

Commentary

An agenda for UK clinical pharmacology

Integrating pharmacology and clinical pharmacology in universities

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Continuing development of safe and effective new medicines is critically important for global health, social prosperity and the economy. The drug discovery–development pipeline depends critically on close partnerships between scientists and clinicians and on educational programmes that ensure that the pharmacological workforce, in its broadest sense, is fit for purpose. Here I consider factors that have influenced the development of basic and clinical pharmacology in UK universities over the past 40 years and discuss ways in which basic pharmacologists, clinical pharmacologists and scientists from different disciplines can work together effectively, while retaining their professional identities and fostering developments in their disciplines. Specifically, I propose the establishment of Institutes of Drug Discovery and Development, whose activities could include development and implementation of a translational pharmacology research strategy, drawing on the collective expertise of the membership and the university as whole; provision of a forum for regular seminars and symposia to promote the discipline, encourage collaboration and develop a cohesive community; provision of a research advisory service, covering, for example, data management, applications for ethics permission, clinical trials design, statistics and regulatory affairs; liaison with potential funders and leadership of major funding bids, including funding for doctoral training; provision of advice on intellectual property protection and the commercialization of research; liaison with corporate partners to facilitate collaboration, knowledge transfer and effective translation; and leadership of undergraduate and postgraduate education in basic and clinical pharmacology and related sciences for medical and science students, including continuing professional development and transferable skills.

Introduction

Writing this article brought a sense of déjà vu and memories of the 1970s. Academia was very different then. Universities were ivory towers that engaged in education, scholarship and research; in my experience, they generally took a rather disparaging view of collaboration with industry or anything that might be viewed as commercial. Intellectual property was rarely, if ever, protected and, to the best of my knowledge, the term 'spinout company' had not been invented. However, departments of basic pharmacology were well established and had led the way in discovering many important compounds, such as neuromuscular blocking drugs. Strangely, though, they were almost always divorced from the clinical arena, even in the stand-alone medical schools. Clinical pharmacology as a discipline was in its infancy, but developing rapidly; however, although collaboration was often mooted, the relationships between scientists and clinicians were all too often ones of

mutual suspicion; hardly the basis for harmonious partnerships. As an undergraduate, I was advised by a very distinguished professor never to consider working with a clinician or in 'one of those terrible medical schools'; when I was awarded my PhD from one such school, the Head of Department, herself an eminent pharmacologist, advised me that I would damage my career beyond repair if I moved to a clinical department!

In the ensuing years, much has changed. Universities have been transformed from ivory towers to global enterprises, with major roles to play in economic growth and social prosperity. Scholarship, education and research are of course still core to their mission, but so too are innovation, translation and entrepreneurship; furthermore, successful partnerships with industry are now loudly applauded. New disciplines have emerged; interdisciplinary research has blurred the barriers between disciplines and led to exciting new discoveries; increased collaboration between clinicians and basic scientists has facilitated

translation in many areas; and several drivers have paved the way for better integration of basic and clinical pharmacology. For example, in the UK: (i) the General Medical Council (GMC) advocated vertical integration in the undergraduate medical curriculum in its original (1993) version of *Tomorrow's Doctors* [1], a document that was designed both to reshape medical undergraduate teaching in the UK and to redefine the knowledge, skills and attributes a medical student is required to demonstrate in order to graduate; (ii) universities have increasingly recognized the value of their intellectual property and have developed robust mechanisms to protect and exploit it; critically, for pharmacology, this includes translating laboratory science to the clinic, with the goal of improving human health, surely the long-term goal of all pharmacologists, basic or clinical; (iii) as examples of successful commercialization of university research have emerged, 'translation' and 'impact' have become increasingly important key performance indicators for universities in the eyes of Government and funders; translational science has become a 'buzz word' in grant applications, and this has focused the minds of many of our scientists and clinicians; and (iv) the growth of the global knowledge-based economy has become a further driver for translational research, as too has the Government's assertion that universities are positioned to make a major and rapid impact on the UK's economy, through knowledge transfer and commercialization of their discoveries.

Opportunities for integration

Against this background, other factors have limited the opportunity for integration of basic and clinical pharmacology in the UK and, in my view, have had a detrimental effect on our discipline as whole.

- While *Tomorrow's Doctors* (1993) [1] argued for vertical integration of teaching, it also advocated a substantial reduction in the basic science content of the undergraduate medical curriculum and the introduction of systems-based rather than discipline-based teaching; basic and clinical pharmacology received scant attention in this document and, consequently, in many schools they were subsumed into systems-based modules and lost as identified disciplines, both in the core curriculum and in examinations.
- At the same time, the structures of basic bioscience degrees (BSc and MSci) underwent significant changes in several universities. 'Modularized' degree programmes, which allowed a broad range of choice, replaced many traditional discipline-based undergraduate degree programmes, and the growth of new areas and important areas such as molecular biology and genetics further diluted core pharmacology teaching. As a result, some key aspects of pharmacology disappeared from many degree programmes; in particular, whole-animal pharmacology and the concepts of quantifying drug action.
- These changes, together with the drive to blur the barriers between the disciplines and encourage interdisciplinary research, resulted in the merger of several basic pharmacology departments with other basic science departments, with a consequent loss of identity of the discipline. In some cases, pharmacology departments were simply dissolved and the staff dispersed into new 'systems-based' academic structures.
- Clinical pharmacology also shrank as a visible discipline, with a reduction in training posts and a tendency for clinical pharmacology research to be embedded in other clinical specialties, further reducing visibility.

Despite these confounding issues, the opportunities for pharmacology to re-establish its position as one of the leading bioscience disciplines and to foster integration of the basic and clinical sciences have, to my mind, never been greater. As discussed earlier, the critical importance of translation to economic growth and social prosperity is well recognized in the UK by universities, funders and Government. Key funders (notably the Wellcome Trust and MRC), supported by pharmaceutical companies, have established funding streams to support research and post-graduate clinical training in 'translational medicine' (essentially clinical pharmacology) and have also recognized the importance of advancing basic science to seed future translation. In addition, there is increasing recognition of the importance of both basic and clinical pharmacology in the undergraduate curriculum.

Triggered by concerns raised by young medical graduates, practising doctors, other healthcare practitioners and the British Pharmacological Society (BPS) about the prescribing competencies of medical graduates, the GMC reconsidered the place of pharmacology in the undergraduate medical curriculum. The 2003 version of *Tomorrow's Doctors* [2] made it clear that medical graduates should know and understand the principles of 'the effective and safe use of medicines as a basis for prescribing, including side effects, harmful interactions, antibiotic resistance and genetic indicators of the appropriateness of drugs' and should be able to 'work out drug dosage and record the outcome accurately' and 'write safe prescriptions for different types of drugs' safely and effectively. *Tomorrow's Doctors* (2009) [3] placed still more emphasis on the importance of pharmacology, stating that graduates must 'demonstrate knowledge of drug actions: therapeutics and pharmacokinetics; drug side effects and interactions, including for multiple treatments, long-term conditions and non-prescribed medication; and also including effects on the population, such as the spread of antibiotic resistance'. It also laid out a clear, comprehensive framework to ensure that graduates have the knowledge necessary to prescribe drugs safely, effectively and economically.

The BPS and UK pharmaceutical companies warned of the growing difficulties in recruiting scientists with

knowledge, understanding and practical expertise in *in vivo* animal physiology/pharmacology. Survey data showed that undergraduates and doctoral scientists received limited training in these areas and that the capacity of universities to deliver such training was diminishing rapidly, partly because of costs, but also because many of those staff with the necessary expertise were approaching retirement. This loss of expertise threatened core pharmacology research in academia and industry and, hence, the drug discovery–development pipeline. In particular, it limited: (i) the opportunity to understand the pathophysiological roles of genes and their products (for example, by studying genetically modified mice) and thereby to capitalize on a wealth of data generated by molecular and genetic studies; and (ii) basic translational and safety pharmacology studies. To address this problem, a consortium comprising AstraZeneca, GlaxoSmithKline, Pfizer, the BBSRC, the MRC, the Higher Education Funding Councils of England and Scotland, and the BPS established a fund (BBSRC Integrative Mammalian Biology Fund) of >£12 million in 2005 to establish and support four centres in the UK (Glasgow/Strathclyde, Imperial College London, King's College London and Manchester/Liverpool) dedicated to providing education and training in *in vivo* science, thereby rebuilding capacity and facilitating translation. The centres have built on their successful research programmes and have developed high-quality training programmes; in addition, they have raised public awareness of the importance of *in vivo* physiology/pharmacology studies in medical research and, in particular, in the drug discovery–drug development cycle.

These changes, together with the social and economic pressures for translational research, must surely support the need for further integration of basic and clinical pharmacology in UK universities. There are, of course, several examples of highly successful integration across the discipline and, for those institutions with strong pharmacology departments (basic, clinical or integrated), there are many opportunities to build on existing strengths and to foster integration. More imaginative solutions are required for institutions in which pharmacology departments no longer exist as independent entities and in which pharmacologists (basic and clinical) are distributed across several departments, sometimes not even recognizing themselves as pharmacologists. Any successful strategy will need a strong, committed and visionary leader with the talent both to draw people together and to convince their university that their vision will deliver clear added value to education, research, translation and innovation, and that their business case will work. Attempts to establish new integrated pharmacology departments by moving staff and thereby potentially destabilizing other viable academic units are, in my view, unlikely to find favour, particularly in the current economic climate.

A proposed solution – Institutes of Drug Discovery and Development

More creative solutions are necessary. Any solution must: (i) respect the contexts in which both scientists and clinicians can best succeed in their work; and (ii) facilitate two-way partnerships that enable not only science to be translated to the clinic, but also the experience of the clinic to inform scientific questions and experiments; only with this two-way dialogue can integration yield maximal benefits. Basic pharmacology research (and education) depends increasingly on interactions with scientists from other disciplines, not only in the biosciences but also in mathematics, physics, chemistry and engineering. Those interactions must continue to flourish for science to move forward, and proximity is key, but an effective model for basic–clinical integration must also enable scientists to work with clinicians and be exposed to a clinical environment, so as to inform their research. Likewise, while clinical practice, research and teaching necessarily require a clinical environment, clinicians also need to work alongside basic pharmacologists and scientists from other disciplines, in order to take best advantage of new scientific developments and apply them appropriately to deliver cutting-edge translational and clinical research. Effective integration thus requires a model in which scientists and clinicians regularly experience and work in each other's environments, while retaining their respective professional bases and identities. Ideally, it should also offer opportunities for both scientists and clinicians to work closely with pharmaceutical and biotechnology companies, perhaps through a system of reciprocal placements, so as to enhance mutual understanding and facilitate effective translation and knowledge transfer.

Creating a structure that both facilitates integration of basic and clinical pharmacology and takes maximal advantage of the cutting-edge science based on a multifaculty campus, with clinical expertise normally based mainly in hospitals remote from the main university campus, is challenging. One potential solution is to form a semi-virtual institute (Figure 1) with a clear remit, a director and a budget to support a basic infrastructure. Members of the institute would be drawn from the academic, clinical, research and technical staff based in the mainstream academic departments and clinical centres and would retain their main bases in their home departments within their faculty or hospital. The institute would provide both a focus to drive and implement an institutional strategy in pharmacology and a space for core activities and services and ideally also for hot desks, particularly for young researchers and visitors, to facilitate collaboration. The success of Australian institutes such as the Walter and Eliza Hall Institute of Medical Research and the Baker IDI Heart And Diabetes Institute testifies to the possibilities.

The remit of an Institute of Drug Discovery and Development might, for example, include the following:

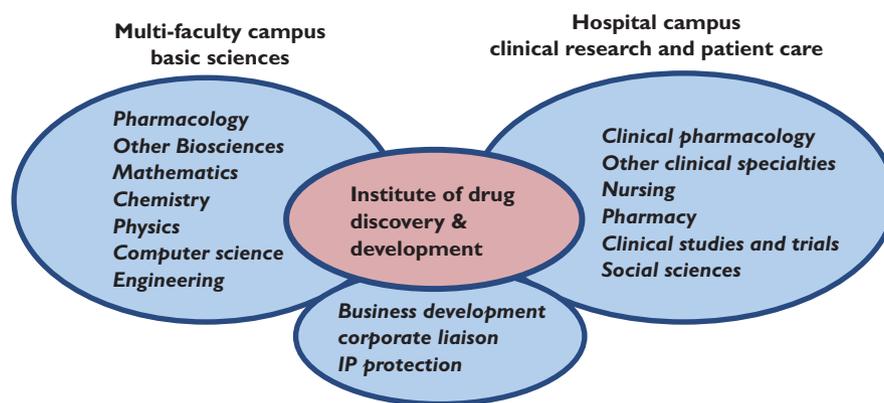


Figure 1

Diagram illustrating how a semi-virtual Institute of Translational Pharmacology could facilitate better integration of basic and clinical pharmacology, especially in universities in which scientists and clinicians operate across different campuses; such a scheme might be particularly valuable in universities in which distinct departments of pharmacology do not exist; such a model could, in the longer term, bring together scientists, clinicians and others to provide a clear focus for all activities relating to drug discovery and development. Abbreviation: IP, intellectual property

(i) development and implementation of a translational pharmacology research strategy that draws on the collective expertise of the membership and the university as whole; (ii) provision of a forum for regular seminars and symposia to promote the discipline, encourage collaboration and develop a cohesive community of pharmacologists, both basic and clinical; (iii) provision of a research advisory service, covering, for example, data management, applications for ethics permission, clinical trials design, statistics and regulatory affairs; (iv) liaison with potential funders and leadership of major funding bids, including funding for doctoral training; (v) provision of advice on intellectual property protection and the commercialization of research; (vi) liaison with corporate partners to facilitate collaboration, knowledge transfer and effective translation; and (vii) leadership of undergraduate and postgraduate education in basic and clinical pharmacology and related sciences for medical and science students, including continuing professional development (CPD) and transferable skills.

Education, in its broadest sense, is likely to be key to success, partly because the postgraduate programme needs some adjustment to facilitate the long-term success of integrated pharmacology research, but also because education is often the glue that holds groups of people together when other pressures tear them apart. Our current approaches to pharmacology education in the UK have evolved to foster the respective interests of clinicians or basic scientists, but have done little to bring the two together. Not surprisingly, undergraduate and CPD programmes for clinicians focus on ensuring that practising doctors are both competent prescribers and equipped to understand advances in pharmacology and therapeutics and apply them safely and appropriately in their practice.

Even for those following an academic career track, they offer few opportunities for the clinician to keep abreast with the science that underpins the discipline or to interact regularly with scientists, unless they work in an integrated basic–clinical environment. For basic scientists, the situation is still less satisfactory. Undergraduate degrees provide core knowledge, understanding and practical expertise in the discipline, while the MRes/PhD provides focused research training, usually with an element of transferable skills training. Thereafter, there is no structured career path in academia and no formal CPD provision; scientists often become increasingly focused on their specific research area as they strive for publications, fellowships and grants, very often with little or no clinical contact or opportunity to gain insight into the clinical problems that their research seeks to address. Effective delivery of cutting-edge bench-to-bedside research requires both scientists and clinicians to develop a sound understanding of the drug discovery–development cycle, from conception to the market, including some insights into the business elements. Good CPD programmes should include this, while at the same time developing the specialist knowledge, skills and attributes of both parties. Importantly, they also should provide opportunities for academic clinicians to develop their scientific knowledge and to work alongside scientists, and for scientists to develop clinical knowledge and to experience the clinical environment.

Conclusions

Integration of basic and clinical pharmacology in UK universities is an old chestnut that badly needs to be cracked. There are many reasons why integration has not been

optimal in the past, but with the current drive for innovation, translation and knowledge transfer, the opportunities have never been greater. However, only people can make it happen.

Competing Interests

There are no competing interests to declare.

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