How academia can help drug discovery

A recent symposium debated the role of academic institutions in producing therapeutic small molecules.

Simon Frantz

When chemists from academia and industry gathered at the recent Horizon Symposium, one of the main points of debate was whether academic institutions can realistically become involved in drug discovery and development programmes.

At the Symposium, entitled 'Charting chemical space — finding new tools to explore biology', which was co-organized by Aventis and Nature Publishing Group, Brent Stockwell, Professor of Biological Sciences at Columbia University, New York, argued that one benefit of academic involvement in drug discovery programmes is that academia can try riskier approaches. (For more information about the Horizon Symposium, visit http://www.horizonsymposia.com/)

"Such riskier approaches can involve using novel types of compounds, novel types of assays, tackling orphan diseases and creating new animal models for disease," said Stockwell. Successful ideas will result in new methods and standards that will eventually be adopted by industry.

Although no-one doubted academia's strength in finding biological targets, mixed feelings were expressed about whether it can produce therapeutically useful small molecules.

After the Symposium, John Schwab, a program director in the Division of Pharmacology, Physiology, and Biological Chemistry at the US National Institute of General Medical Sciences, said that novel small molecules have an integral role in proteomic studies aiming to identify, characterize and validate huge numbers of proteins, many of which will be new drug targets. "These small molecules are unlikely to be supplied by industry," says Schwab who is a member of the NIH committee that is crafting the Molecular Libraries component of the NIH Roadmap.

Christopher Lipinski, now retired from Pfizer, agreed that academia has a positive role in discovering important enabling chemical tools, but added that this is a much easier task than discovering drugs.

Contrary to popular belief, drugs are almost exclusively discovered in industry and not in government laboratories or in academia, says Lipinski. "Profiling performed either computationally or (even better) experimentally by big pharma has very little counterpart in academia," he says. Faced with major problems in lead optimization, an experienced medicinal chemist might consider making a drastic structural change. "Maybe a piece from a compound made 12 years ago is added, or a piece from a literature or patent compound." Here, experience is the key — it could be a 'hunch' or a 'gut feeling' that the change would be beneficial. "When successfully applied, this skill of the medicinal chemist is a beauty to behold," says Lipinski.

It seems that it would be to everyone's advantage if the pharma industry took an active role in teaching medicinal chemistry in academia, says Schwab.

"We are very interested in supporting efforts to better understand the concept of chemical diversity and to develop improved predictive models. However, until we gain a better sense of this correlation, we'll have to rely on more empirical approaches, including high-throughput screening." In terms of assigning function to the genome, Schwab says that academia's ability to predict the biological hotspots in chemical diversity space, and to make libraries to probe these hotspots, will improve. "I don't think that pharma has the resources to do this, so if academia doesn't make the requisite small molecules, then who will?"

Christopher Lipinski at the Horizon Symposium. TIMOTHY P. BYRNE

Lipinski is mystified that although there are programmes for retired business executives to lend their expertise to societal problems, there is no counterpart for retired pharma medicinal chemists to collaborate with academia and government laboratories in enabling tool or orphan-drug discovery. "It seems like such an obvious, cost-effective approach to assist in fulfilling a societal need."