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Dr Falk/Guts UK Awards 2020

MEDICAL STUDENT BURSARY WINNER: **Dylan McClurg MPhil**

PROJECT:

Characterising the Heterogeneity of Barrett's Oesophagus and Oesophageal Adenocarcinoma using a Panel of Patient-Derived Organoid Models for Translational Research and Precision Medicine



Dylan McClurg undertook this research at the MRC Cancer Unit, Hutchison/MRC Research Centre, Cambridge whilst completing an MPhil in Medical Sciences. He is currently completing his 4th year at the University of Aberdeen Medical School.

Dylan McClurg explains:

'With a strong desire to enter the profession of clinical academia and further my knowledge and skills of translational cancer research, I decided to undertake an intercalated MPhil in medical sciences within the MRC Cancer Unit at the University of Cambridge. My research project focused on oesophageal cancer, specifically, Oesophageal adenocarcinoma (OAC). OAC is the dominant subtype of oesophageal cancer in the western world with an increasing incidence and a poor 5-year survival rate at less than 15%. Due to a frequent late presentation at diagnosis and limited available clinical management, research into diagnostic and therapeutic methods remains a high priority. While OAC is often preceded by the premalignant condition Barrett's Oesophagus (BO), the molecular events responsible for this progression remain unclear and accurate preclinical models for investigation are lacking. Currently, OAC patients, dependent on their staging, undergo standardised treatment regimens independent of their molecular features. However, with our increasing knowledge of the genomic heterogeneity of OAC, this 'one size fits all' approach is no longer adequate. Recently, the characterisation of the driver gene landscape of OAC, and the development of patient-derived organoid models (PDO), have provided the opportunity to evaluate new therapeutic targets and precision medicine opportunities.'

Using high-quality clinical annotation, molecular analysis, and immunohistochemical staining for key protein markers, this study aimed to characterise the heterogeneity of OAC and BO and identify novel targeted therapy approaches through a biobank of established organoid models.

This project has significantly increased the quantity of robust OAC organoids available to the research community. It has also provided, for the first time, new biological models of BO which can be used for future studies aimed at understanding the critical genomic alterations involved in BO progression to OAC. Ultimately, this could lead to the identification of molecular stratification biomarkers that could enable prompt pre-emptive OAC treatment. In addition, by targeting specific genetic alterations within a highly characterised OAC organoid panel, we have also identified new avenues for precision medicine approaches and potential biomarkers including novel extrachromosomal DNA events which could help to improve patient outcomes for this grave disease.'

Mr McClurg's Project Supervisor, Consultant Gastroenterologist Professor Rebecca Fitzgerald comments:

'Dylan McClurg is an exceptional medical student who has engaged with research early on in his training – he achieved an incredible amount during his project to characterise 3D models for oesophageal cancer and test their response to targeted drug therapies. The Dr Falk/GUTS UK Award is very well deserved and I do hope that this will encourage Dylan to pursue an exciting career in academic medicine.'

Mr McClurg states:

'I am extremely grateful to receive the Dr Falk / Guts UK Medical Student Prize. I have thoroughly enjoyed my year of research and have gained a solid foundation in translational cancer research. I would like to thank my supervisors Professor Rebecca Fitzgerald and Dr Xiaodun Li for their support, guidance, and expert teaching throughout. This award will be hugely beneficial to my future career aspirations when applying for competitive clinical academic posts.'



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UK--2100036

Date of preparation: February 2021