New feathers in the cap

The Royal Society of London recently announced its list of new Fellows elected in 2015 (ref. 1). There are four eminent Indian academicians among the 59 Fellows and Foreign Members elected. Ajay Sood, Kamal Bawa and Ketan Patel have received the prestigious Fellowship, whereas John Kuriyan has been inducted as the Society's Foreign Member (Figure 1).

Founded in 1660, under the patronage of King Charles II, the Royal Society is one of the oldest scientific communities. Eminent scientists from the UK and Common Wealth Nations are elected each year by the Society's council members as its Fellows. Apart from promoting and supporting excellence in the field of science, the Society promotes the use of science for the benefit of humanity and to foster international and global cooperation. The Society has previously had legendary scientists like Isaac Newton and Alexander Fleming as its Fellows. At present, the Fellows of the Society include 80 Nobel laureates and famous scientists like Stephen Hawking and Richard Dawkins.

Figure 1. (Top left to bottom right) Ajay Sood, Kamal Bawa, Ketan Patel and John Kuriyan (photo credit: www.royalsociety.org).

Ajay Sood (Department of Physics, Indian Institute of Science, Bengaluru) is one of the best experimental physicist from India. His work on condensed matter and related areas of research such as confined and interface phonons in superlattices and generation of electrical voltage by the flow of liquids in nanotubes which is termed the 'Sood effect', is commended worldwide.

Kamal Bawa (University of Massachusetts, Boston) is an evolutionary ecologist with pioneering work on population biology of tropical trees and strategies for their conservation. His work on modelling climate change in eastern Himalaya, has shed light on its impact on biodiversity and agriculture in the region. He is the founder of Ashoka Trust for Research in Ecology and Environment (ATREE), a non-profit establishment that works towards generating interdisciplinary knowledge and plays an influential role in policy making.

Ketan Patel (MRC Laboratory of Molecular Biology, Cambridge, UK) has made ground-breaking discoveries on the Fanconi pathway that plays a major role in DNA repair. Deficiencies in this pathway cause abnormalities in development and also cancer. Patel's research focuses on the mechanism of action of the Fanconi pathway to understand its role in preserving blood stem cells and protection against cancer. In addition, his work offers insights on the fundamental processes involved in DNA replication and repair.

John Kuriyan's (Howard Hughes Medical Institute, University of California, Berkeley) work focuses on the mechanism in which enzymes and molecular switches are responsible for cellular signalling and replication of DNA, using X-ray crystallography. His research has explained how Gleevec, a cancer drug, achieves specificity.

1. www.royalsociety.org (accessed on 18 May 2015).

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MEETING REPORT

Cell death and disease*

Cell death is a completely natural part of recycling of cellular building blocks by the body; it is actually a precondition for life. In every second of our life, about a million new cells are born and a million old or damaged cells die. It is also well conceived that cell death is an important part of the quality and sanitation system of the body that clears away the old and broken bits and replaces them with new ones. Problems arise, however, when something goes wrong with the cell death process. In the case of cancer, cells refuse to die and grow into a tumour. In diseases such as Alzheimer's or Parkinson's the opposite occurs, i.e. brain cells die even though they are not supposed to. In fact, research on cell death was catapulted into the spotlight 13 years ago, when Sydney Brenner and colleagues were awarded the Nobel Prize in Physiology or Medicine in 2002 for their work on programmed cell death. Today, there are more than 50 diseases for which scientists know that the whole reason, or a major part of it, is related to a failure of balance in cell death. This has made the study of different types of cell death the most prolific area of research in the world during the past decade.

The importance of research related to various forms of cell death programmes in relation to health and disease, the need for filling the major scientific data gaps and the relevance of these cell death pathways and drug targets pertaining to

*A report on the national conference on 'Cell Death and Disease' organized by the Department of Biochemistry, University of Madras, under the DST-PURSE programme support, and held on 17 and 18 March 2015.

the clinical setting are less addressed in India at a major level. This formed the premise of organizing a two-day national conference on 'Cell death and disease' in Chennai recently. The purpose of the conference was to provide an informative and interactive forum for the participants to share their experiences regarding the quest for strengthening cell death research in the country.

The conference brought together distinguished researchers in the field of cell death and survival from various parts of the country. The deliberations in a nutshell are presented here. The programme began with an inaugural address by R. Thandavan (University of Madras). The plenary lecture was delivered by Chandrima Shaha (National Institute of Immunology, New Delhi), who spoke on 'Cells at the cross road of life and death'. She elaborated that killing of cancer cells and infectious agents are central to disease treatments, and therefore, understanding of the mechanisms of cell death has translational medical applications. She explained how basic research in organisms as diverse as worms, insects and mammals has identified a process of fundamental importance of cell death to animals, and how this has led to the development of new strategies to treat disease in humans. K. Sankaran (Anna University, Chennai) spoke on: 'Instrumentation development for infectious diseases – the need for paradigm shift in our thinking and method development'. Citing studies of clinical, preclinical and tissue culture nature, M. Balasubramanyam (Madras Diabetes Research Foundation, Chennai) presented his work on 'Cell fate decisions under endoplasmic reticulum (ER) stress and "Stress wars" with special reference to type 2 diabetes'. He emphasized how several cell stressors (inflammation, oxidation, glycation, telomere shortening and senescence) could result in different forms of 'cell fate decisions' mediated by ER stress as a central element of cellular signalling. Citing that all cell death processes are not fatal and detrimental, he delineated that β-cell autophagy is important for its mass, structure and function. He also added that careful design of agents enhancing autophagic activity in β-cells might serve as a novel approach towards therapeutics for the treatment of diabetes. He stressed upon the emergence of 'chemical chaperones' (such as TUDCA [tauroursodeoxycholate] and PBA [4-phenylbutyrate]) as ER stress inhibitors with anti-diabetic potential and several other metabolic benefits. Durgaprasad Mishra (Central Drug Research Institute, Lucknow) discussed 'Trailing TRAIL resistance in cancer cells: path travelled and road ahead'. While TNF-related apoptosis-inducing ligand (TRAIL) is perceived as an attractive chemotherapeutic drug target and TRAIL therapy is selective for eliminating cancer cells, TRAIL resistance by cancer cells is one of the major limitations. Therefore, Mishra emphasized that future work should focus on elucidation of the molecular targets and signalling pathways responsible for TRAIL resistance so as to devise newer and effective therapeutic strategies.

On the second day of the conference, Soma Guhathakurta (Indian Institute of Technology Madras, Chennai) gave a lecture on 'Eryptosis, is it apoptosis of RBC?', which is an emerging and interesting area of cell death research. Despite the fact that erythrocytes are non-nucleated cells, programmed cell death does not spare these cells and it occurs through a process called 'eryptosis'. She delineated how functional eryptosis is important in physiology, including RBC protection from hemolysis and how excessive eryptosis gives rise to many disease-states. M. Rasool (VIT University, Vellore) discussed 'Pathogenesis and therapeutic targets of rheumatoid arthritis: progress and promises'. Citing that current drugs for rheumatoid arthritis have limitations and side effects, he showed some of his laboratory results that demonstrated the potency of natural product principles as therapeutic measures against rheumatoid arthritis. Rajendra Prasad (Annamalai University, Chidambaram) spoke on 'P-glycoprotein as a therapeutic target for overcoming multidrug resistance in cancer'. While multidrug resistance (MDR) is the principal mechanism by which many cancers develop resistance to cell death, he stressed that studying P-glycoprotein and other cellular mechanisms is critical to overcome clinical MDR and this will lead to the development of new treatment regimens for cancer chemotherapy.

The conference attracted 130 participants from various universities, research institutions and colleges all over the country. As the major aim of the conference was to encourage young scientists and research scholars in the area of cell death research, two young research investigators were presented with the Young Investigator awards and three others were chosen for Oral Presentation awards.

The key issues and challenges in the area of cell death in health and disease that emerged from the various plenary and technical sessions formed the subject matter for futuristic recommendations.

- Scientists now know of 12 different types of cell death that occur under different conditions. However, apart from necrosis and apoptosis, the most important and widespread cell death mechanisms are autophagy and mitotic catastrophe. Clarifying the biochemical pathways controlling the variety of cell death programmes will inevitably have clinical benefits, and is expected to result in novel strategies for induction of cell death in certain disease states while preventing cell death in other conditions.
- Although apoptosis is a well-studied cell death phenomenon, now it is time for scientists and clinicians to explore whether apoptosis-resistant tumour cells can be sensitized to other modes of growth control, including necrosis, autophagy, mitotic catastrophe or cellular senescence.
- The successful elucidation of the molecular pathways controlling and mediating apoptosis has come to fruition as agents for cancer and other therapies are entering the clinic. Similar promise exists for other forms of cell death as well, but this needs continuous and expanded research.
- The topic of the conference itself is an appropriate subject for a 'task force' by the funding bodies of the Government of India, through which there is a possibility of time-bound RFA (request for applications) that might encourage research work on cell death all over the country.

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