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Deepak T. Nair obtained his B.Sc (Chemistry; 1994) and M.Sc (Biotechnology; 1996) from the University of Pune. He worked for his Ph.D (Structural Immunology; 2001) at the National Institute of Immunology (New Delhi). After working as a post-doctoral fellow at the Mount Sinai Medical Centre (New York) he joined the National Centre for Biological Sciences (Bangalore) as an independent investigator in 2007.

RESEARCH DESCRIPTION

The blueprint of life for each organism is resident in its genome. Nucleic acid metabolizing enzymes play critical roles in ensuring proper information transfer from the genome for synthesis of effector molecules. Members of this broad group of enzymes are also instrumental in the maintenance of the genome. Perturbation in the function of these enzymes due to mutations or inhibitors has an adverse effect on the survival of the organism. A chemical and topological description of enzymes in their functional state - in the form of three-dimensional structures- has always provided important insights into the mechanism of their action and the molecular basis of related diseases. In my laboratory we are using this approach to study three processes involving the action of nucleic acid metabolizing enzymes on the genome. These processes are (a) DNA Mismatch repair (b) DNA damage tolerance and (c) Japanese Encephalitis Virus Replication. Using X-ray crystallography as the primary tool in conjunction with relevant biochemical methods and allied biophysical techniques, we aim to provide structural insight into the mechanism of action of enzymes/enzyme complexes that are critical in each of these processes. Through ongoing and new collaborative efforts, we aim to shed more light on the relation between biochemical and structural properties of these enzymes and their observed and predicted roles in physiology. Also, generally, for all cellular processes to function optimally, the integrity of the genome has to be maintained. However, it has been seen that creation and retention of error in DNA allows for the evolution of the genome in order to relieve selection pressure imposed by an adverse environment. These two conflicting requirements have led to the presence of molecules and molecular mechanisms that either prevent (e.g. DNA mismatch repair) or facilitate (e.g. error-prone DNA Polymerases) the appearance of mutations. I aim to unearth the chemical and structural strategies employed by such molecules/molecular assemblies to understand how these molecular throttles modulate the rate of evolution.

SELECTED PUBLICATIONS

Amit Sharma, Vidya Subramanian and Deepak T. Nair The PAD region in the mycobacterial dinB homolog MsPolIV exhibits positional heterogeneity Acta Crystallogr D Biol Crystallogr. 2012 (in press).

Amit Sharma and Deepak T. Nair, "MsDpo4-a DinB Homolog from *Mycobacterium smegmatis*-Is an Error-Prone DNA Polymerase That Can Promote G:T and T:G Mismatches," Journal of Nucleic Acids, vol. 2012, Article ID 285481, 8 pages, 2012.

Amit Sharma and Deepak T. Nair. Cloning, expression, purification, crystallization and preliminary crystallographic analysis of MsDpo4: a Y-family DNA polymerase from *Mycobacterium smegmatis.* Acta Crystallogr Sect F Struct Biol Cryst Commun. 2011 Jul 1;67(Pt 7):812-6.

Sivakumar Namadurai, Deepti Jain, Dhananjay S. Kulkarni, Chaitanya R. Tabib, Peter Friedhoff, Desirazu N Rao and Deepak T Nair. The C-terminal domain of the MutL homolog from *Neisseria gonorrhoeae* forms an inverted homodimer. PLoS One. 2010 Oct 28;5(10):e13726.