SCAF/15/01: Generation of Stem-Cell Based Endocrine Tumour Models – Tools for the Development of Personalised Therapies

Biography

Dr Paul Newey is a Clinical Senior Lecturer and Honorary Consultant Endocrinologist at the University of Dundee. He undertook his medical degree in Edinburgh, before moving to Oxford to complete specialty training in Endocrinology. In Oxford, he completed a DPhil in Molecular Genetics and was subsequently appointed as a NIHR Clinical Lecturer in Endocrinology. In 2014, he moved to Dundee to establish his own research group, and in 2015 was awarded a Senior Clinical Academic Fellowship funded by the Chief Scientist Office (CSO)/NHS Research Scotland. His research program focuses on defining the genetic and molecular basis of endocrine disease.

Lay Abstract of Research

Rapid advances in DNA sequencing technologies have provided unprecedented insights into the genetic basis of disease. These include both the accelerated discovery of genes responsible for hereditary disorders, as well as the acquired changes in DNA sequence that result in common diseases such as cancer. These advances afford many potential opportunities, not least the advent of novel treatments and personalised therapies tailored to specific genetic defects. However, in many instances, this improved genetic understanding has not translated into a clinical benefit for patients, and one of the major barriers to progress has been a lack of relevant laboratory model systems to investigate how specific gene mutations affect the cellular environment and contribute to disease pathogenesis.

The apparent failure to translate genetic advance into clinical benefit is evident in the field on endocrine oncology. For example, whilst studies over the past decade have provided increasingly rich genetic characterization of a large number of endocrine tumours occurring in both hereditary and sporadic (i.e. without a family history) settings, little progress has been made in developing new treatments and improving patient outcomes. My research group, funded by the Senior Clinical Academic Fellowship, is focused on investigating how such inherited (i.e. ‘germline’) and acquired (i.e. ‘somatic’) changes in DNA sequence contribute to endocrine tumour formation. To achieve this, we are exploiting recent advances in stem cell biology and gene-editing to establish novel pre-clinical model systems, with the aim of not only understanding early events in tumour formation, but also of establishing a resource for early drug-discovery. The use of human pluripotent stem cells (hPSCs) offers huge potential for disease modelling, highlighted by their ‘normal’ genetic make-up, unlimited capacity for self-renewal and unique ability to undergo differentiation into disease-relevant cell types (e.g. endocrine cells). In addition, when coupled with gene-editing methods, hPSCs offer an unrivalled exploration of cell-type and context-specific gene function, features likely to be critical to understanding disease pathogenesis. In summary, the overarching aim of this research program is to translate the recent advances in endocrine tumour genetics into improved molecular understanding and downstream therapeutic benefit.