Drug discovery

Off-the-shelf Small Molecules on the way

Patrick Walter

A quick, cheap automated process that uses chemical building blocks to make small molecules could replace existing methods of making these molecules, potentially revolutionising small molecule drug discovery.

Chemists behind the new technique at the University of Illinois at Urbana-Champaign, US, have been working with a large chemical company and say a worldwide launch of off-the-shelf chemical building blocks for assembling small molecules is expected in as little as six months.

Small molecule drug development, once the preserve of big pharma, is increasingly being embraced by the biotech industry possibly because patients are more amenable to orally-available small-molecule treatment than injectable protein-based medicines.

The Illinois group led by Martin Burke drew inspiration from the synthesis of peptides whereby amino acids are stitched together to form a short chain using only one reaction.

Burke’s group have not yet made a machine that can churn out complex small molecules, but they have taken an important step. They have created boronic acids with different chemical building blocks that can be used to make specific small molecules. Pyramidal protecting groups direct the reaction so that only the desired linkage is formed. The protecting groups are easily removed and the process repeated. Complex natural products like retinal and half of the fungicide amphotericin B have already been made (JACS 2007, DOI: 10.1021/ja078129s).

The great advantage of their process is its flexibility – a huge number of products could be produced in this way – and its simplicity as it takes out difficult and slow synthesis steps. ‘Aryl and vinyl building blocks appear to be the most accessible at this point, but we are looking to bring alkyll into the mix,’ Burke said.

Ramzi Sweis, senior research scientist at Merck said: ‘At first glance the controlled reactivity would seem to be the greatest advantage. But the simplicity of this method coupled with the mildness of the chemistry is equally advantageous.’ He adds that he anticipates a lot of enthusiasm for this process in pharma. ‘Time will tell if it will displace current methods. If anything has the potential to displace them though, this is it’.

Drug pricing

Drug price reductions greatly exaggerated says ABPI

Marina Murphy

Reports in the Financial Times that government officials are looking for an average 10% reduction in the price the NHS pays for prescription medicines have been dismissed by the industry.

‘We’re in negotiations with the Department of Health (DH) and it would be wrong to comment on any single element or any figures associated with them, but it is safe to say that the 10% figure quoted is entirely speculation by the FT,’ said Richard Ley, spokesperson for the Association of the British Pharmaceutical Industry (ABPI), told C&I.

The ABPI is currently in negotiations with the DH on replacing the current drug pricing system with one in which the price to the NHS reflects its value to patients (C&I 2007, 22, 7). In February, The Office of Fair Trade (OFT) recommended that the current pricing system (Pharmaceutical Price Regulation Scheme (PPRS)) be replaced and the government agreed (C&I, 2007, 4, 4).

The current PPRS, which was last negotiated in 2005, is basically a profit control mechanism. This time, it is not just price but the overall efficiency with which medicines are used in the UK that will be discussed. The industry is likely to also want to discuss the increasing use of generics – medicines that are off patent – and the rate of uptake of new medicines in the UK. The UK is at the bottom of the heap as regards speed with which new medicines are taken up and is at the bottom of 17 EU countries in per capita spend on pharmaceuticals, according to John Melville of Swiss pharmaceutical giant Roche.

In a joint statement, the DH and ABPI said they had agreed on the principles drawn up in response to the 2007 OFT report: value for money, reward for innovation, accelerated uptake of new medicines and sustainability.