Laboratory Researc

This article forms part of a collection of invited articles which will be collated and published as a 'Research Handbook in Dermatology'. Dr Mike Ardern-Jones, Dr Clive Archer, Dr Graham Ogg.

Introduction

Although laboratory research may seem very far away from seeing patients in a busy general dermatology clinic, many advances in patient care have resulted from basic laboratory research. The time taken to translate laboratory research to the clinic can be 10 to 15 years, but it is definitely achievable in a lifetime in cutaneous biology. For example, the type VII collagen gene was cloned in 1994 and over the next few years, clinical trials will start of recombinant type VII collagen in epidermolysis bullosa wounds of patients with type VII collagen gene mutations. Mutations in the ABC-transporter gene, *ABCA12*, were shown to cause harlequin ichthyosis in 2005 and the first preimplantation genetic screening was performed for an affected family in the UK in 2010.

Opportunities

There are more opportunities than ever before to get involved in laboratory research. Medical students in universities where there are active cutaneous biology laboratories can apply for summer scholarships from the Wellcome Trust and other charities and can also undertake intercalated degrees, usually after the 4th year. Final year medical students can apply for academic foundation training programmes to obtain some clinical and basic research exposure.

After obtaining MRCP, interested trainees can apply for Academic Clinical Fellow (ACF or academic NTN) positions in dermatology. Twenty-five percent backfill is provided by the National Institute for Health Research (NIHR) allowing 3 months per annum of laboratory research over 3 years. The outcome is expected to be a successful application to a major funding body for a clinical training fellowship which provides 3 years salary and consumables to undertake a PhD. Being an ACF, however, is not the only route to a clinical training fellowship and Specialist Registrars (SpRs) can also apply and be successful with appropriate support and coaching.

There has never been a better time in dermatology to obtain funding for a PhD. The British Skin Foundation, British Association of Dermatologists and the Medical Research Council are jointly funding 4 fellowships between 2010 and 2013 specifically for trainees in dermatology. Clinical Fellowship funding can also be obtained from the NIHR, Cancer Research UK, Action Research and the Wellcome Trust. Smaller charities generally provide 1 year of funding only, but this can be a great help to obtain preliminary data for a subsequent application to one of the bigger funding bodies.

How it works in practice

To do basic laboratory research, it is helpful to be in a department where there are good core facilities with technical support and a critical mass of scientists with similar interests and an available mentor (this does not have to be a dermatologist, it could be a geneticist immunologist, epidemiologist or other scientist).

For Speciality Registrars who are not in a department where laboratory research and mentorship are available, the BAD Research Committee will be offering bursaries for 'taster weeks' allowing SpRs to visit a dermatology research laboratory of their choice, in the UK or abroad. Since 2010, the BAD Research Committee is also providing 8 annual travel bursaries of £250 each to attend the BSID meeting to SpRs who are interested in research. Another way to gain insight into career paths which combine clinical and research elements is at the THESIS/BAD/BSID meeting.

An important part of working in a laboratory is the cameraderie that develops with other PhD students and post-doctoral researchers. Post-docs help PhD students and more senior PhD students help junior students. This can be very useful, as a naive medic,

Edel O'Toole

immersing oneself into laboratory research for the first time.

Usual laboratory techniques in skin biology include cell culture (for example keratinocytes, fibroblasts, melanocytes or T-cells), protein techniques such as Western blotting, flow-cytometry or immunostaining, molecular techniques such as cloning and PCR and cell biology techiques like invasion or attachment assays.

With the advent of high-throughput technology, it is now possible to obtain a huge amount of data quickly from microarray technology such as gene expression arrays (comparing expression of genes throughout the genome under different conditions) or single nucleotide polymorphism arrays (looking at variation in DNA between individuals). These data can be interpreted using bioinformatics (computer software to analyse large amounts of data).

Laboratory research is a little like gourmet cooking, requiring attention to detail. A minor omission can result in failure of an experiment. Cells do not always behave in the same way. They can be affected by incubator temperature, room temperature, how they were last handled or infection. This can be frustating, but with patience and persistence, experiments eventually start to work. *"It's not that I'm so smart, it's just that I stay with problems longer"* – Albert Einstein.

For clinicians, settling into laboratory life can be challenging. We are accustomed to a tight timetable

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with scheduled outpatient slots etc and many budding clinician scientists find organizing their own work difficult, initially. Some flexibility is also required. For example, one might occasionally need to stay late to finish experiments or come in at the weekend to set up new experiments.

Similar to clinical research, laboratory research sometimes gives the opposite answer to what one had hypothesized. This often opens new avenues of interest with further questions to be answered. In general, during a 3 year PhD, the 'Eureka' moments occur at the end of the 2nd year and then it is time to start finishing up experiments, writing papers and writing the thesis.

A PhD thesis is similar to an 'Unfinished Symphony' in that it is never possible to answer all the questions, so it is important to concentrate on writing up what one can and be awarded a PhD. After obtaining a PhD, interested individuals can consolidate their research experience for 3 to 4 years in a NIHR-funded Clinical Lecturer post which allows 50% time for research and the remainder of the time for completion of clinical competencies.

Conclusion

The human genome has 3 billion bases and with the advent of high-throughput sequencing, the routine availability of sequencing of an individual's entire genome is a reality in our working life times (it is estimated that the cost will decrease 10-fold in the next 5 years to about £300 per genome). High-throughput technology is already producing thousands of biomarkers and targets in cancer and inflammatory skin disease. In the UK, we will need dermatologists who can work with scientists to make this information clinically useful. A mixed laboratory and clinical career is never boring and I always look forward to coming to work!

Edel O'Toole
Barts and the London