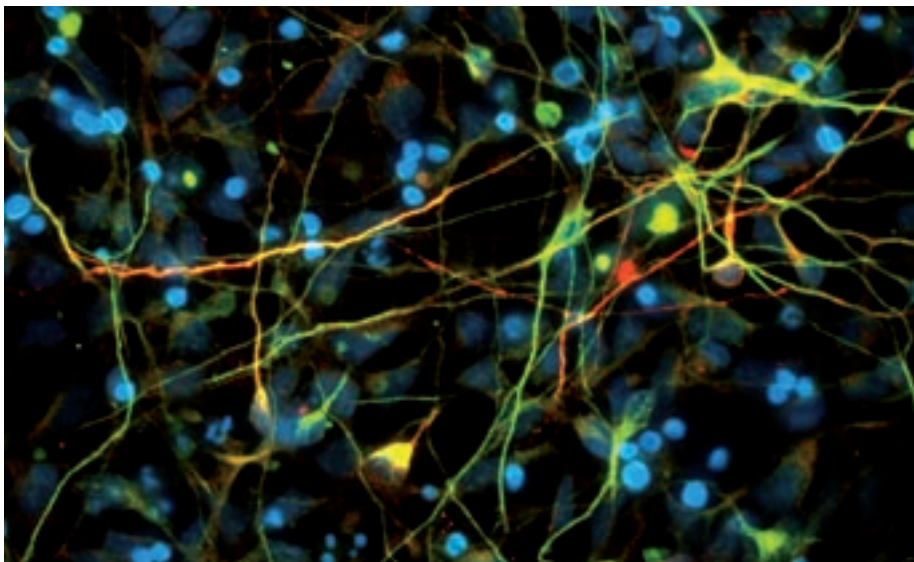


CELL-BASED ASSAYS

INTRO

Biological assays are gaining ground

▶ Drug development costs are on the rise, but pipeline productivity has not kept up with the cost explosion in target and compound identification, clinical studies and marketing. Although neither acceleration of drug development through automation nor reduction of personnel through mergers have brought significant improvements in the last decade, there has been a renaissance in biology in the post-genomics era. Driven by the hope that better assays and disease models would significantly improve the success rate of compounds in the drug development process, the pharma industry is now supporting large initiatives such as the US Critical Path Initiative and its European counterpart, the IMI (Innovative Medicines Initiative - see report on p. 8). One common goal is to establish biological assays that can give more information about the toxicity and efficacy of compounds. Predictive mRNA, protein or metabolic biomarkers and cell-based assays, which are the topic of this special on "Cell-based Assays & Drug discovery" (p. 34-47), are one tool in the box that researchers are using to improve efforts to mimic disease-specific biological processes and reduce candidate failure.



Pharma companies are constantly searching for new ways to gain better information about drug candidates as early as possible in lead discovery and lead optimisation. Problems such as pharmacokinetics/ADME, animal toxicity and side effects/human toxicity plus lack of effi-

cacy are some of the challenges that drug developers face when testing promising drug candidates.

Screening units use cell-based assays as primary detection tools for identifying novel targets and finding those candidates, providing more accurate represen-

tations of the real-life cell model than traditional biochemical endpoint assays.

From data integration to dynamic cell-based assays

Data integration has become an essential tool for analysing the data gained by different new technology platforms such as transcriptomics, proteomics and metabolomics. An IMI forerunner called Innomed Predtox compared the significance of mRNA, protein and metabolite biomarkers for prediction of compound toxicity. A participant in this project was Swiss GeneData AG, which has developed an IT platform for integrating the highly different data (see p. 46). Innomed Predtox ranked mRNA profiling as the technique that gave the most reproducible results.

RNA-interference has developed into an extremely powerful tool for target identification by linking loss of function phenotypes to cellular pathways. Tschulena *et al.*, who used dynamic impedance analysis of knock-downs, report in this issue (see p. 34) that RNAi analyses depend on the time of measurement, and also show unexpected kinetics.

Labeling proteins with fluorescent reporters and following their cell distribution and binding to ligands or interaction partners can offer insights into the role of particular proteins in regulatory networks, especially when carried out in primary human and appropriate animal cell models. Kai Johnsson presents different tags suitable for high-content and high-throughput screening on page 39.

Finally, Funke & Mayer present a 3D tumour model suitable for drug penetration studies and toxicity testing, as well as for cancer migration and responsiveness testing to drugs.

Recent progress in the field of biological space and cell-based assays is the subject of Europe's leading event for drug development this autumn, the Basel-based MipTec (13th-15th Oct.) Its programme includes 110 keynote lectures on drug discovery technologies, biological and chemical space, computational drug discovery, biomarkers, early safety evaluation, pharmacodynamics and biopharmaceuticals. See you there! ◀