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*.[1] Her contribution to cancer genetics has been described in detail elsewhere,[2 3] but in this appreciation, as former coeditors on *JMG*, coauthors[1] 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.[4–6]

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,[7] 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.[8–10] She also defined the role of somatic inactivation of *PTEN* in sporadic tumours including thyroid[11] 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[12]; (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 *JMG* 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 *JMG*, 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 *JMG* 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 *JMG*.[13]

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 good-natured debate with the sommelier regarding the optimum choice 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'.

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.

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