microbial library belonging to Bristol-Myers Squibb.

The new technology is possible, according to Dr Michael Dickman, President of ChromaXome, because of the development of very large vectors for transferring foreign DNA into bacteria. ChromaXome uses standard cosmids to transfer up to 30 to 40 kb of DNA and newly developed bacterial artificial chromosomes to transfer up to 300 to 400 kb of DNA. Assuming that, on average, an enzyme can be encoded in 1 kb of DNA, the genetic information for 30 to 400 enzymes can be transferred at one time into the commercial vector.

In many combinatorial experiments, the DNA from up to 100 different organisms is combined and then randomly transferred into the commercial microbe. To ensure that 90% of the total DNA is represented in the library requires the production of 100–200 million distinct clones. Approximately 1% of the clones produce compounds through pathways transferred from the marine organisms. Screening such a large number of clones is a major challenge, which ChromoXome has met with novel screening assays that use fluorescence-activated cell sorting.

ChromaXome is seeking to establish agreements with several other companies who have expressed an interest in the technology. According to Dickman, "ChromaXome intends to remain small, seek collaborative relationships with major pharmaceutical companies and focus on what we do best – the use of our novel technologies to discover new drug leads. We do not intend to get involved in drug development".

Robert W. Wallace

New Alzheimer's model from Japan

Efforts to discover the underlying mechanism in Alzheimer's disease have been hampered by the lack of a suitable animal model. Attempts have been made to mimic Alzheimer's disease by producing brain lesions surgically or chemically, feeding animals on a choline-deficient diet and using aged animals. However, only humans and chimpanzees are known to suffer from the condition naturally, and the models have achieved very limited success. Now a group led by Professor Toshitaka Nabeshima of the Department of Neuropsychopharmacology at the Nagoya University School of Medicine, Japan, have produced a new model, which appears to be more effective and to mimic the real condition more accurately. They have induced memory impairment and neural dysfunction in rats by infusing β-amyloid protein, the core of the plaques that are so characteristic of the disease, into the cerebral ventricles. The protein is administered by mini-osmotic pump continuously for a period of 2 weeks at doses of 3, 30 and 300 pmol per day.

The performance of the treated animals in standard behavioural tests was impaired, and there was an associated reduction in choline acetyltransferase activity in the frontal cortex and hippocampus. Oral administration of agents known to be potent *in vitro* stimulators of nerve growth factor (NGF) synthesis, such as propentofylline, idebenone and trimethylquinone, produced significant improvements in the behavioural deficits, increased levels of NGF protein and mRNA, and stimulated choline acetyltransferase activity.

The results support the hypothesis that β-amyloid protein deposition in the brain is linked to impaired learning and cholinergic neuronal deterioration. The model should therefore be suitable for rapid screening of the many novel agents in development as potential treatments for this disease.

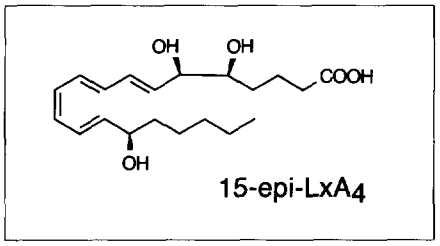
David B. Jack

Better use aspirin

Researchers in the USA have discovered a new mechanism that could help explain some of the pharmacological properties of aspirin (acetylsalicylic acid) that have so far been poorly understood. This may ultimately lead to improved treatment for inflammation and arthritis based on aspirin but without its side-effects, notably gastrointestinal inflammation.

Dr Joan Clària and Professor Charles Serhan at the Department of Medicine, Brigham and Women's Hospital and Harvard Medical School (Boston, MA, USA) have found that aspirin triggers the release of a new group of eicosanoids by a previously unknown biosynthetic pathway [Clària, J. and Serhan, C.N. (1995) *Proc. Natl Acad. Sci. USA* 92, 9475–9479].

Other researchers have demonstrated that the biosynthesis of eicosanoids is influenced by transcellular and cell–cell interactions. Such interactions can amplify and control the release of new mediators in the inflammatory response.



15-epi-LxA$_4$

"We are interested in elucidating the natural 'stop signals' of the inflammatory response – namely chemical mediators that naturally downregulate leukocyte functions" says Serhan. The team were looking at the effects of aspirin on the interaction between white blood cells and blood vessel endothelial cells. They found that they could isolate four members of a new group of compounds belonging to a lipoxin sub-class from their culture. Further biosynthetic studies with human leukocyte and endothelial cells in culture revealed that the production of these lipoxin subtypes resulted from the

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