Protected

by copyright,

includi

Bul

ġ

uses related

to text

and

data

, and

Isimi

a

technologies

## Charis Eng: an appreciation

Dr Charis Eng (17 January 1962-13 August 2024) was a distinguished clinician-scientist whose contributions in research, clinical care and medical education were wide-ranging and highly influential. She held editorial roles, including North American Editor of the Journal of Medical Genetics and Editor-in-Chief of Endocrine-Related Cancer and Human Molecular Genetics. She coauthored many scientific papers and monographs including the third and fourth editions of A Practical Guide to Human *Cancer Genetics.*<sup>1</sup> Her contribution to cancer genetics has been described in detail elsewhere,<sup>2 3</sup> but in this appreciation, as former coeditors on *IMG*, coauthors<sup>1</sup> and colleagues we reflect on her legacy.

Born in Singapore and later moving to the USA via England, Charis was academically gifted, and she was admitted to the University of Chicago aged just 16 years. She attributed her interest in genetics to the influence of her high school biology teacher. After completing her residency in internal medicine at Beth Israel Hospital in Boston and a fellowship in medical oncology at Harvard's Dana-Farber Cancer Institute, she returned to England to undertake a Fellowship in cancer genetics at the University of Cambridge under the mentorship of Professor Sir Bruce Ponder. There, she helped identify germline mutations in RET in multiple endocrine neoplasia type 2 and made key contributions to understanding genotype-phenotype correlations in the disorder.4-

She maintained a lifelong interest in the clinical and molecular features of inherited predisposition to endocrine tumours, particularly phaeochromocytoma/paraganglioma, however, her greatest impact was in the field of PTEN hamartoma tumour syndrome (PHTS). After coleading the research that linked germline PTEN pathogenic variants to Cowden syndrome,<sup>7</sup> she proceeded to demonstrate that several related conditions such as Bannayan-Riley-Ruvalcaba syndrome, a Proteus-like overgrowth disorder and most notably, a subset of individuals with autism spectrum disorders and macrocephaly, were allelic.<sup>8-10</sup> She also defined the role of somatic inactivation of PTEN in sporadic tumours including thyroid<sup>11</sup> and explored the effects of PTEN inactivation in dysregulating the phosphoinositol-3-kinase/Akt and other signalling pathways. Charis' work advanced both laboratory research and clinical management of PHTS, leading to improved diagnostic criteria, tumour surveillance guidelines and the development of the Cleveland Clinic PTEN Risk Calculator<sup>12</sup>; (https://www.lerner.ccf.org/genomic-medicine/ccscore/). For the worldwide cancer genetics community, she was the go-to person for difficult cases.

After Cambridge, Charis held positions at the Dana-Farber Cancer Institute and Ohio State University before she was invited to become the founding director of the Genomic Medicine Institute and the Center for Personalized Genetic Healthcare at the Cleveland Clinic, USA. Her bench to bedside translational research, commitment to precision medicine and her vision for transforming clinical care in inherited cancer predisposition syndromes earned her numerous honours, including election to the National Academy of Medicine (2010) and the American Cancer Society's Medal of Honor for Clinical Research (2018).

Renowned for her mentorship, Charis supported many trainees and mentees, encouraging them to mentor both upwards and among their peers. She fostered a collaborative multidisciplinary environment, and recognising the need to build capacity and

nurture future cancer geneticists, she created a Cancer Genomic Fellowship at the Cleveland Clinic to train future cancer geneticists. This fellowship programme attracted trainees from across the globe and many fellows went on to establish cancer genomic medicine programmes worldwide including in the USA, UK, Australia, Japan and Singapore, Charis inspired others to be better scientists, collaborators and clinicians through her own role modelling.

From 1998 to 2005, she was the North American Editor for the Journal of Medical Genetics. This was a new role established at a time when IMG often considered to be a UK-focused journal. Charis quickly started to change that perception and the number and quality of submissions from the continent increased. During her tenure as an editor at IMG, Charis' academic reputation, proficiency at networking and persuasiveness resulted in the submission and publication of some notable papers in *JMG*. One corresponding author recalled discussing his intention to submit a paper to a renowned North American clinical journal, only to be convinced by Charis that *IMG* was the timely home for their paper. The article went on to be one of the most highly cited papers over its 60-year history of IMG.<sup>13</sup>

Charis was renowned for her commitment to her work, her patients and her mentees. One of her guiding principles was that Serendipity strikes those who work hard. Her family was very important to her, and she attributed her interest in medicine to her uncle who was Professor of Medicine in Singapore. One personal interest in which she excelled was in her knowledge of fine wine. This she attributed to her fellowship and time in Cambridge often finding herself as the youngest person at a College dinner ('High Table') with few shared interests with the other guests. As the quality of the wine served was a frequent topic of dinner conversation, she decided to educate herself in aspects of viniculture. After extensive research and wine tasting, she achieved and frankly excelled in her objective. Her expertise was regularly called on, including at the annual JMG Editorial team dinners held at the American Society of Human Genetics meeting. Here, Charis would engage in a goodnatured debate with the sommelier regarding the optimum choice i mining, of wine. On several of these happy occasions, Charis discussed the qualities she valued most in her colleagues and her friends. Memorably, she observed that 'the most important bone in any person is backbone, closely followed by the funny bone'.

AI training Charis was a highly productive researcher and not only published more than 400 original articles and reviews but also edited and contributed to multiple books on cancer genetics. It was a privilege to know and to collaborate with Charis. Her intellect was accompanied by an infectious humour, huge energy and a generous spirit. Her pioneering work on MEN2 and PHTS was ahead of its time, and she continued to make new discoveries throughout her career. She pioneered the concept of personalised management in individuals predisposed to cancer, she advocated for the importance of clinical education in facilitating the involvement of non-genetic clinicians in delivering clinical cancer genetic services and championed patient involvement.

Charis' remarkable contributions to cancer genetics, her mentorship and her indomitable spirit have left an indelible mark on the field. Her loss will be deeply felt by colleagues, collaborators and patients but her legacy will outlive her and continue to inspire. We all will miss her greatly.

## William D Foulkes <sup>(i)</sup>, <sup>1</sup> Shirley V Hodgson, <sup>2</sup> Eamonn R Maher <sup>(i)</sup>, <sup>3,4</sup> Joanne Ngeow <sup>()</sup>, <sup>5,6</sup> Willie Reardon, <sup>7</sup> Richard Trembath<sup>8</sup>

<sup>1</sup>Departments of Human Genetics, Oncology and Medicine, McGill University, Montreal, Quebec, Canada

<sup>2</sup>Medical Genetics, Clinical Development Sciences, St George's, University of London, London UK

<sup>3</sup>Aston Medical School, Aston University, Birmingham, UK

J Med Genet: first published as 10.1136/jmg-2024-110513 on 31 December 2024. Downloaded from http://jmg.bmj.com/ on May 14, 2025 at Department GEZ-LTA

<sup>4</sup>Department of Medical Genetics, University of Cambridge Clinical School, Cambridge, UK

<sup>5</sup>Genomic Medicine, Lee Kong Chian School of Medicine, Singapore

<sup>6</sup>Division of Medical Oncology, Cancer Genetics Service, National Cancer Centre Singapore, Singapore

<sup>7</sup>Blackrock Clinic, Blackrock, Dublin, Ireland

<sup>8</sup>Department of Medical and Molecular Genetics, King's College London, London, UK

Correspondence to Professor Eamonn R Maher; erm1000@medschl.cam.ac.uk

Contributors All authors contributed to the article. EM is the guarantor.

**Funding** The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval Not applicable.

Provenance and peer review Not commissioned; internally peer-reviewed.

To cite Foulkes WD, Hodgson SV, Maher ER, et al. J Med Genet 2025;62:46-47.

J Med Genet 2025;62:46-47.doi:10.1136/jmg-2024-110513

## ORCID iDs

William D Foulkes http://orcid.org/0000-0001-7427-4651 Eamonn R Maher http://orcid.org/0000-0002-6226-6918 Joanne Ngeow http://orcid.org/0000-0003-1558-3627

## REFERENCES

1 Hodgson SV, Foulkes WD, Eng C, et al. A Practical Guide to Human Cancer Genetics3rd and 4th editions. Springer,

- 2 Cleveland Clinic. Available: https://www.lerner.ccf.org/news/article/?title=Cleveland+ Clinic+mourns+the+loss+of+Dr.+Charis+Eng&id=43fdd17468dbe87cd28f077c5cd2 5a42e9644084
- 3 Available: https://www.brown-forward.com/obituaries/charis-eng-md-phd
- 4 Mulligan LM, Kwok JBJ, Healey CS, *et al*. Germ-line mutations of the RET proto-oncogene in multiple endocrine neoplasia type 2A. *Nature New Biol* 1993;363:458–60.
- 5 Mulligan LM, Eng C, Healey CS, *et al.* Specific mutations of the RET proto-oncogene are related to disease phenotype in MEN 2A and FMTC. *Nat Genet* 1994;6:70–4.
- 6 Eng C, Smith DP, Mulligan LM, et al. Point mutation within the tyrosine kinase domain of the RET proto-oncogene in multiple endocrine neoplasia type 2B and related sporadic tumours. *Hum Mol Genet* 1994;3:237–41.
- 7 Liaw D, Marsh DJ, Li J, *et al*. Germline mutations of the PTEN gene in Cowden disease, an inherited breast and thyroid cancer syndrome. *Nat Genet* 1997;16:64–7.
- 8 Marsh DJ, Dahia PL, Zheng Z, *et al*. Germline mutations in PTEN are present in Bannayan-Zonana syndrome. *Nat Genet* 1997;16:333–4.
- 9 Zhou XP, Marsh DJ, Hampel H, et al. Germline and germline mosaic PTEN mutations associated with a Proteus-like syndrome of hemihypertrophy, lower limb asymmetry, arteriovenous malformations and lipomatosis. *Hum Mol Genet* 2000;9:765–8.
- 10 Butler MG, Dasouki MJ, Zhou XP, et al. Subset of individuals with autism spectrum disorders and extreme macrocephaly associated with germline PTEN tumour suppressor gene mutations. J Med Genet 2005;42:318–21.
- 11 Dahia PL, Marsh DJ, Zheng Z, et al. Somatic deletions and mutations in the Cowden disease gene, PTEN, in sporadic thyroid tumors. *Cancer Res* 1997;57:4710–3.
- 12 Tan MH, Mester J, Peterson C, et al. A clinical scoring system for selection of patients for PTEN mutation testing is proposed on the basis of a prospective study of 3042 probands. Am J Hum Genet 2011;88:42–56.
- 13 Thomson JR, Machado RD, Pauciulo MW, *et al*. Sporadic primary pulmonary hypertension is associated with germline mutations of the gene encoding BMPR-II, a receptor member of the TGF-beta family. *J Med Genet* 2000;37:741–5.