ever, lawmakers should ensure academic freedom and be freed from bureaucratic hassles.

P. N. Tandon, National Brain Research Centre, Haryana, said that since only about a decade, there has been some systematic regulation on animal experimentation. The Indian National Science Academy’s guidelines in 1992 had pointed out major problems in the rules, but these concerns, although mutually agreed upon by members of the CPCSEA and others had not been incorporated in the gazette rules. Furthermore, the use of animals continues to be mandatory to meet statutory regulation requirements and hence animal experimentation would have to continue while efforts are made to develop *in vitro* models. He stated that rules formulated required ample support with the necessary infrastructure.

Ashwini Kumar, Drug Controller General of India, New Delhi spoke of benchmarks for safety, efficacy and quality becoming more stringent in the quest for better drugs. The Government regulations were now in the process of complying with that of the International Conference on Harmonization. In this regard, the Schedule Y of the Drugs and Cosmetics Act is being revised and the draft currently under review.

R. R. Bhande, National Centre for Cell Science, Pune described his institution’s efforts towards evolving alternatives to animal experiments such as cell culture, *in vitro* testing for eye irritation and skin corrosion testing. To minimize role of animals in alternative testing, examples were cited such as about 1500 islets isolated from a single mouse pancreas, islet generation from stem cells, tracheal organ culture, shell-less chick embryo culture, and bone marrow and cord blood cryo preservation.

Sonya Ghosh, University of Delhi, New Delhi said scientists do not use ‘tacit moral judgement’ and called herself and the likes of her as animal welfare and not animal rights persons. Animals possess consciousness and human beings cannot justify invasive use of animals. She reiterated an animal welfare position of accepting the fact that animals could be used for experiments as long as they were treated in a humane way.

K. H. Sreedhara Swamy, Nicholas Piramal India Ltd, Mumbai cited problems in CPCSEA regulations including exhaustive paperwork, justification for repetition of experiments, no additional experiments allowed for training, restrictions on use of large animals, ban on use of mongrel dogs, delay for imports, lack of prompt communication from expert consultants, absence of central breeding facilities and so on. He voiced for a more rational approach and spelt out desired changes called for in the regulations, particularly those pertaining to unclear guidelines.

S. S. Jadhav, Serum Institute of India, Pune spoke of efforts to reduce use of 110 animals to 10 animals in conjugate vaccine testing, soon to be accepted in WHO technical report series and hoped that new molecules released would be done on such lines.

H. L. Attri, CPCSEA, New Delhi stated that recently about 95% of experiments were conducted on small animals. He clarified that CPCSEA was a regulatory body and was not directly responsible for breeding. Clearance of large animals should remain with the CPCSEA, as a national nodal agency for the purpose. There was some discussion and criticism of the lack of clear guidelines by the CPCSEA, to which Attri replied that guidelines do exist and would be circulated. S. C. Adlakha, CPCSEA, New Delhi spoke of the need for harmonization of CPCSEA regulations with those in developed countries such as USA.

Ashok Rattan, Ranbaxy Research Laboratories, New Delhi enumerated the four ‘Rs’ in animal experimentation, namely reduction in animal use, refinement of technology to reduce pain, replacement of animal use, rehabilitation of animals and added the fifth R, namely, responsibility of persons conducting the experiments.

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*Submitted on 01 February 2004. As of 22 February 2004 the author Nirupa Sen joined the Embassy of the United States of America as Scientific Affairs Specialist.*

**K. Kasturirangan takes over as Director, National Institute of Advanced Studies, Bangalore**

Krishnaswamy Kasturirangan, presently nominated Member of the Rajya Sabha and former Chairman of the Indian Space Research Organisation (ISRO) and Space Commission and Secretary, Department of Space, took over as Director of the National Institute of Advanced Studies (NIAS), Bangalore on 31 March 2004. Kasturirangan succeeds Roddam Narasimha, well-known aerospace scientist and former Director of National Aerospace Laboratories. NIAS is a multi-disciplinary research institute with particular focus on the interfaces between natural, social and human sciences. It was established in 1988 at the initiative of the late J.R.D. Tata, who was convinced that the complex problems faced by India and the world need a new leadership equipped with multi-disciplinary perspectives.

Kasturirangan has made significant contributions to the nation in harnessing space technology for national development. His tenure as head of the national space programme (from March 1994 to August 2003) saw ISRO crossing several major milestones, including the successful launch and operationalization of the Polar and the Geosynchronous Satellite Launch Vehicles (PSLV, GSLV), and the growing reputation of the Indian Remote Sensing Satellites (IRS series) as among the world’s best. Kasturirangan’s leadership of the Indian space programme has shown a keen sensitivity to its role as a force for social...
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change, community development and economic growth.

Kasturirangan’s earlier positions included those of Director of the ISRO Satellite Centre and Project Director for India’s first two experimental earth observation satellites, Bhaskara I and II. He started his professional career as an astrophysicist and has done advanced research in the areas of high energy X-ray and gamma-ray astronomy as well as optical astronomy.

Kasturirangan was President of the Indian Academy of Sciences during 2001–2003 and General President of the Indian Science Congress during 2002–2003. He has been honoured widely receiving the Shanti Swarup Bhatnagar Award in 1983 and the Padma Vibhushan in 2000. He was made an Officer of the Legion d’honneur by the President of France in 2002.

RESEARCH NEWS

Towards an effective therapy for Fanconi anaemia

L. Rupachandra Singh* and S. Kunjeshwori Devi

The discovery of a novel enzyme designated FANCL (PHF9) involved in the biochemical processes of development of a hereditary disease known as Fanconi anaemia (FA) has raised a hope towards an effective management of the disease. The detection and molecular identification of the enzyme have enhanced understanding of the common DNA repair pathways involved in the disease, as well as of certain types of cancers and ageing. Better understanding of these pathways could lead to new therapies for FA.

Fanconi anaemia – named after the Swiss paediatrician, Guido Fanconi – is one of the inherited anaemias that leads to bone marrow failure (aplastic anaemia). It is an autosomal recessive disorder. If both parents carry a mutation in the same FA gene, each of their children has a 25% chance of inheriting the defective gene from both the parents. When this happens, the child will have FA. The disease occurs equally in males and females. It is found in all ethnic groups. Though considered primarily a blood disease, it may affect all systems of the body. Many patients eventually develop acute myelogenous leukaemia. Older patients are most likely to develop head and neck, oesophageal, gastrointestinal, vulvar and anal cancers. The first symptoms, such as nosebleeds or easy bruising, usually begin before the age of 12 years. In rare instances, however, symptoms do not become apparent until adulthood. Sometimes, FA is evident at birth through a variety of physical defects such as missing or extra thumbs and skeletal abnormalities of the hips, spine or ribs[1–3].

Though considered a rare and obscure disease earlier, the basis of FA is now linked both functionally and genetically to the genes associated with breast cancers[4,5]. It has generated more widespread interest in the protein molecules underlying FA. Cells from FA patients have more chromosomal breakages compared to those from normal individuals in response to DNA damage particularly interstrand DNA cross-links[6] and it forms the basis of the diagnostic test for the disease. In fact, the definitive test for FA adopted at present is a chromosome breakage test. In this test, some of the patient’s blood cells are treated with a chemical that damages DNA by cross-linking it. Normal cells are able to correct most of the damage and are not severely affected, whereas FA cells show marked net chromosomal breakage due to a poor intracellular repair. The two chemicals commonly used for this test are: diodeoxybutane (DEB) and mitomycin C (MMC)[7,8]. This finding has given rise to the general hypothesis that the FA pathway controls genomic stability (integrity of the set of all genes in an individual) through involvement in DNA repair[9]. The details of the mechanism by which this happens are, however, largely unknown.

The genome protection pathway that is defective in patients with FA is controlled by at least seven genes, including BRCA2 (a breast cancer susceptibility gene). Despite the isolation of these genes, the biochemical functions of FA path-way are still poorly understood[10]. At this juncture lies the importance of the contribution of Meeitei et al., who discovered FANCL, the first FA protein identified by a biochemical approach and also the first FA protein with a defined enzymatic activity[11]. A key step in the FA pathway involves the mono-ubiquitination (attachment of a molecule of ubiquitin, a small protein consisting of 76 amino acid residues) of the FA protein FANC D2, which critically depends on a monoubiquitinated nuclear core complex of at least six FANC proteins—FANCA, FANCC, FANCE, FANCF, FANCG and FANCL. The major contribution of Meeitei et al. is biochemical purification of this nuclear FA complex and identification of all the subunits including five known FA proteins and four new FA-associated proteins (FAAPs) by mass-spectrometric peptide/protein sequencing[12]. After cloning one of the FAAPs namely FAAP43 (molecular mass of 43 kDa), they found that this protein has two interesting domains: (i) WD40 repeats which is implicated in protein–protein interaction, and (ii) ring-finger domain that is commonly found in E3 ubiquitin ligase enzymes. They made and purified both wild type and ring-finder mutant recombinant FAAP43 in Escherichia coli and could demonstrate that FAAP43 indeed has ring-finger dependent E3 ubiquitin ligase activity in vitro. Just to prove that the newly cloned enzyme is the enzyme responsible for ubiquitination of FANC D2, they knocked down FAAP43 in human cell line using small interfering RNA (siRNA) technology and found no ubiquitination of FANC D2. This was the conclusive evidence that FAAP43 is the E3 ligase responsible for ubiquitination of FANC D2 in vivo. They also screened the cells

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