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| Research Article

Undergraduate-level biology students' application of central dogma to understand COVID mRNA vaccines

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ABSTRACT The coronavirus disease 2019 (COVID-19) pandemic has underscored the importance of mRNA vaccines. The mechanism for how such vaccines work is related to the core biology topic of the central dogma, which students often misunderstand despite its importance. Therefore, we wanted to know whether students can apply their biology knowledge of central dogma to the real-world issue of how mRNA COVID vaccines work. Accordingly, we asked college biology students of different expertise levels how the COVID vaccine worked. Later, we cued them by telling them the vaccine contains mRNA and asked them what the mRNA does. We used thematic analysis to find common ideas in their responses. In the uncued condition, fewer than half of the students used central dogma-related ideas to explain what was in the vaccine or how the vaccine worked. Inaccurate ideas were present among all groups of biology students, particularly entering biology majors and non-biology majors, including the idea that the COVID vaccines contain a weakened, dead, or variant form of the COVID virus. After students were cued, many more students in all expertise groups expressed central dogma-related themes, showing that students could apply the knowledge of central dogma if prompted. Advanced biology majors were much more likely to state that the vaccines code for a viral protein, indicating their advanced application of central dogma concepts. These results highlight inaccurate ideas common among students and show changes in the ability to apply knowledge with student expertise level, which could inform future interventions to support student learning about vaccines and central dogma.

KEYWORDS COVID, COVID vaccines, central dogma, misconceptions, mRNA

It is critical for biology educators to prepare students to apply their biology knowledge to understand societally relevant biology topics (1). However, it can be difficult for students to do this, especially without a cue that signals to students that their classroom knowledge may be relevant (2, 3). The coronavirus disease 2019 (COVID-19) pandemic highlighted the importance of vaccination for protecting against infectious disease (4). Yet, studies have found that most college biology students are only partially able to use their knowledge to understand how vaccines function (5, 6).

For students to understand COVID-19 vaccines, they not only need to understand how vaccines work in general but also apply the central dogma of biology, as the most effective vaccines for this disease are mRNA vaccines (4). The central dogma of biology is a key concept that explains the flow of genetic information: DNA is transcribed into RNA, which is then translated into protein. COVID mRNA vaccines contain mRNA that cells translate to produce a version of the virus' spike protein, so understanding the second half of the central dogma is crucial for understanding how these vaccines work (4) (Fig. 1). However, research shows many students incorrectly conceptualize information flow in relation to central dogma (7, 8). For example, many students believe that DNA is chemically transformed into RNA (8). Some inaccurate ideas about mRNA COVID-19

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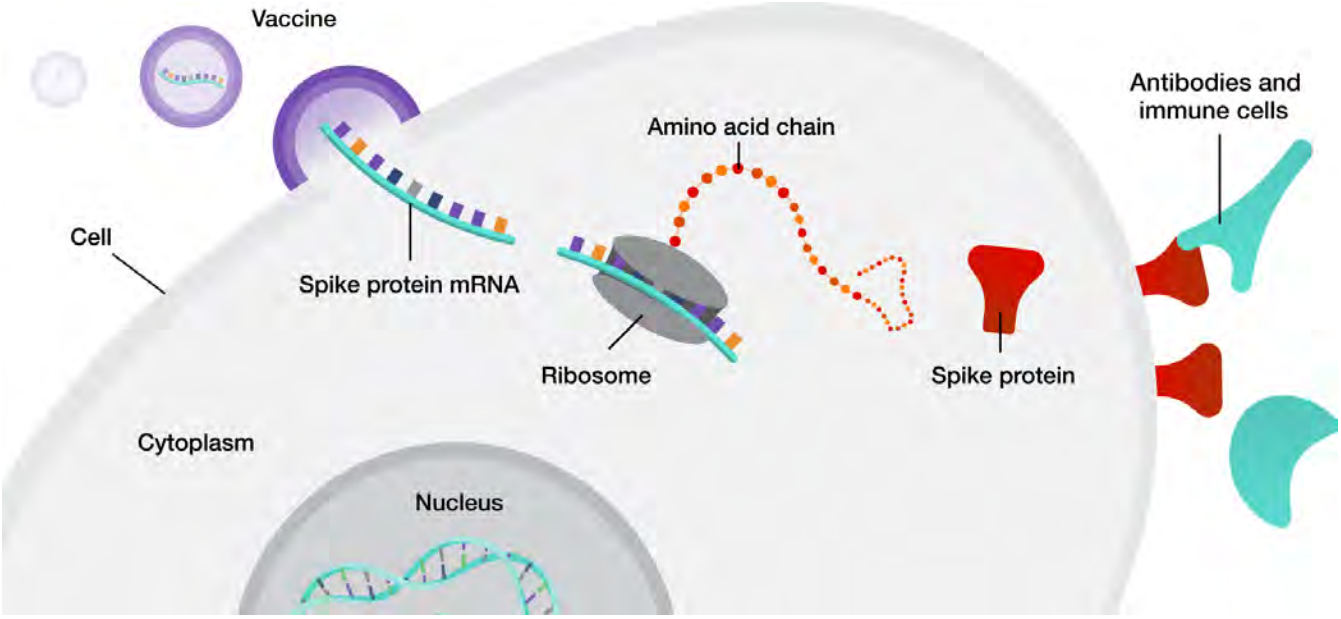

FIG 1 Diagram of how the COVID vaccine works in relation to central dogma. The vaccine delivers the mRNA of severe acute respiratory syndrome coronavirus 2's (SARS-CoV-2's) spike protein to body cells. The cell translates the mRNA into the spike protein, a step that involves the central dogma. The spike protein is then moved to the cell surface, where antibodies and immune cells can interact with the spike protein to produce immunity. Image courtesy of the National Human Genome Research Institute (https://www.genome.gov/about-genomics/fact-sheets/Understanding-COVID-19-mRNA-Vaccines).

vaccines found in members of the public, such as the idea that they can alter one's DNA, relate to misapplications of the central dogma (9). Nevertheless, studies have also shown that students can learn accurate information about the central dogma after instruction (8). Therefore, if students can apply their classroom knowledge about central dogma to mRNA COVID-19 vaccines, they should be able to better explain how these vaccines work.

We analyzed student responses to free-response questions about how mRNA COVID vaccines work to investigate the extent to which college students apply their knowledge of central dogma to the real-world issue of mRNA COVID vaccines. Our work addresses the following questions:

1. What do students believe is in the COVID-19 vaccine?
2. To what extent do college biology students apply central dogma-related ideas when explaining how a COVID-19 vaccine works?
3. When cued with the information that some COVID-19 vaccines contain mRNA, to what extent do college biology students apply central dogma-related ideas when explaining how a COVID-19 vaccine works?

METHODS

Study context

This study occurred at a large, public university in the western United States with very high research activity (10). It was approved by the Human Research Protections Program of the University of California, San Diego (Project #201521 XX).

Survey development

The survey was initially developed to probe student ideas and attitudes about the COVID-19 vaccines. To confirm that the questions were unambiguous and elicited relevant responses (validation evidence based on response processes), we conducted think-aloud interviews with people with PhDs in biology (n = 3 people) and students

taking upper-division ($n = 6$), lower-division ($n = 5$), and non-major ($n = 8$) biology courses (11). Because these interviews are only intended to provide feedback on the questions themselves, it is typically sufficient to interview a handful of people (12). Based on 14 initial interviews, we revised the question about the role of mRNA in the mRNA COVID vaccine to its current form. Later interviews with people from all four categories ($n = 8$) confirmed that the rephrased question was clear and produced responses related to the interviewee's ideas about mRNA, central dogma, COVID vaccines, and immunity. No other questions were altered. The full text of the finalized survey is included in Appendix 1.

Data collection

In the 2020–2021 academic year, students enrolled in seven large-enrollment biology courses were invited, via announcements on the course learning management system, to participate in this study. To participate, students completed an online survey. Invited courses included upper-division (advanced), lower-division (entering), and non-major classes. Students were incentivized by a small amount of extra credit, based on each instructor's discretion. In total, 975 students were invited, and 714 (73%) students participated. These participants were categorized into three expertise-level groups: advanced biology majors (ABM), entering biology majors (EBM), and non-biology majors (NBM) based on their stated major and the course from which they were invited. Participants were excluded if they did not respond to all survey questions or if their stated major and course did not match (i.e., a public health major taking lower-division biology). After exclusions, there were 64 NBMs, 75 EBMs, and 386 ABMs. To avoid overweighting ABM responses, we randomly chose 75 ABM responses to analyze, making the final sample size 75 ABMs. Table 1 contains more information about student demographics and participation rates.

Thematic analysis and inter-rater reliability

The primary questions analyzed here were, "How does a COVID vaccine work?" and "Some of the COVID vaccines have mRNA in them. What is the mRNA's role in how the COVID vaccine works?" These questions were intended to reveal the students'

TABLE 1 Student participant demographics

Group	Advanced biology majors	Entering biology majors	Non-biology majors
No. of students invited	575	288	112
No. of students participated	427	221	66
Participation rate (%)[a]	74.3%	76.7%	58.9%
No. of participants after exclusion criteria applied	386	75	64
No. of participants selected for analysis	75[b]	75	64
Racial and ethnic composition (%)[a]	Asian: 54.7%	Asian: 60.0%	Asian: 32.8%
	Black: 1.3%	Black: 8.0%	Black: 3.1%
	Latinx/Hispanic: 25.3%	Latinx/Hispanic: 25.3%	Latinx/Hispanic 42.2%
	White: 16.0%	White: 6.7%	White: 20.3%
	Prefer not to answer: 2.7%	Prefer not to answer: 0.0%	Prefer not to answer: 1.6%
Gender	Female: 60.0%	Female: 80.0%	Female: 81.3%
	Male: 37.3%	Male: 20.0%	Male: 17.2%
	Non-binary: 1.3%	Non-binary: 0.0%	Non-binary: 1.6%
	Prefer not to answer: 1.3%	Prefer not to answer: 0.0%	Prefer not to answer: 0.0%
Political orientation	Consistently or mostly conservative: 9.3%	Consistently or mostly conservative: 2.7%	Consistently or mostly conservative: 1.6%
	Mixed: 12.0%	Mixed: 21.3%	Mixed: 15.6%
	Consistently or mostly liberal: 57.3%	Consistently or mostly liberal: 53.3%	Consistently or mostly liberal: 68.8%
	Prefer not to answer: 21.3%	Prefer not to answer: 22.7%	Prefer not to answer: 14.1%

[a]Categories where there are significant differences ($P < 0.05$) between student groups by chi-square analysis.
[b]Chosen by random sampling from the total pool of eligible students in this group.

knowledge of how vaccines work and its relation to central dogma. The first question was termed the "uncued" condition because it did not contain any mention of central dogma-related ideas, and the second question was termed the "cued" condition because the question specifically mentioned mRNA. All participants answered both questions, with the uncued question first.

To analyze responses, we used thematic analysis to create two coding guides. The first coding guide was for ideas about the contents of the COVID vaccine, which was developed with and used to analyze responses to the uncued question. If students do not know that the COVID vaccines contain mRNA, they are unlikely to apply central dogma. The second coding guide was for ideas relating to the mechanism of action of the COVID vaccine. It was developed with the responses to the cued question and was used to analyze responses to both the cued and uncued questions. Qualitative coding was performed in Google Sheets and QDA Miner 6.

In both cases, thematic analysis began with one researcher reading a subset of the students' responses to create a preliminary coding guide. Then, to measure inter-rater reliability to characterize the validity and replicability of coding, a second rater recoded a random subset of 10% of the responses for each expertise level of student for each research question. When there were discrepancies in coding, the coding guide was revised. This process was repeated until we achieved at least 85% agreement. Then, for each code, we used Google Sheets to calculate the raw agreement rate and Cohen's kappa, a metric which takes into account agreement occurring by chance (13). After generating codes, we consolidated codes into themes.

When coding the responses, we only considered mention of the idea and did not evaluate scientific accuracy. For example, if a student said that the vaccine contained mRNA but said that the mRNA coded for antibodies, we still coded the student as saying the vaccine contained mRNA. Also, a single student response could be assigned multiple codes if the student expressed multiple ideas.

Statistical analysis

Statistical analysis was performed in Google Sheets. We used chi-square analyses to determine whether certain themes and codes were present at significantly different frequencies in different groups of students or in the uncued vs. the cued condition. Bonferroni correction was used to adjust *P* values for multiple comparisons.

RESULTS

Here, we discuss the most common ideas students have about the contents of COVID vaccines and what ideas they use when thinking about how COVID vaccines work, both with and without a cue. We particularly focus on whether students know the vaccine contains mRNA, as that is a prerequisite to being able to apply the central dogma to vaccine function, and whether students state the mRNA causes production of proteins.

Student ideas about the contents of the COVID vaccine

Students held a variety of ideas about the content of COVID vaccines. Table 2 lists the most common themes and codes. The two most common themes were "COVID virus-based," believing the vaccine contained some version of the COVID virus or some component thereof, and "mRNA-based," believing the vaccine contained mRNA (Fig. 2A). mRNA-based ideas were included significantly more often in ABM responses than in either EBM (ABMs at 62.7%, EBMs at 40.0%, $P = 0.016$) or NBM (34.4%, $P = 0.0027$) responses, while NBMs had more COVID virus-based ideas than ABMs (ABMs at 33.3%, NBMs at 57.8%, $P = 0.011$) (Fig. 2A).

There were also differences among student groups among codes. The code "mRNA" was applied when the student did not specify what the mRNA encoded. This code was not present at significantly different frequencies among the different student groups (ABMs at 17.3%, EBMs at 18.7%, NBMs at 17.2%, $P = 0.96$) (Fig. 2B). However, ABMs were

TABLE 2 Common themes and codes for vaccine contents, with examples and explanations with the overall percent of students citing

Theme/ codes (if theme has codes)	Explanation and example	% of all students citing	% inter-rater agreement	Cohen's kappa[a]
COVID virus-based	**Vaccine contains the COVID virus, some variant of the COVID virus, or some component of the COVID virus.**	**47.2%[b] (101/214)**	–	–
Viral variant	Variant, strain, or mimic of the virus is in the vaccine. "From what I know, there is some way to create a mock invasion of COVID in your body with the shot. Something that mimics COVID virus cells…"	13.1% (28/214)	93.3%	0.63
Live virus	Live or unmodified virus is in the vaccine. "The COVID vaccine contains the live virus and works to acquaint the immune system…"	13.1% (28/214)	86.7%	0.27
Dead virus	Dead or inactive virus is in the vaccine. "I would assume that it works like other vaccines—dead viruses help the immune system help prepare for future attacks."	10.3% (22/214)	93.3%	0.46
mRNA-based	**Vaccine contains mRNA.**	**46.3% (99/214)**	–	–
mRNA	mRNA is in the vaccine, without mention of what the mRNA codes for. "Injecting mRNA into your body, of which your body will recognize..."	17.8% (38/214)	93.3%	0.83
mRNA virus	mRNA of the virus is in the vaccine. "the covid vaccine has mRNA from the covid virus that gives us the blueprint..."	9.4% (20/214)	100.0%	1.00
mRNA spike protein	mRNA of the spike protein is in the vaccine. "It depends on the types of vaccine. Moderna and Pfizer use mRNA vaccines which delivers mRNAs that can copy the spike proteins of Sars-CoV-2…"	7.5% (16/214)	96.7%	0.65
No mention	**Does not mention what is in the vaccine.**	**16.4% (35/214)**	**96.7%**	**0.89**
Uncertainty	**Unsure what is in the vaccine.**	**10.7% (23/214)**	**100.0%**	**1.00**

[a]Cohen's kappas of 0.21–0.40 are considered to be "fair" agreement, 0.41–0.60 to be "moderate" agreement, 0.60–0.80 to be "substantial" agreement," and 0.80–1 to be "excellent" agreement [Landis and Koch (13)].
[b]Bolded lines are themes. Unbolded lines are codes under those themes.

more likely than EBMs (ABMs at 18.7%, EBMs at 1.3%, $P = 0.0012$) to have the code "mRNA virus," which related to the idea that the vaccine contained mRNA from the virus, and they were more likely than EBMs (ABMs at 16.0%, EBMs at 2.7%, $P = 0.015$) and NBMs (3.1%, $P = 0.036$) to have the code "mRNA spike protein," which related to the more specific idea that the vaccine contained mRNA encoding the spike protein (Fig. 2B). On the other hand, EBMs were more likely than ABMs to have the code "virus variant," which related to the idea that the vaccine contained variants of the COVID virus (ABMs at 5.3%, EBMs at 22.7%, $P = 0.007$) (Fig. 2B). The codes "live virus" and "dead virus" were found at similar frequencies between the different groups of students (live virus: ABMs at 9.3%, EBMs at 9.3%, NBMs at 21.9%; dead virus: ABMs at 6.7%, EBMs at 13.3%, NBMs at 10.9%) (Fig. 2B).

Students' uncued application of central dogma in thinking about COVID vaccine function

When students were asked, "How does a COVID vaccine work?," they expressed a variety of ideas, only some of which related to central dogma. Table 3 explains the most common themes and codes. The most common theme cited was "immunity," which related to concepts like vaccines triggering an immune response and protecting against future disease (Fig. 3A). The next most common theme was "pre-existing antigen,"

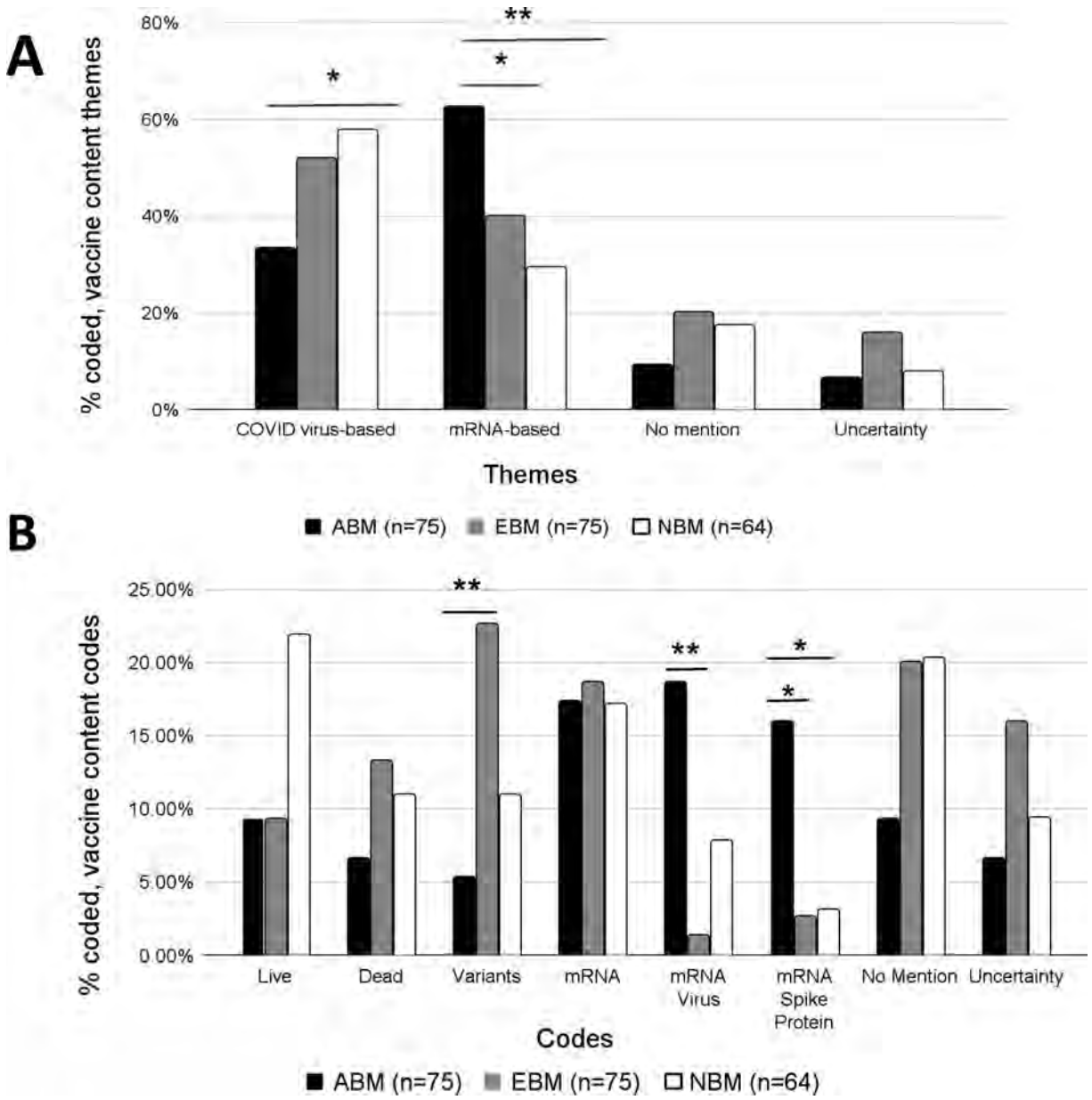

FIG 2 What students of different expertise levels believe is in the SARS-CoV-2 vaccine, at the level of (A) most common themes and (B) most common codes. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$ by chi-square analysis.

which was used when students thought that the vaccine contained an antigen that the body could directly act upon, similar to traditional vaccines (Fig. 3A). The theme "uncertainty" was applied when a student said they did not know or were unsure about how the vaccine worked (Fig. 3A). Most themes were present at non-significantly different frequencies among the three student groups: $P = 0.22$ for immunity, $P = 0.073$ for pre-existing-antigen, and $P = 0.32$ for uncertainty (immunity: ABMs at 78.7%, EBMs at 66.7%, NBMs at 68.8%; pre-existing-antigen: ABMs at 13.3%, EBMs at 25.3%, NBMs at 12.5%; uncertainty: ABMs at 8.0%, EBMs at 16.0%, NBMs at 12.5%) (Fig. 3A). The only theme that was present at significantly different frequencies among different groups of students was "central dogma," which was applied when students mentioned ideas relating to DNA or RNA causing the production of proteins (Fig. 3A). It was present at significantly higher frequencies in ABMs compared to NBMs (ABMs at 36.0%, NBMs at 10.9%, $P = 0.002$) (Fig. 3A).

TABLE 3 Common themes and codes for how the vaccine works, with explanation and examples and overall % of students citing in uncued and cued prompt

Theme/codes (if theme has codes)	Explanation and example	% of students citing in uncued	% of students citing in cued	% inter-rater agreement	Cohen's kappa[a]
Immunity	**Relates to the body producing an immune response.**	**71.4% (153/214)**[b]	**59.3% (127/214)**	–	–
Triggers immune response	The body or immune system responds to create antibodies, activate immune cells, and prepare in a variety of ways. "...they teach our cells how to make a protein—or even just a piece of a protein—that triggers an immune response"	54.2% (116/214)	54.2% (116/214)	88.5%	0.77
Memory	Protection from future infections. "I would assume that they have mRNA to help the cells know what they are fighting or preparing to fight against"	42.5% (91/214)	18.2% (39/214)	92.3%	0.80
Central dogma	**Relates to DNA or RNA causing a protein to be made.**	**22.9% (49/214)**	**62.6% (134/214)**	–	–
mRNA to viral protein	mRNA to "COVID protein," "viral," "crown," and "spike proteins." "The mRNA carries the code for the spike proteins so that our cells can make them and our immune system will know and remember how to attack."	10.8% (23/214)	14.0% (30/214)	100.0%	1.00
Instructions/ blueprint	Discuss mRNA or DNA as instructions for something, not necessarily proteins. "The mRNA is encoded with instructions for the body to create COVID antibodies that will be able to recognize any exposure to COVID in the future to resist them."	7.0% (15/214)	21.5% (46/214)	92.3%	0.81
mRNA to protein	Addresses the idea of the central dogma. "mRNA is like an instruction code that teaches the cell how to make proteins that will activate an immune response."	5.1% (11/214)	28.1% (60/214)	88.5%	0.74
Pre-existing antigen	**Relates to the vaccine containing a pre-existing antigen.**	**15.4% (37/214)**	**8.9% (19/214)**	–	–
Weak/dead COVID virus	Weak or dead version of the COVID virus "It puts dead or weakened versions of the virus into your system..."	14.5% (31/214)	1.9% (4/214)	100.0%	1.00
Uncertainty	**Does not know.**	**12.2% (26/214)**	**13.1% (28/214)**	**100.0%**	**1.00**

[a]Cohen's kappas of 0.61–0.80 are considered to be "substantial" agreement" and 0.81–1 to be "excellent" agreement [Landis and Koch (13)].
[b]Bolded lines represent themes; unbolded lines represent codes.

Given our interest in whether students could apply central dogma, we decided to focus our code-level analysis on the codes in the "central dogma" and the opposing "pre-existing-antigen" themes. Under "central dogma," the code "mRNA to viral protein," which was applied when students said the mRNA in the vaccine caused production of COVID, viral, crown, or spike proteins, was significantly more prevalent in ABMs than EBMs (ABMs at 25.3%, EBMs at 1.3%, $P < 0.001$) or NBMs (4.7%, $P = 0.003$) (Fig. 3B). However, the more generic codes "instructions/blueprints," which represented the idea that DNA or RNA were instructions for producing a product, and "mRNA to protein," where the student did not specify what protein the mRNA encoded, were found at similar frequencies in the three groups (instructions/blueprints: ABMs at 8.0%, EBMs at 9.3%, NBMs at 3.1%, $P = 0.33$; mRNA to protein: ABMs at 4.0%, EBMs at 9.3%, NBMs at 1.6%, $P = 0.10$) (Fig. 3B). Under "pre-existing antigen," students most commonly thought that the vaccine worked by presenting a weak or dead version of the virus to the body. EBMs were significantly more likely to have it than ABMs (ABMs at 6.7%, EBMs at 24.0%, $P = 0.01$) (Fig. 3B).

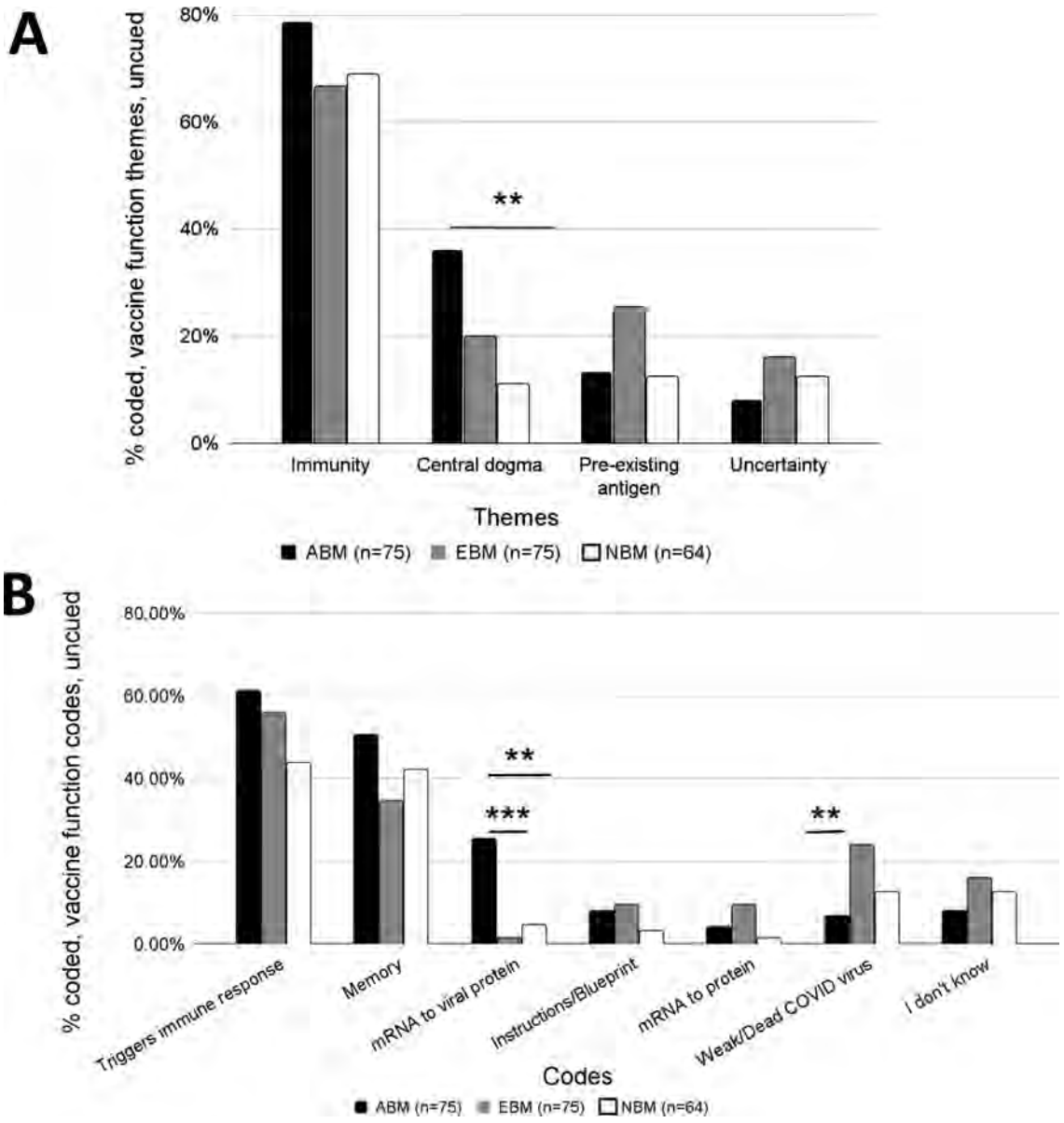

FIG 3 Ideas students of different expertise levels used in describing how the SARS-CoV-2 vaccine works, without cuing, at the level of (A) themes and (B) codes. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$ by chi-square analysis.

Students' application of central dogma to COVID vaccines after cuing

Since cuing might remind students to apply ideas associated with classroom training, we looked at student responses to the question, "Some of the COVID vaccines have mRNA in them. What is the mRNA's role in how the COVID vaccine works?," which specifically cued them to think about mRNA. Here, the most common theme was "central dogma," which was no longer present at significantly different levels between groups (ABMs at 68.0%, EBMs at 64.0%, NBMs at 54.7%, $P = 0.26$) (Fig. 4A). The second most common theme was "immunity," which was present at significantly higher levels in ABMs as compared to NBMs (ABMs at 68.0%, NBMs at 43.8%, $P = 0.012$) (Fig. 4A). The third-most common theme was "uncertainty," which was significantly more frequent in EBMs than ABMs (ABMs at 5.3%, EBMs at 21.3%, $P = 0.014$) (Fig. 4A). The least common theme was "pre-existing-antigen," which was not present at significantly different frequencies among different groups (ABMs at 9.3%, EBMs at 8.0%, NBMs at 9.4%, $P = 0.95$) (Fig. 4A).

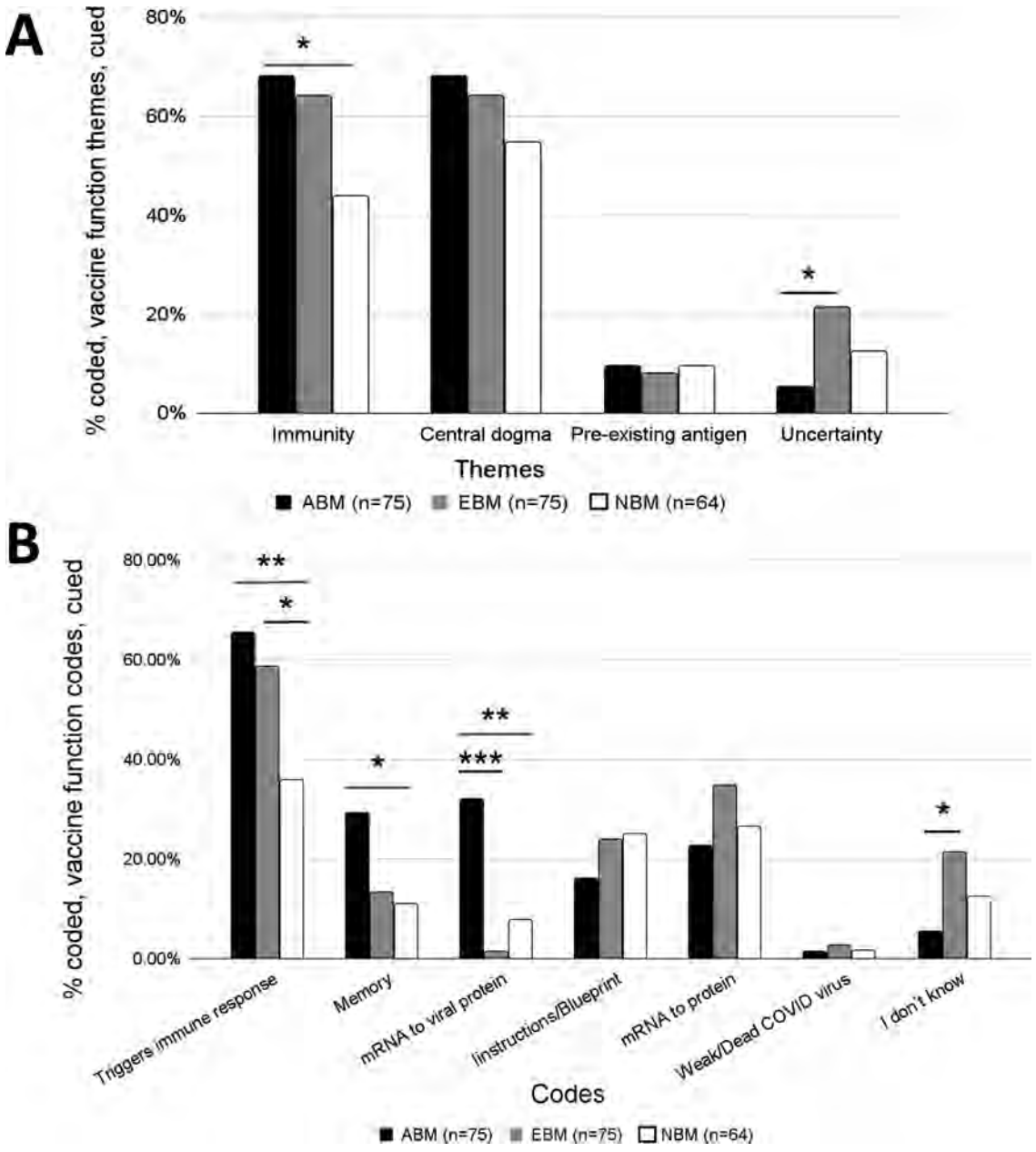

FIG 4 Ideas students of different expertise levels used in describing how the SARS-CoV-2 vaccine works, with cuing, at the level of (A) themes and (B) codes. *P < 0.05, **P < 0.01, ***P < 0.001 by chi-square analysis.

At the code level, patterns for the common "central dogma" codes were similar to those seen with the uncued question. ABMs were still far more likely to have "mRNA to viral protein" than EBMs (ABMs at 32.0%, EBMs at 1.3%, P < 0.001) or NBMs (NBMs at 7.8%, P = 0.001) (Fig. 4B). The frequencies of "instructions/blueprints" and "mRNA to protein" were still similar between all groups (instructions/blueprints: 16.0%, EBMs at 24.0%, NBMs at 25.0%, P = 0.35; mRNA to protein: 22.7%, EBMs at 34.7%, NBMs at 26.6%, P = 0.25) (Fig. 4B). However, unlike in the uncued condition, the code "weak or dead virus," associated with "pre-existing antigen," was present at similar frequencies in all groups (ABMs at 1.3%, EBMs at 2.7%, NBMs at 1.6%, P = 0.81) (Fig. 4B).

Comparing students' uncued and cued application of central dogma

If students lack basic knowledge, cuing will not help them apply it, so it is important to compare the frequency of particular themes and codes between the cued and uncued conditions. The "immunity" theme was significantly more prevalent in the uncued condition among NBMs (uncued at 68.8%, cued at 43.8%, $P = 0.013$), while the "uncertainty" theme was present in similar frequencies in the two conditions for all groups (ABM uncued at 8.0%, ABM cued at 5.3%; EBM uncued at 16.0%, EBM cued at 21.3%; NBM uncued at 12.5.0%, NBM cued at 12.5%; $P = 1$ for all groups) (Fig. 3A; Fig. 4A). The "central dogma" theme was much more frequent in all groups in the cued condition (ABM uncued at 36.0%, ABM cued at 68.0%; EBM uncued at 20.0%, EBM cued at 64.0%; NBM uncued at 10.9%, NBM cued at 54.7%; $P < 0.001$ for all groups), while the "pre-existing antigen" theme was less frequent among EBMs only (EBM uncued at 25.3%, EBM cued at 8.0%, $P = 0.013$) (Fig. 3A; Fig. 4A). For codes, the frequency of "mRNA to viral protein" was not significantly different in the cued condition for any group (ABM uncued at 25.3%, ABM cued at 32.0%; EBM uncued at 1.3%, EBM cued at 1.3%; NBM uncued at 4.7%, NBM cued at 7.8%; $P = 1$ for all groups) (Fig. 3B; Fig. 4B). However, the frequency of the other "central dogma" codes increased in the cued condition. "Instructions/blueprints" occurred more frequently among EBMs (uncued at 9.3%, cued at 24.0%, $P = 0.048$) and NBMs (uncued at 3.1%, cued at 25.0, $P = 0.001$), while "mRNA to protein" occurred more frequently among all groups (ABM uncued at 4.0%, ABM cued at 22.7%; EBM uncued at 9.3%, EBM cued at 34.7%; NBM uncued at 1.6%, NBM cued at 26.6%; $P = 0.002$ or less for all groups) (Fig. 3B; Fig. 4B). In contrast, the frequency of "weak or dead virus" decreased among EBMs (uncued at 24.0%, cued at 2.7%, $P < 0.001$) and NBMs (uncued at 12.5%, cued at 1.6%, $P = 0.047$) (Fig. 3B; Fig. 4B).

Although we saw overall shifts in responses in the cued condition, we wanted to see whether individual students changed their responses between the uncued and cued prompts. For each student, we categorized their use of each theme or code as "maintained" (idea was used in both conditions), "added" (idea was used in the cued but not the uncued condition), "never used" (idea was not used in either condition), or "removed" (idea was in the uncued but not the cued condition). For both "immunity" and "pre-existing antigen," while some students added ideas relating to these themes, slightly more students removed them (Fig. 5A). In contrast, for "central dogma," over a third of students in each group added these ideas, while less than 3% removed them (Fig. 5A). Trends at the code level mirror those at the theme level. The code "weak or dead virus," part of the "pre-existing antigen" theme, was removed by 22.7% of EBM and 10.9% of NBM but was added by only 1.3% and 0.0%, respectively, of these students (Fig. 5B). In contrast, nearly all groups showed a net gain of codes belonging to the "central dogma" theme (Fig. 5B). In all groups, more than 10% of students added "instructions/blueprint," while less than 3% removed it (Fig. 5B). More than 20% of EBMs and NBMs added "mRNA to protein," while 13.3% of ABMs added "mRNA to viral protein." In both cases, fewer than 7% of students removed these ideas (Fig. 5B). Interestingly, the cued condition is the only condition where many students wrote that the mRNA in the vaccine codes for antibodies, which we coded as "mRNA to antibodies." In each group, over 5% of students added this idea (Fig. 5B).

DISCUSSION

We found that students have a variety of ideas about the COVID vaccines and range of ability to apply their knowledge of central dogma to it. Before being cued, many students did not know that COVID vaccines contained mRNA. Instead, many of them believed that they contained a weak or dead virus. Similarly, many students did not apply central dogma-related ideas when they discussed how the COVID vaccines worked. Previous research has indicated that over half of college students know that vaccines contain elements that resemble the pathogen, so these students may have assumed that most COVID vaccines work in the same way as a traditional vaccine (5). However, after being cued with the information that some COVID vaccines contain mRNA, students

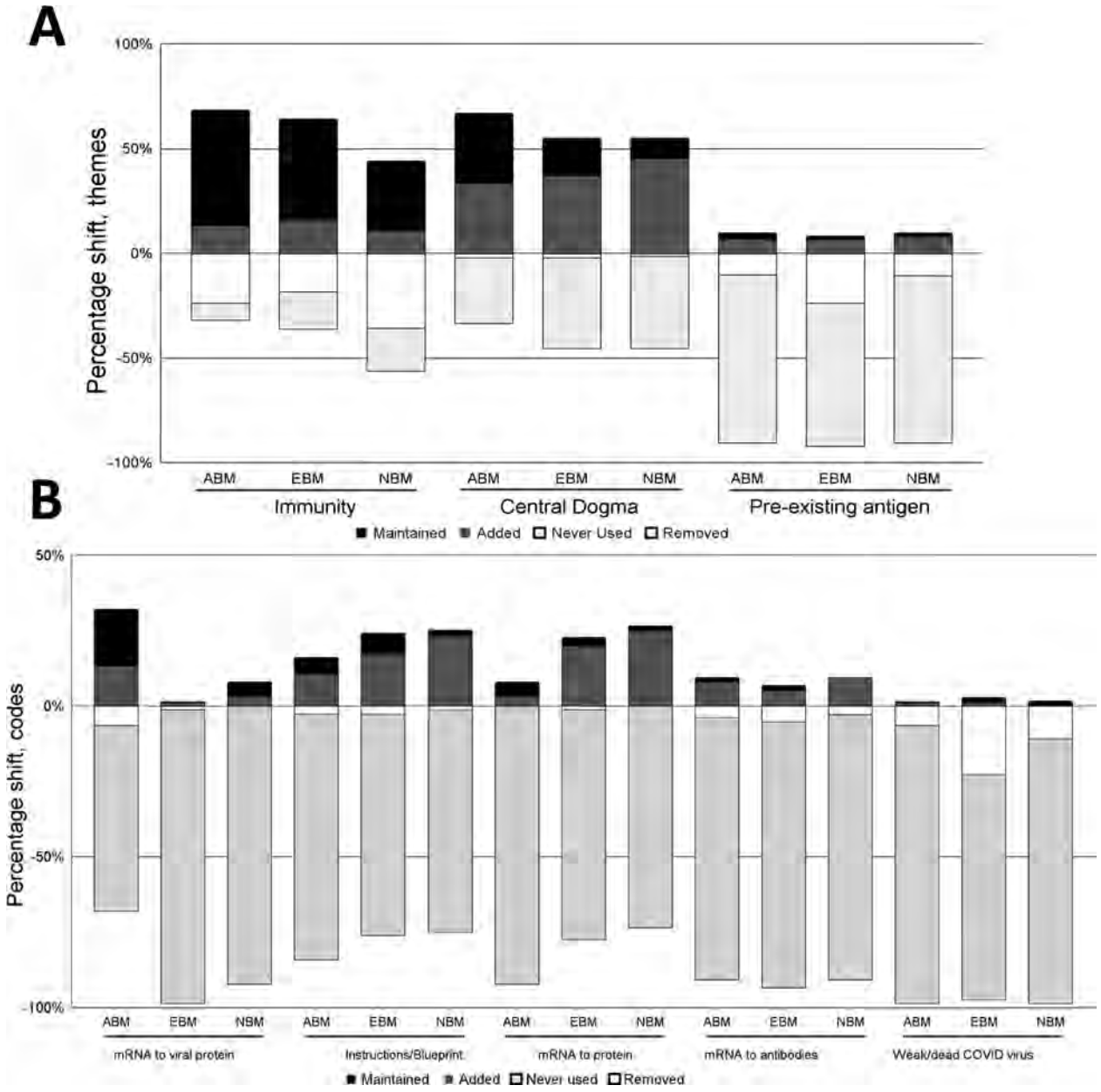

FIG 5 Changes in the ideas of individual students in cued and uncued conditions at the level of (A) themes and (B) codes. "Maintained" means the idea was used in both conditions, "Added" means the idea was used in the cued but not the uncued condition, "Never used" means the idea was not used in either condition, and "Removed" means the idea was in the uncued but not the cued condition.

were able to use that information to make connections to central dogma. After the cue, many more students mentioned that mRNA was used to create proteins or as instructions, and fewer said that the vaccine worked by using a pre-existing antigen. These results indicate that many of the students who initially did not use central dogma-related ideas did possess the basic knowledge about the central dogma and were able to apply it once that knowledge was brought to mind. This finding is useful for vaccine education given that other research has found that the efficacy of cues for prompting students to apply their biology knowledge may differ by topic (2, 14). However, it is also important to note that not all the ideas produced in the cued condition were scientifically accurate. For example, in the cued condition, students were more likely to state the idea that the

mRNA in the vaccine coded for antibodies, which is an idea that uses central dogma but is nevertheless incorrect.

We also found that although students in all groups were able to apply their knowledge of central dogma, at least when cued, ABMs had more accurate and specific knowledge about the COVID vaccines than EBMs and NBMs. ABMs were more likely to know that certain COVID vaccines contained mRNA, that they work through the mRNA being translated into protein, and that the mRNA specifically produced a viral protein. This finding is not surprising given a previous study that found that ABMs were more likely to have accurate knowledge of how vaccines work in general (5). We also found few differences between EBMs and NBMs in their knowledge, even though EBMs intend to major in biology. Since some studies find differences between EBMs and NBMs and others do not (2, 3, 14, 15), our finding may have to do with our particular student context. Even though ABMs were more likely to apply central dogma without the cue, we also found that students in all groups benefited from the cue. A previous study found that ABMs were most able to respond to cues, but that study focused on producing expert-like biology thinking in general, which may be harder to learn and elicit than the idea of applying central dogma (14).

Our results have several implications for biology educators. First, our research uncovers novel inaccurate ideas about the nature of the COVID vaccine, such as it contains a weak or dead virus or that the mRNA codes for antibodies, which instructors could target in their teaching. Second, our results suggest that instructors could provide students with more support in applying their biology knowledge. The fact that the cue was necessary to help large numbers of students in all groups realize central dogma's involvement in the mRNA vaccine means that while many students had some sort of background knowledge about central dogma, they needed instructional support to make connections between course content and real-life biology. Similar results have been reported with other real-world biology-related topics such as genetically modified organisms and antibiotic resistance (2, 3). Educators could be more explicit about these connections and have students practice applying their knowledge. Third, our results suggest that EBMs and NBMs could use greater support in learning to apply central dogma. Our finding that EBMs and NBMs were less likely to cite central dogma-related ideas before cuing is in line with work suggesting that biology novices have trouble understanding and applying the central dogma (7, 16, 17). This is problematic because many college students never go beyond first-year or non-major biology but still need to be equipped to understand topics like the COVID vaccine. Previous research also suggests that students can achieve better understanding with more education, so more intensive or targeted instruction during entry-level biology courses may be able to help these students better understand and apply central dogma more quickly (7).

Limitations and future directions

Our research had several limitations. One set of limitations concerns how we measured student knowledge. Because all students were given the uncued prompt before the cued prompt, increases in mentioning particular ideas may have occurred because answering the uncued prompt simply jogged students' memories. However, it is important to note that substantial numbers of students who mentioned immunity-related ideas in the uncued prompt chose not to do so for the cued prompt (Fig. 5A), suggesting that students did not simply write down all the ideas that occurred to them but were selective about what ideas they found relevant for the cued prompt. In addition, we did not directly measure or control for GPA or any other proxy for general knowledge, nor did we measure or control for students' previous knowledge of the central dogma and mRNA COVID vaccines. We did categorize students by biology level, but these labels may not correlate with understanding of central dogma. Furthermore, in the uncued condition, students who did not mention central dogma may have been thinking about a COVID vaccine based on inactivated virus, such as China's Sinovac vaccine (18). However, this possibility is less likely because at the time of survey administration, all

COVID vaccines widely available in the United States contained nucleic acid of some sort and thus would require knowledge of central dogma to understand.

Another set of limitations concerns student demographics. Unfortunately, the ethnic composition of the three student populations were significantly different (Table 1), which means our results may, in part, arise from differences in these student populations that, in turn, may arise from systemic biases that encourage students from minoritized racial groups to leave STEM (19). In addition, our sample may not be representative of biology students in the United States as a whole. Although our sample was diverse in many aspects, some groups were not well represented, such as Black or politically conservative students (Table 1). Because characteristics, such as racial and political identity, may interact with attitudes toward and knowledge of COVID vaccines in complex ways, it will be important to explore COVID vaccine knowledge in other student samples (20, 21).

Finally, our research did not measure vaccine attitudes, so we cannot draw conclusions about addressing vaccine hesitancy. Studies suggest that providing vaccine-hesitant people with factual information regarding vaccines has little to no impact on how likely they are to take them (22) or can even spark a negative "backlash" against vaccines (23). On the other hand, studies also indicate that younger students' negative attitudes about vaccines might be more malleable, which suggests that we should teach about vaccines earlier (24). Future work could measure student vaccine attitudes to determine how they correlate with knowledge of the mRNA vaccine and the central dogma.

Conclusion

It is important for biology students at all levels to be able to use their biology knowledge to understand real-world topics. Knowing the extent to which students apply the central dogma to COVID vaccines and the misconceptions students have about the vaccine is useful in and of itself, given that COVID remains an endemic disease, new COVID boosters are still being developed, and COVID vaccine misinformation is rife online (9). We also hope that our study can further illuminate the broader issue of how to best guide students in applying their knowledge outside the classroom.

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ADDITIONAL FILES

The following material is available online.

Supplemental Material

Appendix 1 (jmbe00167-23-s0001.pdf). Full text of survey given to students. Course numbers and instructors have been redacted to enhance confidentiality.

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