change, commnity 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

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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 chromosome breakage due to a poor intracellular repair. The two chemicals commonly used for this test are: diepoxybutane (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 Meetei *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[11,12]. 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 FANCD2, which critically depends on a multisubunit nuclear 'core complex' of at least six FANC proteins—FANCA, FANCC, FANCE, FANCF, FANCG and FANCL. The major contribution of Meetei *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[11]. 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-finger 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 FANCD2, they knocked down FAAP43 in human cell line using small interfering RNA (SiRNA) technology and found no ubiquitination of FANCD2. This was the conclusive evidence that FAAP43 is the E3 ligase responsible for ubiquitination of FANCD2 *in vivo*. They also screened the cells

derived from individuals with FA (with unknown complementation group) for the absence of FAAP43 by Western blot using antibody against FAAP43. They found the mutation of *FAAP43* gene in a cell line derived from an individual with FA. Because of this mutation, this cell line could no longer produce FAAP43 protein. They could correct the cellular FA phenotype by introducing their wild type *FAAP43* gene back to the cell but this could not be done by introducing the ring-finger mutant FAAP3 that lacks the E3 ligase activity. Meetei *et al.* named the gene product FAAP43 as FANCL (complementation group L)[11]. An alternative name for the protein is PHF9 (PHD finger protein 9, HGNC ID: 20748) that was recommended by the Human Genome Nomenclature Committee.

One of the important implications of the discovery described here is the suggestion for a possible therapy of the hereditary disease FA. The expression of an enzymatic activity of the newly identified FA protein FANCL (PHF9) suggests that a small molecule could modulate its activity. If such a molecule could stimulate the monoubiquitination of FANCD2 in the absence of the FA 'core complex', that compound may hold hope for preventing the disastrous consequences of genomic instability in individuals with FA[10]. An attempt can now be made to discover such a molecule or to design it after elucidating the specific binding site structure(s) of the enzyme. Besides, inhibitors of the enzyme activity would probably create a FA-like phenotype and would sensitize cells to DNA cross-linkers. DNA cross-linkers such as cisplatin are already among the best currently available cancer chemotherapy agents[10]. As such, inhibitors of the enzyme activity, if discovered or designed, may serve as good cancer drug candidates.

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COMMENTARY

The biodiversity bandwagon: the splitters have it

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The accurate estimation of biodiversity has become one of the most important biological and conservation concerns of the 21st century. An unbiased estimate of biodiversity requires an unambiguous measurement unit. The most commonly used unit is the 'species', and though it is implicitly accepted as valid, consistent and appropriate, there has been little consensus over the many different species concepts proposed over the years[1]. Among these, the Biological Species Concept[2] has been widely used, but it has come under fire due to the arbitrariness of the genetic distance or morphological divergence that is generally used to assign species status[3,4]. Recently, the phylogenetic species concept[5], which recognizes diagnosably distinct taxa, has been used extensively for some groups. In the context of conservation, 'management units' and 'evolutionary significant units' have been proposed[6,7], but most studies still use species as the basic unit without examining or explaining which definition of 'species' they are using.

The core of the species debate revolves around questions over its significance as an evolutionary unit[6], its utility as a taxonomic unit[8] and its place in the phylogenetic tree[9]. These debates have been largely restricted to systematists and evolutionary biologists while conservation biologists have participated little in the debate[10] even though it has direct bearing on conservation prioritization, either through the IUCN Red List or through the designation of biodiversity hotspots[11,12]. Recent conservation paradigms have made species lists paramount, though the biology on which they rest may be suspect. Currently, much of the focus in conservation is on the extinction of described species[13], and the most 'funded' species today are those listed as 'threatened' in the IUCN Red List while the best funded regions are those designated as biodiversity hotspots, namely those with the most numbers of endangered species.

Recent interest in the herpetofauna of southern India and Sri Lanka has resulted in many field studies and publication of results in various forms, including theses[14,15], papers[16–20] and reports[21–23]. In particular, three of these[16,21,22] have announced dramatic increases in species richness in the Western Ghats and Sri Lanka. Given the importance of consistency and precision in assessments of diversity, we examine these publications, in particular, the paper in *Science*[16], which 'describes' more than 100 new species of amphibians to stake the claim that Sri