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## Dr Falk/Guts UK Awards 2024

### MEDICAL STUDENT PRIZE WINNER: MERYL ONG

**PROJECT:**  
**The Systemic Pathology of Dyskeratosis Congenita**



*Ms Ong undertook this project whilst intercalating for an iBSc in Medical Sciences with Gastroenterology and Hepatology, at Imperial College London, Department of Metabolism, Digestion and Reproduction. Ms Ong will return to her medical degree 4th year studies in September at University College, London Medical School.*

#### Ms Ong explains:

'I was keen to seize the opportunity to engage in research and, in particular, to take on the challenge of studying a rare disorder such as Dyskeratosis Congenita. Engaging in pioneering work to understand the biological mechanisms underpinning this disease, imbued the project with profound importance and meaning for me. It was also a rare privilege to be able to examine patient tissue biopsies as well as to learn about and apply cutting-edge AI techniques to histopathology.'

'Dyskeratosis congenita (DC) is an extremely rare, inherited disorder predominantly affecting males, with an estimated incidence of 1 in a million new-borns. The condition is characterised by defective telomere maintenance, leading to premature cellular ageing and senescence (cells lose their ability to divide and grow).'

'DC can manifest in a diverse range of symptoms in childhood; mucocutaneous features include hyperpigmented rashes, nail dystrophy and oral leukoplakia, other features include bone marrow failure, pulmonary fibrosis, and increased cancer susceptibility. This wide variation of features stems from the intricate interplay between genetics and phenotypic expression. Notably, liver disease is emerging as a significant contributor to morbidity and mortality, prevalent in approximately 7% of DC cases, therefore understanding the role of cellular senescence in the liver is crucial for characterising this disease's clinical and pathological features. However, there is currently limited literature exploring the specific hepatic pathology in DC patients. Our study, therefore, aimed to investigate the burden of senescent cells in DC patient liver tissues.'

'Despite the rarity of this condition, St Mary's Hospital London manages a substantial DC cohort due to having an active bone marrow transplant service. Our primary objective was to examine the expression of the senescence biomarker (p16) in DC patient liver biopsies.'

Secondary aims included identifying characteristic DC liver histological features and patterns, and establishing associations between senescence markers, histological findings, and

DC's clinical and pathological manifestations. By leveraging validated artificial intelligence (AI)-based immunohistochemistry image analysis techniques, we quantified senescence markers and histological features. By integrating quantitative analysis with qualitative histological evaluation, we will be able to characterise the role of cellular senescence more comprehensively in DC liver pathology.'

'Ultimately, this exploration will endeavour to deepen our understanding of the fundamental biological mechanisms underlying DC and to propose potential histologic biomarkers for clinically characterising hepatic involvement. Additionally, by investigating cellular senescence more broadly, we aim to gain insights into natural ageing processes and age-related liver diseases. Of note, metabolic dysfunction-associated steatotic liver disease, one of the most common forms of liver disease, is associated with increased hepatocyte senescence.'

'We hope therefore, to lay the foundations for exploring potential therapeutic strategies against DC's multisystemic manifestations. Moreover, this work has the potential to contribute to the broader field of senescence research, providing findings that may inform investigations across an array of age-related pathologies.'

Ms Ong's Project Supervisor Professor Robert Goldin, Consultant Histopathologist specialising in gastro-intestinal and liver disease at Imperial College London, comments:

'This was quite a challenging research project but Meryl more than rose to the occasion. She is obviously intelligent, is very hard working and self-motivated and she also asks very thoughtful questions. Meryl settled in very well to the BSc community, supporting us by taking part in a BSc Fair where she spoke to other students about her project.'

'Meryl clearly has real academic potential and I hope that working on this project has encouraged her to consider an academic career, perhaps to return here to Imperial.'

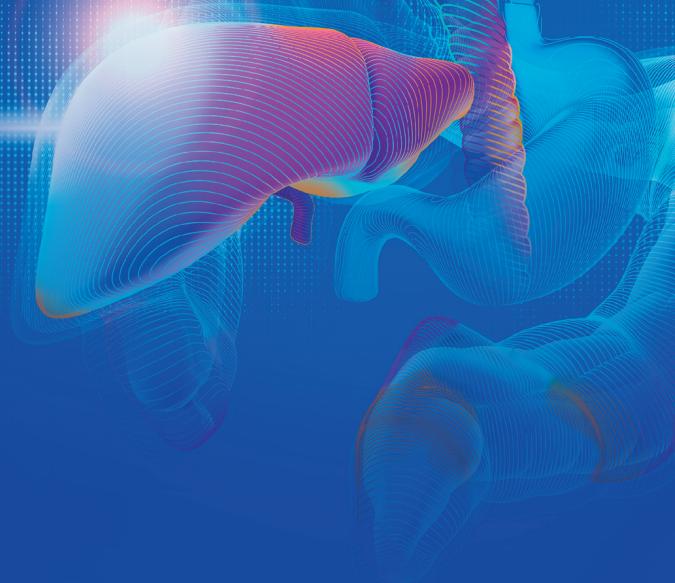
#### Ms Ong states:

'The opportunity to immerse myself in the fields of histopathology, molecular biology, and hepatology through this project resonates strongly with my evolving interests in these disciplines, as well as my career aspirations in academic medicine. I am immensely grateful to my project supervisor, Professor Robert Goldin, whose guidance cultivated a nurturing environment where I could freely explore ideas, ask questions, and embrace the invaluable process of learning from setbacks.'

'This prestigious recognition solidifies my commitment to pursue research opportunities that enrich my medical training, and contributes to 'bench-to-bedside' research aimed at enhancing patient care and improving clinical outcomes.'



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