

NO escape

US researchers think they have found a new way to control the release of nitric oxide in the body so that it can be used in medicine to improve the recovery and prognosis of patients with vascular disorders.

The NO molecule – more commonly known as an environmental pollutant – has become something of a medical superstar recently because it was found to play a leading role in a variety of physiological processes. NO is involved in blood vessel dilation and blood pressure control, neurotransmission and even sexual arousal.

However, NO is very reactive, and so has a very short lifespan in the body. This makes it difficult to study and even harder to control for medical use. Now, Larry Keefer of the National Cancer Institute (Frederick, MD, USA) and his coworkers have devised an NO-releasing compound, which they can use to target particular sites with NO. The compound is a diazeniumdiolate, and was prepared by reacting nitric oxide with L-proline in methanolic sodium methoxide. According to Keefer this compound can be infused

directly as an alkaline solution to generate NO with a two-second half-life, meaning its effects are localized to areas immediately downstream of the site of infusion. [*J. Med. Chem.* (1996) 39, 4361].

The compound could be useful in preventing relapse following vascular surgery. Grafting and by-pass operations often result in tissue scarring and blood clot formation. NO released near the grafted tissue should bring the body's repair systems under control and allow healing to take place more steadily and so be safer.

Infusing this short-acting NO delivery agent at higher rates extends the area that can be treated successfully, Keefer explains. For example, administering it intravenously to sheep with drug-induced pulmonary hypertension selectively reduced the pressure in the pulmonary artery without affecting the blood pressure outside the lung.

Keefer and his coworkers have also blended their diazeniumdiolates into an insoluble polymer. The polymer stops the NO being released from the reactive diazeniumdiolate spontaneously. In contact

with blood plasma, however, NO is rapidly and continuously released. Alternatively, explains Keefer, the non-polymeric NO–diazeniumdiolate complex can be infused slowly into the affected site using a syringe. Either way, the rapid release of NO once at the site means the action is limited to only that area, precluding peripheral side-effects.

The researchers have tested the effects of the NO-polymers on Teflon grafts used to repair damaged blood vessels in laboratory baboons. They found that clotting takes place at a much lower rate than in control animals. Anticoagulant drugs are normally given to human patients with vascular grafts, but these drugs are not without side-effects. Keefer's NO-releasing materials might allow their use to be avoided. "It is early days yet, however," he says, "we must conduct more toxicity studies and further proof-of-concept work before planning clinical applications."

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Unique post-doc system at SUNBOR

SUNBOR (Suntory Institute for Bioorganic Research, Osaka, Japan) was initially set up as the Institute of Food Chemistry in 1946 under the sponsorship of Kotobukia Ltd (Osaka, Japan) as a nonprofit-making organization. In 1963 Kotobukia changed its name to Suntory, and the company is now established as Japan's leading producer and distributor of western-style liquor products and the biggest producer of whisky, with a share of over 60% of the Japanese market. The initial remit was 'to contribute to advancement in health and nutrition of the Japanese people', but this has since expanded to cover many areas of the natural sciences. At its fiftieth anniversary celebration symposium last year, experts were invited to speak on key areas of interest to the institute, including glutamate receptors in brain function, chirality, retinal proteins,

metalloproteins and new approaches to pest control. The institute has expertise in the latest mass spectrometric (MS/MS and LC/MS), NMR (FT-NMR) and other analytical techniques (CD/ORD), and is also experienced in DNA sequencing and synthesis to investigate cellular communication via neurotransmitters and hormones in humans and animals.

One major research programme involves the investigation of toxins, novel peptides and other compounds derived from insects, earthworms, squid and sea-cucumber. Most research is directed toward the investigation of novel leads through detailed structure–activity analysis and the subsequent identification of promising candidates for development.

A unique characteristic of SUNBOR, introduced by Professor Koji Nakanishi, is the 'pair system' of research in which a

senior and junior member of staff work closely on a particular research project. The post-doctoral system, although long established in the West, came late to Japan and is still not fully developed. Professor Nakanishi appreciated the need for external input into the traditional Japanese approach to research. It was his idea to bring foreign staff to SUNBOR to profit from its excellent research facilities while bringing in creativity and a fresh scientific perspective. SUNBOR has been able to recruit post-doctoral researchers from all over the world, and only the very largest corporations, such as Sony and Mitsubishi, have similar systems. As evidence of its success, there is always a waiting list for post-doctoral positions at SUNBOR, and new foreign members of staff integrate quickly with the help of experienced staff members, who help find accommodation

and deal with any administrative problems that arise.

The institute has established long lasting global links through its network of former post-doctoral scientists. The Director,

Professor Terumi Nakajima, an expert on insect toxins, is particularly keen on collaboration with scientists in countries with extensive, but only partially explored, natural resources such as China and Australia.

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BioPartnering on the Net

The 4th annual BioPartnering Europe (BPE) conference took place last October at the Queen Elizabeth II Conference Centre in London. Most conferences revolve around sessions interspersed with visits to the exhibition for light relief. Here the converse is true. BPE offers delegates from investment houses, the major pharmaceutical companies and other potential collaborators the chance to interface with innovative new bioscience companies. In four exhibition sessions held over two days, more than 60 companies are each given a 2–3 hour opportunity to showcase their technologies through interactive poster demonstrations. Each company is assigned a separate room so that conversations can be carried out in moderate privacy, and if the foundation of a deal is being laid, private meeting rooms are always available.

Two plenary sessions each day provide overviews of key areas of interest from senior figures, such as technology transfer, bioinformatics and genomics, and, very importantly, accessing global finance.

Now the organizers, Technology Vision Group, have developed an Internet site, the Global Biopartnering Network (GBNet). According to Dr Birgit Weskamp, a Partner in Technology Vision Group, “delegates have indicated the value of the BPE conference but tell us that once a year is not enough. The new web site will facilitate this flow of information all year round.” This sentiment is symbolized in the web site logo by ripples spreading out over water. All delegates to last year’s meeting were given password access to the site upon registration, as will each registered delegate for the 5th annual BioPartnering Europe, due to take place in London again this October. “Using GBNet’s advanced search capability, delegates are able to focus early on their strategic goals and prepare for productive private meetings in advance,” states Nancy Connelly, BPE Producer. Plans are under way to expand these services on a global scale with the first annual BioPartnering Asia conference being organized for spring 1998.

The site offers every registered company the opportunity to showcase their key characteristics, which include contact details with direct e-mail links, URL of company web sites, company profile, science & technology, commercialization strategy, financing plans, partnering goals, developmental programs, manufacturing capabilities, product opportunities and human resource assets. Jeremy Marshall, Information Manager for Technology Vision Group explains, “our aim is to create a product that is an industry standard, offering companies an efficient means of exchanging ideas and information as part of a package to create new international collaborations”.

Details of BioPartnering Europe are available from the Technology Vision Group (tel: +1 408 464 7100, fax: +1 408 464 4240, e-mail: bpe@techvision.com). The GBNet web site address is <http://www.biopartnering.com>.

David Hughes

SmithKline Beecham first BIA Patron

In his first act as Chairman of the Bio-Industry Association (BIA), Dr John Padfield (Chief Executive, Chiroscience Group plc, Cambridge, UK) opened the third Business for Bioscience meeting, held in London in November. He announced that SmithKline Beecham (SB) has become the first Patron of the Association, which exists to support the growing number of small and medium-sized enterprises in the UK through encouraging communication within the industry and through liaison with Government and

other organizations and institutions. SB spends more than £635 million a year on R&D, and according to Chairman of R&D, Dr George Poste, “The future success of major pharmaceutical companies will be augmented by collaboration with the emerging, innovative sector of new companies. SB’s patronage of the BIA demonstrates our commitment to supporting and encouraging this process.”

Former Chairman, Dr Keith McCullagh (Chief Executive, British Biotech, Oxford, UK) now represents the European

bioindustry as Vice Chairman of the EuropaBio. EuropaBio was formed in September and will represent some 500 companies and 8 national associations. McCullagh will support EuropaBio’s Chairman, Professor Jürgen Drews of Hoffman La Roche.

In the February issue of *Drug Discovery Today*, Professor Drews puts forward *Strategic choices facing the pharmaceutical industry: a case for innovation*.

David Hughes