Pharmaceutical training for clinicians

At the interface between scientific research and patient care lie pharmaceutical companies with their efforts toward drug discovery. Despite the push for clinicians to ‘translate’ the latest research findings into new applications for their patients, few of them have direct experience with drug discovery. Instead, the research options for academic clinicians tend to split into two tracks, either basic research or patient care, with few training opportunities to provide exposure to drug discovery or patient-based clinical trials.

The Wellcome Trust wants to encourage the movement of clinicians into this space by offering training programs to give them experience directly with pharmaceutics. ‘The big question we are faced with is how to train clinicians within the broad field of translational medicine so that they have the skills to become effective translationists. We feel that to do this, we need to leverage the expertise that exists in the university sector with the expertise in the pharma sector,’ explains Dr John Williams, who coordinates the Wellcome Trust Translational Medicine and Therapeutics programs.

‘The interface between pharma and academia is becoming increasingly important. The R&D (research and development) models in pharma are changing to allow them to work more closely with academic partners. We need to train a cadre of bright young clinicians to have the skills, the right kind of awareness and, ultimately, the scientific ideas to cross this interface,’ says Dr Williams. The unique training approach of these fellowships exposes clinicians to research on disease processes, with a focus on how the information might be used to change patient diagnostics or treatment. The Wellcome Trust hopes to strategically provide a subset of clinicians with cooperative understanding of disease physiology and medicine, where they might coordinate medical care with scientific discovery.

‘In the UK, and elsewhere, there is a real decline in the number of people who are able to carry out high-quality patient-based research. These programs establish an environment where bright young clinicians might be drawn, not into the more typical route of molecular biology research, but to research questions that focus on patient-based studies,’ says Dr Williams.

The programs are partnerships between academic institutions and pharmaceutical companies, including: GlaxoSmithKline, Wyeth Research, Roche, AstraZeneca, Sanofi-Aventis, Sirtris Pharmaceuticals and PTC Therapeutics. Academic clinicians, including specialists, can apply to programs through one of the four participating centers: University of Cambridge, University of Newcastle, Imperial College London and the Scottish Consortium. More information about these fellowships that are available from the Wellcome Trust can be found through the websites for the individual centers, or together with information about biomedical science funding from the Wellcome Trust at www.wellcome.ac.uk.

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Alleviating Parkinson’s disease symptoms using chemical chaperones

Parkinson’s disease (PD) is a devastating degenerative neurological disease affecting 1-2% of people over the age of 50. The clinical features of PD include motor impairments, such as resting tremor, bradykinesia, postural instability and rigidity, as well as non-motoric impairments. The causative molecular pathways are obscure, but may involve either environmental or genetic factors, or both.

Treatments for PD are limited and the disease remains progressive. The hallmark of PD is the loss of normal conformation of the $\alpha$-synuclein protein in dopaminergic neurons, followed by its aggregation into toxic oligomers and fibrils known as Lewy bodies. The role of Lewy bodies in pathogenesis is unclear, but emerging data suggests that preventing $\alpha$-synuclein misfolding and aggregation could inhibit the disease process and, thus, it is an attractive therapeutic approach. One approach is to use small molecules, called chemical chaperones, which are capable of crossing the blood-brain barrier (BBB), to promote the normal folding of the $\alpha$-synuclein protein.

DMM Travelling Fellowships

Disease Models and Mechanisms (DMM) offers awards to bring together unique skill sets among researchers with an interest in model organisms of disease. DMM Travelling Fellowships encourage graduate students or postdocs to combine the expertise of their immediate colleagues with the technical or conceptual advancements of scientists outside of their laboratories. These awards offer up to £2500 (or currency equivalent) for collaborative visits to other laboratories. This money is intended to offset the expenses incurred through travel or other expenses related to initiating a new collaboration outside of the host lab institution.

Moran Frenkel-Pinter

Moran Frenkel-Pinter from Prof. Segal’s and Prof. Gazit’s laboratories at the Tel-Aviv University in Israel is identifying compounds that prevent the neurotoxic aggregation of $\alpha$-synuclein and alleviate disease symptoms in a Drosophila model of PD. Her collaboration with Prof. Masliah at the University of San Diego in the USA will expand this work to include mouse models of PD. Taken together, the use of Drosophila and mouse models of PD should provide a powerful system to examine the concept of using...
chemical chaperones for the prevention and treatment of PD, and possibly for treating neurodegenerative disorders in general.

**Screening to reverse melanoma in zebrafish**

Melanoma is the most serious form of skin cancer. It develops in skin cells that produce melanin and aggressively infiltrates body tissues, even with treatment. Patients with metastatic melanoma have a five-year mortality rate of nearly 70%. The cascade of events leading to the development and invasive characteristics of melanoma is still poorly understood. Progress in understanding the origin, nature and mechanisms of the disease should promote the development of more effective treatments.

The transparent zebrafish is an ideal system to study melanoma progression and they provide an inexpensive experimental assay platform for drug screening. Cristina Santoriello, who works in Dr Mione’s laboratory at the IFOM-IEO campus in Italy, developed a transgenic line of zebrafish that express oncogenic Ras driven by the kit promoter. The Ras-expressing fish develop melanomas at between one and three months of age. Transgenic larvae show an overpigmentation phenotype by just three days post-fertilization owing to an increased number and size of melanophores. In collaboration with Dr Kaufman and Dr Zon at the Children’s Hospital in Boston, Cristina will use the transgenic larvae to identify chemicals that can revert the abnormal growth and migration of transformed melanophores.

**Tracing the origin of brain tumors**

Intracranial pediatric germ cell tumors are an unusual class of brain tumor found predominantly in young infants or in teenagers. The prevailing theory is that these tumors arise from germ cell progenitors that aberrantly migrate from the gonadal area to the brain during embryogenesis. As with other types of brain tumors, they are associated with a number of side effects including edema, headaches, vomiting and visual problems. Some tumors require surgical excision, but many respond well to radiation therapy. However, all of the therapies have significant side effects, and their management and prognosis is largely determined by location and tumor histology.

Chris Tan studies at The University of Nottingham with Dr Paul Scotting, who suggests that intracranial pediatric germ cell tumors may actually arise from neural progenitors that normally reside in the developing brain. In collaboration with Dr Val Wilson, at the MRC Centre for Regenerative Medicine in Edinburgh, Chris will use transgenic mice to analyze the potential mechanism by which neural stem cells could become transformed into germ cell tumors. The aim is to provide clear evidence as to whether neural stem cells could indeed be the origin of this class of brain tumor. It is hoped that this study will provide a clear rationale to establish the first animal model in which to study this class of tumor.

**Professor Stephen O’Rahilly wins the 2010 InBev-Baillet Latour Prize**

In Belgium a unique science prize, the InBev-Baillet Latour Health Prize, recognizes someone whose pioneering research has led to the practical application of fundamental research. The international jury chose Professor Stephen O’Rahilly as the 2010 recipient for his work that identified a number of genetic factors that contribute to obesity. His research changed the way that many people think about the causes of obesity and altered the way that many patients are treated for obesity-related disease.

Metabolic diseases, such as obesity and type 2 diabetes, are a growing concern associated with a variety of symptoms including cardiovascular disease, neurological degeneration and some types of cancer. Dr O’Rahilly was the first person to show that a single or very small number of genetic variations can predispose individuals to obesity. He has helped identify many crucial genetic elements that contribute to the complex pathophysiological mechanisms of metabolic diseases. The list of implicated genes that he has linked to metabolic disease continues to grow, but already includes genes that regulate appetite, insulin synthesis, insulin sensitivity and the cellular response to insulin. He and his colleagues have not only showed that a deficiency of leptin, an adipose-derived hormone, predisposed individuals to obesity but they also helped patients normalize their body weight through the administration of recombinant leptin. His work also shows that genetic factors predispose certain individuals to type 2 diabetes. Dr O’Rahilly’s integration of patient information with mouse studies has illuminated new inroads to treating metabolic disease.

DMM would like to congratulate its founding editor, Dr Stephen O’Rahilly for this recognition of his contributions to science and medicine.

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