

*et al*, 2008). These findings identify a specific 5-HT receptor of relevance to a prevalent metabolic disease.

Together, these data indicate that the 5-HT<sub>2C</sub>R is an attractive and tractable potential drug target for the treatment of obesity and/or type 2 diabetes. Recent pharmaceutical efforts have led to the development of at least one compound that is currently in clinical trials for obesity treatment. Results from these trials are awaited with considerable interest.

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## Turning up the pace of ion channel screening in drug discovery

Ion channels represent an important family of integral membrane proteins involved in many diverse physiological processes and are also implicated in a number of pathological conditions in particular of the nervous, cardiovascular, and inflammatory systems. These proteins have proven to be attractive

targets for drug discovery with approximately 13% of marketed drugs having their mechanism of action attributed to activity at ligand- or voltage-gated ion channels (Overington *et al*, 2006). Although this success is noteworthy, there is a general consensus in the field of ion channel-targeted drug discovery that progress has been significantly hampered because of the low-throughput nature of the gold standard assay for electrophysiological assessment of ion channel activity, ie, manual patch clamp electrophysiology in mammalian cell lines expressing channels of interest. Recent innovations in the development of enabling technologies supporting higher throughput and fully automated patch clamp electrophysiology (Dunlop *et al*, 2008; Lu and An, 2008) have provided for a reenergizing of ion channel drug discovery with unprecedented capabilities for compound screening.

Two different approaches to achieving automation of manual patch clamp electrophysiology have recently emerged taking advantage of the so-called planar array of multi-well configurations in either a plate- or chip-based format allowing for multiple parallel recordings replacing the single channel recording typical of manual patch clamp. The IonWorks platform (Schroeder *et al*, 2003) was the first major innovation to be introduced and although this technology did not recapitulate the tight gigaohm seal quality typical of manual recordings, a number of assays have been successfully transferred onto this platform. Most notably, it has been possible to screen small compound libraries using the IonWorks (John *et al*, 2007), representing perhaps the best example of how such technologies have revolutionized ion channel screening as such a feat would be unimaginable with manual recording approaches. The second series of technologies to be introduced in the form of the PatchXpress, QPatch, and Patchliner (Dunlop *et al*, 2008) have successfully recapitulated the gigaohm quality seals typical of manual recordings. Until recently, these systems have

relied on the parallel recording of up to 16 cells, in of itself a significant increase in screening capability. A recent innovation toward unprecedented screening capacity has been introduced in the form of a 48-channel QPatch system, a major advance over the manual recording approach where one can only imagine having 48 different individuals operating manual recording set-ups.

Despite the obvious advantages associated with fully automated ion channel screening there are challenges associated with the implementation of these technologies. Not to be underestimated is the often significant time to generate a cell line compatible with each platform, and not necessarily the cell line you have been using for many years in others applications. This process together with assay optimization and validation can be lengthy and resource intensive. However, these challenges are clearly outweighed by the now unprecedented screening capability to support ion channel-targeted drug discovery, holding much promise for expediting the discovery of new ion channel-targeted drugs.

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### DISCLOSURE/CONFLICT OF INTEREST

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