Drug development needs a new brand of science

We need to break with the past to develop new medicines, says **Garret FitzGerald**. *An interdisciplinary NIH centre points the way.*

Last week, the US National Institutes of Health (NIH) voted to launch a National Center for Advancing Translational Sciences, focusing on translational medicine and therapeutics (TMAT), the growing field that aims to speed therapies from the laboratory to the clinic. NIH director Francis Collins called the decision "momentous" — a "disruptive innovation on an institutional scale" — and I think he is right. Only a translational approach can address the fact that the current model of drug discovery and development is unsustainable. Paradoxically, as we have witnessed a successful revolution in drug discovery, a crisis has emerged in drug development. Targets, and the chemistry needed to probe them, can be selected more rationally than ever — yet more and more candidate drugs are proving expensive failures.

One reason is that too many steps are pursued in specialist isolation, in both academia and industry. Too few people can bridge the translational and interdisciplinary divides. This has led to crucial and expensive mistakes in phase II of drug development — when there is often a failure to see an impact on efficacy, a propensity to ignore risks, or a danger of making errors in dose selection for phase III.

The new NIH centre promises to catalyse a much-needed restructuring of the drug-development process. The centre can foster training by absorbing the Clinical and Translational Science Awards (CTSAs) and their educational infrastructure. This will allow scientists to partner in a modular approach to drug development, in which expertise is drawn from distinct sectors and regions as needed to address particular therapeutic challenges. Furthermore, the broad CTSA-supported programmes and infrastructure — from preclinical science to community outreach — could be harvested to support a more efficient approach to drug development, approval and dissemination.

Why has the need for such a radical change emerged? Thirty years ago, the best clinical pharmacology units housed experts from a range of disciplines. Cell biologists worked side by side with colleagues studying model systems and those involved in mechanistic studies of physiology, disease and drug action in humans and pharmacokinetics. Others were trained in chemistry, statistics and toxicology. Blending these heterogeneous talents fostered what we would now call interdisciplinary science, and, in the context of drug development, T1 translational research.

However, as the economics of academic departments shifted, clinical pharmacology fell from favour. Even the term clinical pharmacology has lost its lustre, and now covers only some of what we need. To attract the best and brightest, we need a new brand, backed by funders, academics and industry. Potential students must perceive the field to be hot.

So what shall we call this interdisciplinary, translational endeavour? It is difficult to imagine anyone rushing to join something called 'T1 translational research'. 'TMAT', on the other hand, captures the fashion for translation, places the discipline in the heart of medicine and indicates the focus on developing novel therapeutics. Adoption of this term by the NIH follows a training programme in TMAT funded by the UK Wellcome Trust. Now we need to realize the potential of this brand and push the idea more widely.

The NIH centre will signal, both to Congress and the biomedical research community, the intimate connection between fundamental science and the accelerated delivery of cures to the general public. This is not a zero-sum game: success of translation requires investment in basic science. By developing sustainable career structures in TMAT, the centre can reverse the flow of bright young scientists into specialist silos. Joint investments in training, infrastructure and programmes would ensure that the efforts of the new centre would improve, not compete with, the translational efforts of disease-focused institutes and centres within the NIH.

The new TMAT centre could also act as a visible point of contact for extramural partners, including industry, charitable foundations and the US Food and Drug Administration, to buy into the restructuring required to move to a more modular approach to drug discovery and development. A looser, more distributed model spanning pharma, biotech and academia could then draw on knowledge more easily, and apply it more efficiently.

It is a big challenge, and two particular obstacles come to mind. First, we must revise how we reward ideas. At present, defence of intellectual property relies on patents on the composition of matter, usually molecules, most of which never become approved drugs. To make sure that they do, many people with diverse skill sets have to work effectively together. Inside a company, it is easy to reward everybody involved. As companies fragment, we should consider new models of intellectual property. Perhaps the financial rewards of a patent should be postponed until a drug is a profitable success — and a formal mechanism found to distribute rewards among all those who helped to make it happen.

Second, we will need common standards of data protection and privacy, and shared infrastructure that allows secure and compliant sharing of diverse types of information, including clinical data, across countries and sectors. This is the foundation upon which a global TMAT enterprise can be established. In some ways, this is the greatest challenge of all, but it can be done. As T. S. Eliot said: "Only those who will risk going too far can possibly find out how far one can go." ■ SEE NEWS P.877

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