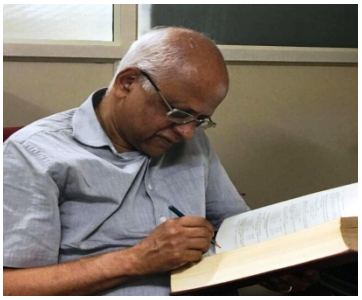
Professor Gautam Radhakrishna Desiraju, FNA



Members of the Council and the Fellows of the Indian Chemical Society feel highly honoured to felicitate Professor Gautam Radhakrishna Desiraju in recognition of his lifetime achievement in teaching and research in the field of Chemistry in general and Crystal Engineering in particular.

Professor Desiraju is a structural chemist who has played a major role in the development and growth of the subject of Crystal Engineering. He is noted for gaining acceptance for the theme of weak hydrogen bonding among chemists and crystallographers. Professor Desiraju is one of the most highly cited Indian scientists with more than 450 research papers, 50000 Scopus citations and H–index of 88. Professor Desiraju was awarded with the Alexander von Humboldt Forschungspreis and the TWAS award in Chemistry.

Professor Desiraju's contribution to the subject of Crystal Engineering has focused on the concept of the Supramolecular Synthon. The Supramolecular Synthon concept is now widely used by crystal engineers in the design of molecular crystals and pharmaceutical co-crystals, which are important from scientific and commercial viewpoints. Crystal Engineering is effectively like supramolecular synthesis in the solid state, and there is a direct analogy between the supramolecular synthon of Professor Desiraju and the molecular synthon that was proposed for organic synthesis by Professor E. J. Corey.

Professor Desiraju has guided the PhD work of around 50 students and has edited three multi-author books in Solid State and Supramolecular Chemistry. He is a member of the Editorial Advisory Boards of Angewandte Chemie and Chemical Communications, Accounts of Chemical Research and a former member of the Editorial Advisory Board of the Journal of the American Chemical Society. He is the former President of the International Union of Crystallography and a champion of the Asian Crystallographic Association. He has also received the Honorary Doctorate degree of the Universidad Nacional de Córdoba, Argentina and of the Rayalaseema University, Kurnool. He was awarded the Acharya P. C. Ray Medal (2015) of the University of Calcutta for innovation in science and technology. He was awarded the ISA medal for science of the University of Bologna for the year 2018.

Presently, Professor Desiraju is the Chairman of the Research Councils of the National Chemical Laboratory, Pune, and the Indian Institute of Chemical Technology, Hyderabad, as well as the Chairman of the Council of the Bose Institute, Kolkata.

Abstract

Halogen bonds and their role in crystal engineering

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The halogen bond is an attractive interaction in which an electrophilic halogen atom approaches a negatively polarized species. Short halogen atom contacts in crystals have been known for around 60 years. Such contacts are found in two varieties: type I, which is symmetrical, and type II, which is bent. Both are influenced by geometric and chemical considerations. Our research group has been using halogen atom interactions as design elements in crystal engineering, for more than 30 years. These interactions include halogen···halogen interactions (X···X) and halogen···heteroatom interactions (X···B). Halogen bonds have electrostatic, polarization and size components. Conclusions may be drawn pertaining to the nature of X···X interactions from the Cambridge Structural Database (CSD). In crystal engineering one builds up from previous knowledge of the halogen bond to construct new crystal architectures. In terms of crystal design, halogen bonds offer a unique opportunity in the strength, atom size and interaction gradation; this may be used in the design of ternary cocrystals. The specific directionality of the halogen bond makes it a good tool to achieve orthogonality in molecular crystals. Mechanical properties can be tuned systematically by varying these orthogonally oriented X···X interactions. With an increasing understanding of these interactions, this may be the right time to look at differences between halogen bonds and hydrogen bonds and exploit them in more subtle ways in crystal engineering.

J. A. R. P. Sarma and G. R. Desiraju, *Acc. Chem. Res*., **19**, 222-8, 1986.
A. Mukherjee, S. Tothadi and G. R. Desiraju, *Acc. Chem. Res*. **47**, 2514-24, 2014.

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Education

M.Sc.: University of Calcutta, India, **Ph.D. :**University of Calcutta, India
Post-Doctoral: University of Texas Medical Branch, USA

Research Interests: DNA damage and Repair | Cancer Biology| Neurodegenerative diseases

The major focus of my lab is to establish the preferential repair of oxidative genomic damage and DNA strand breaks in the transcribed genes. My lab was the first to report preferential repair of oxidative genomic damage both *in vitro* and *in vivo*. We also initiated the work on how DNA repair deficiency is linked to neuropathgogenesis. While investigating the mechanism of Spinocerebellar Ataxia type 3 (SCA3), we found that WT Ataxin 3 (a polyQ repeat-containing protein mutated in SCA3) stimulates, while the mutant Ataxin 3 (ATXN3) abrogates the activity of polynucleotide kinase 3'-phosphatase (PNKP), an essential DNA end-processing enzyme, resulting in the accumulation of DNA strand breaks and consequent constant activation of the DNA damage-response pathway – a plausible cause of SCA3. Our recent studies further revealed that both PNKP and ATXN3 play critical roles in DNA double-strand break repair via non-homologous end joining (NHEJ). Our recent report indicates that C-NHEJ-mediated repair can be error-free, and a homologous nascent RNA provides the template to restore the missing sequence. This seminal work will have profound implications in understanding the molecular basis of various age-related pathologies – such as cancers and neurodegenerative diseases.

Complete List of Published Work in My Bibliography (90 total): (Total Citations 6736; h-index: 48)
https://www.ncbi.nlm.nih.gov/sites/myncbi/145eQfZYKPYAJ/bibliography/47886755/public/?sortby=pubDate&sdirection=descending

Abstract

Chronic inflammation and impaired DNA repair-a double whammy for neurodegenerative diseases

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Spinocerebellar Ataxia Type 3 (SCA3) is a dominantly-inherited autosomal neurodegenerative disease caused by CAG (encoding glutamine) repeat expansion in the Ataxin-3 (ATXN3) gene. However, how the expanded CAG repeats (from 14-41 to 55-82) gains its toxic function is poorly understood. DNA repair deficiencies and neuroinflammation have been implicated in various neurological disorders. Recently, we have shown that wild-type ATXN3 stimulates and by contrast, the mutant form of ATXN3 blocks the activity of polynucleotide kinase 3' phosphatase (PNKP), an essential DNA end-processing enzyme involved in multiple DNA repair pathways including DNA double-strand break (DSB) repair via the classical non-homologous end-joining (C-NHEJ). We thus postulated that ATXN3 is also involved in C-NHEJ-mediated repair of DSBs, and indeed found that ATXN3-depleted cells and SCA3 patients' brain tissue showed increased γH2AX foci formation, a marker for DSBs. Furthermore, Co-IP analysis from mouse cerebellum shows that ATXN3 forms a dynamic complex with C-NHEJ proteins (including PNKP) and RNA Polymerase II (RNAP II) under physiological conditions. Notably, nuclear extract from ATXN3-depleted cells and SCA3 patients' brain tissue showed NFκB activation, RNAP II degradation and also, accumulation of DNA damage mostly in the transcribed genome. We thus conclude that ATXN3 is involved in various cellular processes, including protein quality control, repair of DSBs via the C-NHEJ pathway, and also in maintaining immune-homeostasis. We will discuss how the accumulation of DSBs due to the functional deficiency of PNKP contributes to the pathophysiology of various neurological disorders (Grant support: NINDS NS073976)