

'Calcium signals and short-term synaptic plasticity' was given by another Nobel Laureate, E. Neher. He discussed plastic changes in the connectivity between neurons underlying the adaptive information processing of the central nervous system.

There were altogether 23 different symposia spread over four days. On an average, three symposia were held in parallel. The symposia, covering different aspects of biophysics, were on protein structure and dynamics, protein folding and stability, protein design and ligand binding, DNA structure and dynamics, ribozymes and RNA structures, nucleic acid-protein interaction, membrane structure, dynamics and functions, ion-channels, pumps and carriers, transmembrane signalling and transduction, structure of macromolecular assemblies, biophysics of immune systems, cell surface interaction, metabolic regulatory and control networks, photosynthetic systems and primary processes, electron/proton transport, biomechanics, bioinformatics and data analysis, computational modelling, genomics and proteomics, medical and environmental biophysics, biomaterials and biosensors, innovative biophysical techniques, and education and development. Generally each symposium had two major presentations by invited speakers. There were altogether 57 invited speakers from 17 countries. A larger number of contributed abstracts than in previous Congresses were chosen for oral presen-

tation in the symposia. Of the 55 speakers chosen for contributed oral presentations, 19 were IUPAB young travel fellows and 11 women. The speakers represented 26 different countries. More than 500 posters were presented which were displayed throughout the Congress. Two late afternoon sessions were set apart exclusively for poster viewing. The authors of half the posters were available for discussion on each of the two days. The poster sessions were well attended and the discussions on both the days extended well into the night.

The final (sixth) day of the Congress opened with a plenary session on 'Hot topics' which consisted of a talk on 'Single molecular mechanics and models of myosin motor' by T. Yanagida and a panel discussion on 'Membrane proteins and channels' organized by K. R. K. Easwaran and led by E. Neher, M. Montal and O. Anderson. This was followed by a symposium on 'Biophysics in the 21st century' organized by C. R. Cantor with J. R. Helliwell, J. Garnier, S. I. Chan and Cantor as speakers. Cantor gave an overview of his vision of the likely progress in Biophysics in the next century while the other speakers dealt with specific topics. Helliwell spoke on synchrotron X-radiation and neutron protein crystallography while Garnier was concerned with bioinformatics. The topic of Chan's presentation was protein folding and unfolding.

At the closing ceremony, M. Vijayan,

bade farewell to the participants while M. Parisi invited them to XIV International Biophysics Congress to be held in Argentina in the year 2002. The Congress came to an end with closing remarks by Israel Pecht, the newly elected president of IUPAB.

Close to 650 scientists from 49 different countries participated in the Congress. This is the largest country-wise representation at an international biophysics meeting, with several countries participating for the first time in an IUPAB Congress. Interestingly, almost one-third of the total participants were students coming for the first time to an international congress. Many of them were supported by IUPAB and DST. The presence of such a large proportion of young scientists added to the vitality of the Congress.

The Congress provided a golden opportunity for the nearly 230 Indian participants to discuss their work and rub shoulders with distinguished peers and international leaders from other countries. The abstracts of the Congress were published in the *Journal of Biosciences* of the Indian Academy of Sciences, Bangalore. In addition to the main Congress at New Delhi, three satellite symposia were conducted at Hyderabad, Mumbai and Calcutta.

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## RESEARCH NEWS

### Aspirin hits a new target

Mehran Arabi

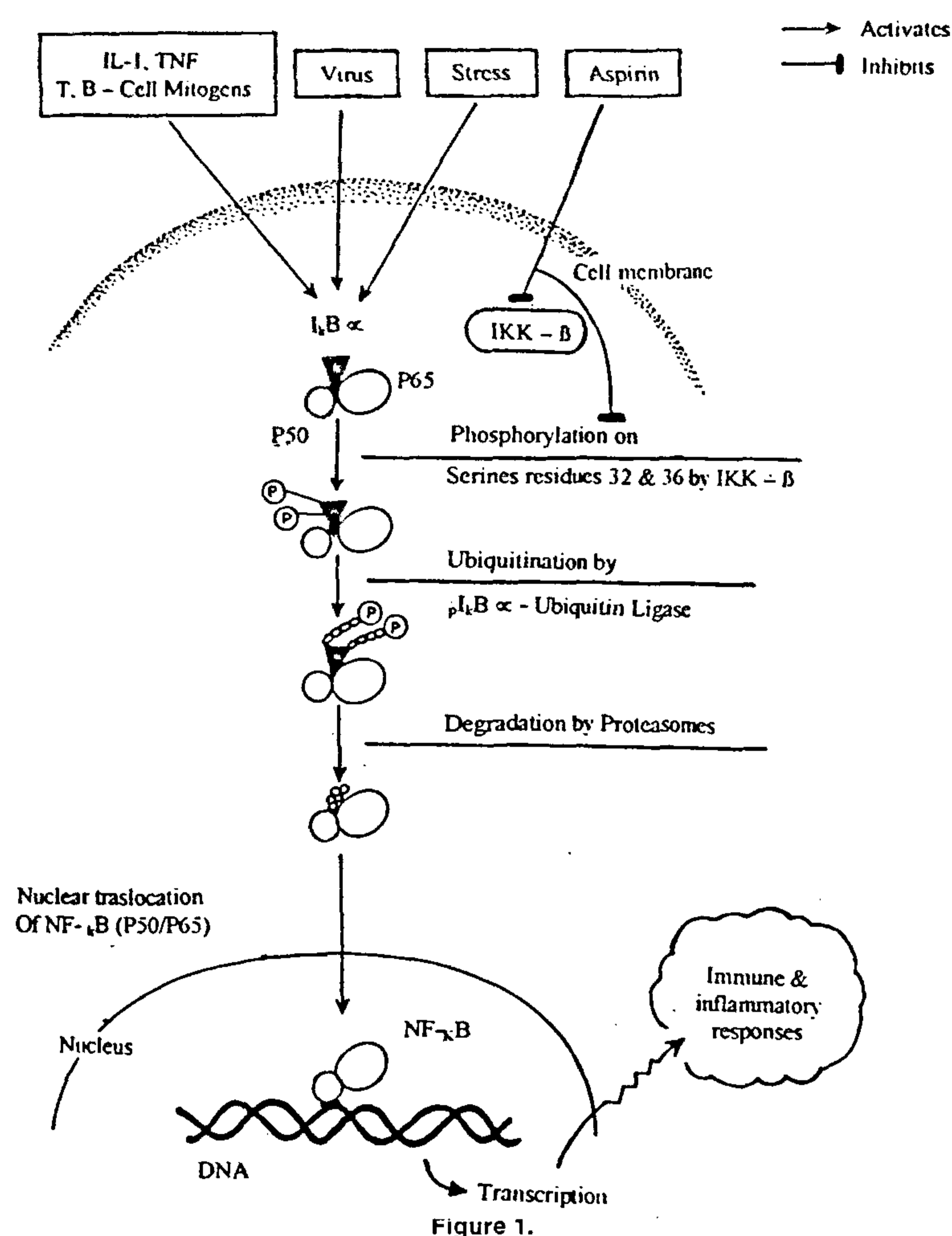
Take two aspirins in the morning and get relief. For many common physical ailments, low doses of aspirin (acetylsalicylic acid) will make you feel better, and high doses of the drug give sustained relief from the symptoms of rheumatoid arthritis. Aspirin irreversibly inhibits cyclo-oxygenases – the enzymes that control the production of prostaglandins (small molecules that induce pain and fever associated with infection and trauma).

However, differences in the clinical activities of aspirin at low and high doses have led to a speculation that not all

the benefits of aspirin are derived by inhibition of cyclo-oxygenases. So what might be the target for high doses of the drug?

For the first time, Yin *et al.*<sup>1</sup> reported that high concentrations of aspirin (IC<sub>50</sub> approximately 50 μM) inhibit the recently discovered enzyme, I<sub>κ</sub>B kinase-β (IKK-β), and they proposed that this effect partially explains the clinical efficacy of high doses of aspirin. IKK enzymes (α and β) catalyse the transfer of phosphate moieties from ATP to I<sub>κ</sub>B. Phosphorylation leads to the degradation of I<sub>κ</sub>B and

release of nuclear factor kappa B (NF-κB) which is a ubiquitous, inducible transcription factor involved in immune, inflammatory, stress and developmental processes, and is retained in a latent form in the cytoplasm of non-stimulated cells by inhibitory molecules, I<sub>κ</sub>Bs. Its activation is a paradigm for a signal-transduction cascade that integrates an inducible kinase and the ubiquitin-proteasome system to eliminate inhibitory regulators, the enzyme pI<sub>κ</sub>Bα-ubiquitin ligase<sup>2</sup>. pI<sub>κ</sub>Bα-E3 attaches ubiquitin – a small protein found universally in eukar-



aspirin, nuclear localization of NF- $\kappa$ B and subsequent transcription is blocked.

It also has been shown that several other kinases, including the homologous and functionally related IKK- $\alpha$ , are not affected by aspirin. The problem with using high doses of aspirin is that it has virtually no therapeutic window, that is the dose at which aspirin gives relief from chronic rheumatic disease is very close to the dose that generates side effects, including headaches, dizziness and tinnitus. However, a hypothesis has been developed wherein IKK- $\beta$  is only one of the several targets for high doses of aspirin, the unwanted side-effects resulting from activity against other targets<sup>5</sup>.

Although there is a broad consensus that aspirin relieves many of the symptoms associated with inflammatory diseases, it does not prevent the hallmark of progressively crippling rheumatoid arthritis – the destruction of joints. This could be due to the limited effect that aspirin can have on NF- $\kappa$ B activation, constrained as it is by the narrow therapeutic window. In light of such findings, we may be able to generate potent molecules that can prevent rheumatoid joint destruction, rather than just relieving the symptoms associated with that destruction. Until then, take two aspirins and get relief in the morning.

1. Yin *et al.*, *Nature*, 1998, 396, 77–80.
2. Yaron *et al.*, *Nature*, 1998, 396, 590–592.
3. Elliott, W. E. and Elliott, D. C., *Biochemistry and Molecular Biology*, Oxford University Press, 1997.
4. Iraël, *Nature*, 1997, 388, 519–521.
5. O’neill, E. A., *Nature*, 1998, 396, 517–518.

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yotes (but not in bacteria, so the name exaggerates somewhat), which marks other proteins for degradation by the proteasome system<sup>3</sup> – to the phosphorylated NF- $\kappa$ B inhibitor I $\kappa$ B $\alpha$  as shown in Figure 1 (ref. 4).

On release, NF- $\kappa$ B rapidly moves to the nucleus where it binds specific DNA sequences, promoting the transcription of genes that influence defence mechanisms such as inflammatory and immune responses. Thus, if IKK- $\beta$  is inhibited by

## Unravelling the biosynthesis of vitamin C in plants

Rajesh Luthra, Pratibha M. Luthra and Sushil Kumar

The importance of vitamin C to human health is well established. Vitamin C, a water soluble vitamin, is chemically defined as ascorbic acid. Ascorbate mainly acts as an antioxidant and has a role in

collagen biosynthesis, the deficiency of which results in scurvy<sup>1</sup>. Animals produce ascorbic acid from glucose via D-glucuronate and L-gulonono-1,4-lactone (Figure 1). D-glucuronate is at first

reduced to L-gulonate which in turn undergoes dehydration to produce L-gulonono-1,4-lactone. L-gulonono-1,4-lactone is oxidized to ascorbic acid by a microsomal L-gulonono-1,4-lactone oxidase (EC