Nanogen (San Diego, CA, USA) has taken a different approach to the new technology. It is developing small electronic chips in which electric fields are used to quickly and quantitatively hybridize and dehybridize DNA to individually addressable oligonucleotides. The assays are designed to monitor fewer genes but to do so quickly and repeatedly, just what some drug discovery scientists might need for an automated high-throughput screen. Nanogen is collaborating with Becton Dickinson (Franklin Lakes, NJ, USA) to develop instrumentation for its system. They plan to focus their combined technology on the diagnosis of infectious diseases. However, their electronic chip product and accompanying instrumentation will likely provide powerful new tools that can also be applied to drug discovery.

Robert W. Wallace
fax: +1 212 254 3322
e-mail: RobWallace@nasw.org

Emerging molecular targets

Ceramide-mediated signaling and vasodilatation

The lipid mediator ceramide is a relative newcomer to our knowledge of intracellular signaling events. It is generated by the hydrolysis of sphingomyelin in the cellular membranes by the enzyme sphingomyelinase (SMase) and is believed to act as an intracellular signaling agent. A ceramide-stimulated protein kinase and phosphatase have been identified. In addition, ceramide inhibits the activity of protein kinase C. Activation of the ceramide-stimulated signaling pathway is believed to occur in response to cellular stimulation of cytokines such as TNF-α, IFN-γ and IL-1β.

Gradually, data is accumulating that links the generation of ceramide by SMase to various physiological functions. In one recent report, Drs Douglas G. Johns, Heather Osborn and R. Clinton Webb from the University of Michigan (Ann Arbor, MI, USA) show that increased levels of ceramide may be linked to the relaxation of vascular smooth muscle cells and vasodilatation [*Biochem. Biophys. Res. Commun.* (1997) 237, 95–97]. They found that the level of ceramide in vascular smooth muscle cells rose more than 15-fold above basal levels within 20 min following the addition of 0.1 U/ml of SMase to the cell culture media. Moreover, they found that the increased elevation of ceramide – either by addition of a ceramide analog or the addition of SMase – correlated with a relaxation of endothelium-denuded phenylephrine-contracted rat thoracic aortic rings. Much more remains to be learned about the Smase; however, if divergent tissue-specific forms of the enzyme exist, it may prove to be an interesting therapeutic target.

Robert W. Wallace
fax: +1 212 254 3322
e-mail: RobWallace@nasw.org

  1359-6446/97/$17.00. PII: S1359-6446(97)01114-8