had been secreted could be identified by colour change, which is measured spectrophotometrically at 405 nm.

"The primary screen consisted of >100,000 discrete compounds. This was achieved in five experiments, taking just 10 days to complete. Assay cost of the whole primary screen was less than £1000", says Phil Robinson, a member of the design team.

The conversion of this 96-well assay to a 384-well format resulted in significant savings in time from reduced handling of plates and reduced demand on tissue culture. This in turn reduced the cost of the assay sevenfold during assay development and optimization, rather than the anticipated fourfold reduction.

In our experience the combined use of 384-well plates and automation represents a major advance in reducing costs and increasing sample throughput and precision.

New high-density plates

Greiner Labortechnik (Frickenhausen, Germany) described their 1536-well plates at the MIPTEC conference. The 1536-well plate was developed in close collaboration with Bayer (Leverkusen, Germany) to fulfil future demands in HTS and is likely to generate much interest from the HTS fraternity. These plates have the length, width and height of a standard 96-well plate. Each well has an internal well area of 2.3 mm^2 with a total well volume of 14 µl. Several plate types are available including transparent, black or white (also available with clear bottom) and tissue-culture treated and sterile plates. Greiner also produce a range of 384-well plates.

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Emerging molecular targets

Immortalized human CNS cell line

A source of neural cells is frequently a limiting factor for research or drug discovery efforts for CNS conditions. Dinah Say, Jasodhara Ray and Fred Gage from Signal Pharmaceuticals (La Jolla, CA, USA) have now demonstrated that a possible solution exists for this dilemma. They report the establishment of an immortalized CNS progenitor cell line from brain tissue of 13-week-old fetuses [*Nat. Biotechnol.* (1997) 15, 574–580].

Two cell lines were obtained using a tetracycline (Tc)-responsive v-*myc* oncogene to immortalize the cells. One of the cell lines possessed a default differentiation into neurons. The other cell line could be differentiated into either neurons or astrocytes. The investigators believe that the development of these cell lines clearly 'demonstrate that bipotent precursor cells exist in the human brain' and that it is possible to establish CNS cells in culture such that 'the fate of these cells can be directed by their environment'. Such cell lines should be an important source of human CNS drug targets as well as a model system for studies on the differentiation of CNS precursor cells.

Y_5-like receptors and epilepsy

Neuropeptide Y binds to a family of G-protein-coupled receptors widely distributed throughout the central nervous system. So far, six different subtypes of the receptor have been identified, all of which appear to act through the inhibition of adenylate cyclase. The receptors for neuropeptide Y are associated with numerous physiological functions, including stimulation of food intake, memory, cardiovascular function and anxiolysis [see *Annu. Rev. Pharmacol. Toxicol.* (1993) 32, 309–352 for a comprehensive overview].

Several lines of evidence support the notion that neuropeptide Y may also function as an endogenous anticonvulsive agent:

- mice deficient in neuropeptide Y sometimes develop spontaneous seizures;
- such mice are more sensitive to the induction of seizures by GABAergic antagonists than those with normal levels of neuropeptide Y; and
- when seizures occur an increase in the level of neuropeptide Y has been observed, possibly as a compensatory mechanism to correct the seizure state.

Now David P.D. Woldbye and associates at the University of Copenhagen (Denmark) and at H.S. Lundbeck A/S (Copenhagen-Valby, Denmark) have provided direct evidence that administration of neuropeptide Y can block seizures in rats that have been induced by kainic acid [*Nat. Med.* (1997) 3, 761–764].

Kainic acid-induced seizures in rats is a well characterized seizure model. Such seizures are caused by the direct perturbation of kainic acid receptors as well as the release of glutamate triggered by kainic acid. Woldbye and coworkers found that a dose of 1.5 nmol or greater of neuropeptide Y – administered through a 22 gauge cannula directly into the right lateral ventricle – completely inhibited kainic acid-induced motor seizures. By comparing the effectiveness of various neuropeptide Y structural analogs, they concluded that the antiepileptic effects were achieved through the perturbation of the Y_5 receptor subtype, the same subtype that has been identified as regulating feeding behavior. They believe that their findings are important; the Y_5 receptor may be an effective target for the discovery of new antiepileptic drugs. However, they caution that weight gain may be an unwanted side effect, because Y_5 antagonists would be expected to increase feeding behavior. They further caution that their data suggest that targeting the Y_5 receptor for development of drugs to decrease appetite may result in a drug with proconvulsant properties. Certainly an area of future research will be an attempt to differentiate the anticonvulsant activity of Y_5 receptors from their effects on feeding behavior, either through the development of chemical compounds with differential activity or the further dissection of subtypes of the Y_5 receptor.

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