The new generation of patch-clamp equipment

During the past few years there has been increasing interest in ion channels as drug targets. The respective therapeutic areas include cardiovascular-, CNS- or metabolic-diseases, cancer, allergy and asthma. However, some interactions with ion channels have been shown to cause side effects, for example, blocking HERG potassium channels might cause drug-induced QT-prolongation. For these reasons there is an increasing need to test compounds on ion-channel targets.

Until today, the technologies that have been used to investigate the effect of compounds on ion channels are either precise but low throughput (e.g. the patch-clamp technique [1]), or high throughput but with limitations in the correlations to physiology (e.g. binding experiments). Recently, several companies have developed new systems to automate the patch clamp technique and to increase the throughput of this technology.

A recent article [2] described the different technologies of specialized companies in detail and compared positive and negative aspects of each. The technologies were compared with respect to throughput, success rate of the experiments, physical parameters of the access to the cell, usability for different ion channels (e.g. voltage-gated or transmitter-gated) and cost. The review provides a very good and comprehensive overview of the literature, concluding that the current automated patch technologies are still not to be seen as high-throughput techniques and that a large number of improvements still have to be made. A clear evaluation of the anticipated projects of the individual pharmaceutical or biotech company has to be done to select the right technology for the individual needs.

For modern drug discovery and development, a combination of different technologies might serve best as a useful strategy to perform screening campaigns. For a variety of ion channels, HTS of 30,000, 100,000 or 500,000 compounds, using either binding-, flux- or fluorescence-based assays [3, 4] can be used for the initial detection of hits. The selected compounds (e.g. 1–2% of the total screened) and those synthesized afterwards in medicinal chemistry can be investigated using automated patch-clamp devices. For this part of the ion-channel drug discovery projects, reliable systems with moderate throughput have to be developed for the market. It is likely that some of the available systems could be optimized within the near future to meet this goal.

References

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Imaging in oncology

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SMi's *Imaging in Oncology* conference, held in London 17–18 March 2004, assembled drug developers, academics, informaticians and data managers, together with the specialist imaging CROs whose expertise is so often essential in delivering usable data from multicentre imaging studies. The meeting covered all aspects of imaging in cancer, including animal models, clinical trials and diagnostics, but the main focus was on biomarkers to support Phase II and III clinical trials. Imaging in oncology is a field of rapidly advancing technology, and as Ellen Feigal from the National Cancer Institute (NCI; http://www.nci.nih.gov) pointed out, received US$170 m in US grant funding in 2003, a fourfold increase since 1996.

Molecular imaging

No imaging meeting is complete without something new on the hot topic of molecular imaging, and delegates were treated to a tantalising glimpse of the future. Willy Eidsaunet from Amersham (http://www.amersham.com) showed beautiful SPECT (single photon emission computed tomography) images in breast cancer using their angiogenesis imaging agent ^{99m}Tc-NC100692, currently in Phase II trials, while Padmaja Yalamanchili [Bristol-Myers Squibb (BMS) http://www.bms.com] described new gamma-emitting imaging agents