	5902.2135	34184.8779	up	2.534	0.032506
hsa-miR-92a-3p	2.928378	16.957612	up	2.5338	0.032625
hsa-miR-181a-2-3p	0.7154	4.40854	up	2.5477	0.034755
hsa-miR-10a-3p	0	0.5357	up	5.7434	0.034783
hsa-miR-3928-3p	0	0.5357	up	5.7434	0.034783
hsa-miR-130b-3p	0	0.5357	up	5.7434	0.034783
hsa-miR-675-3p	0	0.5357	up	5.7434	0.034783
hsa-miR-409-3p	0	0.5357	up	5.7434	0.034783
hsa-miR-548ah-3p	0	0.5357	up	5.7434	0.034783
hsa-miR-4497	12.1076	67.7083	up	2.4834	0.041802
hsa-let-7b-3p	7.154	46.067	up	2.6869	0.04954

Table S6 GSK3β was predicted as a putative miR-1246/27a-3p/92a-3p target through analysis of 4 public prediction databases.

miRNA	**Gene**	**miRDB**	**miRTarBase**	**miRWalk**	**TargetScan**
hsa-miR-1246	GSK3β	0	0	1	1
hsa-miR-27a-3p	GSK3β	1	0	1	1
hsa-miR-92b-3p	GSK3β	0	1	1	0

Table S7 Protein expression profile characteristic to Ex and Fn-Ex.

Ex		Fn-Ex	
Accession	Description	Accession	Description
P98160	Basement membrane-specific heparan sulfate proteoglycan core protein [OS=Homo sapiens]	P98160	Basement membrane-specific heparan sulfate proteoglycan core protein [OS=Homo sapiens]
P01023	alpha-2-macroglobulin [OS=Homo sapiens]	Q08380	Galectin-3-binding protein [OS=Homo sapiens]
P02675	Fibrinogen beta chain [OS=Homo sapiens]	P60709	Actin, cytoplasmic 1 [OS=Homo sapiens]
P02671-1	Fibrinogen alpha chain [OS=Homo sapiens]	P62805	histone H4 [OS=Homo sapiens]
P04114	apolipoprotein B-100 [OS=Homo sapiens]	P62736	Actin, aortic smooth muscle [OS=Homo sapiens]
P02787	Serotransferrin [OS=Homo sapiens]	P01023	alpha-2-macroglobulin [OS=Homo sapiens]
P21333	Filamin-A [OS=Homo sapiens]	P10909-2	Isoform 2 of Clusterin [OS=Homo sapiens]
Q9Y490	Talin-1 [OS=Homo sapiens]	P11142-1	Heat shock cognate 71 kDa protein [OS=Homo sapiens]
P02679-2	Isoform Gamma-A of Fibrinogen gamma chain [OS=Homo sapiens]	P16402	Histone H1.3 [OS=Homo sapiens]
P0DOX5	immunoglobulin gamma-1 heavy chain [OS=Homo sapiens]	Q5QNW6-2	Isoform 2 of Histone H2B type 2-F [OS=Homo sapiens]
P35579-1	Myosin-9 [OS=Homo sapiens]	Q8WUM4-2	Isoform 2 of Programmed cell death 6-interacting protein [OS=Homo sapiens]
P0C0L4-1	Complement C4-A [OS=Homo sapiens]	P23527	Histone H2B type 1-O [OS=Homo sapiens]
P02751	fibronectin [OS=Homo sapiens]	P63104-1	14-3-3 protein zeta/delta [OS=Homo sapiens]
P60709	Actin, cytoplasmic 1 [OS=Homo sapiens]	P62979	Ubiquitin-40S ribosomal protein S27a [OS=Homo sapiens]
Q08380	Galectin-3-binding protein [OS=Homo sapiens]	P0C0S8	histone H2A type 1 [OS=Homo sapiens]
P01859	Immunoglobulin heavy constant gamma 2 [OS=Homo sapiens]	P08238	Heat shock protein HSP 90-beta [OS=Homo sapiens]
Q8WUM4	Programmed cell death 6-interacting protein [OS=Homo sapiens]	Q9P2B2	prostaglandin F2 receptor negative regulator [OS=Homo sapiens]
Q14517	Protocadherin Fat 1 [OS=Homo sapiens]	P02533	Keratin, type I cytoskeletal 14 [OS=Homo sapiens]
Q00610-1	Clathrin heavy chain 1 [OS=Homo sapiens]	P01024	Complement C3 [OS=Homo sapiens]
P01871-2	Isoform 2 of Immunoglobulin heavy constant mu [OS=Homo sapiens]	Q93077	Histone H2A type 1-C [OS=Homo sapiens]
P01860	Immunoglobulin heavy constant gamma 3 [OS=Homo sapiens]	P04083	annexin A1 [OS=Homo sapiens]
P00450	Ceruloplasmin [OS=Homo sapiens]	P06733-1	alpha-enolase [OS=Homo sapiens]
Q9P2B2	prostaglandin F2 receptor negative regulator [OS=Homo sapiens]	Q14517	Protocadherin Fat 1 [OS=Homo sapiens]
P62805	histone H4 [OS=Homo sapiens]	P39060-3	Collagen alpha-1(XVIII) chain [OS=Homo sapiens]
P02774-3	Isoform 3 of Vitamin D-binding protein [OS=Homo sapiens]	P07996	thrombospondin-1 [OS=Homo sapiens]
P01876	immunoglobulin heavy constant alpha 1 [OS=Homo sapiens]	P02787	Serotransferrin [OS=Homo sapiens]
P01834	immunoglobulin kappa constant [OS=Homo sapiens]	Q99715-1	Collagen alpha-1(XII) chain [OS=Homo sapiens]
P0DOX7	immunoglobulin kappa light chain [OS=Homo sapiens]	P0DMV8	heat shock 70 kDa protein 1A [OS=Homo sapiens]
P68032	Actin, alpha cardiac muscle 1 [OS=Homo sapiens]	P07900-2	Isoform 2 of Heat shock protein HSP 90-alpha [OS=Homo sapiens]
P01009-1	alpha-1-antitrypsin [OS=Homo sapiens]	P16422	Epithelial cell adhesion molecule [OS=Homo sapiens]
P08238	Heat shock protein HSP 90-beta [OS=Homo sapiens]	O94907	Dickkopf-related protein 1 [OS=Homo sapiens]
P07996	thrombospondin-1 [OS=Homo sapiens]	P18065	Insulin-like growth factor-binding protein 2 [OS=Homo sapiens]
P00738	Haptoglobin [OS=Homo sapiens]	O00391	Sulfhydryl oxidase 1 [OS=Homo sapiens]
Q08431	Lactadherin [OS=Homo sapiens]	P14618	Pyruvate kinase PKM [OS=Homo sapiens]
P01861	Immunoglobulin heavy constant gamma 4 [OS=Homo sapiens]	P08779	Keratin, type I cytoskeletal 16 [OS=Homo sapiens]
P02647	Apolipoprotein A-I [OS=Homo sapiens]	P62241	40S ribosomal protein S8 [OS=Homo sapiens]
P00747	Plasminogen [OS=Homo sapiens]	Q06830	peroxiredoxin-1 [OS=Homo sapiens]
P19823	Inter-alpha-trypsin inhibitor heavy chain H2 [OS=Homo sapiens]	P68431	Histone H3.1 [OS=Homo sapiens]
P14618	Pyruvate kinase PKM [OS=Homo sapiens]	P00749	Urokinase-type plasminogen activator [OS=Homo sapiens]
P06396	Gelsolin [OS=Homo sapiens]	P68363	Tubulin alpha-1B chain [OS=Homo sapiens]
P11142-1	Heat shock cognate 71 kDa protein [OS=Homo sapiens]	P02774-3	Isoform 3 of Vitamin D-binding protein [OS=Homo sapiens]
P04406-1	glyceraldehyde-3-phosphate dehydrogenase [OS=Homo sapiens]	P02765	Alpha-2-HS-glycoprotein [OS=Homo sapiens]
P07437	tubulin beta chain [OS=Homo sapiens]	P07355-2	Isoform 2 of Annexin A2 [OS=Homo sapiens]
O14672	Disintegrin and metalloproteinase domain-containing protein 10 [OS=Homo sapiens]	P05556-1	Integrin beta-1 [OS=Homo sapiens]
P07900-2	Isoform 2 of Heat shock protein HSP 90-alpha [OS=Homo sapiens]	P01034	Cystatin-C [OS=Homo sapiens]
Q99715-1	Collagen alpha-1(XII) chain [OS=Homo sapiens]	P04406-1	glyceraldehyde-3-phosphate dehydrogenase [OS=Homo sapiens]
P04003	C4b-binding protein alpha chain [OS=Homo sapiens]	P17987	T-complex protein 1 subunit alpha [OS=Homo sapiens]
P68371	Tubulin beta-4B chain [OS=Homo sapiens]	P07195	L-lactate dehydrogenase B chain [OS=Homo sapiens]
P68366	Tubulin alpha-4A chain [OS=Homo sapiens]	P12109	Collagen alpha-1(VI) chain [OS=Homo sapiens]
Q9BQE3	Tubulin alpha-1C chain [OS=Homo sapiens]	P48643	T-complex protein 1 subunit epsilon [OS=Homo sapiens]
P69905	Hemoglobin subunit alpha [OS=Homo sapiens]	P20742	Pregnancy zone protein [OS=Homo sapiens]
Q13748-1	tubulin alpha-3C/D chain [OS=Homo sapiens]	P08727	Keratin, type I cytoskeletal 19 [OS=Homo sapiens]
P0DOY2	immunoglobulin lambda constant 2 [OS=Homo sapiens]	P62280	40S ribosomal protein S11 [OS=Homo sapiens]
P13639	Elongation factor 2 [OS=Homo sapiens]	P16035	Metalloproteinase inhibitor 2 [OS=Homo sapiens]
P00734	Prothrombin [OS=Homo sapiens]	P02545	Prelamin-A/C [OS=Homo sapiens]
P05556-1	Integrin beta-1 [OS=Homo sapiens]	P05787-2	Isoform 2 of Keratin, type II cytoskeletal 8 [OS=Homo sapiens]
P78371-1	T-complex protein 1 subunit beta [OS=Homo sapiens]	P01860	Immunoglobulin heavy constant gamma 3 [OS=Homo sapiens]
Q6FI13	Histone H2A type 2-A [OS=Homo sapiens]	P01859	Immunoglobulin heavy constant gamma 2 [OS=Homo sapiens]
Q5QNW6-2	Isoform 2 of Histone H2B type 2-F [OS=Homo sapiens]	P29692-2	Isoform 2 of Elongation factor 1-delta [OS=Homo sapiens]
P20742	Pregnancy zone protein [OS=Homo sapiens]	P68104	Elongation factor 1-alpha 1 [OS=Homo sapiens]
P05787-2	Isoform 2 of Keratin, type II cytoskeletal 8 [OS=Homo sapiens]	P02679	Fibrinogen gamma chain [OS=Homo sapiens]
P10909-2	Isoform 2 of Clusterin [OS=Homo sapiens]	Q86X29	Lipolysis-stimulated lipoprotein receptor [OS=Homo sapiens]
P12109	Collagen alpha-1(VI) chain [OS=Homo sapiens]	P05452	Tetranectin [OS=Homo sapiens]
Q92626	peroxidasin homolog [OS=Homo sapiens]	P15311	Ezrin [OS=Homo sapiens]
P60033	CD81 antigen [OS=Homo sapiens]	O00560-1	Syntenin-1 [OS=Homo sapiens]
P00338-3	Isoform 3 of L-lactate dehydrogenase A chain [OS=Homo sapiens]	Q14764	major vault protein [OS=Homo sapiens]
P07355-2	Isoform 2 of Annexin A2 [OS=Homo sapiens]	P04075-2	Isoform 2 of Fructose-bisphosphate aldolase A [OS=Homo sapiens]
P16402	Histone H1.3 [OS=Homo sapiens]	P01861	Immunoglobulin heavy constant gamma 4 [OS=Homo sapiens]
P49327	Fatty acid synthase [OS=Homo sapiens]	P69905	Hemoglobin subunit alpha [OS=Homo sapiens]
P39060-3	Collagen alpha-1(XVIII) chain [OS=Homo sapiens]	O43240	Kallikrein-10 [OS=Homo sapiens]
O00560-1	Syntenin-1 [OS=Homo sapiens]	P0DOY3	immunoglobulin lambda constant 3 [OS=Homo sapiens]
P26006-1	Isoform 2 of Integrin alpha-3 [OS=Homo sapiens]	P21741	Midkine [OS=Homo sapiens]
P68871	Hemoglobin subunit beta [OS=Homo sapiens]	P50990	T-complex protein 1 subunit theta [OS=Homo sapiens]
O94985-1	Calsyntenin-1 [OS=Homo sapiens]	P00738	Haptoglobin [OS=Homo sapiens]
P08514-1	integrin alpha-IIb [OS=Homo sapiens]	P09429	High mobility group protein B1 [OS=Homo sapiens]
P23527	Histone H2B type 1-O [OS=Homo sapiens]	P49368-1	T-complex protein 1 subunit gamma [OS=Homo sapiens]
P19827-1	Inter-alpha-trypsin inhibitor heavy chain H1 [OS=Homo sapiens]	Q99988	Growth/differentiation factor 15 [OS=Homo sapiens]
P0DOX8	Immunoglobulin lambda-1 light chain [OS=Homo sapiens]	P35579-1	Myosin-9 [OS=Homo sapiens]
Q04695	Keratin, type I cytoskeletal 17 [OS=Homo sapiens]	P0DOX5	immunoglobulin gamma-1 heavy chain [OS=Homo sapiens]
P13010	X-ray repair cross-complementing protein 5 [OS=Homo sapiens]	Q9GZM7-1	Tubulointerstitial nephritis antigen-like [OS=Homo sapiens]
P05067-1	Amyloid-beta A4 protein [OS=Homo sapiens]	O14672	Disintegrin and metalloproteinase domain-containing protein 10 [OS=Homo sapiens]
Q14624-1	Inter-alpha-trypsin inhibitor heavy chain H4 [OS=Homo sapiens]	O94985-1	Calsyntenin-1 [OS=Homo sapiens]
P63104-1	14-3-3 protein zeta/delta [OS=Homo sapiens]	P09211	Glutathione S-transferase P [OS=Homo sapiens]
O15230	Laminin subunit alpha-5 [OS=Homo sapiens]	P10809	60 kDa heat shock protein, mitochondrial [OS=Homo sapiens]
P02790	Hemopexin [OS=Homo sapiens]	P62937	peptidyl-prolyl cis-trans isomerase A [OS=Homo sapiens]
P18206	Vinculin [OS=Homo sapiens]	P05023	Sodium/potassium-transporting ATPase subunit alpha-1 [OS=Homo sapiens]
P0DMV8	heat shock 70 kDa protein 1A [OS=Homo sapiens]	Q01650	large neutral amino acids transporter small subunit 1 [OS=Homo sapiens]
P12814-4	Isoform 4 of Alpha-actinin-1 [OS=Homo sapiens]	P40227-1	T-complex protein 1 subunit zeta [OS=Homo sapiens]
P04908	histone H2A type 1-B/E [OS=Homo sapiens]	P17096-2	Isoform HMG-Y of High mobility group protein HMG-I/HMG-Y [OS=Homo sapiens]
O43490-1	Prominin-1 [OS=Homo sapiens]	Q8NBP7-1	Proprotein convertase subtilisin/kexin type 9 [OS=Homo sapiens]
Q562R1	Beta-actin-like protein 2 [OS=Homo sapiens]	P07437	tubulin beta chain [OS=Homo sapiens]
P17987	T-complex protein 1 subunit alpha [OS=Homo sapiens]	P0DOX7	immunoglobulin kappa light chain [OS=Homo sapiens]
P08133-1	annexin A6 [OS=Homo sapiens]	P39023	60S ribosomal protein L3 [OS=Homo sapiens]
P05106	Integrin beta-3 [OS=Homo sapiens]	P29401-2	Isoform 2 of Transketolase [OS=Homo sapiens]
P01033	Metalloproteinase inhibitor 1 [OS=Homo sapiens]	Q9NS15-1	Latent-transforming growth factor beta-binding protein 3 [OS=Homo sapiens]
P06733-1	alpha-enolase [OS=Homo sapiens]	P12956	X-ray repair cross-complementing protein 6 [OS=Homo sapiens]
P11387	DNA topoisomerase 1 [OS=Homo sapiens]	P06748	Nucleophosmin [OS=Homo sapiens]
P00558	phosphoglycerate kinase 1 [OS=Homo sapiens]	P13746-2	Isoform 2 of HLA class I histocompatibility antigen, A-11 alpha chain [OS=Homo sapiens]
P50990	T-complex protein 1 subunit theta [OS=Homo sapiens]	P02751-15	Isoform 15 of Fibronectin [OS=Homo sapiens]
Q9H4B7	tubulin beta-1 chain [OS=Homo sapiens]	Q00610-1	Clathrin heavy chain 1 [OS=Homo sapiens]
O75340	programmed cell death protein 6 [OS=Homo sapiens]	P36578	60S ribosomal protein L4 [OS=Homo sapiens]
P00739-2	Isoform 2 of Haptoglobin-related protein [OS=Homo sapiens]	P11047	Laminin subunit gamma-1 [OS=Homo sapiens]
P48643	T-complex protein 1 subunit epsilon [OS=Homo sapiens]	P06396	Gelsolin [OS=Homo sapiens]
P16422	Epithelial cell adhesion molecule [OS=Homo sapiens]	P0DOX6	immunoglobulin mu heavy chain [OS=Homo sapiens]
P49368-1	T-complex protein 1 subunit gamma [OS=Homo sapiens]	P23528	Cofilin-1 [OS=Homo sapiens]
Q14764	major vault protein [OS=Homo sapiens]	P31947-1	14-3-3 protein sigma [OS=Homo sapiens]
P30443	HLA class I histocompatibility antigen, A-1 alpha chain [OS=Homo sapiens]	P15514	Amphiregulin [OS=Homo sapiens]
Q969P0	Immunoglobulin superfamily member 8 [OS=Homo sapiens]	Q92520	Protein FAM3C [OS=Homo sapiens]
Q9Y4K0	Lysyl oxidase homolog 2 [OS=Homo sapiens]	P00338-3	Isoform 3 of L-lactate dehydrogenase A chain [OS=Homo sapiens]
P01031	Complement C5 [OS=Homo sapiens]	P01876	immunoglobulin heavy constant alpha 1 [OS=Homo sapiens]
P15311	Ezrin [OS=Homo sapiens]	P31431-1	syndecan-4 [OS=Homo sapiens]
P62258-1	14-3-3 protein epsilon [OS=Homo sapiens]	P0DOX8	Immunoglobulin lambda-1 light chain [OS=Homo sapiens]
P04083	annexin A1 [OS=Homo sapiens]	P18124	60S ribosomal protein L7 [OS=Homo sapiens]
P22392-2	Isoform 3 of Nucleoside diphosphate kinase B [OS=Homo sapiens]	P81605-2	Isoform 2 of Dermcidin [OS=Homo sapiens]
P04075-2	Isoform 2 of Fructose-bisphosphate aldolase A [OS=Homo sapiens]	P60033	CD81 antigen [OS=Homo sapiens]
P08195-4	Isoform 4 of 4F2 cell-surface antigen heavy chain [OS=Homo sapiens]	P0C0S5	Histone H2A.Z [OS=Homo sapiens]
P12956	X-ray repair cross-complementing protein 6 [OS=Homo sapiens]	P31946	14-3-3 protein beta/alpha [OS=Homo sapiens]
P55072	Transitional endoplasmic reticulum ATPase [OS=Homo sapiens]	Q13444	Disintegrin and metalloproteinase domain-containing protein 15 [OS=Homo sapiens]
P0C0S5	Histone H2A.Z [OS=Homo sapiens]	Q86YZ3	Hornerin [OS=Homo sapiens]
P02649	Apolipoprotein E [OS=Homo sapiens]	P04792	Heat shock protein beta-1 [OS=Homo sapiens]
Q8WWI5	choline transporter-like protein 1 [OS=Homo sapiens]	P60174	Triosephosphate isomerase [OS=Homo sapiens]
P01011-1	Alpha-1-antichymotrypsin [OS=Homo sapiens]	P62263	40S ribosomal protein S14 [OS=Homo sapiens]
P50991	T-complex protein 1 subunit delta [OS=Homo sapiens]	P16870	Carboxypeptidase E [OS=Homo sapiens]
Q99832	T-complex protein 1 subunit eta [OS=Homo sapiens]	P18206	Vinculin [OS=Homo sapiens]
P02765	Alpha-2-HS-glycoprotein [OS=Homo sapiens]	P06454-1	Prothymosin alpha [OS=Homo sapiens]
P07093-3	Isoform 3 of Glia-derived nexin [OS=Homo sapiens]	P61247	40S ribosomal protein S3a [OS=Homo sapiens]
P16870	Carboxypeptidase E [OS=Homo sapiens]	P27635	60S ribosomal protein L10 [OS=Homo sapiens]
P29401-2	Isoform 2 of Transketolase [OS=Homo sapiens]	Q13753-1	Laminin subunit gamma-2 [OS=Homo sapiens]

P08519	apolipoprotein(a) [OS=Homo sapiens]	Q8N5I2	arrestin domain-containing protein 1 [OS=Homo sapiens]
O75531	Barrier-to-autointegration factor [OS=Homo sapiens]	P61026	ras-related protein rab-10 [OS=Homo sapiens]
P01008	Antithrombin-III [OS=Homo sapiens]	P01033	Metalloproteinase inhibitor 1 [OS=Homo sapiens]
A0M8Q6	immunoglobulin lambda constant 7 [OS=Homo sapiens]	P05783	Keratin, type I cytoskeletal 18 [OS=Homo sapiens]
Q9GZM7-1	Tubulointerstitial nephritis antigen-like [OS=Homo sapiens]	P46782	40S ribosomal protein S5 [OS=Homo sapiens]
Q99816	tumor susceptibility gene 101 protein [OS=Homo sapiens]	P36383	gap junction gamma-1 protein [OS=Homo sapiens]
O15240	Neurosecretory protein VGF [OS=Homo sapiens]	P02788	Lactotransferrin [OS=Homo sapiens]
P05023	Sodium/potassium-transporting ATPase subunit alpha-1 [OS=Homo sapiens]	P05067-1	Amyloid-beta A4 protein [OS=Homo sapiens]
P18065	Insulin-like growth factor-binding protein 2 [OS=Homo sapiens]	Q92626	peroxidasin homolog [OS=Homo sapiens]
Q92520	Protein FAM3C [OS=Homo sapiens]	P07737	profilin-1 [OS=Homo sapiens]
P10319	HLA class I histocompatibility antigen, B-58 alpha chain [OS=Homo sapiens]	P62424	60S ribosomal protein L7a [OS=Homo sapiens]
P21741	Midkine [OS=Homo sapiens]	P63000-2	Isoform B of Ras-related C3 botulinum toxin substrate 1 [OS=Homo sapiens]
P62937	peptidyl-prolyl cis-trans isomerase A [OS=Homo sapiens]	P08670	Vimentin [OS=Homo sapiens]
P01034	Cystatin-C [OS=Homo sapiens]	Q07020	60S ribosomal protein L18 [OS=Homo sapiens]
Q06033-1	Inter-alpha-trypsin inhibitor heavy chain H3 [OS=Homo sapiens]	P35998	26S proteasome regulatory subunit 7 [OS=Homo sapiens]
P60174	Triosephosphate isomerase [OS=Homo sapiens]	Q9H2A7	C-X-C motif chemokine 16 [OS=Homo sapiens]
P60900	Proteasome subunit alpha type-6 [OS=Homo sapiens]	P05204	Non-histone chromosomal protein HMG-17 [OS=Homo sapiens]
O43866	CD5 antigen-like [OS=Homo sapiens]	P13611	Versican core protein [OS=Homo sapiens]
P18463	HLA class I histocompatibility antigen, B-37 alpha chain [OS=Homo sapiens]	Q99832	T-complex protein 1 subunit eta [OS=Homo sapiens]
P17096-3	Isoform HMG-R of High mobility group protein HMG-I/HMG-Y [OS=Homo sapiens]	P01009-1	alpha-1-antitrypsin [OS=Homo sapiens]
P07093-1	Glia-derived nexin [OS=Homo sapiens]	Q5D862	Filaggrin-2 [OS=Homo sapiens]
P02766	Transthyretin [OS=Homo sapiens]	Q9Y5Y6	suppressor of tumorigenicity 14 protein [OS=Homo sapiens]
P21926	CD9 antigen [OS=Homo sapiens]	P27348	14-3-3 protein theta [OS=Homo sapiens]
O14792	Heparan sulfate glucosamine 3-O-sulfotransferase 1 [OS=Homo sapiens]	P21926	CD9 antigen [OS=Homo sapiens]
P13611	Versican core protein [OS=Homo sapiens]	P35222	Catenin beta-1 [OS=Homo sapiens]
P07737	profilin-1 [OS=Homo sapiens]	Q02413	Desmoglein-1 [OS=Homo sapiens]
P27918	Properdin [OS=Homo sapiens]	P59665	Neutrophil defensin 1 [OS=Homo sapiens]
P07947	tyrosine-protein kinase Yes [OS=Homo sapiens]	O75462	Cytokine receptor-like factor 1 [OS=Homo sapiens]
P08603-1	complement factor H [OS=Homo sapiens]	Q14103	heterogeneous nuclear ribonucleoprotein D0 [OS=Homo sapiens]
O43707	Alpha-actinin-4 [OS=Homo sapiens]	Q14974	Importin subunit beta-1 [OS=Homo sapiens]
P02788	Lactotransferrin [OS=Homo sapiens]	P62753	40S RIBOSOMAL PROTEIN S6 [OS=Homo sapiens]
Q9NS15-1	Latent-transforming growth factor beta-binding protein 3 [OS=Homo sapiens]	P50991	T-complex protein 1 subunit delta [OS=Homo sapiens]
P00751-1	Complement factor B [OS=Homo sapiens]	P22626	heterogeneous nuclear ribonucleoproteins A2/B1 [OS=Homo sapiens]
P16189	HLA class I histocompatibility antigen, A-31 alpha chain [OS=Homo sapiens]	P29317	Ephrin type-A receptor 2 [OS=Homo sapiens]
P60660	Myosin light polypeptide 6 [OS=Homo sapiens]	P61981	14-3-3 protein gamma [OS=Homo sapiens]
P29317	Ephrin type-A receptor 2 [OS=Homo sapiens]	P62841	40S ribosomal protein S15 [OS=Homo sapiens]
P17301	Integrin alpha-2 [OS=Homo sapiens]	P11166	Solute carrier family 2, facilitated glucose transporter member 1 [OS=Homo sapiens]
P07195	L-lactate dehydrogenase B chain [OS=Homo sapiens]	P04004	Vitronectin [OS=Homo sapiens]
Q06830	peroxiredoxin-1 [OS=Homo sapiens]	Q02818	Nucleobindin-1 [OS=Homo sapiens]
P11047	Laminin subunit gamma-1 [OS=Homo sapiens]	P35443	Thrombospondin-4 [OS=Homo sapiens]
P40227-1	T-complex protein 1 subunit zeta [OS=Homo sapiens]	P02675	Fibrinogen beta chain [OS=Homo sapiens]
P04217	Alpha-1B-glycoprotein [OS=Homo sapiens]	Q9C0H2-4	Isoform 4 of Protein tweety homolog 3 [OS=Homo sapiens]
P61981	14-3-3 protein gamma [OS=Homo sapiens]	P07093-3	Isoform 3 of Glia-derived nexin [OS=Homo sapiens]
P50995	annexin A11 [OS=Homo sapiens]	P01614	Immunoglobulin kappa variable 2D-40 [OS=Homo sapiens]
P07225	Vitamin K-dependent protein S [OS=Homo sapiens]	Q99816	tumor susceptibility gene 101 protein [OS=Homo sapiens]
Q9Y5Y6	suppressor of tumorigenicity 14 protein [OS=Homo sapiens]	Q9H4B7	tubulin beta-1 chain [OS=Homo sapiens]
P36383	gap junction gamma-1 protein [OS=Homo sapiens]	P61586	Transforming protein RhoA [OS=Homo sapiens]
P14923	Junction plakoglobin [OS=Homo sapiens]	P16070	CD44 antigen [OS=Homo sapiens]
P09972	Fructose-bisphosphate aldolase C [OS=Homo sapiens]	P06576	ATP synthase subunit beta, mitochondrial [OS=Homo sapiens]
P06727	Apolipoprotein A-IV [OS=Homo sapiens]	P02671-1	Fibrinogen alpha chain [OS=Homo sapiens]
P52907	F-actin-capping protein subunit alpha-1 [OS=Homo sapiens]	P00734	Prothrombin [OS=Homo sapiens]
Q13421-2	Isoform 3 of Mesothelin [OS=Homo sapiens]	P26006-1	Isoform 2 of Integrin alpha-3 [OS=Homo sapiens]
P01614	Immunoglobulin kappa variable 2D-40 [OS=Homo sapiens]	Q9BSG5-2	Isoform 2 of Retbindin [OS=Homo sapiens]
Q8N2S1	Latent-transforming growth factor beta-binding protein 4 [OS=Homo sapiens]	P02771	Alpha-fetoprotein [OS=Homo sapiens]
P16035	Metalloproteinase inhibitor 2 [OS=Homo sapiens]	P02753	Retinol-binding protein 4 [OS=Homo sapiens]
P68104	Elongation factor 1-alpha 1 [OS=Homo sapiens]	P61254	60S ribosomal protein L26 [OS=Homo sapiens]
P16144-1	Integrin beta-4 [OS=Homo sapiens]	P14625	Endoplasmin [OS=Homo sapiens]
A6NHL2-1	Tubulin alpha chain-like 3 [OS=Homo sapiens]	Q9Y4K0	Lysyl oxidase homolog 2 [OS=Homo sapiens]
P01619	Immunoglobulin kappa variable 3-20 [OS=Homo sapiens]	P46779-3	Isoform 3 of 60S ribosomal protein L28 [OS=Homo sapiens]
P10321	HLA class I histocompatibility antigen, Cw-7 alpha chain [OS=Homo sapiens]	P62910	60S ribosomal protein L32 [OS=Homo sapiens]
P02652	Apolipoprotein A-II [OS=Homo sapiens]	P46776	60S ribosomal protein L27a [OS=Homo sapiens]
P11021	78 kDa glucose-regulated protein [OS=Homo sapiens]	P07225	Vitamin K-dependent protein S [OS=Homo sapiens]
Q71DI3	histone H3.2 [OS=Homo sapiens]	P23246-1	splicing factor, proline- and glutamine-rich [OS=Homo sapiens]
P18669	Phosphoglycerate mutase 1 [OS=Homo sapiens]	Q02878	60S ribosomal protein L6 [OS=Homo sapiens]
Q02809-2	Isoform 2 of Procollagen-lysine,2-oxoglutarate 5-dioxygenase 1 [OS=Homo sapiens]	P13639	Elongation factor 2 [OS=Homo sapiens]
P33908	Mannosyl-oligosaccharide 1,2-alpha-mannosidase IA [OS=Homo sapiens]	Q9H9H4	Vacuolar protein sorting-associated protein 37B [OS=Homo sapiens]
Q8TAA3-1	proteasome subunit alpha type-7-like [OS=Homo sapiens]	P05198	Eukaryotic translation initiation factor 2 subunit 1 [OS=Homo sapiens]
Q6YHK3-1	CD109 antigen [OS=Homo sapiens]	Q8NG11-1	Tetraspanin-14 [OS=Homo sapiens]
P26641-2	Isoform 2 of Elongation factor 1-gamma [OS=Homo sapiens]	Q9Y265	RuvB-like 1 [OS=Homo sapiens]
O60716-1	Catenin delta-1 [OS=Homo sapiens]	P02452	Collagen alpha-1(I) chain [OS=Homo sapiens]
P53396-1	ATP-citrate synthase [OS=Homo sapiens]	O75347	Tubulin-specific chaperone A [OS=Homo sapiens]
A0A0C4DH25	immunoglobulin kappa variable 3D-20 [OS=Homo sapiens]	P49747	Cartilage oligomeric matrix protein [OS=Homo sapiens]
Q8N5I2	arrestin domain-containing protein 1 [OS=Homo sapiens]	P05156	Complement factor I [OS=Homo sapiens]
Q01518-1	adenylyl cyclase-associated protein 1 [OS=Homo sapiens]	O00299	chloride intracellular channel protein 1 [OS=Homo sapiens]
P02776	Platelet factor 4 [OS=Homo sapiens]	A5D8V6	Vacuolar protein sorting-associated protein 37C [OS=Homo sapiens]
P07942	Laminin subunit beta-1 [OS=Homo sapiens]	P42677	40S ribosomal protein S27 [OS=Homo sapiens]
P09382	Galectin-1 [OS=Homo sapiens]	P26373-1	60S ribosomal protein L13 [OS=Homo sapiens]
Q5VW32	BRO1 domain-containing protein BROX [OS=Homo sapiens]	Q13200	26S proteasome non-ATPase regulatory subunit 2 [OS=Homo sapiens]
Q8NBP7-1	Proprotein convertase subtilisin/kexin type 9 [OS=Homo sapiens]	P08195-4	Isoform 4 of 4F2 cell-surface antigen heavy chain [OS=Homo sapiens]
Q14118	Dystroglycan [OS=Homo sapiens]	Q5T749	Keratinocyte proline-rich protein [OS=Homo sapiens]
P63241-2	Isoform 2 of Eukaryotic translation initiation factor 5A-1 [OS=Homo sapiens]	P07910-1	Heterogeneous nuclear ribonucleoproteins C1/C2 [OS=Homo sapiens]
Q05639	Elongation factor 1-alpha 2 [OS=Homo sapiens]	P07305	Histone H1.0 [OS=Homo sapiens]
Q13418	Integrin-linked protein kinase [OS=Homo sapiens]	P08697-1	Alpha-2-antiplasmin [OS=Homo sapiens]
P23284	peptidyl-prolyl cis-trans isomerase B [OS=Homo sapiens]	P52565-1	rho GDP-dissociation inhibitor 1 [OS=Homo sapiens]
P04004	Vitronectin [OS=Homo sapiens]	P02461	Collagen alpha-1(III) chain [OS=Homo sapiens]
Q14766-4	Isoform 4 of Latent-transforming growth factor beta-binding protein 1 [OS=Homo sapiens]	P01591	Immunoglobulin J chain [OS=Homo sapiens]
P02747	Complement C1q subcomponent subunit C [OS=Homo sapiens]	P68371	Tubulin beta-4B chain [OS=Homo sapiens]
Q9H4M9	EH domain-containing protein 1 [OS=Homo sapiens]	Q5JWF2-1	Guanine nucleotide-binding protein G(S) subunit alpha isoforms XLas [OS=Homo sapiens]
P06753	Tropomyosin alpha-3 chain [OS=Homo sapiens]	O75787	Renin receptor [OS=Homo sapiens]
Q13201	Multimerin-1 [OS=Homo sapiens]	P01008	Antithrombin-III [OS=Homo sapiens]
Q13200	26S proteasome non-ATPase regulatory subunit 2 [OS=Homo sapiens]	P55001	Microfibrillar-associated protein 2 [OS=Homo sapiens]
P00736	Complement C1r subcomponent [OS=Homo sapiens]	P13521	Secretogranin-2 [OS=Homo sapiens]
Q9UK41-2	Isoform 2 of Vacuolar protein sorting-associated protein 28 homolog [OS=Homo sapiens]	P61769	Beta-2-microglobulin [OS=Homo sapiens]
P06756	Integrin alpha-V [OS=Homo sapiens]	P62318	small nuclear ribonucleoprotein sm d3 [OS=Homo sapiens]
O75083	WD repeat-containing protein 1 [OS=Homo sapiens]	P19827-1	Inter-alpha-trypsin inhibitor heavy chain H1 [OS=Homo sapiens]
P16070	CD44 antigen [OS=Homo sapiens]	P51148-2	Isoform 2 of Ras-related protein Rab-5C [OS=Homo sapiens]
Q6UWP8-1	Suprabasin [OS=Homo sapiens]	Q86VE9-4	Isoform 4 of Serine incorporator 5 [OS=Homo sapiens]
Q14974	Importin subunit beta-1 [OS=Homo sapiens]	P23396-2	Isoform 2 of 40S ribosomal protein S3 [OS=Homo sapiens]
Q06481	Amyloid-like protein 2 [OS=Homo sapiens]	P15880	40S ribosomal protein S2 [OS=Homo sapiens]
P28066-1	Proteasome subunit alpha type-5 [OS=Homo sapiens]	P62888	60S ribosomal protein L30 [OS=Homo sapiens]
P62979	Ubiquitin-40S ribosomal protein S27a [OS=Homo sapiens]	P22090	40S ribosomal protein S4, Y isoform 1 [OS=Homo sapiens]
Q99988	Growth/differentiation factor 15 [OS=Homo sapiens]	P30041	Peroxiredoxin-6 [OS=Homo sapiens]
P25787	Proteasome subunit alpha type-2 [OS=Homo sapiens]	P16949-2	Isoform 2 of Stathmin [OS=Homo sapiens]
P23142	Fibulin-1 [OS=Homo sapiens]	P39019	40S ribosomal protein S19 [OS=Homo sapiens]
P35613	Basigin [OS=Homo sapiens]	P02652	Apolipoprotein A-II [OS=Homo sapiens]
P04275	Von Willebrand factor [OS=Homo sapiens]	Q15828	Cystatin-M [OS=Homo sapiens]
P28074-1	proteasome subunit beta type-5 [OS=Homo sapiens]	P40925-3	Isoform 3 of Malate dehydrogenase, cytoplasmic [OS=Homo sapiens]
P19338	Nucleolin [OS=Homo sapiens]	P34096	Ribonuclease 4 [OS=Homo sapiens]
O00391	Sulfhydryl oxidase 1 [OS=Homo sapiens]	P20618	proteasome subunit beta type-1 [OS=Homo sapiens]
Q13443	disintegrin and metalloproteinase domain-containing protein 9 [OS=Homo sapiens]	P14649	Myosin light chain 6B [OS=Homo sapiens]
O00299	chloride intracellular channel protein 1 [OS=Homo sapiens]	P08603-1	complement factor H [OS=Homo sapiens]
P21579	Synaptotagmin-1 [OS=Homo sapiens]	P12259	Coagulation factor V [OS=Homo sapiens]
O00468-7	Isoform 7 of Agrin [OS=Homo sapiens]	P50914	60S ribosomal protein L14 [OS=Homo sapiens]
P48960-1	CD97 antigen [OS=Homo sapiens]	P26641-2	Isoform 2 of Elongation factor 1-gamma [OS=Homo sapiens]
Q6PCB0	von Willebrand factor A domain-containing protein 1 [OS=Homo sapiens]	Q15019-2	Isoform 2 of Septin-2 [OS=Homo sapiens]
P09429	High mobility group protein B1 [OS=Homo sapiens]	P0C0L4-1	Complement C4-A [OS=Homo sapiens]
P60953	Cell division control protein 42 homolog [OS=Homo sapiens]	P62826	GTP-binding nuclear protein RAN [OS=Homo sapiens]
P00387-3	Isoform 3 of NADH-cytochrome b5 reductase 3 [OS=Homo sapiens]	Q14624-1	Inter-alpha-trypsin inhibitor heavy chain H4 [OS=Homo sapiens]
P55001	Microfibrillar-associated protein 2 [OS=Homo sapiens]	P61224-1	Ras-related protein Rap-1b [OS=Homo sapiens]
O60635	Tetraspanin-1 [OS=Homo sapiens]	Q5SSJ5-1	Heterochromatin protein 1-binding protein 3 [OS=Homo sapiens]
P61769	Beta-2-microglobulin [OS=Homo sapiens]	Q8NBS9-1	Thioredoxin domain-containing protein 5 [OS=Homo sapiens]
Q99985	Semaphorin-3C [OS=Homo sapiens]	P55058	phospholipid transfer protein [OS=Homo sapiens]
P06310	Immunoglobulin kappa variable 2-30 [OS=Homo sapiens]	P47914	60S ribosomal protein L29 [OS=Homo sapiens]
Q13308-6	Isoform 6 of Inactive tyrosine-protein kinase 7 [OS=Homo sapiens]	P61313-1	60S ribosomal protein L15 [OS=Homo sapiens]
P12931-2	Isoform 2 of Proto-oncogene tyrosine-protein kinase Src [OS=Homo sapiens]	P09382	Galectin-1 [OS=Homo sapiens]
Q14697-2	Isoform 2 of Neutral alpha-glucosidase AB [OS=Homo sapiens]	Q99436	Proteasome subunit beta type-7 [OS=Homo sapiens]
P25786-2	Isoform Long of Proteasome subunit alpha type-1 [OS=Homo sapiens]	P10145	interleukin-8 [OS=Homo sapiens]
P02746	Complement C1q subcomponent subunit B [OS=Homo sapiens]	P62851	40S ribosomal protein S25 [OS=Homo sapiens]
P29692-2	Isoform 2 of Elongation factor 1-delta [OS=Homo sapiens]	P28072	Proteasome subunit beta type-6 [OS=Homo sapiens]
P01591	Immunoglobulin J chain [OS=Homo sapiens]	P07947	tyrosine-protein kinase Yes [OS=Homo sapiens]
Q92876-1	Kallikrein-6 [OS=Homo sapiens]	P21583-1	Kit ligand [OS=Homo sapiens]
P49411	elongation factor Tu, mitochondrial [OS=Homo sapiens]	P23142	Fibulin-1 [OS=Homo sapiens]

Q14152	Eukaryotic translation initiation factor 3 subunit A [OS=Homo sapiens]	P62258-1	14-3-3 protein epsilon [OS=Homo sapiens]
P23526-1	Adenosylhomocysteinase [OS=Homo sapiens]	P78371-1	T-complex protein 1 subunit beta [OS=Homo sapiens]
P06748	Nucleophosmin [OS=Homo sapiens]	P19021-5	Isoform 5 of Peptidyl-glycine alpha-amidating monooxygenase [OS=Homo sapiens]
P01042	kininogen-1 [OS=Homo sapiens]	P02749	Beta-2-glycoprotein 1 [OS=Homo sapiens]
Q12906-7	Isoform 7 of Interleukin enhancer-binding factor 3 [OS=Homo sapiens]	Q07955-2	Isoform ASF-2 of Serine/arginine-rich splicing factor 1 [OS=Homo sapiens]
Q13753-1	Laminin subunit gamma-2 [OS=Homo sapiens]	P62277	40S ribosomal protein S13 [OS=Homo sapiens]
P13497	Bone morphogenetic protein 1 [OS=Homo sapiens]	Q96RF0	Sorting nexin-18 [OS=Homo sapiens]
P11166	Solute carrier family 2, facilitated glucose transporter member 1 [OS=Homo sapiens]	P61353	60S ribosomal protein L27 [OS=Homo sapiens]
O43657	Tetraspanin-6 [OS=Homo sapiens]	P14174	Macrophage Migration inhibitory factor [OS=Homo sapiens]
P61204	ADP-ribosylation factor 3 [OS=Homo sapiens]	P57721-1	Poly(rC)-binding protein 3 [OS=Homo sapiens]
P05546	Heparin cofactor 2 [OS=Homo sapiens]	P60866-2	Isoform 2 of 40S ribosomal protein S20 [OS=Homo sapiens]
Q9H013-1	Disintegrin and metalloproteinase domain-containing protein 19 [OS=Homo sapiens]	P31943	Heterogeneous nuclear ribonucleoprotein H [OS=Homo sapiens]
P25705-1	ATP synthase subunit alpha, mitochondrial [OS=Homo sapiens]	P19823	Inter-alpha-trypsin inhibitor heavy chain H2 [OS=Homo sapiens]
Q13740-1	CD166 antigen [OS=Homo sapiens]	P02790	Hemopexin [OS=Homo sapiens]
O75367-1	Core histone macro-H2A.1 [OS=Homo sapiens]	O76061	Stanniocalcin-2 [OS=Homo sapiens]
P08134	Rho-related GTP-binding protein RhoC [OS=Homo sapiens]	Q02809-2	Isoform 2 of Procollagen-lysine,2-oxoglutarate 5-dioxygenase 1 [OS=Homo sapiens]
P62873	Guanine nucleotide-binding protein G(I)/G(S)/G(T) subunit beta-1 [OS=Homo sapiens]	P35268	60S ribosomal protein L22 [OS=Homo sapiens]
Q9BRK5-1	45 kDa calcium-binding protein [OS=Homo sapiens]	P23284	peptidyl-prolyl cis-trans isomerase B [OS=Homo sapiens]
P67809	Nuclease-sensitive element-binding protein 1 [OS=Homo sapiens]	Q9Y490	Talin-1 [OS=Homo sapiens]
Q9UGM3-9	Isoform 9 of Deleted in malignant brain tumors 1 protein [OS=Homo sapiens]	P00747	Plasminogen [OS=Homo sapiens]
P04792	Heat shock protein beta-1 [OS=Homo sapiens]	P14923	Junction plakoglobin [OS=Homo sapiens]
P09211	Glutathione S-transferase P [OS=Homo sapiens]	P63220	40S ribosomal protein S21 [OS=Homo sapiens]
Q14126	Desmoglein-2 [OS=Homo sapiens]	Q9UK73	Protein fem-1 homolog B [OS=Homo sapiens]
P30101	Protein disulfide-isomerase A3 [OS=Homo sapiens]	O95782	AP-2 complex subunit alpha-1 [OS=Homo sapiens]
P04196	Histidine-rich glycoprotein [OS=Homo sapiens]	Q9H444	Charged multivesicular body protein 4b [OS=Homo sapiens]
P04899-4	Isoform sGi2 of Guanine nucleotide-binding protein G(i) subunit alpha-2 [OS=Homo sapiens]	P62857	40S ribosomal protein S28 [OS=Homo sapiens]
P35222	Catenin beta-1 [OS=Homo sapiens]	P83881	60S ribosomal protein L36a [OS=Homo sapiens]
P78539-1	Sushi repeat-containing protein SRPX [OS=Homo sapiens]	P55072	Transitional endoplasmic reticulum ATPase [OS=Homo sapiens]
Q96EY5-1	Multivesicular body subunit 12A [OS=Homo sapiens]	P02647	Apolipoprotein A-I [OS=Homo sapiens]
P01624	Immunoglobulin kappa variable 3-15 [OS=Homo sapiens]	Q9HD42-1	Charged multivesicular body protein 1a [OS=Homo sapiens]
P02749	Beta-2-glycoprotein 1 [OS=Homo sapiens]	Q9NRY6	Phospholipid scramblase 3 [OS=Homo sapiens]
P07357	Complement component C8 alpha chain [OS=Homo sapiens]	B5ME19	eukaryotic translation initiation factor 3 subunit C-like protein [OS=Homo sapiens]
Q96PD5-2	Isoform 2 of N-acetylmuramoyl-L-alanine amidase [OS=Homo sapiens]	Q15631-1	Translin [OS=Homo sapiens]
P12259	Coagulation factor V [OS=Homo sapiens]	O95750	Fibroblast growth factor 19 [OS=Homo sapiens]
P09871	Complement C1s subcomponent [OS=Homo sapiens]	P04114	apolipoprotein B-100 [OS=Homo sapiens]
O75674	TOM1-like protein 1 [OS=Homo sapiens]	P09874	Poly [ADP-ribose] polymerase 1 [OS=Homo sapiens]
Q96QD8	sodium-coupled neutral amino acid transporter 2 [OS=Homo sapiens]	Q99996-6	Isoform 6 of A-kinase anchor protein 9 [OS=Homo sapiens]
P54709	sodium/potassium-transporting ATPase subunit beta-3 [OS=Homo sapiens]	P46777	60S ribosomal protein L5 [OS=Homo sapiens]
Q9ULF5	Zinc transporter ZIP10 [OS=Homo sapiens]	P84098	60S ribosomal protein L19 [OS=Homo sapiens]
P62879	Guanine nucleotide-binding protein G(I)/G(S)/G(T) subunit beta-2 [OS=Homo sapiens]	Q8R5X6	10 kDa chaperonin OS=Fusobacterium nucleatum (strain ATCC 25586)
P68400	Casein kinase II subunit alpha [OS=Homo sapiens]	Q8RG30	Glutamate dehydrogenase OS=Fusobacterium nucleatum (strain ATCC 25586)
P21589-1	5'-nucleotidase [OS=Homo sapiens]	Q8R5X7	60 kDa chaperonin OS=Fusobacterium nucleatum (strain ATCC 25586)
Q8IWA5-2	Isoform 2 of Choline transporter-like protein 2 [OS=Homo sapiens]	Q8R643	Pyruvate-flavodoxin oxidoreductase OS=Fusobacterium nucleatum (strain ATCC 25586)
Q99873	protein arginine N-methyltransferase 1 [OS=Homo sapiens]	Q8RES5	3-hydroxybutyryl-CoA dehydrogenase OS=Fusobacterium nucleatum (strain ATCC 25586)
Q8IUL8	Cartilage intermediate layer protein 2 [OS=Homo sapiens]	Q8RIN6	Acyl-CoA dehydrogenase, short-chain specific OS=Fusobacterium nucleatum (strain ATCC 25586)
P30989	Neurotensin receptor type 1 [OS=Homo sapiens]	Q8RI55	Enolase OS=Fusobacterium nucleatum (strain ATCC 25586)
P10809	60 kDa heat shock protein, mitochondrial [OS=Homo sapiens]	Q8RFC6	Electron transfer flavoprotein alpha-subunit OS=Fusobacterium nucleatum (strain ATCC 25586)
Q15149-1	plectin [OS=Homo sapiens]	Q8R6D3	Alkyl hydroperoxide reductase C22 protein OS=Fusobacterium nucleatum (strain ATCC 25586)
O15427	Monocarboxylate transporter 4 [OS=Homo sapiens]	Q8R603	Elongation factor Tu OS=Fusobacterium nucleatum (strain ATCC 25586)
O95297-1	Myelin protein zero-like protein 1 [OS=Homo sapiens]	Q8RHQ6	Tryptophanase OS=Fusobacterium nucleatum (strain ATCC 25586)
Q12907	Vesicular integral-membrane protein VIP36 [OS=Homo sapiens]	Q8R600	Elongation factor Ts OS=Fusobacterium nucleatum (strain ATCC 25586)
P18428	lipopolysaccharide-binding protein [OS=Homo sapiens]	Q8RG24	Acetyl-CoA acetyltransferase OS=Fusobacterium nucleatum (strain ATCC 25586)
P55268	laminin subunit beta-2 [OS=Homo sapiens]	Q8RHN0	Thioredoxin reductase OS=Fusobacterium nucleatum (strain ATCC 25586)
Q9C0H2-4	Isoform 4 of Protein tweety homolog 3 [OS=Homo sapiens]	Q8REE2	D-galactose-binding protein OS=Fusobacterium nucleatum (strain ATCC 25586)
P23528	Cofilin-1 [OS=Homo sapiens]	Q8R609	Pyruvate-flavodoxin oxidoreductase OS=Fusobacterium nucleatum (strain ATCC 25586)
P02771	Alpha-fetoprotein [OS=Homo sapiens]	Q8RFN9	Glyceraldehyde-3-phosphate dehydrogenase OS=Fusobacterium nucleatum (strain ATCC 25586)
Q9UN37	Vacuolar protein sorting-associated protein 4A [OS=Homo sapiens]	Q8RF98	DNA-binding protein HU OS=Fusobacterium nucleatum (strain ATCC 25586)
P40926	Malate dehydrogenase, mitochondrial [OS=Homo sapiens]	Q8RI44	Uncharacterized protein OS=Fusobacterium nucleatum (strain ATCC 25586)
P07237	Protein disulfide-isomerase [OS=Homo sapiens]	Q8RH05	Chaperone protein DnaK OS=Fusobacterium nucleatum (strain ATCC 25586)
P06576	ATP synthase subunit beta, mitochondrial [OS=Homo sapiens]	Q8RE69	Uncharacterized protein OS=Fusobacterium nucleatum (strain ATCC 25586)
Q15828	Cystatin-M [OS=Homo sapiens]	Q8R608	Serine protease OS=Fusobacterium nucleatum (strain ATCC 25586)
P59190-1	Ras-related protein Rab-15 [OS=Homo sapiens]	Q8RFC7	Electron transfer flavoprotein beta-subunit OS=Fusobacterium nucleatum (strain ATCC 25586)
P78417	Glutathione S-transferase omega-1 [OS=Homo sapiens]	Q8RDT9	Threonine dehydratase OS=Fusobacterium nucleatum (strain ATCC 25586)
O75636-1	Ficolin-3 [OS=Homo sapiens]	Q8RED7	Acetate kinase OS=Fusobacterium nucleatum (strain ATCC 25586)
O14950	Myosin regulatory light chain 12B [OS=Homo sapiens]	Q8RHT8	Probable cytosol aminopeptidase OS=Fusobacterium nucleatum (strain ATCC 25586)
Q9Y624	Junctional adhesion molecule A [OS=Homo sapiens]	Q8RES4	3-hydroxybutyryl-CoA dehydratase OS=Fusobacterium nucleatum (strain ATCC 25586)
P25788-1	Proteasome subunit alpha type-3 [OS=Homo sapiens]	Q8RHY3	Acetoacetate:butyrate/acetate coenzyme A transferase OS=Fusobacterium nucleatum (strain ATCC 25586)
P28072	Proteasome subunit beta type-6 [OS=Homo sapiens]	Q8RHY1	Major outer membrane protein OS=Fusobacterium nucleatum (strain ATCC 25586)
Q8NFJ5	Retinoic acid-induced protein 3 [OS=Homo sapiens]	Q8RIF3	Uncharacterized protein OS=Fusobacterium nucleatum (strain ATCC 25586)
Q15185	Prostaglandin E synthase 3 [OS=Homo sapiens]	Q8RE11	Acetoacetate metabolism regulatory protein atoC OS=Fusobacterium nucleatum (strain ATCC 25586)
Q93084-5	Isoform SERCA3E of Sarcoplasmic/endoplasmic reticulum calcium ATPase 3 [OS=Homo sapiens]	Q8RGS8	Glutaconyl-CoA decarboxylase A subunit OS=Fusobacterium nucleatum (strain ATCC 25586)
Q86X29	Lipolysis-stimulated lipoprotein receptor [OS=Homo sapiens]	Q8RGT0	Glutaconate CoA-transferase subunit A OS=Fusobacterium nucleatum (strain ATCC 25586)
P31947-1	14-3-3 protein sigma [OS=Homo sapiens]	Q8RHQ8	Chaperone protein ClpB OS=Fusobacterium nucleatum (strain ATCC 25586)
O00151	PDZ and LIM domain protein 1 [OS=Homo sapiens]	Q8RHF4	Formate--tetrahydrofolate ligase OS=Fusobacterium nucleatum (strain ATCC 25586)
Q9H9H4	Vacuolar protein sorting-associated protein 37B [OS=Homo sapiens]	Q8RE65	C4-dicarboxylate-binding protein OS=Fusobacterium nucleatum (strain ATCC 25586)
P37802-2	Isoform 2 of Transgelin-2 [OS=Homo sapiens]	Q8RIB8	N-acetylneuraminate synthase OS=Fusobacterium nucleatum (strain ATCC 25586)
P02794	Ferritin heavy chain [OS=Homo sapiens]	Q8RE60	Outer membrane protein OS=Fusobacterium nucleatum (strain ATCC 25586)
P55786	puromycin-sensitive aminopeptidase [OS=Homo sapiens]	Q8RG53	Uncharacterized protein OS=Fusobacterium nucleatum (strain ATCC 25586)
P22090	40S ribosomal protein S4, Y isoform 1 [OS=Homo sapiens]	Q8RDW4	Citrate lyase alpha chain OS=Fusobacterium nucleatum (strain ATCC 25586
A0A0A0MRZ	immunoglobulin kappa variable 3D-11 [OS=Homo sapiens]	Q8RDX7	Triosephosphate isomerase OS=Fusobacterium nucleatum (strain ATCC 25586)
P19021-5	Isoform 5 of Peptidyl-glycine alpha-amidating monooxygenase [OS=Homo sapiens]	Q8R602	Elongation factor G OS=Fusobacterium nucleatum subsp. nucleatum (strain ATCC 25586)
P26583	High mobility group protein B2 [OS=Homo sapiens]	Q8RIJ6	Ion-translocating oxidoreductase complex subunit C OS=Fusobacterium nucleatum (strain ATCC 25586)
Q8WUJ3-1	Cell migration-inducing and hyaluronan-binding protein [OS=Homo sapiens]	Q8R6H3	Probable electron transfer flavoprotein-quinone oxidoreductase ydiS OS=Fusobacterium nucleatum (strain ATCC 25586)
Q86UX7	Fermitin family homolog 3 [OS=Homo sapiens]	Q8RES0	DNA-binding protein HU OS=Fusobacterium nucleatum (strain ATCC 25586)
P08567	pleckstrin [OS=Homo sapiens]	Q8RFS6	Threonine--tRNA ligase OS=Fusobacterium nucleatum (strain ATCC 25586)
Q99497	protein/nucleic acid deglycase DJ-1 [OS=Homo sapiens]	Q8RIN5	(S)-2-hydroxy-acid oxidase chain D OS=Fusobacterium nucleatum (strain ATCC 25586)
P02452	Collagen alpha-1(I) chain [OS=Homo sapiens]	Q8REM0	Neutrophil-activating protein A OS=Fusobacterium nucleatum (strain ATCC 25586)
P00750-1	Tissue-type plasminogen activator [OS=Homo sapiens]	Q8RHI5	50S ribosomal protein L7/L12 OS=Fusobacterium nucleatum (strain ATCC 25586)
P63096-1	Guanine nucleotide-binding protein G(i) subunit alpha-1 [OS=Homo sapiens]	Q8RI77	V-type sodium ATP synthase subunit A OS=Fusobacterium nucleatum (strain ATCC 25586)
P02748	complement component C9 [OS=Homo sapiens]	Q8RFC1	Urocanate hydratase OS=Fusobacterium nucleatum (strain ATCC 25586)
O15551	Claudin-3 [OS=Homo sapiens]	Q8RGS9	Glutaconate CoA-transferase subunit B OS=Fusobacterium nucleatum (strain ATCC 25586)
P14625	Endoplasmin [OS=Homo sapiens]	Q8RI92	Uncharacterized protein OS=Fusobacterium nucleatum (strain ATCC 25586)
P05387	60S acidic ribosomal protein P2 [OS=Homo sapiens]	Q8R5Y8	Biotin carboxyl carrier protein of glutaconyl-COA decarboxylase OS=Fusobacterium nucleatum (strain ATCC 25586)
Q13867	bleomycin hydrolase [OS=Homo sapiens]	Q8R6B3	(R)-2-hydroxyglutaryl-CoA dehydratase beta-subunit OS=Fusobacterium nucleatum (strain ATCC 25586)
P62316	Small nuclear ribonucleoprotein Sm D2 [OS=Homo sapiens]	Q8R674	Acyl-CoA dehydrogenase OS=Fusobacterium nucleatum (strain ATCC 25586)
Q9P265	Disco-interacting protein 2 homolog B [OS=Homo sapiens]	Q8RIH8	Hypothetical cytosolic protein OS=Fusobacterium nucleatum (strain ATCC 25586)
P01137	Transforming growth factor beta-1 [OS=Homo sapiens]	Q8RG80	50S ribosomal protein L19 OS=Fusobacterium nucleatum (strain ATCC 25586)
Q8N1N4	Keratin, type II cytoskeletal 78 [OS=Homo sapiens]	Q8RFL4	Transcriptional regulator, MarR family OS=Fusobacterium nucleatum (strain ATCC 25586)
P48509	CD151 antigen [OS=Homo sapiens]	Q8REM1	Hypothetical exported 24-amino acid repeat protein OS=Fusobacterium nucleatum (strain ATCC 25586)
O95471	Claudin-7 [OS=Homo sapiens]	Q8RFW8	Hypothetical cytosolic protein OS=Fusobacterium nucleatum (strain ATCC 25586)
P06737-1	Glycogen phosphorylase, liver form [OS=Homo sapiens]	Q8RGB0	Dipeptide-binding protein OS=Fusobacterium nucleatum (strain ATCC 25586)
Q9NP79	Vacuolar protein sorting-associated protein VTA1 homolog [OS=Homo sapiens]	Q8RG09	Flavodoxin OS=Fusobacterium nucleatum (strain ATCC 25586)
P61916	Epididymal secretory protein E1 [OS=Homo sapiens]	Q8RFG1	Imidazolonepropionase OS=Fusobacterium nucleatum (strain ATCC 25586)
P25789	Proteasome subunit alpha type-4 [OS=Homo sapiens]	Q8RGE2	ATP synthase subunit beta OS=Fusobacterium nucleatum (strain ATCC 25586)
P07358	Complement component C8 beta chain [OS=Homo sapiens]	Q8RET7	Outer membrane protein P1 OS=Fusobacterium nucleatum (strain ATCC 25586)
P08758	annexin A5 [OS=Homo sapiens]	Q8RDM5	UPF0735 ACT domain-containing protein FN1487 OS=Fusobacterium nucleatum (strain ATCC 25586)
P00390	Glutathione reductase, mitochondrial [OS=Homo sapiens]	Q8RDT4	L-methionine gamma-lyase OS=Fusobacterium nucleatum (strain ATCC 25586)
Q00796	Sorbitol dehydrogenase [OS=Homo sapiens]	Q8RGE5	S-adenosylmethionine synthase OS=Fusobacterium nucleatum (strain ATCC 25586)
Q8NG11-1	Tetraspanin-14 [OS=Homo sapiens]	Q8RG46	Flavodoxin OS=Fusobacterium nucleatum (strain ATCC 25586)
P05109	Protein S100-A8 [OS=Homo sapiens]	Q8R6H9	Uncharacterized protein OS=Fusobacterium nucleatum (strain ATCC 25586)
P01824	immunoglobulin heavy variable 4-39 [OS=Homo sapiens]	Q8RI54	Pyruvate kinase OS=Fusobacterium nucleatum (strain ATCC 25586)
P11908-2	Isoform 2 of Ribose-phosphate pyrophosphokinase 2 [OS=Homo sapiens]	Q8RDY4	Dipeptide-binding protein OS=Fusobacterium nucleatum (strain ATCC 25586)
P31689-1	DnaJ homolog subfamily A member 1 [OS=Homo sapiens]	Q8RED6	Phosphate acetyltransferase OS=Fusobacterium nucleatum (strain ATCC 25586)
O14791-2	Isoform 2 of Apolipoprotein L1 [OS=Homo sapiens]	Q8RH03	Chaperone protein DnaJ OS=Fusobacterium nucleatum (strain ATCC 25586)
Q86VE9-4	Isoform 4 of Serine incorporator 5 [OS=Homo sapiens]	Q8RGL8	Butyrate-acetoacetate CoA-transferase subunit B OS=Fusobacterium nucleatum (strain ATCC 25586)
Q9H0E2	Toll-interacting protein [OS=Homo sapiens]	Q8RIN1	Iron-sulfur cluster-binding protein OS=Fusobacterium nucleatum (strain ATCC 25586)
O75487	Glypican-4 [OS=Homo sapiens]	Q8RDP7	Pyridoxal 5'-phosphate synthase subunit PdxS OS=Fusobacterium nucleatum (strain ATCC 25586)
P36955	Pigment epithelium-derived factor [OS=Homo sapiens]	Q8RGH3	Fructose-bisphosphate aldolase class 1 OS=Fusobacterium nucleatum (strain ATCC 25586)
P0DME0	Protein SETSIP [OS=Homo sapiens]	Q8REG8	Phosphonates-binding protein OS=Fusobacterium nucleatum (strain ATCC 25586)
P20618	proteasome subunit beta type-1 [OS=Homo sapiens]	Q8RE27	Uncharacterized protein OS=Fusobacterium nucleatum (strain ATCC 25586)
P48059-3	Isoform 3 of LIM and senescent cell antigen-like-containing domain protein 1 [OS=Homo sapiens]	Q8RIG8	50S ribosomal protein L5 OS=Fusobacterium nucleatum (strain ATCC 25586)
Q9UMF0	intercellular adhesion molecule 5 [OS=Homo sapiens]	Q8RHM6	Tyrosine phenol-lyase OS=Fusobacterium nucleatum (strain ATCC 25586)
Q96F07	Cytoplasmic FMR1-interacting protein 2 [OS=Homo sapiens]	Q8RFG0	Glutamate formiminotransferase OS=Fusobacterium nucleatum (strain ATCC 25586)
P00488	Coagulation factor XIII A chain [OS=Homo sapiens]	Q8RHI6	DNA-directed RNA polymerase subunit beta OS=Fusobacterium nucleatum (strain ATCC 25586)
O95497	Pantetheinase [OS=Homo sapiens]		
P36551	Oxygen-dependent coproporphyrinogen-III oxidase, mitochondrial [OS=Homo sapiens]		
Q9NZM1	Myoferlin [OS=Homo sapiens]		
Q16787-2	Laminin subunit alpha-3 [OS=Homo sapiens]		
P23142-4	Isoform C of Fibulin-1 [OS=Homo sapiens]		
O95819-3	Isoform 3 of Mitogen-activated protein kinase kinase kinase kinase 4 [OS=Homo sapiens]		
Q9H5V8-1	CUB domain-containing protein 1 [OS=Homo sapiens]		
P13671	Complement component c6 [OS=Homo sapiens]		

O43240	Kallikrein-10 [OS=Homo sapiens]		
Q13126-2	Isoform 2 of S-methyl-5'-thioadenosine phosphorylase [OS=Homo sapiens]		
P10643	Complement component C7 [OS=Homo sapiens]		
P11234-2	Isoform 2 of Ras-related protein Ral-B [OS=Homo sapiens]		
P07910-1	Heterogeneous nuclear ribonucleoproteins C1/C2 [OS=Homo sapiens]		
O95866-2	Isoform A of Megakaryocyte and platelet inhibitory receptor G6b [OS=Homo sapiens]		
Q5SSJ5-1	Heterochromatin protein 1-binding protein 3 [OS=Homo sapiens]		
Q9UQ80	proliferation-associated protein 2G4 [OS=Homo sapiens]		
P14678-3	Isoform SM-B1 of Small nuclear ribonucleoprotein-associated proteins B and B' [OS=Homo sapiens]		
Q01469	Fatty acid-binding protein, epidermal [OS=Homo sapiens]		
P23229-1	integrin alpha-6 [OS=Homo sapiens]		
Q12841	Follistatin-related protein 1 [OS=Homo sapiens]		
Q86YZ3	Hornerin [OS=Homo sapiens]		
P63313	thymosin beta-10 [OS=Homo sapiens]		
Q15651-1	High mobility group nucleosome-binding domain-containing protein 3 [OS=Homo sapiens]		
P61247	40S ribosomal protein S3a [OS=Homo sapiens]		
P01780	Immunoglobulin heavy variable 3-7 [OS=Homo sapiens]		
A0A075B6I0	immunoglobulin lambda variable 8-61 [OS=Homo sapiens]		
P35052	Glypican-1 [OS=Homo sapiens]		
Q15758-1	Neutral amino acid transporter B(0) [OS=Homo sapiens]		
P32119	Peroxiredoxin-2 [OS=Homo sapiens]		
P61224-1	Ras-related protein Rap-1b [OS=Homo sapiens]		
P63000-2	Isoform B of Ras-related C3 botulinum toxin substrate 1 [OS=Homo sapiens]		
P12277	Creatine kinase B-type [OS=Homo sapiens]		
P61158	actin-related protein 3 [OS=Homo sapiens]		
A0A0C4DH38	immunoglobulin heavy variable 5-51 [OS=Homo sapiens]		
P05543	thyroxine-binding globulin [OS=Homo sapiens]		
P08697-1	Alpha-2-antiplasmin [OS=Homo sapiens]		
Q53H96	Pyrroline-5-carboxylate reductase 3 [OS=Homo sapiens]		
P25398	40S ribosomal protein S12 [OS=Homo sapiens]		
P03950	angiogenin [OS=Homo sapiens]		
P60981-1	Destrin [OS=Homo sapiens]		
Q9NZN3	EH domain-containing protein 3 [OS=Homo sapiens]		
P04062	glucosylceramidase [OS=Homo sapiens]		
P62888	60S ribosomal protein L30 [OS=Homo sapiens]		
O95750	Fibroblast growth factor 19 [OS=Homo sapiens]		
P05204	Non-histone chromosomal protein HMG-17 [OS=Homo sapiens]		
P55854-2	Isoform 2 of Small ubiquitin-related modifier 3 [OS=Homo sapiens]		
Q86XX4-2	Isoform 2 of Extracellular matrix protein FRAS1 [OS=Homo sapiens]		
P15514	Amphiregulin [OS=Homo sapiens]		
O94907	Dickkopf-related protein 1 [OS=Homo sapiens]		
P05164-3	Isoform H7 of Myeloperoxidase [OS=Homo sapiens]		
P17096-2	Isoform HMG-Y of High mobility group protein HMG-I/HMG-Y [OS=Homo sapiens]		
P38646	Stress-70 protein, mitochondrial [OS=Homo sapiens]		
Q9Y376	Calcium-binding protein 39 [OS=Homo sapiens]		
P02461	Collagen alpha-1(III) chain [OS=Homo sapiens]		
Q8IUE6	Histone H2A type 2-B [OS=Homo sapiens]		
P14770	Platelet glycoprotein IX [OS=Homo sapiens]		
P36871-2	Isoform 2 of Phosphoglucomutase-1 [OS=Homo sapiens]		
O75955	Flotillin-1 [OS=Homo sapiens]		
Q14254	Flotillin-2 [OS=Homo sapiens]		
O75954	tetraspanin-9 [OS=Homo sapiens]		
Q641Q3	Meteorin-like protein [OS=Homo sapiens]		
Q02413	Desmoglein-1 [OS=Homo sapiens]		
Q9NZN4	EH domain-containing protein 2 [OS=Homo sapiens]		
Q9Y5K6	CD2-associated protein [OS=Homo sapiens]		
Q96DG6	Carboxymethylenebutenolidase homolog [OS=Homo sapiens]		
P40925-3	Isoform 3 of Malate dehydrogenase, cytoplasmic [OS=Homo sapiens]		
Q9P258	Protein RCC2 [OS=Homo sapiens]		
Q92485-1	acid sphingomyelinase-like phosphodiesterase 3B [OS=Homo sapiens]		
P61313-1	60S ribosomal protein L15 [OS=Homo sapiens]		
P22061-2	Isoform 2 of Protein-L-isoaspartate(D-aspartate) O-methyltransferase [OS=Homo sapiens]		
P34932	Heat shock 70 kDa protein 4 [OS=Homo sapiens]		
P02545	Prelamin-A/C [OS=Homo sapiens]		
Q9HBI1-2	Isoform 2 of Beta-parvin [OS=Homo sapiens]		
P62826	GTP-binding nuclear protein RAN [OS=Homo sapiens]		
O43491-1	band 4.1-like protein 2 [OS=Homo sapiens]		
O00339-1	Matrilin-2 [OS=Homo sapiens]		
Q9Y617-1	phosphoserine aminotransferase [OS=Homo sapiens]		
P22626	heterogeneous nuclear ribonucleoproteins A2/B1 [OS=Homo sapiens]		
O60888-2	Isoform A of Protein CutA [OS=Homo sapiens]		
P35244	Replication protein A 14 kDa subunit [OS=Homo sapiens]		
P15151-1	Poliovirus receptor [OS=Homo sapiens]		
P49588-2	Isoform 2 of Alanine--tRNA ligase, cytoplasmic [OS=Homo sapiens]		
P37837	Transaldolase [OS=Homo sapiens]		
A0A0C4DH68	immunoglobulin kappa variable 2-24 [OS=Homo sapiens]		
Q9H9K5	Endogenous retrovirus group MER34 member 1 Env polyprotein [OS=Homo sapiens]		
Q14978-2	Isoform Beta of Nucleolar and coiled-body phosphoprotein 1 [OS=Homo sapiens]		
P24592	insulin-like growth factor-binding protein 6 [OS=Homo sapiens]		
O43278	Kunitz-type protease inhibitor 1 [OS=Homo sapiens]		
P62318	small nuclear ribonucleoprotein sm d3 [OS=Homo sapiens]		
Q9UBQ0-2	Isoform 2 of Vacuolar protein sorting-associated protein 29 [OS=Homo sapiens]		
Q9BWS9-2	Isoform 2 of Chitinase domain-containing protein 1 [OS=Homo sapiens]		
P62837	ubiquitin-conjugating enzyme E2 D2 [OS=Homo sapiens]		
Q68E01	Integrator complex subunit 3 [OS=Homo sapiens]		
P81605	Dermcidin [OS=Homo sapiens]		
Q96AG4	Leucine-rich repeat-containing protein 59 [OS=Homo sapiens]		
P62280	40S ribosomal protein S11 [OS=Homo sapiens]		
P62136-1	serine/threonine-protein phosphatase PP1-alpha catalytic subunit [OS=Homo sapiens]		
Q9Y4L1	Hypoxia up-regulated protein 1 [OS=Homo sapiens]		
O43488	aflatoxin B1 aldehyde reductase member 2 [OS=Homo sapiens]		
A0A0C4DH29	Immunoglobulin heavy variable 1-3 [OS=Homo sapiens]		
P02730	Band 3 anion transport protein [OS=Homo sapiens]		
P13798	Acylamino-acid-releasing enzyme [OS=Homo sapiens]		
Q7Z2W4	zinc finger CCCH-type antiviral protein 1 [OS=Homo sapiens]		
Q04917	14-3-3 protein eta [OS=Homo sapiens]		
O75390	citrate synthase, mitochondrial [OS=Homo sapiens]		
P08962	CD63 antigen [OS=Homo sapiens]		
P50552	Vasodilator-stimulated phosphoprotein [OS=Homo sapiens]		
O00410-3	Isoform 3 of Importin-5 [OS=Homo sapiens]		
Q9H0C2	ADP/ATP translocase 4 [OS=Homo sapiens]		
P10114	Ras-related protein Rap-2a [OS=Homo sapiens]		
P00740	Coagulation factor IX [OS=Homo sapiens]		
Q9ULA0	Aspartyl aminopeptidase [OS=Homo sapiens]		
P31146	Coronin-1A [OS=Homo sapiens]		
P55060-1	Exportin-2 [OS=Homo sapiens]		
P15153	Ras-related C3 botulinum toxin substrate 2 [OS=Homo sapiens]		
P09012	U1 SMALL NUCLEAR RIBONUCLEOPROTEIN A [OS=Homo sapiens]		
P35573-1	glycogen debranching enzyme [OS=Homo sapiens]		
P53621-2	Isoform 2 of Coatomer subunit alpha [OS=Homo sapiens]		
Q96J02	E3 ubiquitin-protein ligase Itchy homolog [OS=Homo sapiens]		
P02760	Protein AMBP [OS=Homo sapiens]		
Q14515	SPARC-like protein 1 [OS=Homo sapiens]		
P40429	60S ribosomal protein L13a [OS=Homo sapiens]		
P00749	Urokinase-type plasminogen activator [OS=Homo sapiens]		
P27105	erythrocyte band 7 integral membrane protein [OS=Homo sapiens]		
P10301	Ras-related protein R-Ras [OS=Homo sapiens]		
Q9NPH2	Inositol-3-phosphate synthase 1 [OS=Homo sapiens]		
P03973	Antileukoproteinase [OS=Homo sapiens]		
P01111	GTPase NRas [OS=Homo sapiens]		
P61978-2	Isoform 2 of Heterogeneous nuclear ribonucleoprotein K [OS=Homo sapiens]		
O43252	bifunctional 3'-phosphoadenosine 5'-phosphosulfate synthase 1 [OS=Homo sapiens]		
P17980	26S proteasome regulatory subunit 6A [OS=Homo sapiens]		
Q6ZVX7	F-box only protein 50 [OS=Homo sapiens]		
Q9HBH0	Rho-related GTP-binding protein RhoF [OS=Homo sapiens]		
P18124	60S ribosomal protein L7 [OS=Homo sapiens]		
P46777	60S ribosomal protein L5 [OS=Homo sapiens]		
Q9UNM6-2	Isoform 2 of 26S proteasome non-ATPase regulatory subunit 13 [OS=Homo sapiens]		
P60866-2	Isoform 2 of 40S ribosomal protein S20 [OS=Homo sapiens]		
P49407-1	Beta-arrestin-1 [OS=Homo sapiens]		
O75347-2	Isoform 2 of Tubulin-specific chaperone A [OS=Homo sapiens]		
P05386	60S acidic ribosomal protein P1 [OS=Homo sapiens]		

P01699	Immunoglobulin lambda variable 1-44 [OS=Homo sapiens]		
P21583-1	Kit ligand [OS=Homo sapiens]		
A0A0B4J1X5	immunoglobulin heavy variable 3-74 [OS=Homo sapiens]		
Q6UXI9-6	Isoform 6 of Nephronectin [OS=Homo sapiens]		
P11717	Cation-independent mannose-6-phosphate receptor [OS=Homo sapiens]		
Q9Y6C2	EMILIN-1 [OS=Homo sapiens]		
Q9UNN8	Endothelial protein C receptor [OS=Homo sapiens]		
P05388	60S acidic ribosomal protein P0 [OS=Homo sapiens]		
P00533-1	epidermal growth factor receptor [OS=Homo sapiens]		
Q9Y6W3	Calpain-7 [OS=Homo sapiens]		
Q9NZZ3	Charged multivesicular body protein 5 [OS=Homo sapiens]		
P14174	Macrophage Migration inhibitory factor [OS=Homo sapiens]		
P23396-2	Isoform 2 of 40S ribosomal protein S3 [OS=Homo sapiens]		
P38159-1	RNA-binding motif protein, X chromosome [OS=Homo sapiens]		
P07359	Platelet glycoprotein Ib alpha chain [OS=Homo sapiens]		
B5ME19	eukaryotic translation initiation factor 3 subunit C-like protein [OS=Homo sapiens]		
Q9UHL4	Dipeptidyl peptidase 2 [OS=Homo sapiens]		
P50502	Hsc70-interacting protein [OS=Homo sapiens]		
P62942	Peptidyl-prolyl cis-trans isomerase FKBP1A [OS=Homo sapiens]		
P41091	eukaryotic translation initiation factor 2 subunit 3 [OS=Homo sapiens]		
P62079	Tetraspanin-5 [OS=Homo sapiens]		
P15169	Carboxypeptidase N catalytic chain [OS=Homo sapiens]		
Q9ULV4-3	Isoform 3 of Coronin-1C [OS=Homo sapiens]		
P62249	40S ribosomal protein S16 [OS=Homo sapiens]		
Q04760-1	lactoylglutathione lyase [OS=Homo sapiens]		
Q9Y277-2	Isoform 2 of Voltage-dependent anion-selective channel protein 3 [OS=Homo sapiens]		

Table S8 KEGG pathway analysis showed that these Fn-Ex unique cell proteins.

pathway	pathway_name	class	diff_KO2acc	p value
hsa04062	Ribosome	Genetic Information Processing	hsa:6159(P47914);hsa:6187(P15880);hsa:6230(P62851);hsa:100529097(P83881);hsa:6157(P46776);hsa:6154(P61254);hsa:6155(P61353);hsa:6234(P62857);hsa:6232(P42677);hsa:6173(P83881);hsa:6130(P62424);hsa:6134(P27635);hsa:51121(P61254);hsa:6194(P62753);hsa:6193(P46782);hsa:6227(P63220);hsa:6202(P62241);hsa:6146(P35268);hsa:6141(Q07020);hsa:6207(P62277);hsa:6143(P84098);hsa:6166(P83881);hsa:6208(P62263);hsa:6209(P62841);hsa:6161(P62910);hsa:6223(P39019);hsa:6122(P39023);hsa:6124(P36578);hsa:6128(Q02878);hsa:9045(P50914)	1.53E-07
hsa04810	Chemokine signaling pathway	Organismal Systems	hsa:387(P61586);hsa:3576(P10145);hsa:58191(Q9H2A7)	0.055461
hsa04150	mTOR signaling pathway	Environmental Information Processing	hsa:6194(P62753);hsa:387(P61586);hsa:8140(Q01650)	0.062763
hsa04810	Regulation of actin cytoskeleton	Cellular Processes	hsa:387(P61586)	0.062763
hsa04270	Vascular smooth muscle contraction	Organismal Systems	hsa:140465(P14649);hsa:387(P61586);hsa:59(P62736);hsa:72(P62736)	0.062763
hsa05200	Pathways in cancer	Human Diseases	hsa:387(P61586);hsa:3576(P10145)	0.083066
hsa04015	Rap1 signaling pathway	Environmental Information Processing	hsa:387(P61586)	0.084432
hsa05205	Proteoglycans in cancer	Human Diseases	hsa:6194(P62753);hsa:387(P61586)	0.116169
hsa05150	Staphylococcus aureus infection	Human Diseases	hsa:102723407(P0DOX6);hsa:3426(P05156);hsa:718(P01024);hsa:2266(P02679);hsa:728358(P59665);hsa:1668(P59665);hsa:1667(P59665)	0.123359
hsa04510	Focal adhesion	Cellular Processes	hsa:1311(P49747);hsa:387(P61586);hsa:7060(P35443)	0.138822
hsa04610	Complement and coagulation cascades	Organismal Systems	hsa:718(P01024);hsa:2266(P02679);hsa:3426(P05156)	0.138822
hsa05133	Pertussis	Human Diseases	hsa:718(P01024);hsa:387(P61586);hsa:3576(P10145)	0.15324
hsa05161	Hepatitis B	Human Diseases	hsa:7529(P31946);hsa:3576(P10145);hsa:10971(P27348)	0.15324
hsa04621	NOD-like receptor signaling pathway	Organismal Systems	hsa:1667(P59665);hsa:728358(P59665);hsa:387(P61586);hsa:1668(P59665);hsa:3576(P10145)	0.15324
hsa04512	ECM-receptor interaction	Environmental Information Processing	hsa:1311(P49747);hsa:7060(P35443)	0.158097
hsa05165	Human papillomavirus infection	Human Diseases	hsa:1311(P49747);hsa:7060(P35443)	0.158097
hsa04371	Apelin signaling pathway	Environmental Information Processing	hsa:6194(P62753);hsa:59(P62736)	0.159481
hsa05142	Chagas disease (American trypanosomiasis)	Human Diseases	hsa:718(P01024);hsa:3576(P10145)	0.159481
hsa04932	Non-alcoholic fatty liver disease (NAFLD)	Human Diseases	hsa:1965(P05198);hsa:3576(P10145)	0.159481
hsa04144	Endocytosis	Cellular Processes	hsa:10890(P61026);hsa:55048(A5D8V6);hsa:128866(Q9H444);hsa:160(O95782);hsa:387(P61586)	0.169516
hsa04151	PI3K-Akt signaling pathway	Environmental Information Processing	hsa:102723407(P0DOX6);hsa:1311(P49747);hsa:7529(P31946);hsa:6194(P62753);hsa:7060(P35443);hsa:10971(P27348)	0.1703
hsa05418	Fluid shear stress and atherosclerosis	Human Diseases	hsa:387(P61586)	0.183131
hsa05202	Transcriptional misregulation in cancer	Human Diseases	hsa:102723407(P0DOX6);hsa:8358(P68431);hsa:653604(P68431);hsa:333932(P68431);hsa:3576(P10145);hsa:8352(P68431);hsa:8353(P68431);hsa:8350(P68431);hsa:8351(P68431);hsa:8356(P68431);hsa:8357(P68431);hsa:8354(P68431);hsa:8355(P68431);hsa:126961(P68431);hsa:1668(P59665);hsa:8968(P68431)	0.196016
hsa04915	Estrogen signaling pathway	Organismal Systems	hsa:3861(P02533);hsa:3868(P08779);hsa:3875(P05783);hsa:3880(P08727)	0.196016
hsa05322	Systemic lupus erythematosus	Human Diseases	hsa:102723407(P0DOX6);hsa:8358(P68431);hsa:8352(P68431);hsa:8353(P68431);hsa:8350(P68431);hsa:8351(P68431);hsa:8356(P68431);hsa:8357(P68431);hsa:8354(P68431);hsa:8355(P68431);hsa:8330(P0C0S8;Q93077);hsa:8331(P0C0S8);hsa:8332(P0C0S8;Q93077);hsa:8334(P0C0S8;Q93077);hsa:8335(P0C0S8;Q93077);hsa:8336(P0C0S8;Q93077);hsa:8337(P0C0S8;Q93077);hsa:8969(P0C0S8;Q93077);hsa:8968(P68431);hsa:723790(P0C0S8;Q93077);hsa:92815(Q93077);hsa:718(P01024);hsa:8329(P0C0S8;Q93077);hsa:653604(P68431);hsa:85235(P0C0S8;Q93077);hsa:333932(P68431);hsa:126961(P68431);hsa:3012(P0C0S8;Q93077);hsa:3013(P0C0S8)	0.206168
hsa05146	Amoebiasis	Human Diseases	hsa:102723407(P0DOX6);hsa:3576(P10145)	0.208201
hsa04611	Platelet activation	Organismal Systems	hsa:2266(P02679);hsa:387(P61586)	0.208201
hsa04145	Phagosome	Cellular Processes	hsa:102723407(P0DOX6);hsa:1311(P49747);hsa:7060(P35443);hsa:718(P01024);hsa:7846(P68363);hsa:10376(P68363)	0.228841
hsa04210	Apoptosis	Cellular Processes	hsa:7846(P68363);hsa:1965(P05198);hsa:142(P09874);hsa:10376(P68363)	0.232865
hsa04530	Tight junction	Cellular Processes	hsa:7846(P68363);hsa:140465(P14649);hsa:387(P61586);hsa:10376(P68363)	0.232865
hsa04072	Phospholipase D signaling pathway	Environmental Information Processing	hsa:102723407(P0DOX6);hsa:387(P61586);hsa:3576(P10145)	0.232865
hsa04064	NF-kappa B signaling pathway	Environmental Information Processing	hsa:102723407(P0DOX6);hsa:3576(P10145);hsa:142(P09874)	0.232865
hsa05152	Tuberculosis	Human Diseases	hsa:718(P01024);hsa:387(P61586);hsa:102723407(P0DOX6)	0.232865
hsa04217	Necroptosis	Cellular Processes	hsa:8969(P0C0S8;Q93077);hsa:3012(P0C0S8;Q93077);hsa:8336(P0C0S8;Q93077);hsa:142(P09874);hsa:92815(Q93077);hsa:8329(P0C0S8;Q93077);hsa:128866(Q9H444);hsa:723790(P0C0S8;Q93077);hsa:3013(P0C0S8);hsa:8330(P0C0S8;Q93077);hsa:8331(P0C0S8);hsa:8332(P0C0S8;Q93077);hsa:8334(P0C0S8;Q93077);hsa:8335(P0C0S8;Q93077);hsa:85235(P0C0S8;Q93077);hsa:8337(P0C0S8;Q93077)	0.237833
hsa04520	Adherens junction	Cellular Processes	hsa:387(P61586)	0.25774
hsa04066	HIF-1 signaling pathway	Environmental Information Processing	hsa:6194(P62753)	0.25774
hsa04141	Protein processing in endoplasmic reticulum	Genetic Information Processing	hsa:1965(P05198)	0.25774
hsa03013	RNA transport	Genetic Information Processing	hsa:1965(P05198)	0.25774
hsa05131	Shigellosis	Human Diseases	hsa:3576(P10145)	0.25774
hsa04979	Cholesterol metabolism	Organismal Systems	hsa:5360(P55058)	0.25774
hsa04670	Leukocyte transendothelial migration	Organismal Systems	hsa:387(P61586)	0.25774
hsa05203	Viral carcinogenesis	Human Diseases	hsa:718(P01024);hsa:7529(P31946);hsa:387(P61586);hsa:10971(P27348)	0.258583
hsa05130	Pathogenic Escherichia coli infection	Human Diseases	hsa:7846(P68363);hsa:3875(P05783);hsa:387(P61586);hsa:10376(P68363);hsa:10971(P27348)	0.259166
hsa04390	Hippo signaling pathway	Environmental Information Processing	hsa:7529(P31946);hsa:10971(P27348)	0.263175
hsa05206	MicroRNAs in cancer	Human Diseases	hsa:7431(P08670);hsa:387(P61586)	0.263175
hsa05034	Alcoholism	Human Diseases	hsa:8358(P68431);hsa:8352(P68431);hsa:8353(P68431);hsa:8350(P68431);hsa:8351(P68431);hsa:8356(P68431);hsa:8357(P68431);hsa:8354(P68431);hsa:8355(P68431);hsa:8330(P0C0S8;Q93077);hsa:8331(P0C0S8);hsa:8332(P0C0S8;Q93077);hsa:8334(P0C0S8;Q93077);hsa:8335(P0C0S8;Q93077);hsa:8336(P0C0S8;Q93077);hsa:8337(P0C0S8;Q93077);hsa:8969(P0C0S8;Q93077);hsa:8968(P68431);hsa:723790(P0C0S8;Q93077);hsa:92815(Q93077);hsa:8329(P0C0S8;Q93077);hsa:653604(P68431);hsa:85235(P0C0S8;Q93077);hsa:333932(P68431);hsa:126961(P68431);hsa:3012(P0C0S8;Q93077);hsa:3013(P0C0S8)	0.28189
hsa05144	Malaria	Human Diseases	hsa:1311(P49747);hsa:3576(P10145);hsa:7060(P35443)	0.28189
hsa05160	Hepatitis C	Human Diseases	hsa:7529(P31946);hsa:1965(P05198);hsa:10971(P27348)	0.28189
hsa04110	Cell cycle	Cellular Processes	hsa:7529(P31946);hsa:10971(P27348)	0.290152
hsa04114	Oocyte meiosis	Cellular Processes	hsa:7529(P31946);hsa:10971(P27348)	0.290152
hsa04060	Cytokine-cytokine receptor interaction	Environmental Information Processing	hsa:58191(Q9H2A7);hsa:3576(P10145)	0.290152
hsa05323	Rheumatoid arthritis	Human Diseases	hsa:102723407(P0DOX6);hsa:3576(P10145)	0.290152
hsa05140	Leishmaniasis	Human Diseases	hsa:718(P01024);hsa:102723407(P0DOX6)	0.290152
hsa05168	Herpes simplex virus 1 infection	Human Diseases	hsa:718(P01024);hsa:1965(P05198)	0.290152
hsa05135	Yersinia infection	Human Diseases	hsa:387(P61586);hsa:3576(P10145)	0.290152
hsa05169	Epstein-Barr virus infection	Human Diseases	hsa:102723407(P0DOX6);hsa:7431(P08670);hsa:5701(P35998)	0.297291
hsa05134	Legionellosis	Human Diseases	hsa:718(P01024);hsa:3576(P10145)	0.315393
hsa04540	Gap junction	Cellular Processes	hsa:7846(P68363);hsa:10376(P68363)	0.346675
hsa05100	Bacterial invasion of epithelial cells	Human Diseases	hsa:387(P61586)	0.346675
hsa05143	African trypanosomiasis	Human Diseases	hsa:102723407(P0DOX6)	0.346675
hsa05230	Central carbon metabolism in cancer	Human Diseases	hsa:8140(Q01650)	0.346675
hsa03320	PPAR signaling pathway	Organismal Systems	hsa:5360(P55058)	0.346675
hsa04640	Hematopoietic cell lineage	Organismal Systems	hsa:102723407(P0DOX6)	0.346675
hsa04666	Fc gamma R-mediated phagocytosis	Organismal Systems	hsa:102723407(P0DOX6)	0.346675
hsa04310	Wnt signaling pathway	Environmental Information Processing	hsa:8607(Q9Y265);hsa:387(P61586)	0.350443
hsa05163	Human cytomegalovirus infection	Human Diseases	hsa:387(P61586);hsa:3576(P10145)	0.350443
hsa05164	Influenza A	Human Diseases	hsa:1965(P05198);hsa:3576(P10145)	0.350443
hsa05167	Kaposi sarcoma-associated herpesvirus infection	Human Diseases	hsa:718(P01024);hsa:3576(P10145)	0.350443

hsa04921	Oxytocin signaling pathway	Organismal Systems	hsa:140465(P14649);hsa:387(P61586)	0.350443
hsa03050	Proteasome	Genetic Information Processing	hsa:5695(Q99436);hsa:5701(P35998)	0.351207
hsa05414	Dilated cardiomyopathy (DCM)	Human Diseases	hsa:102723407(P0DOX6);hsa:70(P62736)	0.351207
hsa04218	Cellular senescence	Cellular Processes	hsa:3576(P10145)	0.401274
hsa04071	Sphingolipid signaling pathway	Environmental Information Processing	hsa:387(P61586)	0.401274
hsa04061	Viral protein interaction with cytokine and cytokine receptor	Environmental Information Processing	hsa:3576(P10145)	0.401274
hsa04910	Insulin signaling pathway	Organismal Systems	hsa:6194(P62753)	0.401274
hsa04928	Parathyroid hormone synthesis, secretion and action	Organismal Systems	hsa:387(P61586)	0.401274
hsa04625	C-type lectin receptor signaling pathway	Organismal Systems	hsa:387(P61586)	0.401274
hsa04620	Toll-like receptor signaling pathway	Organismal Systems	hsa:3576(P10145)	0.401274
hsa04722	Neurotrophin signaling pathway	Organismal Systems	hsa:387(P61586)	0.401274
hsa04614	Renin-angiotensin system	Organismal Systems	hsa:10159(O75787)	0.401274
hsa04721	Synaptic vesicle cycle	Organismal Systems	hsa:160(O95782)	0.401274
hsa04622	RIG-I-like receptor signaling pathway	Organismal Systems	hsa:3576(P10145)	0.401274
hsa04660	T cell receptor signaling pathway	Organismal Systems	hsa:387(P61586)	0.401274
hsa04014	Ras signaling pathway	Environmental Information Processing	hsa:387(P61586)	0.435228
hsa04080	Neuroactive ligand-receptor interaction	Environmental Information Processing	hsa:718(P01024)	0.435228
hsa05416	Viral myocarditis	Human Diseases	hsa:102723407(P0DOX6)	0.435228
hsa04933	AGE-RAGE signaling pathway in diabetic complications	Human Diseases	hsa:3576(P10145)	0.435228
hsa05132	Salmonella infection	Human Diseases	hsa:3576(P10145)	0.435228
hsa05410	Hypertrophic cardiomyopathy (HCM)	Human Diseases	hsa:70(P62736)	0.435228
hsa05210	Colorectal cancer	Human Diseases	hsa:387(P61586)	0.435228
hsa04360	Axon guidance	Organismal Systems	hsa:387(P61586)	0.435228
hsa04657	IL-17 signaling pathway	Organismal Systems	hsa:3576(P10145)	0.435228
hsa04662	B cell receptor signaling pathway	Organismal Systems	hsa:102723407(P0DOX6)	0.435228
hsa04926	Relaxin signaling pathway	Organismal Systems	hsa:59(P62736)	0.435228
hsa04714	Thermogenesis	Organismal Systems	hsa:6194(P62753)	0.435228
hsa04140	Autophagy - animal	Cellular Processes	hsa:1965(P05198)	0.483586
hsa04152	AMPK signaling pathway	Environmental Information Processing	hsa:10890(P61026)	0.483586
hsa04020	Calcium signaling pathway	Environmental Information Processing	hsa:102723407(P0DOX6)	0.483586
hsa04350	TGF-beta signaling pathway	Environmental Information Processing	hsa:387(P61586)	0.483586
hsa04022	cGMP-PKG signaling pathway	Environmental Information Processing	hsa:387(P61586)	0.483586
hsa04024	cAMP signaling pathway	Environmental Information Processing	hsa:387(P61586)	0.483586
hsa03410	Base excision repair	Genetic Information Processing	hsa:142(P09874)	0.483586
hsa05016	Huntington disease	Human Diseases	hsa:160(O95782)	0.483586
hsa05219	Bladder cancer	Human Diseases	hsa:3576(P10145)	0.483586
hsa05320	Autoimmune thyroid disease	Human Diseases	hsa:102723407(P0DOX6)	0.483586
hsa05340	Primary immunodeficiency	Human Diseases	hsa:102723407(P0DOX6)	0.483586
hsa05162	Measles	Human Diseases	hsa:1965(P05198)	0.483586
hsa05330	Allograft rejection	Human Diseases	hsa:102723407(P0DOX6)	0.483586
hsa05120	Epithelial cell signaling in Helicobacter pylori infection	Human Diseases	hsa:3576(P10145)	0.483586
hsa05310	Asthma	Human Diseases	hsa:102723407(P0DOX6)	0.483586
hsa04672	Intestinal immune network for IgA production	Organismal Systems	hsa:102723407(P0DOX6)	0.483586
hsa04261	Adrenergic signaling in cardiomyocytes	Organismal Systems	hsa:70(P62736)	0.483586
hsa04961	Endocrine and other factor-regulated calcium reabsorption	Organismal Systems	hsa:160(O95782)	0.483586
hsa04650	Natural killer cell mediated cytotoxicity	Organismal Systems	hsa:102723407(P0DOX6)	0.483586
hsa04972	Pancreatic secretion	Organismal Systems	hsa:387(P61586)	0.483586
hsa04260	Cardiac muscle contraction	Organismal Systems	hsa:70(P62736)	0.483586
hsa04664	Fc epsilon RI signaling pathway	Organismal Systems	hsa:102723407(P0DOX6)	0.483586

Table S9 The relationship between the fecal Fn abundance or serum exosomes miR-1246/92b-3p/27a-3p levels and the clinicopathological variables of the 82 CRC patients.

Characteristics	**cases (n)**	***Fn* -log10**	***p***	**miR-1246 -log10**	***p***	**miR-92b-3p -log10**	***p***	**miR-27a-3p -log10**	***p***	**CXCL16 log10 pg/ml**	***P***
Gender			0.51		0.46		0.16		0.3		0.4
Male	54	4.44±1.31		3.18±1.32		3.59±1.29		4.47±0.75		1.71±0.79	
Female	28	4.23±1.54		3.39±0.97		3.14±1.46		4.30±0.69		1.55±0.78	
Age(y)			0.34		0.97		0.69		0.22		0.33
<60	43	4.30±1.40		3.25±1.20		3.50±1.47		4.32±0.70		1.73±0.79	
≥60	39	4.52±1.37		3.26±1.25		3.37±1.25		4.52±0.77		1.56±0.79	
Location			0.66		0.95		0.58		0.95		0.67
Colon	53	4.32±1.39		3.24±1.27		3.50±1.40		4.41±0.68		1.68±0.76	
Rectal	29	4.46±1.38		3.26±1.13		5.32±1.30		4.42±0.81		1.60±0.85	
Stage			0.11		0.59		0.1		0.04		0.45
Ⅰ+Ⅱ	45	4.59±1.49		3.32±1.16		3.21±1.30		4.57±23.93		1.59±0.80	
Ⅲ+Ⅳ	37	4.10±1.20		3.20±1.28		3.70±1.40		4.23±20.81		1.73±0.78	
T status			0.92		0.26		0.71		0.62		0.09
T1+T2	13	4.33±1.77		3.48±0.65		3.31±1.26		4.51±0.58		1.32±0.76	
T3+T4	69	4.38±1.31		3.21±1.29		3.46±1.39		4.40±0.76		1.72±0.78	
N status			0.13		0.6		0.09		0.43		0.73
No	44	4.58±1.51		3.32±1.18		3.20±1.31		4.56±0.71		1.68±0.68	
Yes	38	4.12±1.19		3.18±1.27		3.71±1.38		4.24±0.73		1.62±0.73	
Metastasis			0.72		0.47		0.17		0.62		0.006
No	66	4.40±1.46		3.30±1.21		3.34±1.33		4.43±0.72		1.54±0.71	
Yes	16	4.26±1.06		3.05±1.23		3.86±1.44		4.33±0.79		2.13±0.94	
CEA (μg/ml)			0.21		0.24		0.59		0.88		0.07
<5	53	4.22±1.30		3.37±1.07		3.50±1.36		4.40±0.72		1.54±0.83	
≥5	29	4.63±1.52		3.04±1.43		3.33±1.38		4.43±0.77		1.87±0.71	
CA19-9 (U/ml)			0.34		0.4		0.85		0.17		0.72
<35	69	6.31±1.40		3.20±1.23		3.42±1.30		4.36±0.40		1.64±0.77	
≥35	13	4.70±1.29		3.51±1.09		3.50±1.72		4.67±0.65		1.73±0.69	
gFOBT			0.62		0.95		0.19		0.76		0.65
Positive	8	4.05±1.26		3.38±1.39		4.05±1.24		4.23±0.68		1.86±0.54	
Weakly positive	12	4.14±1.44		3.21±1.42		2.93±1.15		4.46±0.81		1.64±0.69	
Negative	62	4.45±1.40		3.24±1.17		3.46±1.39		4.43±0.73		1.63±0.70	

Supplementary Figure

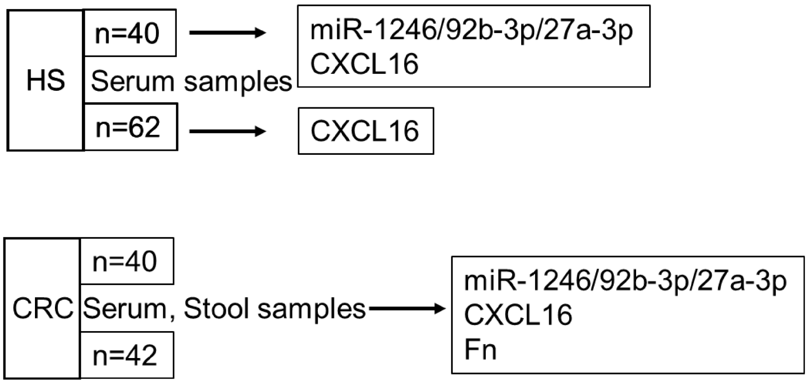


Figure S1 Background grouping of the study cohorts.

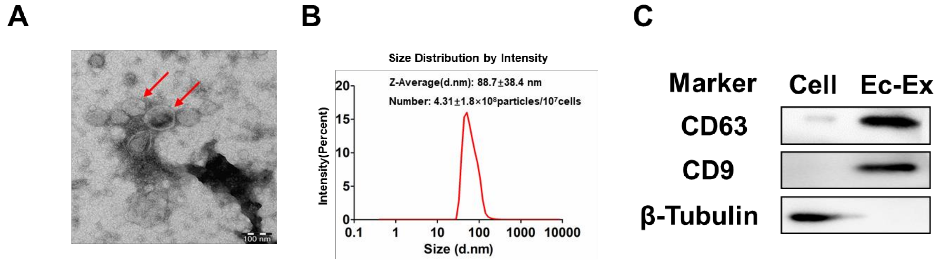


Figure S2 Identification of exosomes derived from *E.coli*-infected HCT116 cell (Ec -Ex). HCT116 cell were infected with live *E.coli* at an MOI of 1:1000 (bacteria: cells) and then were cultured for 24 h. **(A)** TEM images of purified Ec-Ex. Scale bar = 100 nm. **(B)** Nanoparticle tracking analysis (NTA) analysis of size distribution. **(C)** Western blot analysis of markers (CD63 and CD9) in exosomal protein purified from *E.coli*-infected HCT116 cell supernatants, tubulin served as an internal control in whole-cell lysates.

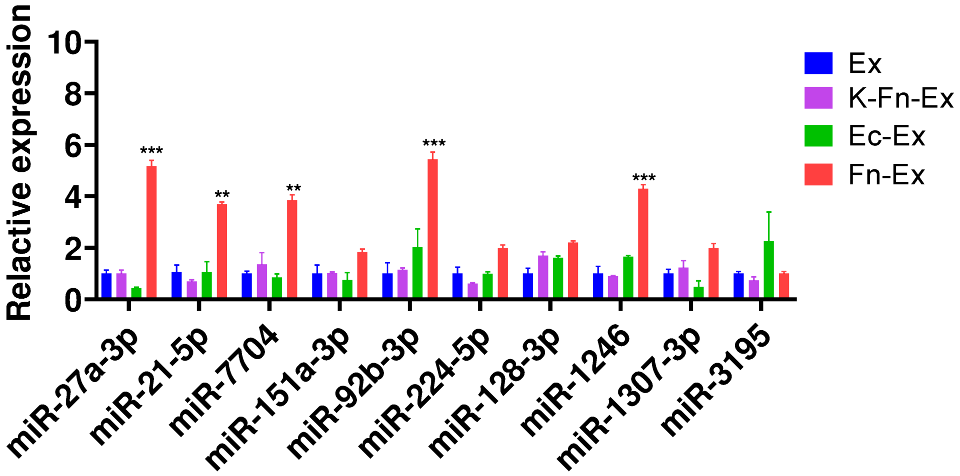
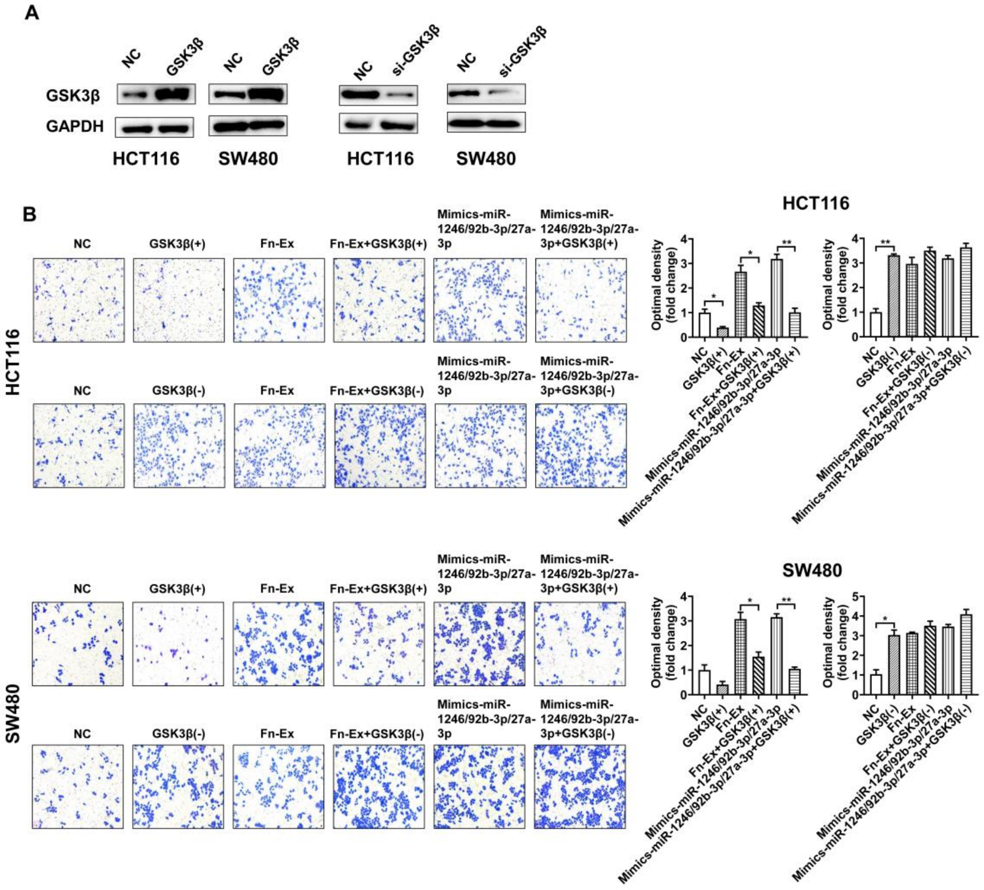


Figure S3 Screen and identification the results of RNA sequence in exosome from HCT116 cells (Ex), *E.coli*-infected HCT116 cells (Ec-Ex), Fn-infected HCT116 cells (Fn-Ex), and heat-killed Fn-infected HCT116 cells (K-Fn-Ex). Quantitative real-time PCR indicating relative expression of selected miRNA in Ex, K-Fn-Ex, Ec-Ex and Fn-Ex. Error bars, SD. **, $P < 0.01$; ***, $P < 0.001$.


A
NC
GSK3β
NC
GSK3β
NC
si-GSK3β
NC
si-GSK3β
GSK3β
GAPDH
HCT116
SW480
HCT116
SW480
B
HCT116
NC
GSK3β(+)
Fn-Ex
Fn-Ex+GSK3β(+)
Mimics-miR-1246/92b-3p/27a-3p
Mimics-miR-1246/92b-3p/27a-3p+GSK3β(+)
NC
GSK3β(-)
Fn-Ex
Fn-Ex+GSK3β(-)
Mimics-miR-1246/92b-3p/27a-3p
Mimics-miR-1246/92b-3p/27a-3p+GSK3β(-)
Optimal density (fold change)
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SW480
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0
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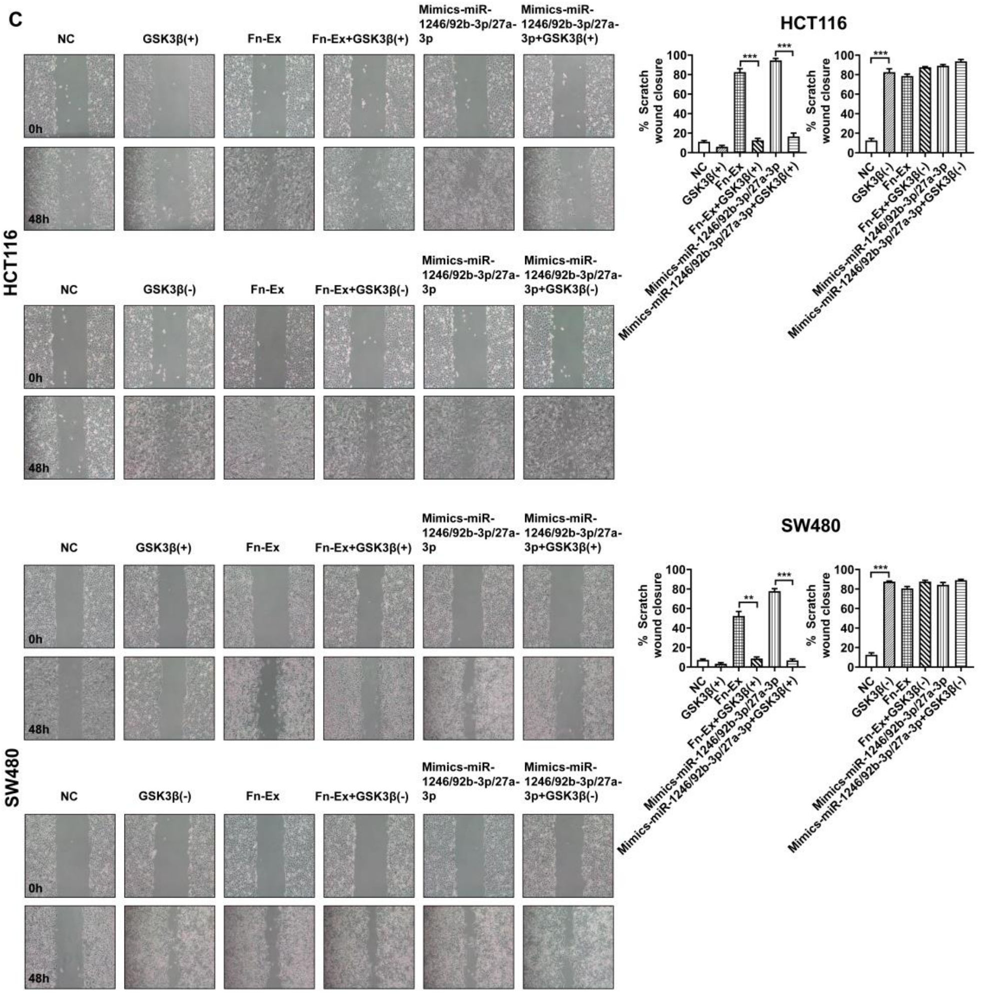

Figure S4 miR-1246/92b-3p/27a-3p of Fn-Ex to promote CRC cells migration through inhibition of GSK3β. (A) Expression of GSK3β in HCT116 and SW480 cells after transfection with GSK3β overexpression plasmid GSK3β(+) or siRNAs GSK3β(-). **(B)** The migration of CRC cells was assessed using a Transwell migration assays. Representative images of the assay (right). **(C)** Analysis of CRC cells migration by *in vitro* scratch assays. Images were acquired at 0 and 48 h. Right quantitative analysis of scratch wound closure. Data represent at least three experiments performed in triplicate. Scale bar = 200 μm; Error bars, SD. **, $P < 0.01$; and ***, $P < 0.001$.

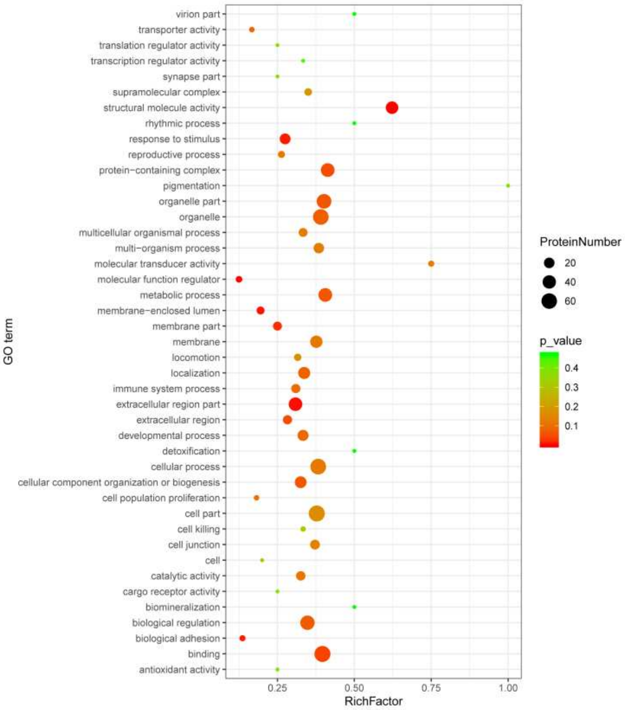

Figure S5 Gene ontology (GO) enrichment analysis of the Fn-infected HCT116 cells derived exosomes (Fn-Ex) unique cell proteins.

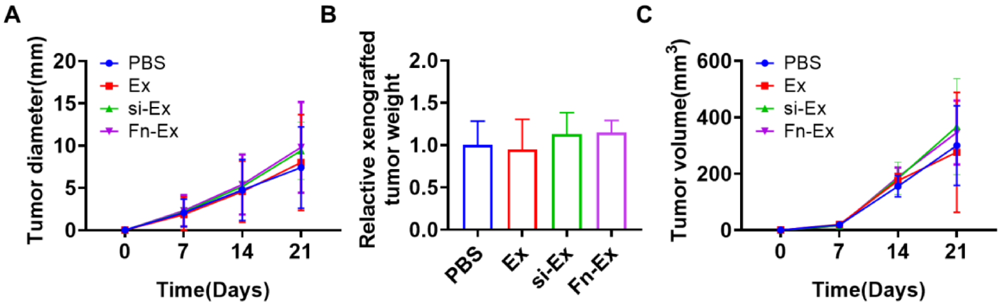

Figure S6 *In vivo* verification shows that Fn-Ex promotes migration. Quantitative analysis of xenografted tumor diameter **(A)**, weight **(B)**, and volume **(C)** (n = 5). Error bars, SD.

Exosomes derived from *Fusobacterium nucleatum*-infected colorectal cancer cells facilitate tumor metastasis by selectively carrying miR-1246/92b-3p/27a-3p and CXCL16

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Supplementary Information

Materials and Methods

Patients and samples

The serum and stool samples from 82 patients with primary CRC were selected from an archive of blood samples at the Cancer Center of Sun Yat-sen University (SYSUCC). Ethics approval was granted by the Ethics Committee of SYSUCC. In addition, healthy blood samples were obtained from 102 subjects without any malignancy. All experiments were carried out in accordance with the approved guidelines and related regulations.

Bacterial culture

Fn ATCC 25586 was purchased from the Institute of Microbiology of Chinese Academy of Sciences. Fn was grown anaerobically at 37 °C for 48 h in brain heart infusion broth (BHI, Oxoid, UK). Heat-killed (dead) Fn was made by heating at 100 °C for 10 min. *E. coli* (DH5α; Tiangen, China) was cultured aerobically at 37°C for 24 h in an LB agar plate. Bacteria were centrifuged and then suspended to a concentration of 1×10^8 colony-forming units (CFUs)/ml with RPMI 1640 (Gibco, USA) for the infection experiment.

Cell culture

The human CRC cell lines HCT116 and SW480 and the mouse CRC cell line CT26 were cultured in the recommended medium supplemented with 10% fetal bovine serum (FBS, Gibco, USA) in a humidified incubator at 37°C with 5% CO_2.

Exosome isolation, characterization and nanoparticle tracking analysis

Exosomes were isolated by differential centrifugation. Briefly, the cell supernatant was centrifuged at 16,500 g for 20 min and then passed through a 0.22 μm filter. Then, the filtered supernatant was subjected to ultracentrifugation at 120,000 g for 70 min at 4°C and the exosomal pellet was resuspended in PBS to produce exosome-enriched fractions. Serum samples (2 ml) from CRC patients and healthy subjects (HS) were collected from the same volume serum as a quantitative indicator of exosome and diluted eight-fold with PBS and the exosome-enriched fractions were prepared as described above. The exosome size and number were measured by a nanoparticle tracking analysis (NTA) using a Zetasizer Nano S90 system (Malvern Instruments, England) equipped with a blue laser (405 nm). The movement under Brownian motion was recorded in 9 s sample videos which were analyzed with NTA analytical software (version 2.2). Purified exosomes were observed with a JEM1400 transmission electron microscope (TEM) operated at 120 kV (JEOL, Japan) and photographs were captured with a Canon A650 digital camera.

PKH26 staining for exosomes

Exosomes were labeled using PKH26 red fluorescent cell linker kits (Sigma, USA) according to the manufacturer’s instructions. Briefly, exosomes were resuspended in 100 μl of Diluent C. Then, 5 μM PKH26 dye was added, which was followed by 15 min of incubation at room temperature in the dark. The staining was stopped by adding 200 μl of bovine serum and incubating for 1 min. The stained exosomes were evaluated by CLSM (OLYMPUS-FV3000, Japan).

miRNA library construction and sequencing

Total RNA from exosomes was used for miRNA library preparation and sequencing. Library preparation and sequencing were conducted by Guangzhou RiboBio Co., Ltd. Briefly, total RNA samples were separated on a 15% Tris-borate-EDTA (TBE) polyacrylamide gel (Invitrogen, USA) and small RNAs ranging between 18 and 30 nucleotides (nt) were used for library preparation. Small RNAs were reverse transcribed and amplified by PCR. The PCR products were sequenced using an Illumina HiSeq 2500 platform (Illumina, USA).

RNA isolation and quantitative RT-PCR

Total RNA from exosomes was extracted using a total exosome RNA and protein isolation kit (Thermo Fisher Scientific, USA) according to the instructions of the manufacturer. cDNA was synthesized using PrimeScript™ RT Master Mix (TaKaRa, Japan). Quantification of miRNA expression was performed using a Mir-X™ miRNA RT-qPCR TB Green™ Kit (TaKaRa, Japan) on a Light Cycler® 480 II (Roche, Applied Science). The data were normalized to U6 small nuclear RNA expression and was calculated as $2^{-\triangle\triangle CT}$ expression.

Cell proliferation assay

Cells were seeded into 96-well plates at a density of 3,000 cells/well and cocultured with PBS, Ex，Ec-Ex or Fn-Ex at a concentration of 10 μg/ml. Cells were incubated at

37 ˚C in an incubator supplied with 5% CO_2 for 0, 24, 48 and 72 h. Cell Counting kit-8 (CCK8; Sigma) assays were performed according to the manufacturer’s protocol. Finally, the absorbance of each sample was detected at a wavelength of 450 nm using a plate reader (Bio-Rad, USA).

miRNA transfection

Cells were transfected with miR-1246/27a-3p/92a-3p mimics, inhibitors, or negative control (NC) chemical synthesis oligonucleotides (Gene Pharma, China) at a final concentration of 50 nM using Lipofectamine 3000 reagent (Invitrogen, USA) at the indicated concentrations according to the supplier’s instructions.

Stool sample DNA extraction and bacterial quantification

DNA was extracted using a TIANamp Stool DNA Kit (Tiangen, China) according to the manufacturer’s instructions and was stored at -20 °C prior to amplification steps. The quantification of Fn was performed as described previously.[1]

miRNA target prediction and luciferase activity assay

miRNA target prediction and analysis were performed with the algorithms from TargetScan (http://www.targetscan.org/vert_72/), PicTar (https://pictar.mdc-berlin.de/), and miRanda (http://miranda.org.uk/). Wild-type GSK3β-3′untranslated regions (UTRs) or GSK3β-3′UTRs with various miRNA-binding site mutations were placed in a pmirGLO vector (Gene Pharma, China).

Luciferase reporter assays were performed using a dual-specific luciferase assay kit (Promega, USA) according to the manufacturer's protocol. The reporters were transfected into cells using Lipofectamine 3000 (Invitrogen, USA). The relative expression of firefly luciferase activity was normalized to Renilla luciferase activity.

GSK3β overexpression and knockdown

To generate GSK3β overexpression cells, cells were transfected with pcDNA3.1-GSK3β or pcDNA3.1 vector control using Lipofectamine 3000 reagent (Invitrogen, USA). For GSK3β knockdown, cells were transfected with si-GSK3β RNA (si-GSK3β, sense: 5’-CCACTCAAGAACTGTCAAGTA-3’; anti-sense: 5’-UUCUCCGAACGUGUCACGUTT-3’, GenePharma, China) at a working concentration of 50 nM using Lipofectamine 3000 reagent (Invitrogen, USA).

Wound healing assay

Cells were seeded in 60-mm dishes to create a confluent monolayer. The cell monolayer was then scraped with a p200 pipette tip in a straight line to create a "scratch". After the first image of the scratch was acquired, cells were cocultured with Ex (10 μg/ml)，Ec-Ex (10 μg/ml)，Fn-Ex (10 μg/ml)，CXCL16 (20 ng/ml, Sinobiological, China)，or Fn-Ex (10 μg/ml) and CXCR6 (10 ng/ml, Sinobiological, China) for 48 h prior to acquisition of the second image. The percent wound closure (%) = migrated cell surface area/total surface area ×100.

Transwell migration assay

The effect of exosomes on the migration of cancer cells was determined by using Transwell 24-well plates (8-μm pores; Corning). Ex (10 μg/ml), Ec-Ex (10 μg/ml)， Fn-Ex (10 μg/ml), CXCL16 (20 ng/ml, Sinobiological, China), or Fn-Ex (10 μg/ml) and CXCR6 (10 ng/ml, Sinobiological, China) were added to the bottom chambers to act as chemoattractants. Cells across pores were fixed with 4% paraformaldehyde and stained with 1% crystal violet solution. For each chamber, three fields were randomly chosen and cells were counted.

Western blotting

Cellular and exosomal proteins were separated by 12% SDS-PAGE, transferred to polyvinylidene difluoride membranes, and probed with antibodies against GSK3β and IL8 (1:1,000, BOSTER), CXCL16 and RhoA (1:2,000, BOSTER), β-Catenin and E-cadherin (1:2,000, Abcam), C-Myc, Vimentin and CyclinD1 (1:1,000, CST). Horseradish peroxidase (HRP)-conjugated anti-rabbit or anti-mouse antibodies (1:1,000, BOSTER) were used as secondary antibodies. GAPDH/β-Tubulin protein levels were determined by using the specific antibodies (1:5,000, BOSTER), and their levels were used as a loading control for samples, CD9 and CD63 (1:1,000, Abcam) antibodies were used as markers for exosomes.

Protein analysis

a. Sample preparation for proteomic analysis

Exosome-protein pellets were re-suspended in digestion buffer (8 M urea, 100 mM Tris-HCl; pH 8.5). The mixture was brought to 5 mM Tris [2-carboxyethyl] phosphine (TCEP) and incubated at room temperature (RT) for 15 min. Iodoacetamide was then added to a final concentration of 10 mM and the resultant mixture was incubated at RT for 20 min in the dark, when Lys-C was added at 1:50 (enzyme to substrate ratio) followed by incubation at 37 °C for 4 h. The digest was then diluted to achieve a final concentration of 2 M urea with 100 mM Tris-HCl; pH 8.5 and trypsin digestion (1:50 protease to protein ratio) was carried out at 37 °C overnight. Protein digestion was stopped by the addition of formic acid at 4% final concentration.

b. Nano-LC–MS/MS analysis of proteins

Analysis by Nano LC-Q Exactive Plus (Thermo Fisher). The injection volume was 10μl, and the flow rate was 500 nl/min. The mobile phases consisted of 0.5% acetic acid (A) and 0.5% acetic acid and 80% acetonitrile (B). A three-step linear gradient of 5–10% B in 5 min, 10–40% B in 60 min, 40–100% B in 5 min, and 100% B for 10 min was used. A spray voltage of 2400 V was applied *via* the metal connector. The MS was operated in data-dependent MS/MS mode in which each full MS scan was collected in the orbitrap, precursor ion range of 300–1600 m/z (R = 6000 @ 400 m/z), followed by up to eight MS/MS scans performed in the linear ion trap where the most abundant peptide molecular ions were selected for collision-induced dissociation (CID), using a normalized collision energy of 35%.

c. Database searches

Data from the first set of samples was searched against the human proteome (Uniprot) with no enzyme constraint, methionine oxidation as variable modification, using average mass with a peptide tolerance of 1.4 Da and a MS/MS tolerance of 0.5 Da using Mascot (v2.4.0, Matrix Science Ltd.). Filtering the data was performed using Scaffold (version 4.2.0, Proteome Software Inc., Portland, OR). Peptide identifications were accepted if they could be established at greater than 95.0% probability by the Scaffold Local FDR algorithm. Protein identifications were accepted if they could be established at greater than 99.0% probability.

ELISA

The quantification of serum exosome cytokines was determined using a Quantibody Human CXCL16 Array 1 Kit (MEIMIAN, China) following the manufacturers' protocol. Briefly, 0.5 μg of serum exosomes or a standard was added to a 96-well ELISA plate and then reacted with their cognate primary antibodies and HRP-conjugated secondary antibodies. 3, 3′, 5, 5′-Tetramethylbenzidine (TMB) was used as the substrate, and the absorbance was measured at 450 nm with a microplate reader (Bio-Rad, USA)

CXCL16 knockdown

Cells were cultured in 6-well plates with a 5×10^5/ml density. The cells were then transfected with 50 nM siCXCL16 RNA (si-CXCL16, sense: 5'-CAAAGAAUGUGGACAUGCU-3' ;anti-sense:

5’-AGCAUGUCCACAUUCUUU-3’; GenePharma, China) using the Lipofectamine 3000 reagent (Invitrogen，USA) for 48 h. The scrambled siRNA (GenePharma, China) was used as a negative control. The efficiency of knockdown was examined by RT-qPCR. The expression of target gene CXCL16 was detected by RT-qPCR and Western blot.

Experimental mouse techniques

Mice were obtained from the Model Animal Center of Nanjing University (Nanjing, China) and were raised under pathogen-free conditions in Sun Yat-sen University Animal Center (Guangzhou, China). All of the animal studies were conducted in accordance with protocols approved by the Institutional Animal Care and Research Advisory Committee.

To establish a human CRC xenograft model, six-week-old BALB/c nude mice were subcutaneously (*s.c.*) inoculated with 2×10^6 HCT116 cell. To establish a mouse CRC homograft model, six-week-old BALB/c mice were inoculated with 2×10^6 CT26 cells by tail vein injection. After tumor transplantation, Fn-Ex, si-Ex or Ex (10 μg) were injected intratumorally (*i.t.*) or intravenously (*i.v.*) every other day. PBS were injected as a control. Tumor growth and body weight were monitored every 2 days. Xenograft tumor growth was measured in three dimensions twice a week with a caliper. Tumor volume was calculated using the following formula: $(\text{length}\times\text{width}^2)/2$. The mice were sacrificed two weeks after the treatment began, and the tumors were surgically removed and counted.

Histology

Tissues were fixed in 10% buffered formalin for 24 h, processed, and embedded in paraffin for sectioning according to the conventional methods. The paraffin-embedded tissues were cut into 5-μm-thick sections. The sections were dewaxed, rehydrated and rinsed.

The tumor cell density in H&E stained sections was calculated by scanning the tissue sections under a microscope at ×40-power and counting the number of nuclei in each histological image in ten different, randomly selected fields. Data were averaged over the ten fields for statistical analysis.

Histology immunohistochemical assays

Tissue sections were incubated with a primary antibody GSK3β (1:50, BOSTER) at 4°C overnight. After washing with PBST, the sections were incubated with an HRP-conjugated anti-mouse or anti-rabbit secondary antibody (1:5000, BOSTER) at room temperature for 2 h. The sections were developed with 3-diaminobenzidine tetrahydrochloride for 10 s, which was followed by counterstaining with 10% Mayer's haematoxylin.

Statistical analyses

The data represent the mean ± SD unless otherwise indicated. Data were analyzed by two-tailed unpaired Student's t-test between two groups and by One-Way ANOVA followed by Bonferroni test for multiple comparisons. Significance was considered $P < 0.05$. Statistical analyses were performed using GraphPad 6.0.

References

1 Guo S, Li L, Xu B*, et al.* A Simple and Novel Fecal Biomarker for Colorectal Cancer: Ratio of Fusobacterium Nucleatum to Probiotics Populations, Based on Their Antagonistic Effect. Clin Chem 2018;**64**:1327-37.

Supplementary Table

Table S1 Sequence of primer.

miRNA	Primer (5'-3')
hsa-miR-1246	AATGGATTTTTGGAGCAGGAA
hsa-miR-92b-3p	GCACTCGTCCCGGCCTCC
hsa-miR-27a-3p	TCACAGTGGCTAAGTTCCGC
hsa-miR-128-3p	TCACAGTGAACCGGTCTCTTT
hsa-miR-7704	GGGTCGGCGGCGACGTG
hsa-miR-3195	CGCGCCGGGCCCGGGTT
hsa-miR-224-5p	CAAGTCACTAGTGGTTCCGTT
hsa-miR-151a-3p	CTAGACTGAAGCTCCTTGAG
hsa-miR-1307-3p	GCGTGGCGTCGGTCGTG
hsa-miR-21-5p	TAGCTTATCAGACTGATGTTGA
U6	F: CTCGCTTCGGCAGCACA
	R: AACGCTTCACGAATTTGCGT

Table S2 Sequences for microRNA mimics and inhibitors.

Name	Sequence (5'-3')
miR-1246 mimics	AAUGGAUUUUUGGAGCAGG
miR-1246 inhibitor	CCUGCUCCAAAAAUCCAUU
miR-92b-3p mimics	GCACUCGUCCCGGCCUCC
miR-92b-3p inhibitor	GGAGGCCGGGACGAGUGC
miR-27a-3p mimics	UCACAGUGGCUAAGUUCCGC
miR-27a-3p inhibitor	GCGGAACUUAGCCACUGTGA
negative control (NC)	ACUAGUCGAUCUAUGUGUGAUATT

Table S3 Summary of small RNA sequencing of Fn-infected and non-infected exosomes (Fn-Ex and Ex).

Categories	**Ex**		**Fn-Ex**	
	Clean Reads	**percent**	**Clean Reads**	**percent**
All	18170471	100%	18668313	100%
miRNA	2408579	13.26%	3089284	16.55%
tRNA	202727	1.12%	274875	1.47%
rRNA	11175946	61.51%	12192919	65.31%
snRNA	920965	5.07%	584985	3.13%
snoRNA	132751	0.73%	65536	0.35%
piRNA	2522604	13.88%	1502548	8.05%
Y_RNA	348825	1.92%	112815	0.60%
Others	458074	2.52%	845351	4.53%

Table S4 Number of miRNA identified in each sample.

Ex		
miRNA_ID	**Total_Count**	**Normalized_Value**
hsa-let-7a-3p	44	2.4215
hsa-let-7a-5p	7718	424.7551
hsa-let-7b-3p	130	7.154
hsa-let-7b-5p	1891	104.0699
hsa-let-7c-5p	871	47.9349
hsa-let-7d-3p	88	4.843
hsa-let-7d-5p	455	25.0406
hsa-let-7e-5p	305	16.7855
hsa-let-7f-1-3p	16	0.8805
hsa-let-7f-5p	28025	1542.3376
hsa-let-7g-5p	4376	240.8303
hsa-let-7i-5p	29850	1642.7752
hsa-miR-100-5p	11846	651.9369
hsa-miR-101-3p	210	11.5572
hsa-miR-103a-3p	591	32.5253
hsa-miR-105-5p	60	3.3021
hsa-miR-106a-5p	43	2.3665
hsa-miR-106b-3p	587	32.3052
hsa-miR-106b-5p	17	0.9356
hsa-miR-107	12	0.6604
hsa-miR-10a-5p	3929	216.2299
hsa-miR-10b-5p	832	45.7886
hsa-miR-1180-3p	52	2.8618
hsa-miR-122-5p	122	6.7142
hsa-miR-1246	107246	5902.2135
hsa-miR-1248	131	7.2095
hsa-miR-1255a	19	1.0457
hsa-miR-125a-5p	389	21.4084
hsa-miR-125b-1-3	18	0.9906
hsa-miR-125b-2-3	10	0.5503
hsa-miR-125b-5p	170	9.3558
hsa-miR-126-3p	315	17.3358
hsa-miR-1273g-3p	30	1.651
hsa-miR-127-3p	13	0.7154
hsa-miR-1283	36	1.9812
hsa-miR-128-3p	691	38.0287
hsa-miR-1290	10	0.5503
hsa-miR-1291	40	2.2014
hsa-miR-129-5p	69	3.7974
hsa-miR-1301-3p	15	0.8255
hsa-miR-1304-3p	23	1.2658
hsa-miR-1307-3p	196	10.7867
hsa-miR-130a-3p	16	0.8805
hsa-miR-130b-5p	44	2.4215
hsa-miR-132-3p	79	4.3477
hsa-miR-132-5p	20	1.1007
hsa-miR-139-5p	16	0.8805
hsa-miR-1-3p	44	2.4215
hsa-miR-140-3p	256	14.0888
hsa-miR-140-5p	18	0.9906
hsa-miR-143-3p	684	37.6435
hsa-miR-145-5p	10	0.5503
hsa-miR-146a-5p	19	1.0457
hsa-miR-146b-5p	102	5.6135
hsa-miR-148a-3p	3879	213.4782
hsa-miR-148b-3p	682	37.5334
hsa-miR-149-5p	42	2.3114
hsa-miR-151a-3p	3365	185.1906
hsa-miR-152-3p	175	9.631
hsa-miR-15b-3p	32	1.7611
hsa-miR-15b-5p	27	1.4859
hsa-miR-16-2-3p	73	4.0175
hsa-miR-16-5p	67	3.6873
hsa-miR-17-5p	205	11.282
hsa-miR-181a-2-3	13	0.7154

Fn-Ex		
miRNA_ID	**Total_Count**	**Normalized_Value**
hsa-miR-16-5p	99	5.3031
hsa-miR-92a-3p	31	16.957612
hsa-miR-221-5p	26	1.3927
hsa-miR-182-5p	4814	257.8701
hsa-miR-320a	2528	135.4166
hsa-miR-361-3p	222	11.8918
hsa-miR-20a-5p	1172	62.7802
hsa-miR-152-3p	650	34.8184
hsa-miR-516a-5p	32	1.7141
hsa-let-7i-5p	70993	3802.861
hsa-let-7g-5p	10444	559.4507
hsa-let-7f-5p	98404	5271.178
hsa-let-7a-5p	35131	1881.8519
hsa-miR-222-3p	464	24.855
hsa-miR-4497	1264	67.7083
hsa-miR-584-5p	131	7.0172
hsa-miR-574-3p	98	5.2495
hsa-miR-582-3p	1240	66.4227
hsa-miR-4746-5p	34	1.8213
hsa-miR-30b-5p	23	1.232
hsa-miR-10a-5p	8727	467.4766
hsa-miR-423-3p	2218	118.8109
hsa-miR-24-2-5p	107	5.7316
hsa-miR-203a-3p	273	14.6237
hsa-miR-1246	638174	34184.8779
hsa-miR-7706	282	15.1058
hsa-miR-3934-5p	36	1.9284
hsa-miR-98-5p	1049	56.1915
hsa-miR-15b-3p	35	1.8748
hsa-miR-335-5p	20	1.0713
hsa-miR-335-3p	340	18.2127
hsa-miR-1307-3p	778	41.6749
hsa-miR-425-5p	59	3.1604
hsa-miR-194-5p	25	1.3392
hsa-miR-1304-3p	74	3.9639
hsa-miR-7704	2167	116.079
hsa-miR-17-5p	251	13.4452
hsa-miR-3656	85	4.5532
hsa-miR-5701	142	7.6065
hsa-miR-31-5p	28	1.4999
hsa-miR-1273g-3p	43	2.3034
hsa-miR-95-3p	397	21.266
hsa-miR-1255a	31	1.6606
hsa-miR-548o-3p	99	5.3031
hsa-miR-365b-3p	192	10.2848
hsa-miR-1301-3p	38	2.0355
hsa-miR-378d	32	1.7141
hsa-miR-374a-3p	99	5.3031
hsa-miR-26b-5p	600	32.14
hsa-miR-378g	35	1.8748
hsa-miR-30e-3p	1998	107.0263
hsa-miR-331-3p	20	1.0713
hsa-miR-19a-3p	37	1.982
hsa-miR-486-5p	246	13.1774
hsa-miR-941	7223	386.9123
hsa-miR-106b-3p	1981	106.1156
hsa-miR-501-3p	89	4.7674
hsa-miR-26a-5p	6808	364.6821
hsa-miR-140-3p	371	19.8732
hsa-miR-193a-5p	72	3.8568
hsa-miR-1283	56	2.9997
hsa-miR-129-5p	160	8.5707
hsa-miR-1180-3p	141	7.5529
hsa-let-7d-3p	457	24.48
hsa-miR-93-5p	293	15.695

hsa-miR-181a-5p	119	6.5491
hsa-miR-181b-5p	86	4.733
hsa-miR-181d-5p	29	1.596
hsa-miR-182-5p	4624	254.4788
hsa-miR-183-5p	1846	101.5934
hsa-miR-185-5p	345	18.9868
hsa-miR-186-5p	201	11.0619
hsa-miR-191-5p	636	35.0018
hsa-miR-192-5p	1419	78.0937
hsa-miR-193a-5p	18	0.9906
hsa-miR-193b-3p	29	1.596
hsa-miR-194-5p	26	1.4309
hsa-miR-196a-5p	1586	87.2845
hsa-miR-196b-5p	161	8.8605
hsa-miR-197-3p	75	4.1276
hsa-miR-199a-3p	21	1.1557
hsa-miR-199b-3p	21	1.1557
hsa-miR-19a-3p	42	2.3114
hsa-miR-19b-3p	45	2.4765
hsa-miR-200b-3p	42	2.3114
hsa-miR-200c-3p	36	1.9812
hsa-miR-203a-3p	92	5.0632
hsa-miR-20a-5p	618	34.0112
hsa-miR-210-3p	60	3.3021
hsa-miR-212-5p	43	2.3665
hsa-miR-215-5p	28	1.541
hsa-miR-21-5p	35446	1950.7475
hsa-miR-218-5p	15	0.8255
hsa-miR-221-3p	362	19.9224
hsa-miR-221-5p	31	1.7061
hsa-miR-222-3p	205	11.282
hsa-miR-22-3p	72	3.9625
hsa-miR-224-5p	1310	72.095
hsa-miR-23a-3p	596	32.8005
hsa-miR-23b-3p	307	16.8955
hsa-miR-24-2-5p	61	3.3571
hsa-miR-24-3p	942	51.8424
hsa-miR-25-3p	1729	95.1544
hsa-miR-26a-5p	2410	132.6328
hsa-miR-26b-5p	338	18.6016
hsa-miR-27a-3p	321	17.666
hsa-miR-27b-3p	1157	63.6747
hsa-miR-27b-5p	10	0.5503
hsa-miR-28-3p	463	25.4809
hsa-miR-28-5p	14	0.7705
hsa-miR-29a-3p	162	8.9156
hsa-miR-29b-3p	13	0.7154
hsa-miR-3065-5p	12	0.6604
hsa-miR-30a-3p	1149	63.2345
hsa-miR-30a-5p	3126	172.0374
hsa-miR-30b-5p	16	0.8805
hsa-miR-30c-2-3p	84	4.6229
hsa-miR-30c-5p	881	48.4853
hsa-miR-30d-5p	2837	156.1324
hsa-miR-30e-3p	550	30.2689
hsa-miR-30e-5p	74	4.0725
hsa-miR-3135b	24	1.3208
hsa-miR-3195	14	0.7705
hsa-miR-3196	22	1.2108
hsa-miR-320a	1569	86.3489
hsa-miR-320b	57	3.137
hsa-miR-320c	71	3.9074
hsa-miR-320d	65	3.5772
hsa-miR-32-5p	30	1.651
hsa-miR-328-3p	13	0.7154
hsa-miR-330-3p	177	9.7411
hsa-miR-331-3p	15	0.8255
hsa-miR-335-3p	76	4.1826

hsa-miR-320b	271	14.5166
hsa-miR-132-3p	214	11.4633
hsa-miR-132-5p	58	3.1069
hsa-miR-148a-3p	13493	722.7755
hsa-miR-30d-5p	4467	239.2825
hsa-miR-125a-5p	894	47.8886
hsa-miR-125b-5p	444	23.7836
hsa-miR-30c-5p	1967	105.3657
hsa-miR-99b-5p	3626	194.2329
hsa-miR-345-5p	34	1.8213
hsa-miR-125b-1-3p	58	3.1069
hsa-miR-32-5p	54	2.8926
hsa-miR-183-5p	4247	227.4978
hsa-miR-320c	321	17.1949
hsa-miR-105-5p	175	9.3742
hsa-let-7f-1-3p	39	2.0891
hsa-miR-1-3p	39	2.0891
hsa-miR-200b-3p	95	5.0888
hsa-miR-424-3p	102	5.4638
hsa-miR-149-5p	93	4.9817
hsa-miR-193b-3p	75	4.0175
hsa-miR-197-3p	237	12.6953
hsa-miR-532-5p	1930	103.3837
hsa-miR-4516	130	6.9637
hsa-miR-340-5p	96	5.1424
hsa-miR-338-5p	56	2.9997
hsa-miR-21-5p	112217	6011.0948
hsa-miR-130a-3p	29	1.5534
hsa-miR-185-5p	945	50.6205
hsa-miR-30e-5p	71	3.8032
hsa-miR-23b-3p	455	24.3729
hsa-miR-4508	149	7.9814
hsa-miR-30a-5p	3542	189.7333
hsa-let-7d-5p	1647	88.2244
hsa-miR-1290	71	3.81395
hsa-miR-342-3p	131	7.0172
hsa-miR-27b-3p	2975	159.3609
hsa-miR-99a-5p	4345	232.7473
hsa-miR-25-3p	6441	345.0231
hsa-miR-181a-2-3p	82	4.40854
hsa-miR-191-5p	806	43.1748
hsa-let-7c-5p	3362	180.0913
hsa-miR-1261	21	1.1249
hsa-miR-23a-3p	1184	63.423
hsa-miR-340-3p	28	1.4999
hsa-miR-320d	335	17.9448
hsa-miR-140-5p	25	1.3392
hsa-miR-450a-5p	23	1.232
hsa-miR-196a-5p	3116	166.9139
hsa-let-7b-5p	6766	362.4323
hsa-miR-3135b	32	1.7141
hsa-miR-130b-5p	203	10.874
hsa-miR-92b-3p	2646	141.7375
hsa-miR-7-5p	6443	345.1303
hsa-miR-103a-3p	1193	63.9051
hsa-miR-330-3p	161	8.6242
hsa-miR-21-3p	43	2.3034
hsa-miR-451a	28	1.4999
hsa-miR-760	40	2.1427
hsa-miR-378a-3p	3876	207.6245
hsa-miR-744-5p	110	5.8923
hsa-let-7a-3p	144	7.7136
hsa-miR-22-3p	132	7.0708
hsa-miR-210-3p	62	3.3211
hsa-miR-19b-3p	24	1.2856
hsa-miR-186-5p	377	20.1946
hsa-miR-502-3p	29	1.5534
hsa-miR-629-5p	181	9.6956

hsa-miR-338-5p	29	1.596
hsa-miR-340-5p	38	2.0913
hsa-miR-342-3p	145	7.98
hsa-miR-345-5p	13	0.7154
hsa-miR-34a-5p	11	0.6054
hsa-miR-361-3p	126	6.9343
hsa-miR-3615	27	1.4859
hsa-miR-361-5p	16	0.8805
hsa-miR-3656	60	3.3021
hsa-miR-365a-3p	157	8.6404
hsa-miR-365b-3p	157	8.6404
hsa-miR-374a-3p	59	3.247
hsa-miR-374a-5p	22	1.2108
hsa-miR-374b-5p	79	4.3477
hsa-miR-378a-3p	1268	69.7836
hsa-miR-378f	14	0.7705
hsa-miR-3934-5p	17	0.9356
hsa-miR-3960	12	0.6604
hsa-miR-421	19	1.0457
hsa-miR-423-3p	605	33.2958
hsa-miR-423-5p	236	12.9881
hsa-miR-425-5p	182	10.0163
hsa-miR-4488	116	6.384
hsa-miR-4492	21	1.1557
hsa-miR-4497	220	12.1076
hsa-miR-4508	29	1.596
hsa-miR-450b-5p	42	2.3114
hsa-miR-4516	119	6.5491
hsa-miR-451a	12	0.6604
hsa-miR-452-5p	238	13.0982
hsa-miR-454-3p	30	1.651
hsa-miR-455-3p	11	0.6054
hsa-miR-455-5p	47	2.5866
hsa-miR-4634	10	0.5503
hsa-miR-4664-3p	26	1.4309
hsa-miR-484	105	5.7786
hsa-miR-486-5p	947	52.1175
hsa-miR-500a-3p	42	2.3114
hsa-miR-501-3p	25	1.3759
hsa-miR-505-3p	11	0.6054
hsa-miR-516a-5p	11	0.6054
hsa-miR-522-3p	70	3.8524
hsa-miR-532-5p	593	32.6354
hsa-miR-548e-3p	10	0.5503
hsa-miR-548o-3p	73	4.0175
hsa-miR-5701	48	2.6416
hsa-miR-574-3p	45	2.4765
hsa-miR-576-3p	33	1.8161
hsa-miR-582-3p	425	23.3896
hsa-miR-584-5p	31	1.7061
hsa-miR-589-5p	136	7.4847
hsa-miR-615-3p	8	0.41276
hsa-miR-619-5p	18	0.9906
hsa-miR-625-3p	11	0.6054
hsa-miR-629-5p	49	2.6967
hsa-miR-641	12	0.6604
hsa-miR-651-5p	22	1.2108
hsa-miR-6516-3p	25	1.3759
hsa-miR-664a-3p	26	1.4309
hsa-miR-671-3p	23	1.2658
hsa-miR-744-5p	35	1.9262
hsa-miR-7-5p	10799	594.3159
hsa-miR-7641	23832	1311.5785
hsa-miR-767-5p	25	1.3759
hsa-miR-769-5p	39	2.1463
hsa-miR-7704	197	10.8418
hsa-miR-7706	66	3.6323
hsa-miR-92a-3p	53	2.928378

hsa-miR-15b-5p	58	3.1069
hsa-miR-200c-3p	82	4.3925
hsa-miR-589-5p	294	15.7486
hsa-miR-6130	24	1.2856
hsa-miR-18a-3p	22	1.1785
hsa-miR-96-5p	275	14.7308
hsa-miR-181d-5p	55	2.9462
hsa-miR-3196	31	1.6606
hsa-miR-3195	124	6.6423
hsa-miR-181a-5p	308	16.4985
hsa-miR-16-2-3p	305	16.3378
hsa-miR-450b-5p	111	5.9459
hsa-miR-374a-5p	42	2.2498
hsa-miR-30c-2-3p	183	9.8027
hsa-miR-192-5p	3458	185.2337
hsa-miR-106b-5p	27	1.4463
hsa-miR-151a-5p	32	1.7141
hsa-miR-1281	23	1.232
hsa-miR-651-5p	36	1.9284
hsa-miR-28-3p	1758	94.1703
hsa-miR-143-3p	521	27.9083
hsa-miR-29a-3p	385	20.6232
hsa-miR-4488	261	13.9809
hsa-miR-455-3p	39	2.0891
hsa-miR-101-3p	493	26.4084
hsa-miR-125b-2-3p	56	2.9997
hsa-let-7b-3p	860	46.067
hsa-miR-484	263	14.088
hsa-miR-330-5p	23	1.232
hsa-let-7e-5p	575	30.8009
hsa-miR-215-5p	61	3.2676
hsa-miR-421	21	1.1249
hsa-miR-146b-5p	103	5.5174
hsa-miR-199b-3p	19	1.0178
hsa-miR-625-3p	52	2.7855
hsa-miR-181b-5p	256	13.7131
hsa-miR-128-3p	3116	166.9139
hsa-miR-122-5p	88	4.7139
hsa-miR-106a-5p	50	2.6783
hsa-miR-22-5p	21	1.1249
hsa-miR-27b-5p	22	1.1785
hsa-miR-522-3p	143	7.66
hsa-miR-10b-5p	1470	78.7431
hsa-miR-199a-3p	19	1.0178
hsa-miR-3615	149	7.9814
hsa-miR-455-5p	105	5.6245
hsa-miR-671-3p	101	5.4102
hsa-miR-374b-5p	73	3.9104
hsa-miR-148b-3p	1168	62.5659
hsa-miR-4664-3p	68	3.6425
hsa-miR-99b-3p	284	15.2129
hsa-miR-196b-5p	166	8.8921
hsa-miR-542-3p	34	1.8213
hsa-miR-454-3p	21	1.1249
hsa-miR-500a-3p	105	5.6245
hsa-miR-135b-5p	23	1.232
hsa-miR-4448	41	2.1962
hsa-miR-576-3p	44	2.3569
hsa-miR-361-5p	54	2.8926
hsa-miR-139-5p	43	2.3034
hsa-miR-769-5p	73	3.9104
hsa-miR-7641	34912	1870.1208
hsa-miR-100-5p	39358	2108.2783
hsa-miR-767-5p	46	2.4641
hsa-miR-4492	83	4.446
hsa-miR-126-3p	417	22.3373
hsa-miR-212-5p	137	7.3386
hsa-miR-151a-3p	16153	865.263

hsa-miR-92b-3p	301	16.5653
hsa-miR-93-5p	286	15.7398
hsa-miR-941	1932	106.3264
hsa-miR-95-3p	162	8.9156
hsa-miR-96-5p	239	13.1532
hsa-miR-98-3p	22	1.2108
hsa-miR-98-5p	591	32.5253
hsa-miR-99a-5p	1466	80.6804
hsa-miR-99b-3p	84	4.6229
hsa-miR-99b-5p	940	51.7323

hsa-miR-221-3p	628	33.6399
hsa-miR-615-3p	62	3.32114
hsa-miR-224-5p	5314	284.6535
hsa-miR-452-5p	329	17.6234
hsa-miR-423-5p	588	31.4972
hsa-miR-28-5p	42	2.2498
hsa-miR-27a-3p	1378	73.8149
hsa-miR-30a-3p	3788	202.9107
hsa-miR-365a-3p	192	10.2848
hsa-miR-24-3p	2800	149.9868
hsa-miR-148b-5p	19	1.0178
hsa-miR-29b-3p	18	0.9642
hsa-miR-219a-1-3p	18	0.9642
hsa-miR-125a-3p	18	0.9642
hsa-miR-576-5p	18	0.9642
hsa-miR-454-5p	18	0.9642
hsa-miR-1291	18	0.9642
hsa-miR-664a-5p	18	0.9642
hsa-miR-92b-5p	17	0.9106
hsa-miR-1254	17	0.9106
hsa-miR-93-3p	16	0.8571
hsa-miR-107	16	0.8571
hsa-miR-519c-5p	16	0.8571
hsa-miR-519b-5p	16	0.8571
hsa-miR-523-5p	16	0.8571
hsa-miR-518e-5p	16	0.8571
hsa-miR-522-5p	16	0.8571
hsa-miR-519a-5p	16	0.8571
hsa-miR-942-5p	16	0.8571
hsa-miR-378f	16	0.8571
hsa-miR-4791	16	0.8571
hsa-miR-6747-3p	16	0.8571
hsa-miR-98-3p	15	0.8035
hsa-miR-422a	15	0.8035
hsa-miR-548e-3p	15	0.8035
hsa-miR-1248	15	0.8035
hsa-miR-2110	15	0.8035
hsa-miR-3622a-5p	15	0.8035
hsa-miR-331-5p	14	0.7499
hsa-miR-652-3p	14	0.7499
hsa-miR-1303	14	0.7499
hsa-miR-4485-3p	14	0.7499
hsa-miR-23b-5p	13	0.6964
hsa-miR-339-3p	13	0.6964
hsa-miR-505-3p	13	0.6964
hsa-miR-3690	13	0.6964
hsa-miR-378e	13	0.6964
hsa-miR-4677-3p	13	0.6964
hsa-miR-218-5p	12	0.6428
hsa-miR-126-5p	12	0.6428
hsa-miR-328-3p	12	0.6428
hsa-miR-1827	12	0.6428
hsa-miR-548aq-3p	12	0.6428
hsa-miR-6720-3p	12	0.6428
hsa-miR-9-5p	11	0.5892
hsa-miR-185-3p	11	0.5892
hsa-miR-324-3p	11	0.5892
hsa-miR-532-3p	11	0.5892
hsa-miR-641	11	0.5892
hsa-miR-1250-5p	11	0.5892
hsa-miR-664a-3p	11	0.5892
hsa-miR-3065-5p	11	0.5892
hsa-miR-3960	11	0.5892
hsa-miR-4661-5p	11	0.5892
hsa-miR-30d-3p	10	0.5357
hsa-miR-10a-3p	10	0.5357
hsa-miR-146a-5p	10	0.5357
hsa-miR-130b-3p	10	0.5357

hsa-miR-338-3p	10	0.5357
hsa-miR-409-3p	10	0.5357
hsa-miR-675-3p	10	0.5357
hsa-miR-320e	10	0.5357
hsa-miR-4326	10	0.5357
hsa-miR-3928-3p	10	0.5357
hsa-miR-548ah-3p	10	0.5357
hsa-miR-4634	10	0.5357

Table S5 miRNA with significantly different expression levels between Ex and Fn-Ex.

miRNA_ID	Ex (normalized value)	Fn-Ex(normalized value)	up/down	log2(foldchange)	P-value
hsa-miR-1248	7.2095	0.8035	down	-3.1655	1.91E-07
hsa-miR-6516-3p	1.3759	0	down	-7.1042	9.48E-06
hsa-miR-619-5p	0.9906	0	down	-6.6302	7.45E-05
hsa-miR-425-5p	10.0163	3.1604	down	-1.6642	0.000154
hsa-miR-127-3p	0.7154	0	down	-6.1607	0.00053
hsa-miR-34a-5p	0.6054	0	down	-5.9198	0.001409
hsa-miR-145-5p	0.5503	0	down	-5.7821	0.001996
hsa-miR-1291	2.2014	0.9642	down	-1.191	0.003964
hsa-miR-664a-3p	1.4309	0.5892	down	-1.2801	0.008158
hsa-miR-486-5p	13.1774	52.1175	up	1.9837	1.47E-05
hsa-miR-424-3p	0	5.4638	up	9.0938	3.19E-07
hsa-miR-21-3p	0	2.3034	up	7.8476	0.000157
hsa-miR-760	0	2.1427	up	7.7433	0.000244
hsa-miR-4448	0	2.1962	up	7.7789	0.000244
hsa-miR-542-3p	0	1.8213	up	7.5088	0.000622
hsa-miR-378g	0	1.8748	up	7.5506	0.000622
hsa-miR-4746-5p	0	1.8213	up	7.5088	0.000622
hsa-miR-7704	10.8418	116.079	up	3.4204	0.000857
hsa-miR-450a-5p	0	1.232	up	6.9449	0.001006
hsa-miR-330-5p	0	1.232	up	6.9449	0.001006
hsa-miR-135b-5p	0	1.232	up	6.9449	0.001006
hsa-miR-1281	0	1.232	up	6.9449	0.001006
hsa-miR-151a-5p	0	1.7141	up	7.4213	0.001028
hsa-miR-378d	0	1.7141	up	7.4213	0.001028
hsa-miR-18a-3p	0	1.1785	up	6.8808	0.001409
hsa-miR-1261	0	1.1249	up	6.8137	0.001409
hsa-miR-22-5p	0	1.1249	up	6.8137	0.001409
hsa-miR-31-5p	0	1.4999	up	7.2287	0.001744
hsa-miR-340-3p	0	1.4999	up	7.2287	0.001744
hsa-miR-502-3p	0	1.5534	up	7.2793	0.001744
hsa-miR-335-5p	0	1.0713	up	6.7432	0.001996
hsa-miR-125a-3p	0	0.9642	up	6.5913	0.002864
hsa-miR-576-5p	0	0.9642	up	6.5913	0.002864
hsa-miR-454-5p	0	0.9642	up	6.5913	0.002864
hsa-miR-148b-5p	0	1.0178	up	6.6693	0.002864
hsa-miR-664a-5p	0	0.9642	up	6.5913	0.002864
hsa-miR-219a-1-3p	0	0.9642	up	6.5913	0.002864
hsa-miR-92b-3p	16.5653	141.7375	up	3.097	0.003633
hsa-miR-6130	0	1.2856	up	7.0063	0.004066
hsa-miR-92b-5p	0	0.9106	up	6.5087	0.004166
hsa-miR-519a-5p	0	0.8571	up	6.4214	0.006149
hsa-miR-422a	0	0.8035	up	6.3282	0.006149
hsa-miR-6747-3p	0	0.8571	up	6.4214	0.006149
hsa-miR-518e-5p	0	0.8571	up	6.4214	0.006149
hsa-miR-615-3p	0.41276	3.2114	up	3.0083	0.006575
hsa-miR-3615	1.4859	7.9814	up	2.4253	0.007351
hsa-let-7d-3p	4.843	24.48	up	2.3376	0.007357
hsa-miR-320d	3.5772	17.9448	up	2.3267	0.008072
hsa-miR-4485-3p	0	0.7499	up	6.2286	0.009224
hsa-miR-1303	0	0.7499	up	6.2286	0.009224
hsa-miR-652-3p	0	0.7499	up	6.2286	0.009224
hsa-miR-331-5p	0	0.7499	up	6.2286	0.009224
hsa-miR-27a-3p	185.1906	865.263	up	2.2241	0.00923
hsa-miR-4508	1.596	7.9814	up	2.3222	0.009773
hsa-miR-3195	0.7705	6.6423	up	3.1078	0.011498
hsa-miR-1307-3p	424.7551	1881.8519	up	2.1474	0.011623
hsa-miR-320b	3.137	14.5166	up	2.2102	0.011661
hsa-miR-128-3p	38.0287	166.9139	up	2.1339	0.012266
hsa-miR-125b-2-3p	0.5503	2.9997	up	2.4465	0.01307
hsa-miR-130b-5p	2.4215	10.874	up	2.1669	0.013488
hsa-miR-320c	3.9074	17.1949	up	2.1377	0.013557
hsa-miR-4677-3p	0	0.6964	up	6.1218	0.014079
hsa-miR-339-3p	0	0.6964	up	6.1218	0.014079
hsa-miR-3690	0	0.6964	up	6.1218	0.014079
hsa-miR-378e	0	0.6964	up	6.1218	0.014079
hsa-miR-23b-5p	0	0.6964	up	6.1218	0.014079

hsa-miR-335-3p	4.1826	18.2127	up	2.1225	0.014249
hsa-miR-151a-3p	17.666	73.8149	up	2.0629	0.015305
hsa-miR-7706	3.6323	15.1058	up	2.0561	0.017318
hsa-miR-1290	0.5503	3.81395	up	2.7363	0.017994
hsa-let-7a-5p	10.7867	41.6749	up	1.9499	0.018158
hsa-miR-21-5p	1950.7475	6011.0948	up	1.6236	0.018331
hsa-miR-16-2-3p	4.0175	16.3378	up	2.0238	0.018517
hsa-miR-224-5p	72.095	284.6535	up	1.9812	0.018688
hsa-miR-221-5p	69.7836	207.6245	up	1.573	0.019129
hsa-miR-671-3p	1.2658	5.4102	up	2.0956	0.01997
hsa-miR-185-3p	0	0.5892	up	5.8807	0.0219
hsa-miR-1250-5p	0	0.5892	up	5.8807	0.0219
hsa-miR-9-5p	0	0.5892	up	5.8807	0.0219
hsa-miR-548aq-3p	0	0.6428	up	6.0063	0.0219
hsa-miR-1246	5902.2135	34184.8779	up	2.534	0.032506
hsa-miR-92a-3p	2.928378	16.957612	up	2.5338	0.032625
hsa-miR-181a-2-3p	0.7154	4.40854	up	2.5477	0.034755
hsa-miR-10a-3p	0	0.5357	up	5.7434	0.034783
hsa-miR-3928-3p	0	0.5357	up	5.7434	0.034783
hsa-miR-130b-3p	0	0.5357	up	5.7434	0.034783
hsa-miR-675-3p	0	0.5357	up	5.7434	0.034783
hsa-miR-409-3p	0	0.5357	up	5.7434	0.034783
hsa-miR-548ah-3p	0	0.5357	up	5.7434	0.034783
hsa-miR-4497	12.1076	67.7083	up	2.4834	0.041802
hsa-let-7b-3p	7.154	46.067	up	2.6869	0.04954

Table S6 GSK3β was predicted as a putative miR-1246/27a-3p/92a-3p target through analysis of 4 public prediction databases.

miRNA	**Gene**	**miRDB**	**miRTarBase**	**miRWalk**	**TargetScan**
hsa-miR-1246	GSK3β	0	0	1	1
hsa-miR-27a-3p	GSK3β	1	0	1	1
hsa-miR-92b-3p	GSK3β	0	1	1	0

Table S7 Protein expression profile characteristic to Ex and Fn-Ex.

Ex		Fn-Ex	
Accession	Description	Accession	Description
P98160	Basement membrane-specific heparan sulfate proteoglycan core protein [OS=Homo sapiens]	P98160	Basement membrane-specific heparan sulfate proteoglycan core protein [OS=Homo sapiens]
P01023	alpha-2-macroglobulin [OS=Homo sapiens]	Q08380	Galectin-3-binding protein [OS=Homo sapiens]
P02675	Fibrinogen beta chain [OS=Homo sapiens]	P60709	Actin, cytoplasmic 1 [OS=Homo sapiens]
P02671-1	Fibrinogen alpha chain [OS=Homo sapiens]	P62805	histone H4 [OS=Homo sapiens]
P04114	apolipoprotein B-100 [OS=Homo sapiens]	P62736	Actin, aortic smooth muscle [OS=Homo sapiens]
P02787	Serotransferrin [OS=Homo sapiens]	P01023	alpha-2-macroglobulin [OS=Homo sapiens]
P21333	Filamin-A [OS=Homo sapiens]	P10909-2	Isoform 2 of Clusterin [OS=Homo sapiens]
Q9Y490	Talin-1 [OS=Homo sapiens]	P11142-1	Heat shock cognate 71 kDa protein [OS=Homo sapiens]
P02679-2	Isoform Gamma-A of Fibrinogen gamma chain [OS=Homo sapiens]	P16402	Histone H1.3 [OS=Homo sapiens]
P0DOX5	immunoglobulin gamma-1 heavy chain [OS=Homo sapiens]	Q5QNW6-2	Isoform 2 of Histone H2B type 2-F [OS=Homo sapiens]
P35579-1	Myosin-9 [OS=Homo sapiens]	Q8WUM4-2	Isoform 2 of Programmed cell death 6-interacting protein [OS=Homo sapiens]
P0C0L4-1	Complement C4-A [OS=Homo sapiens]	P23527	Histone H2B type 1-O [OS=Homo sapiens]
P02751	fibronectin [OS=Homo sapiens]	P63104-1	14-3-3 protein zeta/delta [OS=Homo sapiens]
P60709	Actin, cytoplasmic 1 [OS=Homo sapiens]	P62979	Ubiquitin-40S ribosomal protein S27a [OS=Homo sapiens]
Q08380	Galectin-3-binding protein [OS=Homo sapiens]	P0C0S8	histone H2A type 1 [OS=Homo sapiens]
P01859	Immunoglobulin heavy constant gamma 2 [OS=Homo sapiens]	P08238	Heat shock protein HSP 90-beta [OS=Homo sapiens]
Q8WUM4	Programmed cell death 6-interacting protein [OS=Homo sapiens]	Q9P2B2	prostaglandin F2 receptor negative regulator [OS=Homo sapiens]
Q14517	Protocadherin Fat 1 [OS=Homo sapiens]	P02533	Keratin, type I cytoskeletal 14 [OS=Homo sapiens]
Q00610-1	Clathrin heavy chain 1 [OS=Homo sapiens]	P01024	Complement C3 [OS=Homo sapiens]
P01871-2	Isoform 2 of Immunoglobulin heavy constant mu [OS=Homo sapiens]	Q93077	Histone H2A type 1-C [OS=Homo sapiens]
P01860	Immunoglobulin heavy constant gamma 3 [OS=Homo sapiens]	P04083	annexin A1 [OS=Homo sapiens]
P00450	Ceruloplasmin [OS=Homo sapiens]	P06733-1	alpha-enolase [OS=Homo sapiens]
Q9P2B2	prostaglandin F2 receptor negative regulator [OS=Homo sapiens]	Q14517	Protocadherin Fat 1 [OS=Homo sapiens]
P62805	histone H4 [OS=Homo sapiens]	P39060-3	Collagen alpha-1(XVIII) chain [OS=Homo sapiens]
P02774-3	Isoform 3 of Vitamin D-binding protein [OS=Homo sapiens]	P07996	thrombospondin-1 [OS=Homo sapiens]
P01876	immunoglobulin heavy constant alpha 1 [OS=Homo sapiens]	P02787	Serotransferrin [OS=Homo sapiens]
P01834	immunoglobulin kappa constant [OS=Homo sapiens]	Q99715-1	Collagen alpha-1(XII) chain [OS=Homo sapiens]
P0DOX7	immunoglobulin kappa light chain [OS=Homo sapiens]	P0DMV8	heat shock 70 kDa protein 1A [OS=Homo sapiens]
P68032	Actin, alpha cardiac muscle 1 [OS=Homo sapiens]	P07900-2	Isoform 2 of Heat shock protein HSP 90-alpha [OS=Homo sapiens]
P01009-1	alpha-1-antitrypsin [OS=Homo sapiens]	P16422	Epithelial cell adhesion molecule [OS=Homo sapiens]
P08238	Heat shock protein HSP 90-beta [OS=Homo sapiens]	O94907	Dickkopf-related protein 1 [OS=Homo sapiens]
P07996	thrombospondin-1 [OS=Homo sapiens]	P18065	Insulin-like growth factor-binding protein 2 [OS=Homo sapiens]
P00738	Haptoglobin [OS=Homo sapiens]	O00391	Sulfhydryl oxidase 1 [OS=Homo sapiens]
Q08431	Lactadherin [OS=Homo sapiens]	P14618	Pyruvate kinase PKM [OS=Homo sapiens]
P01861	Immunoglobulin heavy constant gamma 4 [OS=Homo sapiens]	P08779	Keratin, type I cytoskeletal 16 [OS=Homo sapiens]
P02647	Apolipoprotein A-I [OS=Homo sapiens]	P62241	40S ribosomal protein S8 [OS=Homo sapiens]
P00747	Plasminogen [OS=Homo sapiens]	Q06830	peroxiredoxin-1 [OS=Homo sapiens]
P19823	Inter-alpha-trypsin inhibitor heavy chain H2 [OS=Homo sapiens]	P68431	Histone H3.1 [OS=Homo sapiens]
P14618	Pyruvate kinase PKM [OS=Homo sapiens]	P00749	Urokinase-type plasminogen activator [OS=Homo sapiens]
P06396	Gelsolin [OS=Homo sapiens]	P68363	Tubulin alpha-1B chain [OS=Homo sapiens]
P11142-1	Heat shock cognate 71 kDa protein [OS=Homo sapiens]	P02774-3	Isoform 3 of Vitamin D-binding protein [OS=Homo sapiens]
P04406-1	glyceraldehyde-3-phosphate dehydrogenase [OS=Homo sapiens]	P02765	Alpha-2-HS-glycoprotein [OS=Homo sapiens]
P07437	tubulin beta chain [OS=Homo sapiens]	P07355-2	Isoform 2 of Annexin A2 [OS=Homo sapiens]
O14672	Disintegrin and metalloproteinase domain-containing protein 10 [OS=Homo sapiens]	P05556-1	Integrin beta-1 [OS=Homo sapiens]
P07900-2	Isoform 2 of Heat shock protein HSP 90-alpha [OS=Homo sapiens]	P01034	Cystatin-C [OS=Homo sapiens]
Q99715-1	Collagen alpha-1(XII) chain [OS=Homo sapiens]	P04406-1	glyceraldehyde-3-phosphate dehydrogenase [OS=Homo sapiens]
P04003	C4b-binding protein alpha chain [OS=Homo sapiens]	P17987	T-complex protein 1 subunit alpha [OS=Homo sapiens]
P68371	Tubulin beta-4B chain [OS=Homo sapiens]	P07195	L-lactate dehydrogenase B chain [OS=Homo sapiens]
P68366	Tubulin alpha-4A chain [OS=Homo sapiens]	P12109	Collagen alpha-1(VI) chain [OS=Homo sapiens]
Q9BQE3	Tubulin alpha-1C chain [OS=Homo sapiens]	P48643	T-complex protein 1 subunit epsilon [OS=Homo sapiens]
P69905	Hemoglobin subunit alpha [OS=Homo sapiens]	P20742	Pregnancy zone protein [OS=Homo sapiens]
Q13748-1	tubulin alpha-3C/D chain [OS=Homo sapiens]	P08727	Keratin, type I cytoskeletal 19 [OS=Homo sapiens]
P0DOY2	immunoglobulin lambda constant 2 [OS=Homo sapiens]	P62280	40S ribosomal protein S11 [OS=Homo sapiens]
P13639	Elongation factor 2 [OS=Homo sapiens]	P16035	Metalloproteinase inhibitor 2 [OS=Homo sapiens]
P00734	Prothrombin [OS=Homo sapiens]	P02545	Prelamin-A/C [OS=Homo sapiens]
P05556-1	Integrin beta-1 [OS=Homo sapiens]	P05787-2	Isoform 2 of Keratin, type II cytoskeletal 8 [OS=Homo sapiens]
P78371-1	T-complex protein 1 subunit beta [OS=Homo sapiens]	P01860	Immunoglobulin heavy constant gamma 3 [OS=Homo sapiens]
Q6FI13	Histone H2A type 2-A [OS=Homo sapiens]	P01859	Immunoglobulin heavy constant gamma 2 [OS=Homo sapiens]
Q5QNW6-2	Isoform 2 of Histone H2B type 2-F [OS=Homo sapiens]	P29692-2	Isoform 2 of Elongation factor 1-delta [OS=Homo sapiens]
P20742	Pregnancy zone protein [OS=Homo sapiens]	P68104	Elongation factor 1-alpha 1 [OS=Homo sapiens]
P05787-2	Isoform 2 of Keratin, type II cytoskeletal 8 [OS=Homo sapiens]	P02679	Fibrinogen gamma chain [OS=Homo sapiens]
P10909-2	Isoform 2 of Clusterin [OS=Homo sapiens]	Q86X29	Lipolysis-stimulated lipoprotein receptor [OS=Homo sapiens]
P12109	Collagen alpha-1(VI) chain [OS=Homo sapiens]	P05452	Tetranectin [OS=Homo sapiens]
Q92626	peroxidasin homolog [OS=Homo sapiens]	P15311	Ezrin [OS=Homo sapiens]
P60033	CD81 antigen [OS=Homo sapiens]	O00560-1	Syntenin-1 [OS=Homo sapiens]
P00338-3	Isoform 3 of L-lactate dehydrogenase A chain [OS=Homo sapiens]	Q14764	major vault protein [OS=Homo sapiens]
P07355-2	Isoform 2 of Annexin A2 [OS=Homo sapiens]	P04075-2	Isoform 2 of Fructose-bisphosphate aldolase A [OS=Homo sapiens]
P16402	Histone H1.3 [OS=Homo sapiens]	P01861	Immunoglobulin heavy constant gamma 4 [OS=Homo sapiens]
P49327	Fatty acid synthase [OS=Homo sapiens]	P69905	Hemoglobin subunit alpha [OS=Homo sapiens]
P39060-3	Collagen alpha-1(XVIII) chain [OS=Homo sapiens]	O43240	Kallikrein-10 [OS=Homo sapiens]
O00560-1	Syntenin-1 [OS=Homo sapiens]	P0DOY3	immunoglobulin lambda constant 3 [OS=Homo sapiens]
P26006-1	Isoform 2 of Integrin alpha-3 [OS=Homo sapiens]	P21741	Midkine [OS=Homo sapiens]
P68871	Hemoglobin subunit beta [OS=Homo sapiens]	P50990	T-complex protein 1 subunit theta [OS=Homo sapiens]
O94985-1	Calsyntenin-1 [OS=Homo sapiens]	P00738	Haptoglobin [OS=Homo sapiens]
P08514-1	integrin alpha-IIb [OS=Homo sapiens]	P09429	High mobility group protein B1 [OS=Homo sapiens]
P23527	Histone H2B type 1-O [OS=Homo sapiens]	P49368-1	T-complex protein 1 subunit gamma [OS=Homo sapiens]
P19827-1	Inter-alpha-trypsin inhibitor heavy chain H1 [OS=Homo sapiens]	Q99988	Growth/differentiation factor 15 [OS=Homo sapiens]
P0DOX8	Immunoglobulin lambda-1 light chain [OS=Homo sapiens]	P35579-1	Myosin-9 [OS=Homo sapiens]
Q04695	Keratin, type I cytoskeletal 17 [OS=Homo sapiens]	P0DOX5	immunoglobulin gamma-1 heavy chain [OS=Homo sapiens]
P13010	X-ray repair cross-complementing protein 5 [OS=Homo sapiens]	Q9GZM7-1	Tubulointerstitial nephritis antigen-like [OS=Homo sapiens]
P05067-1	Amyloid-beta A4 protein [OS=Homo sapiens]	O14672	Disintegrin and metalloproteinase domain-containing protein 10 [OS=Homo sapiens]
Q14624-1	Inter-alpha-trypsin inhibitor heavy chain H4 [OS=Homo sapiens]	O94985-1	Calsyntenin-1 [OS=Homo sapiens]
P63104-1	14-3-3 protein zeta/delta [OS=Homo sapiens]	P09211	Glutathione S-transferase P [OS=Homo sapiens]
O15230	Laminin subunit alpha-5 [OS=Homo sapiens]	P10809	60 kDa heat shock protein, mitochondrial [OS=Homo sapiens]
P02790	Hemopexin [OS=Homo sapiens]	P62937	peptidyl-prolyl cis-trans isomerase A [OS=Homo sapiens]
P18206	Vinculin [OS=Homo sapiens]	P05023	Sodium/potassium-transporting ATPase subunit alpha-1 [OS=Homo sapiens]
P0DMV8	heat shock 70 kDa protein 1A [OS=Homo sapiens]	Q01650	large neutral amino acids transporter small subunit 1 [OS=Homo sapiens]
P12814-4	Isoform 4 of Alpha-actinin-1 [OS=Homo sapiens]	P40227-1	T-complex protein 1 subunit zeta [OS=Homo sapiens]
P04908	histone H2A type 1-B/E [OS=Homo sapiens]	P17096-2	Isoform HMG-Y of High mobility group protein HMG-I/HMG-Y [OS=Homo sapiens]
O43490-1	Prominin-1 [OS=Homo sapiens]	Q8NBP7-1	Proprotein convertase subtilisin/kexin type 9 [OS=Homo sapiens]
Q562R1	Beta-actin-like protein 2 [OS=Homo sapiens]	P07437	tubulin beta chain [OS=Homo sapiens]
P17987	T-complex protein 1 subunit alpha [OS=Homo sapiens]	P0DOX7	immunoglobulin kappa light chain [OS=Homo sapiens]
P08133-1	annexin A6 [OS=Homo sapiens]	P39023	60S ribosomal protein L3 [OS=Homo sapiens]
P05106	Integrin beta-3 [OS=Homo sapiens]	P29401-2	Isoform 2 of Transketolase [OS=Homo sapiens]
P01033	Metalloproteinase inhibitor 1 [OS=Homo sapiens]	Q9NS15-1	Latent-transforming growth factor beta-binding protein 3 [OS=Homo sapiens]
P06733-1	alpha-enolase [OS=Homo sapiens]	P12956	X-ray repair cross-complementing protein 6 [OS=Homo sapiens]
P11387	DNA topoisomerase 1 [OS=Homo sapiens]	P06748	Nucleophosmin [OS=Homo sapiens]
P00558	phosphoglycerate kinase 1 [OS=Homo sapiens]	P13746-2	Isoform 2 of HLA class I histocompatibility antigen, A-11 alpha chain [OS=Homo sapiens]
P50990	T-complex protein 1 subunit theta [OS=Homo sapiens]	P02751-15	Isoform 15 of Fibronectin [OS=Homo sapiens]
Q9H4B7	tubulin beta-1 chain [OS=Homo sapiens]	Q00610-1	Clathrin heavy chain 1 [OS=Homo sapiens]
O75340	programmed cell death protein 6 [OS=Homo sapiens]	P36578	60S ribosomal protein L4 [OS=Homo sapiens]
P00739-2	Isoform 2 of Haptoglobin-related protein [OS=Homo sapiens]	P11047	Laminin subunit gamma-1 [OS=Homo sapiens]
P48643	T-complex protein 1 subunit epsilon [OS=Homo sapiens]	P06396	Gelsolin [OS=Homo sapiens]
P16422	Epithelial cell adhesion molecule [OS=Homo sapiens]	P0DOX6	immunoglobulin mu heavy chain [OS=Homo sapiens]
P49368-1	T-complex protein 1 subunit gamma [OS=Homo sapiens]	P23528	Cofilin-1 [OS=Homo sapiens]
Q14764	major vault protein [OS=Homo sapiens]	P31947-1	14-3-3 protein sigma [OS=Homo sapiens]
P30443	HLA class I histocompatibility antigen, A-1 alpha chain [OS=Homo sapiens]	P15514	Amphiregulin [OS=Homo sapiens]
Q969P0	Immunoglobulin superfamily member 8 [OS=Homo sapiens]	Q92520	Protein FAM3C [OS=Homo sapiens]
Q9Y4K0	Lysyl oxidase homolog 2 [OS=Homo sapiens]	P00338-3	Isoform 3 of L-lactate dehydrogenase A chain [OS=Homo sapiens]
P01031	Complement C5 [OS=Homo sapiens]	P01876	immunoglobulin heavy constant alpha 1 [OS=Homo sapiens]
P15311	Ezrin [OS=Homo sapiens]	P31431-1	syndecan-4 [OS=Homo sapiens]
P62258-1	14-3-3 protein epsilon [OS=Homo sapiens]	P0DOX8	Immunoglobulin lambda-1 light chain [OS=Homo sapiens]
P04083	annexin A1 [OS=Homo sapiens]	P18124	60S ribosomal protein L7 [OS=Homo sapiens]
P22392-2	Isoform 3 of Nucleoside diphosphate kinase B [OS=Homo sapiens]	P81605-2	Isoform 2 of Dermcidin [OS=Homo sapiens]
P04075-2	Isoform 2 of Fructose-bisphosphate aldolase A [OS=Homo sapiens]	P60033	CD81 antigen [OS=Homo sapiens]
P08195-4	Isoform 4 of 4F2 cell-surface antigen heavy chain [OS=Homo sapiens]	P0C0S5	Histone H2A.Z [OS=Homo sapiens]
P12956	X-ray repair cross-complementing protein 6 [OS=Homo sapiens]	P31946	14-3-3 protein beta/alpha [OS=Homo sapiens]
P55072	Transitional endoplasmic reticulum ATPase [OS=Homo sapiens]	Q13444	Disintegrin and metalloproteinase domain-containing protein 15 [OS=Homo sapiens]
P0C0S5	Histone H2A.Z [OS=Homo sapiens]	Q86YZ3	Hornerin [OS=Homo sapiens]
P02649	Apolipoprotein E [OS=Homo sapiens]	P04792	Heat shock protein beta-1 [OS=Homo sapiens]
Q8WWI5	choline transporter-like protein 1 [OS=Homo sapiens]	P60174	Triosephosphate isomerase [OS=Homo sapiens]
P01011-1	Alpha-1-antichymotrypsin [OS=Homo sapiens]	P62263	40S ribosomal protein S14 [OS=Homo sapiens]
P50991	T-complex protein 1 subunit delta [OS=Homo sapiens]	P16870	Carboxypeptidase E [OS=Homo sapiens]
Q99832	T-complex protein 1 subunit eta [OS=Homo sapiens]	P18206	Vinculin [OS=Homo sapiens]
P02765	Alpha-2-HS-glycoprotein [OS=Homo sapiens]	P06454-1	Prothymosin alpha [OS=Homo sapiens]
P07093-3	Isoform 3 of Glia-derived nexin [OS=Homo sapiens]	P61247	40S ribosomal protein S3a [OS=Homo sapiens]
P16870	Carboxypeptidase E [OS=Homo sapiens]	P27635	60S ribosomal protein L10 [OS=Homo sapiens]
P29401-2	Isoform 2 of Transketolase [OS=Homo sapiens]	Q13753-1	Laminin subunit gamma-2 [OS=Homo sapiens]

P08519	apolipoprotein(a) [OS=Homo sapiens]	Q8N5I2	arrestin domain-containing protein 1 [OS=Homo sapiens]
O75531	Barrier-to-autointegration factor [OS=Homo sapiens]	P61026	ras-related protein rab-10 [OS=Homo sapiens]
P01008	Antithrombin-III [OS=Homo sapiens]	P01033	Metalloproteinase inhibitor 1 [OS=Homo sapiens]
A0M8Q6	immunoglobulin lambda constant 7 [OS=Homo sapiens]	P05783	Keratin, type I cytoskeletal 18 [OS=Homo sapiens]
Q9GZM7-1	Tubulointerstitial nephritis antigen-like [OS=Homo sapiens]	P46782	40S ribosomal protein S5 [OS=Homo sapiens]
Q99816	tumor susceptibility gene 101 protein [OS=Homo sapiens]	P36383	gap junction gamma-1 protein [OS=Homo sapiens]
O15240	Neurosecretory protein VGF [OS=Homo sapiens]	P02788	Lactotransferrin [OS=Homo sapiens]
P05023	Sodium/potassium-transporting ATPase subunit alpha-1 [OS=Homo sapiens]	P05067-1	Amyloid-beta A4 protein [OS=Homo sapiens]
P18065	Insulin-like growth factor-binding protein 2 [OS=Homo sapiens]	Q92626	peroxidasin homolog [OS=Homo sapiens]
Q92520	Protein FAM3C [OS=Homo sapiens]	P07737	profilin-1 [OS=Homo sapiens]
P10319	HLA class I histocompatibility antigen, B-58 alpha chain [OS=Homo sapiens]	P62424	60S ribosomal protein L7a [OS=Homo sapiens]
P21741	Midkine [OS=Homo sapiens]	P63000-2	Isoform B of Ras-related C3 botulinum toxin substrate 1 [OS=Homo sapiens]
P62937	peptidyl-prolyl cis-trans isomerase A [OS=Homo sapiens]	P08670	Vimentin [OS=Homo sapiens]
P01034	Cystatin-C [OS=Homo sapiens]	Q07020	60S ribosomal protein L18 [OS=Homo sapiens]
Q06033-1	Inter-alpha-trypsin inhibitor heavy chain H3 [OS=Homo sapiens]	P35998	26S proteasome regulatory subunit 7 [OS=Homo sapiens]
P60174	Triosephosphate isomerase [OS=Homo sapiens]	Q9H2A7	C-X-C motif chemokine 16 [OS=Homo sapiens]
P60900	Proteasome subunit alpha type-6 [OS=Homo sapiens]	P05204	Non-histone chromosomal protein HMG-17 [OS=Homo sapiens]
O43866	CD5 antigen-like [OS=Homo sapiens]	P13611	Versican core protein [OS=Homo sapiens]
P18463	HLA class I histocompatibility antigen, B-37 alpha chain [OS=Homo sapiens]	Q99832	T-complex protein 1 subunit eta [OS=Homo sapiens]
P17096-3	Isoform HMG-R of High mobility group protein HMG-I/HMG-Y [OS=Homo sapiens]	P01009-1	alpha-1-antitrypsin [OS=Homo sapiens]
P07093-1	Glia-derived nexin [OS=Homo sapiens]	Q5D862	Filaggrin-2 [OS=Homo sapiens]
P02766	Transthyretin [OS=Homo sapiens]	Q9Y5Y6	suppressor of tumorigenicity 14 protein [OS=Homo sapiens]
P21926	CD9 antigen [OS=Homo sapiens]	P27348	14-3-3 protein theta [OS=Homo sapiens]
O14792	Heparan sulfate glucosamine 3-O-sulfotransferase 1 [OS=Homo sapiens]	P21926	CD9 antigen [OS=Homo sapiens]
P13611	Versican core protein [OS=Homo sapiens]	P35222	Catenin beta-1 [OS=Homo sapiens]
P07737	profilin-1 [OS=Homo sapiens]	Q02413	Desmoglein-1 [OS=Homo sapiens]
P27918	Properdin [OS=Homo sapiens]	P59665	Neutrophil defensin 1 [OS=Homo sapiens]
P07947	tyrosine-protein kinase Yes [OS=Homo sapiens]	O75462	Cytokine receptor-like factor 1 [OS=Homo sapiens]
P08603-1	complement factor H [OS=Homo sapiens]	Q14103	heterogeneous nuclear ribonucleoprotein D0 [OS=Homo sapiens]
O43707	Alpha-actinin-4 [OS=Homo sapiens]	Q14974	Importin subunit beta-1 [OS=Homo sapiens]
P02788	Lactotransferrin [OS=Homo sapiens]	P62753	40S RIBOSOMAL PROTEIN S6 [OS=Homo sapiens]
Q9NS15-1	Latent-transforming growth factor beta-binding protein 3 [OS=Homo sapiens]	P50991	T-complex protein 1 subunit delta [OS=Homo sapiens]
P00751-1	Complement factor B [OS=Homo sapiens]	P22626	heterogeneous nuclear ribonucleoproteins A2/B1 [OS=Homo sapiens]
P16189	HLA class I histocompatibility antigen, A-31 alpha chain [OS=Homo sapiens]	P29317	Ephrin type-A receptor 2 [OS=Homo sapiens]
P60660	Myosin light polypeptide 6 [OS=Homo sapiens]	P61981	14-3-3 protein gamma [OS=Homo sapiens]
P29317	Ephrin type-A receptor 2 [OS=Homo sapiens]	P62841	40S ribosomal protein S15 [OS=Homo sapiens]
P17301	Integrin alpha-2 [OS=Homo sapiens]	P11166	Solute carrier family 2, facilitated glucose transporter member 1 [OS=Homo sapiens]
P07195	L-lactate dehydrogenase B chain [OS=Homo sapiens]	P04004	Vitronectin [OS=Homo sapiens]
Q06830	peroxiredoxin-1 [OS=Homo sapiens]	Q02818	Nucleobindin-1 [OS=Homo sapiens]
P11047	Laminin subunit gamma-1 [OS=Homo sapiens]	P35443	Thrombospondin-4 [OS=Homo sapiens]
P40227-1	T-complex protein 1 subunit zeta [OS=Homo sapiens]	P02675	Fibrinogen beta chain [OS=Homo sapiens]
P04217	Alpha-1B-glycoprotein [OS=Homo sapiens]	Q9C0H2-4	Isoform 4 of Protein tweety homolog 3 [OS=Homo sapiens]
P61981	14-3-3 protein gamma [OS=Homo sapiens]	P07093-3	Isoform 3 of Glia-derived nexin [OS=Homo sapiens]
P50995	annexin A11 [OS=Homo sapiens]	P01614	Immunoglobulin kappa variable 2D-40 [OS=Homo sapiens]
P07225	Vitamin K-dependent protein S [OS=Homo sapiens]	Q99816	tumor susceptibility gene 101 protein [OS=Homo sapiens]
Q9Y5Y6	suppressor of tumorigenicity 14 protein [OS=Homo sapiens]	Q9H4B7	tubulin beta-1 chain [OS=Homo sapiens]
P36383	gap junction gamma-1 protein [OS=Homo sapiens]	P61586	Transforming protein RhoA [OS=Homo sapiens]
P14923	Junction plakoglobin [OS=Homo sapiens]	P16070	CD44 antigen [OS=Homo sapiens]
P09972	Fructose-bisphosphate aldolase C [OS=Homo sapiens]	P06576	ATP synthase subunit beta, mitochondrial [OS=Homo sapiens]
P06727	Apolipoprotein A-IV [OS=Homo sapiens]	P02671-1	Fibrinogen alpha chain [OS=Homo sapiens]
P52907	F-actin-capping protein subunit alpha-1 [OS=Homo sapiens]	P00734	Prothrombin [OS=Homo sapiens]
Q13421-2	Isoform 3 of Mesothelin [OS=Homo sapiens]	P26006-1	Isoform 2 of Integrin alpha-3 [OS=Homo sapiens]
P01614	Immunoglobulin kappa variable 2D-40 [OS=Homo sapiens]	Q9BSG5-2	Isoform 2 of Retbindin [OS=Homo sapiens]
Q8N2S1	Latent-transforming growth factor beta-binding protein 4 [OS=Homo sapiens]	P02771	Alpha-fetoprotein [OS=Homo sapiens]
P16035	Metalloproteinase inhibitor 2 [OS=Homo sapiens]	P02753	Retinol-binding protein 4 [OS=Homo sapiens]
P68104	Elongation factor 1-alpha 1 [OS=Homo sapiens]	P61254	60S ribosomal protein L26 [OS=Homo sapiens]
P16144-1	Integrin beta-4 [OS=Homo sapiens]	P14625	Endoplasmin [OS=Homo sapiens]
A6NHL2-1	Tubulin alpha chain-like 3 [OS=Homo sapiens]	Q9Y4K0	Lysyl oxidase homolog 2 [OS=Homo sapiens]
P01619	Immunoglobulin kappa variable 3-20 [OS=Homo sapiens]	P46779-3	Isoform 3 of 60S ribosomal protein L28 [OS=Homo sapiens]
P10321	HLA class I histocompatibility antigen, Cw-7 alpha chain [OS=Homo sapiens]	P62910	60S ribosomal protein L32 [OS=Homo sapiens]
P02652	Apolipoprotein A-II [OS=Homo sapiens]	P46776	60S ribosomal protein L27a [OS=Homo sapiens]
P11021	78 kDa glucose-regulated protein [OS=Homo sapiens]	P07225	Vitamin K-dependent protein S [OS=Homo sapiens]
Q71DI3	histone H3.2 [OS=Homo sapiens]	P23246-1	splicing factor, proline- and glutamine-rich [OS=Homo sapiens]
P18669	Phosphoglycerate mutase 1 [OS=Homo sapiens]	Q02878	60S ribosomal protein L6 [OS=Homo sapiens]
Q02809-2	Isoform 2 of Procollagen-lysine,2-oxoglutarate 5-dioxygenase 1 [OS=Homo sapiens]	P13639	Elongation factor 2 [OS=Homo sapiens]
P33908	Mannosyl-oligosaccharide 1,2-alpha-mannosidase IA [OS=Homo sapiens]	Q9H9H4	Vacuolar protein sorting-associated protein 37B [OS=Homo sapiens]
Q8TAA3-1	proteasome subunit alpha type-7-like [OS=Homo sapiens]	P05198	Eukaryotic translation initiation factor 2 subunit 1 [OS=Homo sapiens]
Q6YHK3-1	CD109 antigen [OS=Homo sapiens]	Q8NG11-1	Tetraspanin-14 [OS=Homo sapiens]
P26641-2	Isoform 2 of Elongation factor 1-gamma [OS=Homo sapiens]	Q9Y265	RuvB-like 1 [OS=Homo sapiens]
O60716-1	Catenin delta-1 [OS=Homo sapiens]	P02452	Collagen alpha-1(I) chain [OS=Homo sapiens]
P53396-1	ATP-citrate synthase [OS=Homo sapiens]	O75347	Tubulin-specific chaperone A [OS=Homo sapiens]
A0A0C4DH25	immunoglobulin kappa variable 3D-20 [OS=Homo sapiens]	P49747	Cartilage oligomeric matrix protein [OS=Homo sapiens]
Q8N5I2	arrestin domain-containing protein 1 [OS=Homo sapiens]	P05156	Complement factor I [OS=Homo sapiens]
Q01518-1	adenylyl cyclase-associated protein 1 [OS=Homo sapiens]	O00299	chloride intracellular channel protein 1 [OS=Homo sapiens]
P02776	Platelet factor 4 [OS=Homo sapiens]	A5D8V6	Vacuolar protein sorting-associated protein 37C [OS=Homo sapiens]
P07942	Laminin subunit beta-1 [OS=Homo sapiens]	P42677	40S ribosomal protein S27 [OS=Homo sapiens]
P09382	Galectin-1 [OS=Homo sapiens]	P26373-1	60S ribosomal protein L13 [OS=Homo sapiens]
Q5VW32	BRO1 domain-containing protein BROX [OS=Homo sapiens]	Q13200	26S proteasome non-ATPase regulatory subunit 2 [OS=Homo sapiens]
Q8NBP7-1	Proprotein convertase subtilisin/kexin type 9 [OS=Homo sapiens]	P08195-4	Isoform 4 of 4F2 cell-surface antigen heavy chain [OS=Homo sapiens]
Q14118	Dystroglycan [OS=Homo sapiens]	Q5T749	Keratinocyte proline-rich protein [OS=Homo sapiens]
P63241-2	Isoform 2 of Eukaryotic translation initiation factor 5A-1 [OS=Homo sapiens]	P07910-1	Heterogeneous nuclear ribonucleoproteins C1/C2 [OS=Homo sapiens]
Q05639	Elongation factor 1-alpha 2 [OS=Homo sapiens]	P07305	Histone H1.0 [OS=Homo sapiens]
Q13418	Integrin-linked protein kinase [OS=Homo sapiens]	P08697-1	Alpha-2-antiplasmin [OS=Homo sapiens]
P23284	peptidyl-prolyl cis-trans isomerase B [OS=Homo sapiens]	P52565-1	rho GDP-dissociation inhibitor 1 [OS=Homo sapiens]
P04004	Vitronectin [OS=Homo sapiens]	P02461	Collagen alpha-1(III) chain [OS=Homo sapiens]
Q14766-4	Isoform 4 of Latent-transforming growth factor beta-binding protein 1 [OS=Homo sapiens]	P01591	Immunoglobulin J chain [OS=Homo sapiens]
P02747	Complement C1q subcomponent subunit C [OS=Homo sapiens]	P68371	Tubulin beta-4B chain [OS=Homo sapiens]
Q9H4M9	EH domain-containing protein 1 [OS=Homo sapiens]	Q5JWF2-1	Guanine nucleotide-binding protein G(S) subunit alpha isoforms XLas [OS=Homo sapiens]
P06753	Tropomyosin alpha-3 chain [OS=Homo sapiens]	O75787	Renin receptor [OS=Homo sapiens]
Q13201	Multimerin-1 [OS=Homo sapiens]	P01008	Antithrombin-III [OS=Homo sapiens]
Q13200	26S proteasome non-ATPase regulatory subunit 2 [OS=Homo sapiens]	P55001	Microfibrillar-associated protein 2 [OS=Homo sapiens]
P00736	Complement C1r subcomponent [OS=Homo sapiens]	P13521	Secretogranin-2 [OS=Homo sapiens]
Q9UK41-2	Isoform 2 of Vacuolar protein sorting-associated protein 28 homolog [OS=Homo sapiens]	P61769	Beta-2-microglobulin [OS=Homo sapiens]
P06756	Integrin alpha-V [OS=Homo sapiens]	P62318	small nuclear ribonucleoprotein sm d3 [OS=Homo sapiens]
O75083	WD repeat-containing protein 1 [OS=Homo sapiens]	P19827-1	Inter-alpha-trypsin inhibitor heavy chain H1 [OS=Homo sapiens]
P16070	CD44 antigen [OS=Homo sapiens]	P51148-2	Isoform 2 of Ras-related protein Rab-5C [OS=Homo sapiens]
Q6UWP8-1	Suprabasin [OS=Homo sapiens]	Q86VE9-4	Isoform 4 of Serine incorporator 5 [OS=Homo sapiens]
Q14974	Importin subunit beta-1 [OS=Homo sapiens]	P23396-2	Isoform 2 of 40S ribosomal protein S3 [OS=Homo sapiens]
Q06481	Amyloid-like protein 2 [OS=Homo sapiens]	P15880	40S ribosomal protein S2 [OS=Homo sapiens]
P28066-1	Proteasome subunit alpha type-5 [OS=Homo sapiens]	P62888	60S ribosomal protein L30 [OS=Homo sapiens]
P62979	Ubiquitin-40S ribosomal protein S27a [OS=Homo sapiens]	P22090	40S ribosomal protein S4, Y isoform 1 [OS=Homo sapiens]
Q99988	Growth/differentiation factor 15 [OS=Homo sapiens]	P30041	Peroxiredoxin-6 [OS=Homo sapiens]
P25787	Proteasome subunit alpha type-2 [OS=Homo sapiens]	P16949-2	Isoform 2 of Stathmin [OS=Homo sapiens]
P23142	Fibulin-1 [OS=Homo sapiens]	P39019	40S ribosomal protein S19 [OS=Homo sapiens]
P35613	Basigin [OS=Homo sapiens]	P02652	Apolipoprotein A-II [OS=Homo sapiens]
P04275	Von Willebrand factor [OS=Homo sapiens]	Q15828	Cystatin-M [OS=Homo sapiens]
P28074-1	proteasome subunit beta type-5 [OS=Homo sapiens]	P40925-3	Isoform 3 of Malate dehydrogenase, cytoplasmic [OS=Homo sapiens]
P19338	Nucleolin [OS=Homo sapiens]	P34096	Ribonuclease 4 [OS=Homo sapiens]
O00391	Sulfhydryl oxidase 1 [OS=Homo sapiens]	P20618	proteasome subunit beta type-1 [OS=Homo sapiens]
Q13443	disintegrin and metalloproteinase domain-containing protein 9 [OS=Homo sapiens]	P14649	Myosin light chain 6B [OS=Homo sapiens]
O00299	chloride intracellular channel protein 1 [OS=Homo sapiens]	P08603-1	complement factor H [OS=Homo sapiens]
P21579	Synaptotagmin-1 [OS=Homo sapiens]	P12259	Coagulation factor V [OS=Homo sapiens]
O00468-7	Isoform 7 of Agrin [OS=Homo sapiens]	P50914	60S ribosomal protein L14 [OS=Homo sapiens]
P48960-1	CD97 antigen [OS=Homo sapiens]	P26641-2	Isoform 2 of Elongation factor 1-gamma [OS=Homo sapiens]
Q6PCB0	von Willebrand factor A domain-containing protein 1 [OS=Homo sapiens]	Q15019-2	Isoform 2 of Septin-2 [OS=Homo sapiens]
P09429	High mobility group protein B1 [OS=Homo sapiens]	P0C0L4-1	Complement C4-A [OS=Homo sapiens]
P60953	Cell division control protein 42 homolog [OS=Homo sapiens]	P62826	GTP-binding nuclear protein RAN [OS=Homo sapiens]
P00387-3	Isoform 3 of NADH-cytochrome b5 reductase 3 [OS=Homo sapiens]	Q14624-1	Inter-alpha-trypsin inhibitor heavy chain H4 [OS=Homo sapiens]
P55001	Microfibrillar-associated protein 2 [OS=Homo sapiens]	P61224-1	Ras-related protein Rap-1b [OS=Homo sapiens]
O60635	Tetraspanin-1 [OS=Homo sapiens]	Q5SSJ5-1	Heterochromatin protein 1-binding protein 3 [OS=Homo sapiens]
P61769	Beta-2-microglobulin [OS=Homo sapiens]	Q8NBS9-1	Thioredoxin domain-containing protein 5 [OS=Homo sapiens]
Q99985	Semaphorin-3C [OS=Homo sapiens]	P55058	phospholipid transfer protein [OS=Homo sapiens]
P06310	Immunoglobulin kappa variable 2-30 [OS=Homo sapiens]	P47914	60S ribosomal protein L29 [OS=Homo sapiens]
Q13308-6	Isoform 6 of Inactive tyrosine-protein kinase 7 [OS=Homo sapiens]	P61313-1	60S ribosomal protein L15 [OS=Homo sapiens]
P12931-2	Isoform 2 of Proto-oncogene tyrosine-protein kinase Src [OS=Homo sapiens]	P09382	Galectin-1 [OS=Homo sapiens]
Q14697-2	Isoform 2 of Neutral alpha-glucosidase AB [OS=Homo sapiens]	Q99436	Proteasome subunit beta type-7 [OS=Homo sapiens]
P25786-2	Isoform Long of Proteasome subunit alpha type-1 [OS=Homo sapiens]	P10145	interleukin-8 [OS=Homo sapiens]
P02746	Complement C1q subcomponent subunit B [OS=Homo sapiens]	P62851	40S ribosomal protein S25 [OS=Homo sapiens]
P29692-2	Isoform 2 of Elongation factor 1-delta [OS=Homo sapiens]	P28072	Proteasome subunit beta type-6 [OS=Homo sapiens]
P01591	Immunoglobulin J chain [OS=Homo sapiens]	P07947	tyrosine-protein kinase Yes [OS=Homo sapiens]
Q92876-1	Kallikrein-6 [OS=Homo sapiens]	P21583-1	Kit ligand [OS=Homo sapiens]
P49411	elongation factor Tu, mitochondrial [OS=Homo sapiens]	P23142	Fibulin-1 [OS=Homo sapiens]

Q14152	Eukaryotic translation initiation factor 3 subunit A [OS=Homo sapiens]	P62258-1	14-3-3 protein epsilon [OS=Homo sapiens]
P23526-1	Adenosylhomocysteinase [OS=Homo sapiens]	P78371-1	T-complex protein 1 subunit beta [OS=Homo sapiens]
P06748	Nucleophosmin [OS=Homo sapiens]	P19021-5	Isoform 5 of Peptidyl-glycine alpha-amidating monooxygenase [OS=Homo sapiens]
P01042	kininogen-1 [OS=Homo sapiens]	P02749	Beta-2-glycoprotein 1 [OS=Homo sapiens]
Q12906-7	Isoform 7 of Interleukin enhancer-binding factor 3 [OS=Homo sapiens]	Q07955-2	Isoform ASF-2 of Serine/arginine-rich splicing factor 1 [OS=Homo sapiens]
Q13753-1	Laminin subunit gamma-2 [OS=Homo sapiens]	P62277	40S ribosomal protein S13 [OS=Homo sapiens]
P13497	Bone morphogenetic protein 1 [OS=Homo sapiens]	Q96RF0	Sorting nexin-18 [OS=Homo sapiens]
P11166	Solute carrier family 2, facilitated glucose transporter member 1 [OS=Homo sapiens]	P61353	60S ribosomal protein L27 [OS=Homo sapiens]
O43657	Tetraspanin-6 [OS=Homo sapiens]	P14174	Macrophage Migration inhibitory factor [OS=Homo sapiens]
P61204	ADP-ribosylation factor 3 [OS=Homo sapiens]	P57721-1	Poly(rC)-binding protein 3 [OS=Homo sapiens]
P05546	Heparin cofactor 2 [OS=Homo sapiens]	P60866-2	Isoform 2 of 40S ribosomal protein S20 [OS=Homo sapiens]
Q9H013-1	Disintegrin and metalloproteinase domain-containing protein 19 [OS=Homo sapiens]	P31943	Heterogeneous nuclear ribonucleoprotein H [OS=Homo sapiens]
P25705-1	ATP synthase subunit alpha, mitochondrial [OS=Homo sapiens]	P19823	Inter-alpha-trypsin inhibitor heavy chain H2 [OS=Homo sapiens]
Q13740-1	CD166 antigen [OS=Homo sapiens]	P02790	Hemopexin [OS=Homo sapiens]
O75367-1	Core histone macro-H2A.1 [OS=Homo sapiens]	O76061	Stanniocalcin-2 [OS=Homo sapiens]
P08134	Rho-related GTP-binding protein RhoC [OS=Homo sapiens]	Q02809-2	Isoform 2 of Procollagen-lysine,2-oxoglutarate 5-dioxygenase 1 [OS=Homo sapiens]
P62873	Guanine nucleotide-binding protein G(I)/G(S)/G(T) subunit beta-1 [OS=Homo sapiens]	P35268	60S ribosomal protein L22 [OS=Homo sapiens]
Q9BRK5-1	45 kDa calcium-binding protein [OS=Homo sapiens]	P23284	peptidyl-prolyl cis-trans isomerase B [OS=Homo sapiens]
P67809	Nuclease-sensitive element-binding protein 1 [OS=Homo sapiens]	Q9Y490	Talin-1 [OS=Homo sapiens]
Q9UGM3-9	Isoform 9 of Deleted in malignant brain tumors 1 protein [OS=Homo sapiens]	P00747	Plasminogen [OS=Homo sapiens]
P04792	Heat shock protein beta-1 [OS=Homo sapiens]	P14923	Junction plakoglobin [OS=Homo sapiens]
P09211	Glutathione S-transferase P [OS=Homo sapiens]	P63220	40S ribosomal protein S21 [OS=Homo sapiens]
Q14126	Desmoglein-2 [OS=Homo sapiens]	Q9UK73	Protein fem-1 homolog B [OS=Homo sapiens]
P30101	Protein disulfide-isomerase A3 [OS=Homo sapiens]	O95782	AP-2 complex subunit alpha-1 [OS=Homo sapiens]
P04196	Histidine-rich glycoprotein [OS=Homo sapiens]	Q9H444	Charged multivesicular body protein 4b [OS=Homo sapiens]
P04899-4	Isoform sGi2 of Guanine nucleotide-binding protein G(i) subunit alpha-2 [OS=Homo sapiens]	P62857	40S ribosomal protein S28 [OS=Homo sapiens]
P35222	Catenin beta-1 [OS=Homo sapiens]	P83881	60S ribosomal protein L36a [OS=Homo sapiens]
P78539-1	Sushi repeat-containing protein SRPX [OS=Homo sapiens]	P55072	Transitional endoplasmic reticulum ATPase [OS=Homo sapiens]
Q96EY5-1	Multivesicular body subunit 12A [OS=Homo sapiens]	P02647	Apolipoprotein A-I [OS=Homo sapiens]
P01624	Immunoglobulin kappa variable 3-15 [OS=Homo sapiens]	Q9HD42-1	Charged multivesicular body protein 1a [OS=Homo sapiens]
P02749	Beta-2-glycoprotein 1 [OS=Homo sapiens]	Q9NRY6	Phospholipid scramblase 3 [OS=Homo sapiens]
P07357	Complement component C8 alpha chain [OS=Homo sapiens]	B5ME19	eukaryotic translation initiation factor 3 subunit C-like protein [OS=Homo sapiens]
Q96PD5-2	Isoform 2 of N-acetylmuramoyl-L-alanine amidase [OS=Homo sapiens]	Q15631-1	Translin [OS=Homo sapiens]
P12259	Coagulation factor V [OS=Homo sapiens]	O95750	Fibroblast growth factor 19 [OS=Homo sapiens]
P09871	Complement C1s subcomponent [OS=Homo sapiens]	P04114	apolipoprotein B-100 [OS=Homo sapiens]
O75674	TOM1-like protein 1 [OS=Homo sapiens]	P09874	Poly [ADP-ribose] polymerase 1 [OS=Homo sapiens]
Q96QD8	sodium-coupled neutral amino acid transporter 2 [OS=Homo sapiens]	Q99996-6	Isoform 6 of A-kinase anchor protein 9 [OS=Homo sapiens]
P54709	sodium/potassium-transporting ATPase subunit beta-3 [OS=Homo sapiens]	P46777	60S ribosomal protein L5 [OS=Homo sapiens]
Q9ULF5	Zinc transporter ZIP10 [OS=Homo sapiens]	P84098	60S ribosomal protein L19 [OS=Homo sapiens]
P62879	Guanine nucleotide-binding protein G(I)/G(S)/G(T) subunit beta-2 [OS=Homo sapiens]	Q8R5X6	10 kDa chaperonin OS=Fusobacterium nucleatum (strain ATCC 25586)
P68400	Casein kinase II subunit alpha [OS=Homo sapiens]	Q8RG30	Glutamate dehydrogenase OS=Fusobacterium nucleatum (strain ATCC 25586)
P21589-1	5'-nucleotidase [OS=Homo sapiens]	Q8R5X7	60 kDa chaperonin OS=Fusobacterium nucleatum (strain ATCC 25586)
Q8IWA5-2	Isoform 2 of Choline transporter-like protein 2 [OS=Homo sapiens]	Q8R643	Pyruvate-flavodoxin oxidoreductase OS=Fusobacterium nucleatum (strain ATCC 25586)
Q99873	protein arginine N-methyltransferase 1 [OS=Homo sapiens]	Q8RES5	3-hydroxybutyryl-CoA dehydrogenase OS=Fusobacterium nucleatum (strain ATCC 25586)
Q8IUL8	Cartilage intermediate layer protein 2 [OS=Homo sapiens]	Q8RIN6	Acyl-CoA dehydrogenase, short-chain specific OS=Fusobacterium nucleatum (strain ATCC 25586)
P30989	Neurotensin receptor type 1 [OS=Homo sapiens]	Q8RI55	Enolase OS=Fusobacterium nucleatum (strain ATCC 25586)
P10809	60 kDa heat shock protein, mitochondrial [OS=Homo sapiens]	Q8RFC6	Electron transfer flavoprotein alpha-subunit OS=Fusobacterium nucleatum (strain ATCC 25586)
Q15149-1	plectin [OS=Homo sapiens]	Q8R6D3	Alkyl hydroperoxide reductase C22 protein OS=Fusobacterium nucleatum (strain ATCC 25586)
O15427	Monocarboxylate transporter 4 [OS=Homo sapiens]	Q8R603	Elongation factor Tu OS=Fusobacterium nucleatum (strain ATCC 25586)
O95297-1	Myelin protein zero-like protein 1 [OS=Homo sapiens]	Q8RHQ6	Tryptophanase OS=Fusobacterium nucleatum (strain ATCC 25586)
Q12907	Vesicular integral-membrane protein VIP36 [OS=Homo sapiens]	Q8R600	Elongation factor Ts OS=Fusobacterium nucleatum (strain ATCC 25586)
P18428	lipopolysaccharide-binding protein [OS=Homo sapiens]	Q8RG24	Acetyl-CoA acetyltransferase OS=Fusobacterium nucleatum (strain ATCC 25586)
P55268	laminin subunit beta-2 [OS=Homo sapiens]	Q8RHN0	Thioredoxin reductase OS=Fusobacterium nucleatum (strain ATCC 25586)
Q9C0H2-4	Isoform 4 of Protein tweety homolog 3 [OS=Homo sapiens]	Q8REE2	D-galactose-binding protein OS=Fusobacterium nucleatum (strain ATCC 25586)
P23528	Cofilin-1 [OS=Homo sapiens]	Q8R609	Pyruvate-flavodoxin oxidoreductase OS=Fusobacterium nucleatum (strain ATCC 25586)
P02771	Alpha-fetoprotein [OS=Homo sapiens]	Q8RFN9	Glyceraldehyde-3-phosphate dehydrogenase OS=Fusobacterium nucleatum (strain ATCC 25586)
Q9UN37	Vacuolar protein sorting-associated protein 4A [OS=Homo sapiens]	Q8RF98	DNA-binding protein HU OS=Fusobacterium nucleatum (strain ATCC 25586)
P40926	Malate dehydrogenase, mitochondrial [OS=Homo sapiens]	Q8RI44	Uncharacterized protein OS=Fusobacterium nucleatum (strain ATCC 25586)
P07237	Protein disulfide-isomerase [OS=Homo sapiens]	Q8RH05	Chaperone protein DnaK OS=Fusobacterium nucleatum (strain ATCC 25586)
P06576	ATP synthase subunit beta, mitochondrial [OS=Homo sapiens]	Q8RE69	Uncharacterized protein OS=Fusobacterium nucleatum (strain ATCC 25586)
Q15828	Cystatin-M [OS=Homo sapiens]	Q8R608	Serine protease OS=Fusobacterium nucleatum (strain ATCC 25586)
P59190-1	Ras-related protein Rab-15 [OS=Homo sapiens]	Q8RFC7	Electron transfer flavoprotein beta-subunit OS=Fusobacterium nucleatum (strain ATCC 25586)
P78417	Glutathione S-transferase omega-1 [OS=Homo sapiens]	Q8RDT9	Threonine dehydratase OS=Fusobacterium nucleatum (strain ATCC 25586)
O75636-1	Ficolin-3 [OS=Homo sapiens]	Q8RED7	Acetate kinase OS=Fusobacterium nucleatum (strain ATCC 25586)
O14950	Myosin regulatory light chain 12B [OS=Homo sapiens]	Q8RHT8	Probable cytosol aminopeptidase OS=Fusobacterium nucleatum (strain ATCC 25586)
Q9Y624	Junctional adhesion molecule A [OS=Homo sapiens]	Q8RES4	3-hydroxybutyryl-CoA dehydratase OS=Fusobacterium nucleatum (strain ATCC 25586)
P25788-1	Proteasome subunit alpha type-3 [OS=Homo sapiens]	Q8RHY3	Acetoacetate:butyrate/acetate coenzyme A transferase OS=Fusobacterium nucleatum (strain ATCC 25586)
P28072	Proteasome subunit beta type-6 [OS=Homo sapiens]	Q8RHY1	Major outer membrane protein OS=Fusobacterium nucleatum (strain ATCC 25586)
Q8NFJ5	Retinoic acid-induced protein 3 [OS=Homo sapiens]	Q8RIF3	Uncharacterized protein OS=Fusobacterium nucleatum (strain ATCC 25586)
Q15185	Prostaglandin E synthase 3 [OS=Homo sapiens]	Q8RE11	Acetoacetate metabolism regulatory protein atoC OS=Fusobacterium nucleatum (strain ATCC 25586)
Q93084-5	Isoform SERCA3E of Sarcoplasmic/endoplasmic reticulum calcium ATPase 3 [OS=Homo sapiens]	Q8RGS8	Glutaconyl-CoA decarboxylase A subunit OS=Fusobacterium nucleatum (strain ATCC 25586)
Q86X29	Lipolysis-stimulated lipoprotein receptor [OS=Homo sapiens]	Q8RGT0	Glutaconate CoA-transferase subunit A OS=Fusobacterium nucleatum (strain ATCC 25586)
P31947-1	14-3-3 protein sigma [OS=Homo sapiens]	Q8RHQ8	Chaperone protein ClpB OS=Fusobacterium nucleatum (strain ATCC 25586)
O00151	PDZ and LIM domain protein 1 [OS=Homo sapiens]	Q8RHF4	Formate--tetrahydrofolate ligase OS=Fusobacterium nucleatum (strain ATCC 25586)
Q9H9H4	Vacuolar protein sorting-associated protein 37B [OS=Homo sapiens]	Q8RE65	C4-dicarboxylate-binding protein OS=Fusobacterium nucleatum (strain ATCC 25586)
P37802-2	Isoform 2 of Transgelin-2 [OS=Homo sapiens]	Q8RIB8	N-acetylneuraminate synthase OS=Fusobacterium nucleatum (strain ATCC 25586)
P02794	Ferritin heavy chain [OS=Homo sapiens]	Q8RE60	Outer membrane protein OS=Fusobacterium nucleatum (strain ATCC 25586)
P55786	puromycin-sensitive aminopeptidase [OS=Homo sapiens]	Q8RG53	Uncharacterized protein OS=Fusobacterium nucleatum (strain ATCC 25586)
P22090	40S ribosomal protein S4, Y isoform 1 [OS=Homo sapiens]	Q8RDW4	Citrate lyase alpha chain OS=Fusobacterium nucleatum (strain ATCC 25586
A0A0A0MRZ	immunoglobulin kappa variable 3D-11 [OS=Homo sapiens]	Q8RDX7	Triosephosphate isomerase OS=Fusobacterium nucleatum (strain ATCC 25586)
P19021-5	Isoform 5 of Peptidyl-glycine alpha-amidating monooxygenase [OS=Homo sapiens]	Q8R602	Elongation factor G OS=Fusobacterium nucleatum subsp. nucleatum (strain ATCC 25586)
P26583	High mobility group protein B2 [OS=Homo sapiens]	Q8RIJ6	Ion-translocating oxidoreductase complex subunit C OS=Fusobacterium nucleatum (strain ATCC 25586)
Q8WUJ3-1	Cell migration-inducing and hyaluronan-binding protein [OS=Homo sapiens]	Q8R6H3	Probable electron transfer flavoprotein-quinone oxidoreductase ydiS OS=Fusobacterium nucleatum (strain ATCC 25586)
Q86UX7	Fermitin family homolog 3 [OS=Homo sapiens]	Q8RES0	DNA-binding protein HU OS=Fusobacterium nucleatum (strain ATCC 25586)
P08567	pleckstrin [OS=Homo sapiens]	Q8RFS6	Threonine--tRNA ligase OS=Fusobacterium nucleatum (strain ATCC 25586)
Q99497	protein/nucleic acid deglycase DJ-1 [OS=Homo sapiens]	Q8RIN5	(S)-2-hydroxy-acid oxidase chain D OS=Fusobacterium nucleatum (strain ATCC 25586)
P02452	Collagen alpha-1(I) chain [OS=Homo sapiens]	Q8REM0	Neutrophil-activating protein A OS=Fusobacterium nucleatum (strain ATCC 25586)
P00750-1	Tissue-type plasminogen activator [OS=Homo sapiens]	Q8RHI5	50S ribosomal protein L7/L12 OS=Fusobacterium nucleatum (strain ATCC 25586)
P63096-1	Guanine nucleotide-binding protein G(i) subunit alpha-1 [OS=Homo sapiens]	Q8RI77	V-type sodium ATP synthase subunit A OS=Fusobacterium nucleatum (strain ATCC 25586)
P02748	complement component C9 [OS=Homo sapiens]	Q8RFC1	Urocanate hydratase OS=Fusobacterium nucleatum (strain ATCC 25586)
O15551	Claudin-3 [OS=Homo sapiens]	Q8RGS9	Glutaconate CoA-transferase subunit B OS=Fusobacterium nucleatum (strain ATCC 25586)
P14625	Endoplasmin [OS=Homo sapiens]	Q8RI92	Uncharacterized protein OS=Fusobacterium nucleatum (strain ATCC 25586)
P05387	60S acidic ribosomal protein P2 [OS=Homo sapiens]	Q8R5Y8	Biotin carboxyl carrier protein of glutaconyl-COA decarboxylase OS=Fusobacterium nucleatum (strain ATCC 25586)
Q13867	bleomycin hydrolase [OS=Homo sapiens]	Q8R6B3	(R)-2-hydroxyglutaryl-CoA dehydratase beta-subunit OS=Fusobacterium nucleatum (strain ATCC 25586)
P62316	Small nuclear ribonucleoprotein Sm D2 [OS=Homo sapiens]	Q8R674	Acyl-CoA dehydrogenase OS=Fusobacterium nucleatum (strain ATCC 25586)
Q9P265	Disco-interacting protein 2 homolog B [OS=Homo sapiens]	Q8RIH8	Hypothetical cytosolic protein OS=Fusobacterium nucleatum (strain ATCC 25586)
P01137	Transforming growth factor beta-1 [OS=Homo sapiens]	Q8RG80	50S ribosomal protein L19 OS=Fusobacterium nucleatum (strain ATCC 25586)
Q8N1N4	Keratin, type II cytoskeletal 78 [OS=Homo sapiens]	Q8RFL4	Transcriptional regulator, MarR family OS=Fusobacterium nucleatum (strain ATCC 25586)
P48509	CD151 antigen [OS=Homo sapiens]	Q8REM1	Hypothetical exported 24-amino acid repeat protein OS=Fusobacterium nucleatum (strain ATCC 25586)
O95471	Claudin-7 [OS=Homo sapiens]	Q8RFW8	Hypothetical cytosolic protein OS=Fusobacterium nucleatum (strain ATCC 25586)
P06737-1	Glycogen phosphorylase, liver form [OS=Homo sapiens]	Q8RGB0	Dipeptide-binding protein OS=Fusobacterium nucleatum (strain ATCC 25586)
Q9NP79	Vacuolar protein sorting-associated protein VTA1 homolog [OS=Homo sapiens]	Q8RG09	Flavodoxin OS=Fusobacterium nucleatum (strain ATCC 25586)
P61916	Epididymal secretory protein E1 [OS=Homo sapiens]	Q8RFG1	Imidazolonepropionase OS=Fusobacterium nucleatum (strain ATCC 25586)
P25789	Proteasome subunit alpha type-4 [OS=Homo sapiens]	Q8RGE2	ATP synthase subunit beta OS=Fusobacterium nucleatum (strain ATCC 25586)
P07358	Complement component C8 beta chain [OS=Homo sapiens]	Q8RET7	Outer membrane protein P1 OS=Fusobacterium nucleatum (strain ATCC 25586)
P08758	annexin A5 [OS=Homo sapiens]	Q8RDM5	UPF0735 ACT domain-containing protein FN1487 OS=Fusobacterium nucleatum (strain ATCC 25586)
P00390	Glutathione reductase, mitochondrial [OS=Homo sapiens]	Q8RDT4	L-methionine gamma-lyase OS=Fusobacterium nucleatum (strain ATCC 25586)
Q00796	Sorbitol dehydrogenase [OS=Homo sapiens]	Q8RGE5	S-adenosylmethionine synthase OS=Fusobacterium nucleatum (strain ATCC 25586)
Q8NG11-1	Tetraspanin-14 [OS=Homo sapiens]	Q8RG46	Flavodoxin OS=Fusobacterium nucleatum (strain ATCC 25586)
P05109	Protein S100-A8 [OS=Homo sapiens]	Q8R6H9	Uncharacterized protein OS=Fusobacterium nucleatum (strain ATCC 25586)
P01824	immunoglobulin heavy variable 4-39 [OS=Homo sapiens]	Q8RI54	Pyruvate kinase OS=Fusobacterium nucleatum (strain ATCC 25586)
P11908-2	Isoform 2 of Ribose-phosphate pyrophosphokinase 2 [OS=Homo sapiens]	Q8RDY4	Dipeptide-binding protein OS=Fusobacterium nucleatum (strain ATCC 25586)
P31689-1	DnaJ homolog subfamily A member 1 [OS=Homo sapiens]	Q8RED6	Phosphate acetyltransferase OS=Fusobacterium nucleatum (strain ATCC 25586)
O14791-2	Isoform 2 of Apolipoprotein L1 [OS=Homo sapiens]	Q8RH03	Chaperone protein DnaJ OS=Fusobacterium nucleatum (strain ATCC 25586)
Q86VE9-4	Isoform 4 of Serine incorporator 5 [OS=Homo sapiens]	Q8RGL8	Butyrate-acetoacetate CoA-transferase subunit B OS=Fusobacterium nucleatum (strain ATCC 25586)
Q9H0E2	Toll-interacting protein [OS=Homo sapiens]	Q8RIN1	Iron-sulfur cluster-binding protein OS=Fusobacterium nucleatum (strain ATCC 25586)
O75487	Glypican-4 [OS=Homo sapiens]	Q8RDP7	Pyridoxal 5'-phosphate synthase subunit PdxS OS=Fusobacterium nucleatum (strain ATCC 25586)
P36955	Pigment epithelium-derived factor [OS=Homo sapiens]	Q8RGH3	Fructose-bisphosphate aldolase class 1 OS=Fusobacterium nucleatum (strain ATCC 25586)
P0DME0	Protein SETSIP [OS=Homo sapiens]	Q8REG8	Phosphonates-binding protein OS=Fusobacterium nucleatum (strain ATCC 25586)
P20618	proteasome subunit beta type-1 [OS=Homo sapiens]	Q8RE27	Uncharacterized protein OS=Fusobacterium nucleatum (strain ATCC 25586)
P48059-3	Isoform 3 of LIM and senescent cell antigen-like-containing domain protein 1 [OS=Homo sapiens]	Q8RIG8	50S ribosomal protein L5 OS=Fusobacterium nucleatum (strain ATCC 25586)
Q9UMF0	intercellular adhesion molecule 5 [OS=Homo sapiens]	Q8RHM6	Tyrosine phenol-lyase OS=Fusobacterium nucleatum (strain ATCC 25586)
Q96F07	Cytoplasmic FMR1-interacting protein 2 [OS=Homo sapiens]	Q8RFG0	Glutamate formiminotransferase OS=Fusobacterium nucleatum (strain ATCC 25586)
P00488	Coagulation factor XIII A chain [OS=Homo sapiens]	Q8RHI6	DNA-directed RNA polymerase subunit beta OS=Fusobacterium nucleatum (strain ATCC 25586)
O95497	Pantetheinase [OS=Homo sapiens]		
P36551	Oxygen-dependent coproporphyrinogen-III oxidase, mitochondrial [OS=Homo sapiens]		
Q9NZM1	Myoferlin [OS=Homo sapiens]		
Q16787-2	Laminin subunit alpha-3 [OS=Homo sapiens]		
P23142-4	Isoform C of Fibulin-1 [OS=Homo sapiens]		
O95819-3	Isoform 3 of Mitogen-activated protein kinase kinase kinase kinase 4 [OS=Homo sapiens]		
Q9H5V8-1	CUB domain-containing protein 1 [OS=Homo sapiens]		
P13671	Complement component c6 [OS=Homo sapiens]		

O43240	Kallikrein-10 [OS=Homo sapiens]		
Q13126-2	Isoform 2 of S-methyl-5'-thioadenosine phosphorylase [OS=Homo sapiens]		
P10643	Complement component C7 [OS=Homo sapiens]		
P11234-2	Isoform 2 of Ras-related protein Ral-B [OS=Homo sapiens]		
P07910-1	Heterogeneous nuclear ribonucleoproteins C1/C2 [OS=Homo sapiens]		
O95866-2	Isoform A of Megakaryocyte and platelet inhibitory receptor G6b [OS=Homo sapiens]		
Q5SSJ5-1	Heterochromatin protein 1-binding protein 3 [OS=Homo sapiens]		
Q9UQ80	proliferation-associated protein 2G4 [OS=Homo sapiens]		
P14678-3	Isoform SM-B1 of Small nuclear ribonucleoprotein-associated proteins B and B' [OS=Homo sapiens]		
Q01469	Fatty acid-binding protein, epidermal [OS=Homo sapiens]		
P23229-1	integrin alpha-6 [OS=Homo sapiens]		
Q12841	Follistatin-related protein 1 [OS=Homo sapiens]		
Q86YZ3	Hornerin [OS=Homo sapiens]		
P63313	thymosin beta-10 [OS=Homo sapiens]		
Q15651-1	High mobility group nucleosome-binding domain-containing protein 3 [OS=Homo sapiens]		
P61247	40S ribosomal protein S3a [OS=Homo sapiens]		
P01780	Immunoglobulin heavy variable 3-7 [OS=Homo sapiens]		
A0A075B6I0	immunoglobulin lambda variable 8-61 [OS=Homo sapiens]		
P35052	Glypican-1 [OS=Homo sapiens]		
Q15758-1	Neutral amino acid transporter B(0) [OS=Homo sapiens]		
P32119	Peroxiredoxin-2 [OS=Homo sapiens]		
P61224-1	Ras-related protein Rap-1b [OS=Homo sapiens]		
P63000-2	Isoform B of Ras-related C3 botulinum toxin substrate 1 [OS=Homo sapiens]		
P12277	Creatine kinase B-type [OS=Homo sapiens]		
P61158	actin-related protein 3 [OS=Homo sapiens]		
A0A0C4DH38	immunoglobulin heavy variable 5-51 [OS=Homo sapiens]		
P05543	thyroxine-binding globulin [OS=Homo sapiens]		
P08697-1	Alpha-2-antiplasmin [OS=Homo sapiens]		
Q53H96	Pyrroline-5-carboxylate reductase 3 [OS=Homo sapiens]		
P25398	40S ribosomal protein S12 [OS=Homo sapiens]		
P03950	angiogenin [OS=Homo sapiens]		
P60981-1	Destrin [OS=Homo sapiens]		
Q9NZN3	EH domain-containing protein 3 [OS=Homo sapiens]		
P04062	glucosylceramidase [OS=Homo sapiens]		
P62888	60S ribosomal protein L30 [OS=Homo sapiens]		
O95750	Fibroblast growth factor 19 [OS=Homo sapiens]		
P05204	Non-histone chromosomal protein HMG-17 [OS=Homo sapiens]		
P55854-2	Isoform 2 of Small ubiquitin-related modifier 3 [OS=Homo sapiens]		
Q86XX4-2	Isoform 2 of Extracellular matrix protein FRAS1 [OS=Homo sapiens]		
P15514	Amphiregulin [OS=Homo sapiens]		
O94907	Dickkopf-related protein 1 [OS=Homo sapiens]		
P05164-3	Isoform H7 of Myeloperoxidase [OS=Homo sapiens]		
P17096-2	Isoform HMG-Y of High mobility group protein HMG-I/HMG-Y [OS=Homo sapiens]		
P38646	Stress-70 protein, mitochondrial [OS=Homo sapiens]		
Q9Y376	Calcium-binding protein 39 [OS=Homo sapiens]		
P02461	Collagen alpha-1(III) chain [OS=Homo sapiens]		
Q8IUE6	Histone H2A type 2-B [OS=Homo sapiens]		
P14770	Platelet glycoprotein IX [OS=Homo sapiens]		
P36871-2	Isoform 2 of Phosphoglucomutase-1 [OS=Homo sapiens]		
O75955	Flotillin-1 [OS=Homo sapiens]		
Q14254	Flotillin-2 [OS=Homo sapiens]		
O75954	tetraspanin-9 [OS=Homo sapiens]		
Q641Q3	Meteorin-like protein [OS=Homo sapiens]		
Q02413	Desmoglein-1 [OS=Homo sapiens]		
Q9NZN4	EH domain-containing protein 2 [OS=Homo sapiens]		
Q9Y5K6	CD2-associated protein [OS=Homo sapiens]		
Q96DG6	Carboxymethylenebutenolidase homolog [OS=Homo sapiens]		
P40925-3	Isoform 3 of Malate dehydrogenase, cytoplasmic [OS=Homo sapiens]		
Q9P258	Protein RCC2 [OS=Homo sapiens]		
Q92485-1	acid sphingomyelinase-like phosphodiesterase 3B [OS=Homo sapiens]		
P61313-1	60S ribosomal protein L15 [OS=Homo sapiens]		
P22061-2	Isoform 2 of Protein-L-isoaspartate(D-aspartate) O-methyltransferase [OS=Homo sapiens]		
P34932	Heat shock 70 kDa protein 4 [OS=Homo sapiens]		
P02545	Prelamin-A/C [OS=Homo sapiens]		
Q9HBI1-2	Isoform 2 of Beta-parvin [OS=Homo sapiens]		
P62826	GTP-binding nuclear protein RAN [OS=Homo sapiens]		
O43491-1	band 4.1-like protein 2 [OS=Homo sapiens]		
O00339-1	Matrilin-2 [OS=Homo sapiens]		
Q9Y617-1	phosphoserine aminotransferase [OS=Homo sapiens]		
P22626	heterogeneous nuclear ribonucleoproteins A2/B1 [OS=Homo sapiens]		
O60888-2	Isoform A of Protein CutA [OS=Homo sapiens]		
P35244	Replication protein A 14 kDa subunit [OS=Homo sapiens]		
P15151-1	Poliovirus receptor [OS=Homo sapiens]		
P49588-2	Isoform 2 of Alanine--tRNA ligase, cytoplasmic [OS=Homo sapiens]		
P37837	Transaldolase [OS=Homo sapiens]		
A0A0C4DH68	immunoglobulin kappa variable 2-24 [OS=Homo sapiens]		
Q9H9K5	Endogenous retrovirus group MER34 member 1 Env polyprotein [OS=Homo sapiens]		
Q14978-2	Isoform Beta of Nucleolar and coiled-body phosphoprotein 1 [OS=Homo sapiens]		
P24592	insulin-like growth factor-binding protein 6 [OS=Homo sapiens]		
O43278	Kunitz-type protease inhibitor 1 [OS=Homo sapiens]		
P62318	small nuclear ribonucleoprotein sm d3 [OS=Homo sapiens]		
Q9UBQ0-2	Isoform 2 of Vacuolar protein sorting-associated protein 29 [OS=Homo sapiens]		
Q9BWS9-2	Isoform 2 of Chitinase domain-containing protein 1 [OS=Homo sapiens]		
P62837	ubiquitin-conjugating enzyme E2 D2 [OS=Homo sapiens]		
Q68E01	Integrator complex subunit 3 [OS=Homo sapiens]		
P81605	Dermcidin [OS=Homo sapiens]		
Q96AG4	Leucine-rich repeat-containing protein 59 [OS=Homo sapiens]		
P62280	40S ribosomal protein S11 [OS=Homo sapiens]		
P62136-1	serine/threonine-protein phosphatase PP1-alpha catalytic subunit [OS=Homo sapiens]		
Q9Y4L1	Hypoxia up-regulated protein 1 [OS=Homo sapiens]		
O43488	aflatoxin B1 aldehyde reductase member 2 [OS=Homo sapiens]		
A0A0C4DH29	Immunoglobulin heavy variable 1-3 [OS=Homo sapiens]		
P02730	Band 3 anion transport protein [OS=Homo sapiens]		
P13798	Acylamino-acid-releasing enzyme [OS=Homo sapiens]		
Q7Z2W4	zinc finger CCCH-type antiviral protein 1 [OS=Homo sapiens]		
Q04917	14-3-3 protein eta [OS=Homo sapiens]		
O75390	citrate synthase, mitochondrial [OS=Homo sapiens]		
P08962	CD63 antigen [OS=Homo sapiens]		
P50552	Vasodilator-stimulated phosphoprotein [OS=Homo sapiens]		
O00410-3	Isoform 3 of Importin-5 [OS=Homo sapiens]		
Q9H0C2	ADP/ATP translocase 4 [OS=Homo sapiens]		
P10114	Ras-related protein Rap-2a [OS=Homo sapiens]		
P00740	Coagulation factor IX [OS=Homo sapiens]		
Q9ULA0	Aspartyl aminopeptidase [OS=Homo sapiens]		
P31146	Coronin-1A [OS=Homo sapiens]		
P55060-1	Exportin-2 [OS=Homo sapiens]		
P15153	Ras-related C3 botulinum toxin substrate 2 [OS=Homo sapiens]		
P09012	U1 SMALL NUCLEAR RIBONUCLEOPROTEIN A [OS=Homo sapiens]		
P35573-1	glycogen debranching enzyme [OS=Homo sapiens]		
P53621-2	Isoform 2 of Coatomer subunit alpha [OS=Homo sapiens]		
Q96J02	E3 ubiquitin-protein ligase Itchy homolog [OS=Homo sapiens]		
P02760	Protein AMBP [OS=Homo sapiens]		
Q14515	SPARC-like protein 1 [OS=Homo sapiens]		
P40429	60S ribosomal protein L13a [OS=Homo sapiens]		
P00749	Urokinase-type plasminogen activator [OS=Homo sapiens]		
P27105	erythrocyte band 7 integral membrane protein [OS=Homo sapiens]		
P10301	Ras-related protein R-Ras [OS=Homo sapiens]		
Q9NPH2	Inositol-3-phosphate synthase 1 [OS=Homo sapiens]		
P03973	Antileukoproteinase [OS=Homo sapiens]		
P01111	GTPase NRas [OS=Homo sapiens]		
P61978-2	Isoform 2 of Heterogeneous nuclear ribonucleoprotein K [OS=Homo sapiens]		
O43252	bifunctional 3'-phosphoadenosine 5'-phosphosulfate synthase 1 [OS=Homo sapiens]		
P17980	26S proteasome regulatory subunit 6A [OS=Homo sapiens]		
Q6ZVX7	F-box only protein 50 [OS=Homo sapiens]		
Q9HBH0	Rho-related GTP-binding protein RhoF [OS=Homo sapiens]		
P18124	60S ribosomal protein L7 [OS=Homo sapiens]		
P46777	60S ribosomal protein L5 [OS=Homo sapiens]		
Q9UNM6-2	Isoform 2 of 26S proteasome non-ATPase regulatory subunit 13 [OS=Homo sapiens]		
P60866-2	Isoform 2 of 40S ribosomal protein S20 [OS=Homo sapiens]		
P49407-1	Beta-arrestin-1 [OS=Homo sapiens]		
O75347-2	Isoform 2 of Tubulin-specific chaperone A [OS=Homo sapiens]		
P05386	60S acidic ribosomal protein P1 [OS=Homo sapiens]		

P01699	Immunoglobulin lambda variable 1-44 [OS=Homo sapiens]		
P21583-1	Kit ligand [OS=Homo sapiens]		
A0A0B4J1X5	immunoglobulin heavy variable 3-74 [OS=Homo sapiens]		
Q6UXI9-6	Isoform 6 of Nephronectin [OS=Homo sapiens]		
P11717	Cation-independent mannose-6-phosphate receptor [OS=Homo sapiens]		
Q9Y6C2	EMILIN-1 [OS=Homo sapiens]		
Q9UNN8	Endothelial protein C receptor [OS=Homo sapiens]		
P05388	60S acidic ribosomal protein P0 [OS=Homo sapiens]		
P00533-1	epidermal growth factor receptor [OS=Homo sapiens]		
Q9Y6W3	Calpain-7 [OS=Homo sapiens]		
Q9NZZ3	Charged multivesicular body protein 5 [OS=Homo sapiens]		
P14174	Macrophage Migration inhibitory factor [OS=Homo sapiens]		
P23396-2	Isoform 2 of 40S ribosomal protein S3 [OS=Homo sapiens]		
P38159-1	RNA-binding motif protein, X chromosome [OS=Homo sapiens]		
P07359	Platelet glycoprotein Ib alpha chain [OS=Homo sapiens]		
B5ME19	eukaryotic translation initiation factor 3 subunit C-like protein [OS=Homo sapiens]		
Q9UHL4	Dipeptidyl peptidase 2 [OS=Homo sapiens]		
P50502	Hsc70-interacting protein [OS=Homo sapiens]		
P62942	Peptidyl-prolyl cis-trans isomerase FKBP1A [OS=Homo sapiens]		
P41091	eukaryotic translation initiation factor 2 subunit 3 [OS=Homo sapiens]		
P62079	Tetraspanin-5 [OS=Homo sapiens]		
P15169	Carboxypeptidase N catalytic chain [OS=Homo sapiens]		
Q9ULV4-3	Isoform 3 of Coronin-1C [OS=Homo sapiens]		
P62249	40S ribosomal protein S16 [OS=Homo sapiens]		
Q04760-1	lactoylglutathione lyase [OS=Homo sapiens]		
Q9Y277-2	Isoform 2 of Voltage-dependent anion-selective channel protein 3 [OS=Homo sapiens]		

Table S8 KEGG pathway analysis showed that these Fn-Ex unique cell proteins.

pathway	pathway_name	class	diff_KO2acc	p value
hsa04062	Ribosome	Genetic Information Processing	hsa:6159(P47914);hsa:6187(P15880);hsa:6230(P62851);hsa:100529097(P83881);hsa:6157(P46776);hsa:6154(P61254);hsa:6155(P61353);hsa:6234(P62857);hsa:6232(P42677);hsa:6173(P83881);hsa:6130(P62424);hsa:6134(P27635);hsa:51121(P61254);hsa:6194(P62753);hsa:6193(P46782);hsa:6227(P63220);hsa:6202(P62241);hsa:6146(P35268);hsa:6141(Q07020);hsa:6207(P62277);hsa:6143(P84098);hsa:6166(P83881);hsa:6208(P62263);hsa:6209(P62841);hsa:6161(P62910);hsa:6223(P39019);hsa:6122(P39023);hsa:6124(P36578);hsa:6128(Q02878);hsa:9045(P50914)	1.53E-07
hsa04810	Chemokine signaling pathway	Organismal Systems	hsa:387(P61586);hsa:3576(P10145);hsa:58191(Q9H2A7)	0.055461
hsa04150	mTOR signaling pathway	Environmental Information Processing	hsa:6194(P62753);hsa:387(P61586);hsa:8140(Q01650)	0.062763
hsa04810	Regulation of actin cytoskeleton	Cellular Processes	hsa:387(P61586)	0.062763
hsa04270	Vascular smooth muscle contraction	Organismal Systems	hsa:140465(P14649);hsa:387(P61586);hsa:59(P62736);hsa:72(P62736)	0.062763
hsa05200	Pathways in cancer	Human Diseases	hsa:387(P61586);hsa:3576(P10145)	0.083066
hsa04015	Rap1 signaling pathway	Environmental Information Processing	hsa:387(P61586)	0.084432
hsa05205	Proteoglycans in cancer	Human Diseases	hsa:6194(P62753);hsa:387(P61586)	0.116169
hsa05150	Staphylococcus aureus infection	Human Diseases	hsa:102723407(P0DOX6);hsa:3426(P05156);hsa:718(P01024);hsa:2266(P02679);hsa:728358(P59665);hsa:1668(P59665);hsa:1667(P59665)	0.123359
hsa04510	Focal adhesion	Cellular Processes	hsa:1311(P49747);hsa:387(P61586);hsa:7060(P35443)	0.138822
hsa04610	Complement and coagulation cascades	Organismal Systems	hsa:718(P01024);hsa:2266(P02679);hsa:3426(P05156)	0.138822
hsa05133	Pertussis	Human Diseases	hsa:718(P01024);hsa:387(P61586);hsa:3576(P10145)	0.15324
hsa05161	Hepatitis B	Human Diseases	hsa:7529(P31946);hsa:3576(P10145);hsa:10971(P27348)	0.15324
hsa04621	NOD-like receptor signaling pathway	Organismal Systems	hsa:1667(P59665);hsa:728358(P59665);hsa:387(P61586);hsa:1668(P59665);hsa:3576(P10145)	0.15324
hsa04512	ECM-receptor interaction	Environmental Information Processing	hsa:1311(P49747);hsa:7060(P35443)	0.158097
hsa05165	Human papillomavirus infection	Human Diseases	hsa:1311(P49747);hsa:7060(P35443)	0.158097
hsa04371	Apelin signaling pathway	Environmental Information Processing	hsa:6194(P62753);hsa:59(P62736)	0.159481
hsa05142	Chagas disease (American trypanosomiasis)	Human Diseases	hsa:718(P01024);hsa:3576(P10145)	0.159481
hsa04932	Non-alcoholic fatty liver disease (NAFLD)	Human Diseases	hsa:1965(P05198);hsa:3576(P10145)	0.159481
hsa04144	Endocytosis	Cellular Processes	hsa:10890(P61026);hsa:55048(A5D8V6);hsa:128866(Q9H444);hsa:160(O95782);hsa:387(P61586)	0.169516
hsa04151	PI3K-Akt signaling pathway	Environmental Information Processing	hsa:102723407(P0DOX6);hsa:1311(P49747);hsa:7529(P31946);hsa:6194(P62753);hsa:7060(P35443);hsa:10971(P27348)	0.1703
hsa05418	Fluid shear stress and atherosclerosis	Human Diseases	hsa:387(P61586)	0.183131
hsa05202	Transcriptional misregulation in cancer	Human Diseases	hsa:102723407(P0DOX6);hsa:8358(P68431);hsa:653604(P68431);hsa:333932(P68431);hsa:3576(P10145);hsa:8352(P68431);hsa:8353(P68431);hsa:8350(P68431);hsa:8351(P68431);hsa:8356(P68431);hsa:8357(P68431);hsa:8354(P68431);hsa:8355(P68431);hsa:126961(P68431);hsa:1668(P59665);hsa:8968(P68431)	0.196016
hsa04915	Estrogen signaling pathway	Organismal Systems	hsa:3861(P02533);hsa:3868(P08779);hsa:3875(P05783);hsa:3880(P08727)	0.196016
hsa05322	Systemic lupus erythematosus	Human Diseases	hsa:102723407(P0DOX6);hsa:8358(P68431);hsa:8352(P68431);hsa:8353(P68431);hsa:8350(P68431);hsa:8351(P68431);hsa:8356(P68431);hsa:8357(P68431);hsa:8354(P68431);hsa:8355(P68431);hsa:8330(P0C0S8;Q93077);hsa:8331(P0C0S8);hsa:8332(P0C0S8;Q93077);hsa:8334(P0C0S8;Q93077);hsa:8335(P0C0S8;Q93077);hsa:8336(P0C0S8;Q93077);hsa:8337(P0C0S8;Q93077);hsa:8969(P0C0S8;Q93077);hsa:8968(P68431);hsa:723790(P0C0S8;Q93077);hsa:92815(Q93077);hsa:718(P01024);hsa:8329(P0C0S8;Q93077);hsa:653604(P68431);hsa:85235(P0C0S8;Q93077);hsa:333932(P68431);hsa:126961(P68431);hsa:3012(P0C0S8;Q93077);hsa:3013(P0C0S8)	0.206168
hsa05146	Amoebiasis	Human Diseases	hsa:102723407(P0DOX6);hsa:3576(P10145)	0.208201
hsa04611	Platelet activation	Organismal Systems	hsa:2266(P02679);hsa:387(P61586)	0.208201
hsa04145	Phagosome	Cellular Processes	hsa:102723407(P0DOX6);hsa:1311(P49747);hsa:7060(P35443);hsa:718(P01024);hsa:7846(P68363);hsa:10376(P68363)	0.228841
hsa04210	Apoptosis	Cellular Processes	hsa:7846(P68363);hsa:1965(P05198);hsa:142(P09874);hsa:10376(P68363)	0.232865
hsa04530	Tight junction	Cellular Processes	hsa:7846(P68363);hsa:140465(P14649);hsa:387(P61586);hsa:10376(P68363)	0.232865
hsa04072	Phospholipase D signaling pathway	Environmental Information Processing	hsa:102723407(P0DOX6);hsa:387(P61586);hsa:3576(P10145)	0.232865
hsa04064	NF-kappa B signaling pathway	Environmental Information Processing	hsa:102723407(P0DOX6);hsa:3576(P10145);hsa:142(P09874)	0.232865
hsa05152	Tuberculosis	Human Diseases	hsa:718(P01024);hsa:387(P61586);hsa:102723407(P0DOX6)	0.232865
hsa04217	Necroptosis	Cellular Processes	hsa:8969(P0C0S8;Q93077);hsa:3012(P0C0S8;Q93077);hsa:8336(P0C0S8;Q93077);hsa:142(P09874);hsa:92815(Q93077);hsa:8329(P0C0S8;Q93077);hsa:128866(Q9H444);hsa:723790(P0C0S8;Q93077);hsa:3013(P0C0S8);hsa:8330(P0C0S8;Q93077);hsa:8331(P0C0S8);hsa:8332(P0C0S8;Q93077);hsa:8334(P0C0S8;Q93077);hsa:8335(P0C0S8;Q93077);hsa:85235(P0C0S8;Q93077);hsa:8337(P0C0S8;Q93077)	0.237833
hsa04520	Adherens junction	Cellular Processes	hsa:387(P61586)	0.25774
hsa04066	HIF-1 signaling pathway	Environmental Information Processing	hsa:6194(P62753)	0.25774
hsa04141	Protein processing in endoplasmic reticulum	Genetic Information Processing	hsa:1965(P05198)	0.25774
hsa03013	RNA transport	Genetic Information Processing	hsa:1965(P05198)	0.25774
hsa05131	Shigellosis	Human Diseases	hsa:3576(P10145)	0.25774
hsa04979	Cholesterol metabolism	Organismal Systems	hsa:5360(P55058)	0.25774
hsa04670	Leukocyte transendothelial migration	Organismal Systems	hsa:387(P61586)	0.25774
hsa05203	Viral carcinogenesis	Human Diseases	hsa:718(P01024);hsa:7529(P31946);hsa:387(P61586);hsa:10971(P27348)	0.258583
hsa05130	Pathogenic Escherichia coli infection	Human Diseases	hsa:7846(P68363);hsa:3875(P05783);hsa:387(P61586);hsa:10376(P68363);hsa:10971(P27348)	0.259166
hsa04390	Hippo signaling pathway	Environmental Information Processing	hsa:7529(P31946);hsa:10971(P27348)	0.263175
hsa05206	MicroRNAs in cancer	Human Diseases	hsa:7431(P08670);hsa:387(P61586)	0.263175
hsa05034	Alcoholism	Human Diseases	hsa:8358(P68431);hsa:8352(P68431);hsa:8353(P68431);hsa:8350(P68431);hsa:8351(P68431);hsa:8356(P68431);hsa:8357(P68431);hsa:8354(P68431);hsa:8355(P68431);hsa:8330(P0C0S8;Q93077);hsa:8331(P0C0S8);hsa:8332(P0C0S8;Q93077);hsa:8334(P0C0S8;Q93077);hsa:8335(P0C0S8;Q93077);hsa:8336(P0C0S8;Q93077);hsa:8337(P0C0S8;Q93077);hsa:8969(P0C0S8;Q93077);hsa:8968(P68431);hsa:723790(P0C0S8;Q93077);hsa:92815(Q93077);hsa:8329(P0C0S8;Q93077);hsa:653604(P68431);hsa:85235(P0C0S8;Q93077);hsa:333932(P68431);hsa:126961(P68431);hsa:3012(P0C0S8;Q93077);hsa:3013(P0C0S8)	0.28189
hsa05144	Malaria	Human Diseases	hsa:1311(P49747);hsa:3576(P10145);hsa:7060(P35443)	0.28189
hsa05160	Hepatitis C	Human Diseases	hsa:7529(P31946);hsa:1965(P05198);hsa:10971(P27348)	0.28189
hsa04110	Cell cycle	Cellular Processes	hsa:7529(P31946);hsa:10971(P27348)	0.290152
hsa04114	Oocyte meiosis	Cellular Processes	hsa:7529(P31946);hsa:10971(P27348)	0.290152
hsa04060	Cytokine-cytokine receptor interaction	Environmental Information Processing	hsa:58191(Q9H2A7);hsa:3576(P10145)	0.290152
hsa05323	Rheumatoid arthritis	Human Diseases	hsa:102723407(P0DOX6);hsa:3576(P10145)	0.290152
hsa05140	Leishmaniasis	Human Diseases	hsa:718(P01024);hsa:102723407(P0DOX6)	0.290152
hsa05168	Herpes simplex virus 1 infection	Human Diseases	hsa:718(P01024);hsa:1965(P05198)	0.290152
hsa05135	Yersinia infection	Human Diseases	hsa:387(P61586);hsa:3576(P10145)	0.290152
hsa05169	Epstein-Barr virus infection	Human Diseases	hsa:102723407(P0DOX6);hsa:7431(P08670);hsa:5701(P35998)	0.297291
hsa05134	Legionellosis	Human Diseases	hsa:718(P01024);hsa:3576(P10145)	0.315393
hsa04540	Gap junction	Cellular Processes	hsa:7846(P68363);hsa:10376(P68363)	0.346675
hsa05100	Bacterial invasion of epithelial cells	Human Diseases	hsa:387(P61586)	0.346675
hsa05143	African trypanosomiasis	Human Diseases	hsa:102723407(P0DOX6)	0.346675
hsa05230	Central carbon metabolism in cancer	Human Diseases	hsa:8140(Q01650)	0.346675
hsa03320	PPAR signaling pathway	Organismal Systems	hsa:5360(P55058)	0.346675
hsa04640	Hematopoietic cell lineage	Organismal Systems	hsa:102723407(P0DOX6)	0.346675
hsa04666	Fc gamma R-mediated phagocytosis	Organismal Systems	hsa:102723407(P0DOX6)	0.346675
hsa04310	Wnt signaling pathway	Environmental Information Processing	hsa:8607(Q9Y265);hsa:387(P61586)	0.350443
hsa05163	Human cytomegalovirus infection	Human Diseases	hsa:387(P61586);hsa:3576(P10145)	0.350443
hsa05164	Influenza A	Human Diseases	hsa:1965(P05198);hsa:3576(P10145)	0.350443
hsa05167	Kaposi sarcoma-associated herpesvirus infection	Human Diseases	hsa:718(P01024);hsa:3576(P10145)	0.350443

hsa04921	Oxytocin signaling pathway	Organismal Systems	hsa:140465(P14649);hsa:387(P61586)	0.350443
hsa03050	Proteasome	Genetic Information Processing	hsa:5695(Q99436);hsa:5701(P35998)	0.351207
hsa05414	Dilated cardiomyopathy (DCM)	Human Diseases	hsa:102723407(P0DOX6);hsa:70(P62736)	0.351207
hsa04218	Cellular senescence	Cellular Processes	hsa:3576(P10145)	0.401274
hsa04071	Sphingolipid signaling pathway	Environmental Information Processing	hsa:387(P61586)	0.401274
hsa04061	Viral protein interaction with cytokine and cytokine receptor	Environmental Information Processing	hsa:3576(P10145)	0.401274
hsa04910	Insulin signaling pathway	Organismal Systems	hsa:6194(P62753)	0.401274
hsa04928	Parathyroid hormone synthesis, secretion and action	Organismal Systems	hsa:387(P61586)	0.401274
hsa04625	C-type lectin receptor signaling pathway	Organismal Systems	hsa:387(P61586)	0.401274
hsa04620	Toll-like receptor signaling pathway	Organismal Systems	hsa:3576(P10145)	0.401274
hsa04722	Neurotrophin signaling pathway	Organismal Systems	hsa:387(P61586)	0.401274
hsa04614	Renin-angiotensin system	Organismal Systems	hsa:10159(O75787)	0.401274
hsa04721	Synaptic vesicle cycle	Organismal Systems	hsa:160(O95782)	0.401274
hsa04622	RIG-I-like receptor signaling pathway	Organismal Systems	hsa:3576(P10145)	0.401274
hsa04660	T cell receptor signaling pathway	Organismal Systems	hsa:387(P61586)	0.401274
hsa04014	Ras signaling pathway	Environmental Information Processing	hsa:387(P61586)	0.435228
hsa04080	Neuroactive ligand-receptor interaction	Environmental Information Processing	hsa:718(P01024)	0.435228
hsa05416	Viral myocarditis	Human Diseases	hsa:102723407(P0DOX6)	0.435228
hsa04933	AGE-RAGE signaling pathway in diabetic complications	Human Diseases	hsa:3576(P10145)	0.435228
hsa05132	Salmonella infection	Human Diseases	hsa:3576(P10145)	0.435228
hsa05410	Hypertrophic cardiomyopathy (HCM)	Human Diseases	hsa:70(P62736)	0.435228
hsa05210	Colorectal cancer	Human Diseases	hsa:387(P61586)	0.435228
hsa04360	Axon guidance	Organismal Systems	hsa:387(P61586)	0.435228
hsa04657	IL-17 signaling pathway	Organismal Systems	hsa:3576(P10145)	0.435228
hsa04662	B cell receptor signaling pathway	Organismal Systems	hsa:102723407(P0DOX6)	0.435228
hsa04926	Relaxin signaling pathway	Organismal Systems	hsa:59(P62736)	0.435228
hsa04714	Thermogenesis	Organismal Systems	hsa:6194(P62753)	0.435228
hsa04140	Autophagy - animal	Cellular Processes	hsa:1965(P05198)	0.483586
hsa04152	AMPK signaling pathway	Environmental Information Processing	hsa:10890(P61026)	0.483586
hsa04020	Calcium signaling pathway	Environmental Information Processing	hsa:102723407(P0DOX6)	0.483586
hsa04350	TGF-beta signaling pathway	Environmental Information Processing	hsa:387(P61586)	0.483586
hsa04022	cGMP-PKG signaling pathway	Environmental Information Processing	hsa:387(P61586)	0.483586
hsa04024	cAMP signaling pathway	Environmental Information Processing	hsa:387(P61586)	0.483586
hsa03410	Base excision repair	Genetic Information Processing	hsa:142(P09874)	0.483586
hsa05016	Huntington disease	Human Diseases	hsa:160(O95782)	0.483586
hsa05219	Bladder cancer	Human Diseases	hsa:3576(P10145)	0.483586
hsa05320	Autoimmune thyroid disease	Human Diseases	hsa:102723407(P0DOX6)	0.483586
hsa05340	Primary immunodeficiency	Human Diseases	hsa:102723407(P0DOX6)	0.483586
hsa05162	Measles	Human Diseases	hsa:1965(P05198)	0.483586
hsa05330	Allograft rejection	Human Diseases	hsa:102723407(P0DOX6)	0.483586
hsa05120	Epithelial cell signaling in Helicobacter pylori infection	Human Diseases	hsa:3576(P10145)	0.483586
hsa05310	Asthma	Human Diseases	hsa:102723407(P0DOX6)	0.483586
hsa04672	Intestinal immune network for IgA production	Organismal Systems	hsa:102723407(P0DOX6)	0.483586
hsa04261	Adrenergic signaling in cardiomyocytes	Organismal Systems	hsa:70(P62736)	0.483586
hsa04961	Endocrine and other factor-regulated calcium reabsorption	Organismal Systems	hsa:160(O95782)	0.483586
hsa04650	Natural killer cell mediated cytotoxicity	Organismal Systems	hsa:102723407(P0DOX6)	0.483586
hsa04972	Pancreatic secretion	Organismal Systems	hsa:387(P61586)	0.483586
hsa04260	Cardiac muscle contraction	Organismal Systems	hsa:70(P62736)	0.483586
hsa04664	Fc epsilon RI signaling pathway	Organismal Systems	hsa:102723407(P0DOX6)	0.483586

Table S9 The relationship between the fecal Fn abundance or serum exosomes miR-1246/92b-3p/27a-3p levels and the clinicopathological variables of the 82 CRC patients.

Characteristics	**cases (n)**	***Fn* -log10**	***p***	**miR-1246 -log10**	***p***	**miR-92b-3p -log10**	***p***	**miR-27a-3p -log10**	***p***	**CXCL16 log10 pg/ml**	***P***
Gender			0.51		0.46		0.16		0.3		0.4
Male	54	4.44±1.31		3.18±1.32		3.59±1.29		4.47±0.75		1.71±0.79	
Female	28	4.23±1.54		3.39±0.97		3.14±1.46		4.30±0.69		1.55±0.78	
Age(y)			0.34		0.97		0.69		0.22		0.33
<60	43	4.30±1.40		3.25±1.20		3.50±1.47		4.32±0.70		1.73±0.79	
≥60	39	4.52±1.37		3.26±1.25		3.37±1.25		4.52±0.77		1.56±0.79	
Location			0.66		0.95		0.58		0.95		0.67
Colon	53	4.32±1.39		3.24±1.27		3.50±1.40		4.41±0.68		1.68±0.76	
Rectal	29	4.46±1.38		3.26±1.13		5.32±1.30		4.42±0.81		1.60±0.85	
Stage			0.11		0.59		0.1		0.04		0.45
Ⅰ+Ⅱ	45	4.59±1.49		3.32±1.16		3.21±1.30		4.57±23.93		1.59±0.80	
Ⅲ+Ⅳ	37	4.10±1.20		3.20±1.28		3.70±1.40		4.23±20.81		1.73±0.78	
T status			0.92		0.26		0.71		0.62		0.09
T1+T2	13	4.33±1.77		3.48±0.65		3.31±1.26		4.51±0.58		1.32±0.76	
T3+T4	69	4.38±1.31		3.21±1.29		3.46±1.39		4.40±0.76		1.72±0.78	
N status			0.13		0.6		0.09		0.43		0.73
No	44	4.58±1.51		3.32±1.18		3.20±1.31		4.56±0.71		1.68±0.68	
Yes	38	4.12±1.19		3.18±1.27		3.71±1.38		4.24±0.73		1.62±0.73	
Metastasis			0.72		0.47		0.17		0.62		0.006
No	66	4.40±1.46		3.30±1.21		3.34±1.33		4.43±0.72		1.54±0.71	
Yes	16	4.26±1.06		3.05±1.23		3.86±1.44		4.33±0.79		2.13±0.94	
CEA (μg/ml)			0.21		0.24		0.59		0.88		0.07
<5	53	4.22±1.30		3.37±1.07		3.50±1.36		4.40±0.72		1.54±0.83	
≥5	29	4.63±1.52		3.04±1.43		3.33±1.38		4.43±0.77		1.87±0.71	
CA19-9 (U/ml)			0.34		0.4		0.85		0.17		0.72
<35	69	6.31±1.40		3.20±1.23		3.42±1.30		4.36±0.40		1.64±0.77	
≥35	13	4.70±1.29		3.51±1.09		3.50±1.72		4.67±0.65		1.73±0.69	
gFOBT			0.62		0.95		0.19		0.76		0.65
Positive	8	4.05±1.26		3.38±1.39		4.05±1.24		4.23±0.68		1.86±0.54	
Weakly positive	12	4.14±1.44		3.21±1.42		2.93±1.15		4.46±0.81		1.64±0.69	
Negative	62	4.45±1.40		3.24±1.17		3.46±1.39		4.43±0.73		1.63±0.70	

Supplementary Figure

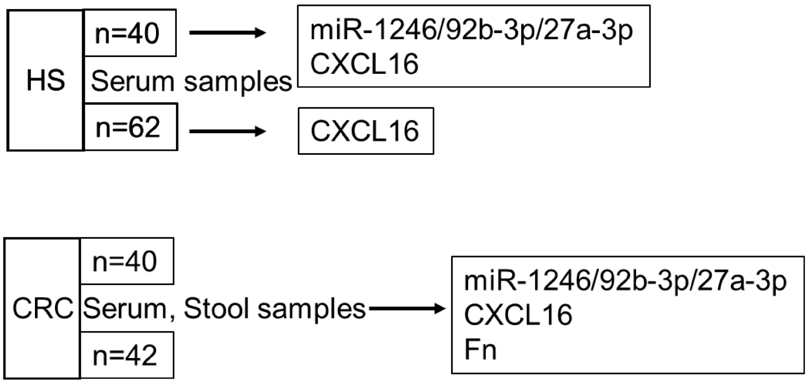


Figure S1 Background grouping of the study cohorts.

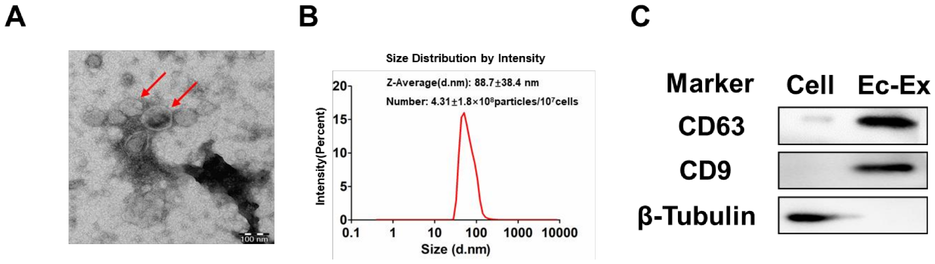


Figure S2 Identification of exosomes derived from *E.coli*-infected HCT116 cell (Ec -Ex). HCT116 cell were infected with live *E.coli* at an MOI of 1:1000 (bacteria: cells) and then were cultured for 24 h. **(A)** TEM images of purified Ec-Ex. Scale bar = 100 nm. **(B)** Nanoparticle tracking analysis (NTA) analysis of size distribution. **(C)** Western blot analysis of markers (CD63 and CD9) in exosomal protein purified from *E.coli*-infected HCT116 cell supernatants, tubulin served as an internal control in whole-cell lysates.

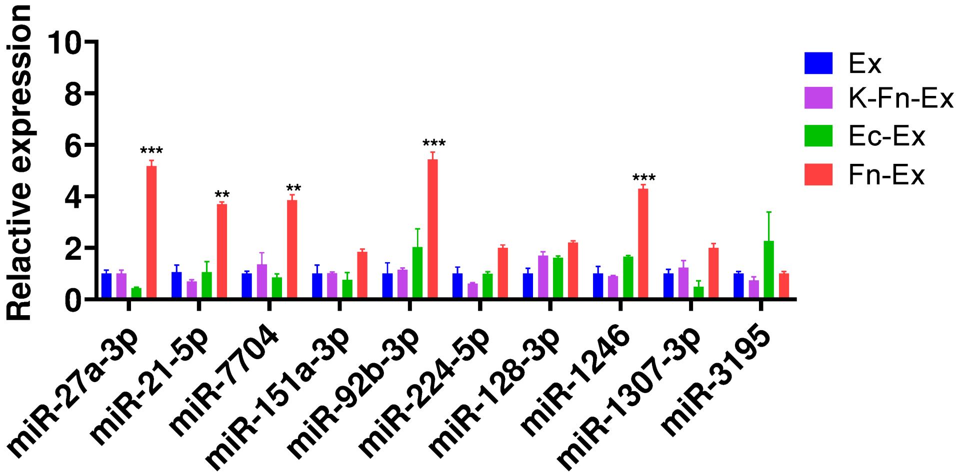
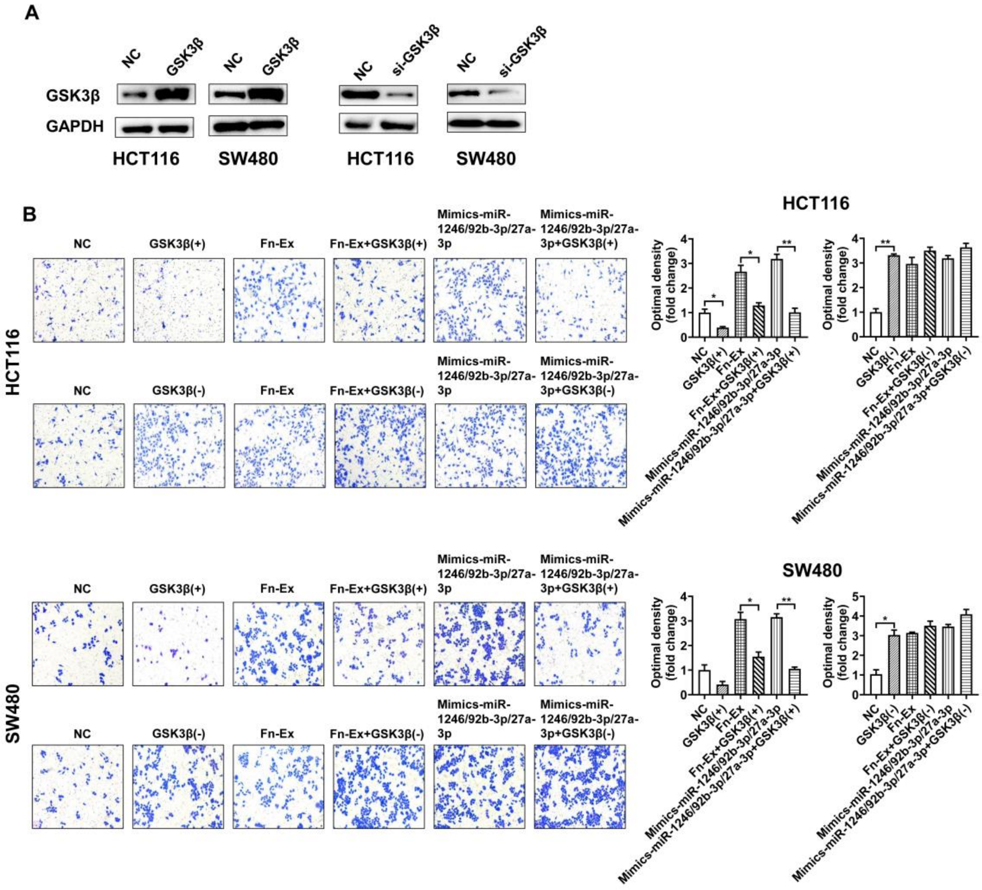


Figure S3 Screen and identification the results of RNA sequence in exosome from HCT116 cells (Ex), *E.coli*-infected HCT116 cells (Ec-Ex), Fn-infected HCT116 cells (Fn-Ex), and heat-killed Fn-infected HCT116 cells (K-Fn-Ex). Quantitative real-time PCR indicating relative expression of selected miRNA in Ex, K-Fn-Ex, Ec-Ex and Fn-Ex. Error bars, SD. **, *P* < 0.01; ***, *P* < 0.001.


A
NC
GSK3β
NC
GSK3β
NC
si-GSK3β
NC
si-GSK3β
GSK3β
GAPDH
HCT116
SW480
HCT116
SW480
B
HCT116
NC
GSK3β(+)
Fn-Ex
Fn-Ex+GSK3β(+)
Mimics-miR-1246/92b-3p/27a-3p
Mimics-miR-1246/92b-3p/27a-3p+GSK3β(+)
NC
GSK3β(-)
Fn-Ex
Fn-Ex+GSK3β(-)
Mimics-miR-1246/92b-3p/27a-3p
Mimics-miR-1246/92b-3p/27a-3p+GSK3β(-)
Optimal density (fold change)
0
1
2
3
4
*
*
**
NC
GSK3β(+)
Fn-Ex
Fn-Ex+GSK3β(+)
Mimics-miR-1246/92b-3p/27a-3p
Mimics-miR-1246/92b-3p/27a-3p+GSK3β(+)
**
NC
GSK3β(-)
Fn-Ex
Fn-Ex+GSK3β(-)
Mimics-miR-1246/92b-3p/27a-3p
Mimics-miR-1246/92b-3p/27a-3p+GSK3β(-)
SW480
NC
GSK3β(+)
Fn-Ex
Fn-Ex+GSK3β(+)
Mimics-miR-1246/92b-3p/27a-3p
Mimics-miR-1246/92b-3p/27a-3p+GSK3β(+)
NC
GSK3β(-)
Fn-Ex
Fn-Ex+GSK3β(-)
Mimics-miR-1246/92b-3p/27a-3p
Mimics-miR-1246/92b-3p/27a-3p+GSK3β(-)
Optimal density (fold change)
0
1
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5
*
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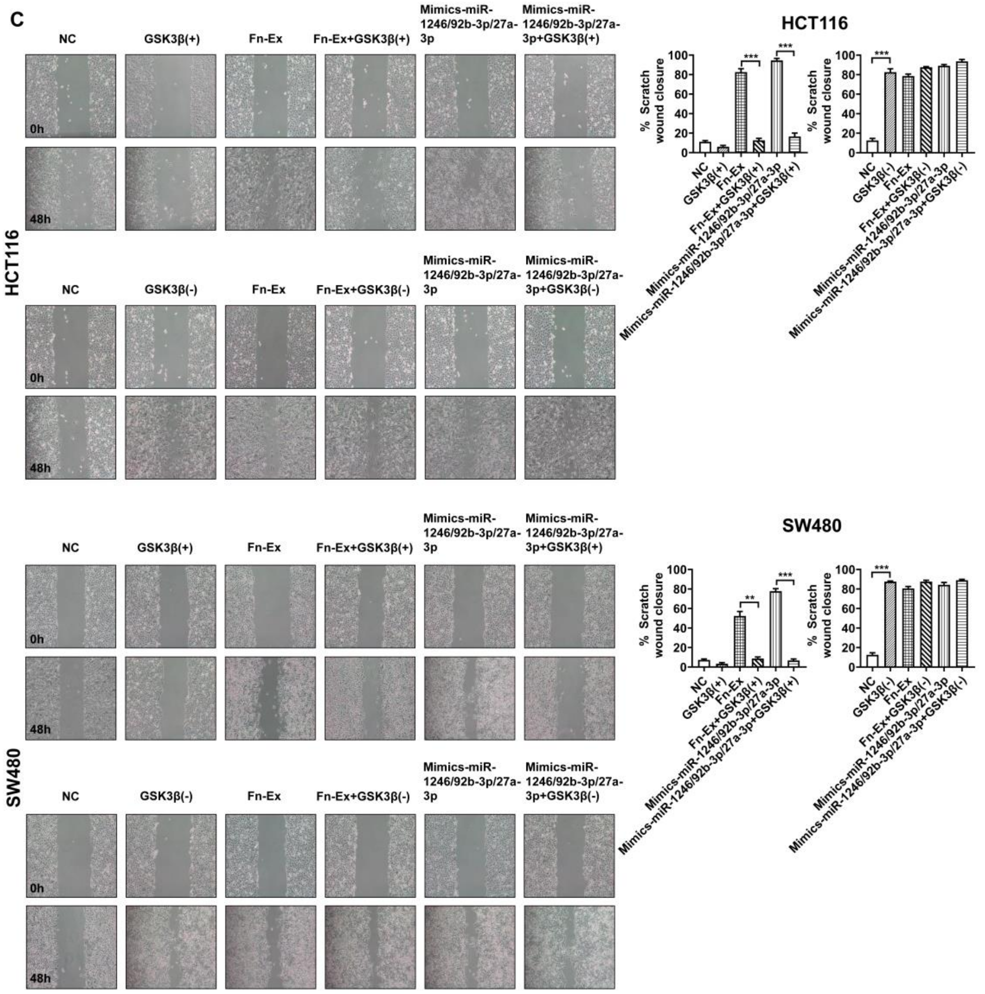

Figure S4 miR-1246/92b-3p/27a-3p of Fn-Ex to promote CRC cells migration through inhibition of GSK3β. (A) Expression of GSK3β in HCT116 and SW480 cells after transfection with GSK3β overexpression plasmid GSK3β(+) or siRNAs GSK3β(-). **(B)** The migration of CRC cells was assessed using a Transwell migration assays. Representative images of the assay (right). **(C)** Analysis of CRC cells migration by *in vitro* scratch assays. Images were acquired at 0 and 48 h. Right quantitative analysis of scratch wound closure. Data represent at least three experiments performed in triplicate. Scale bar = 200 μm; Error bars, SD. **, $P < 0.01$; and ***, $P < 0.001$.

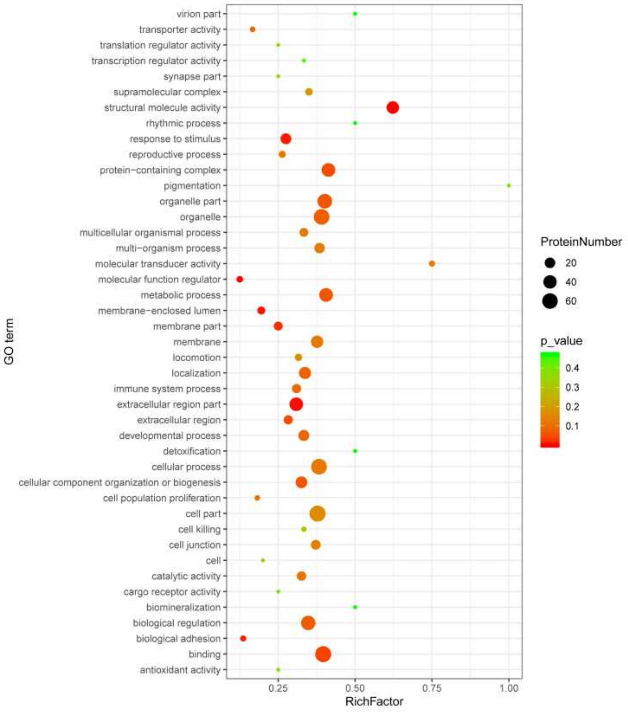

Figure S5 Gene ontology (GO) enrichment analysis of the Fn-infected HCT116 cells derived exosomes (Fn-Ex) unique cell proteins.

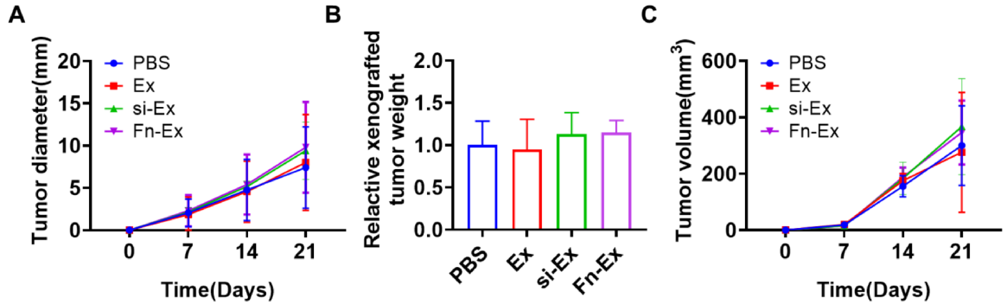

Figure S6 *In vivo* verification shows that Fn-Ex promotes migration. Quantitative analysis of xenografted tumor diameter **(A)**, weight **(B)**, and volume **(C)** (n = 5). Error bars, SD.