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Structural and functional analysis of human ERG oncoprotein: A potential target to develop the prostate cancer drug

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ERG oncoprotein belongs to ETS (E26 transformation specific domain transcription factor) family of eukaryotic proteins with highly conserved winged helix-turn-helix DNA binding domain. The ETS gene encoding domains are frequent target for chromosomal translocation that result in various types of leukemia's, Ewing sarcoma and over-expression of some genes are implicated in other human diseases. TMPRSS2-ERG fusion also occurs in more than 50% of prostate cancer.

Erg protein is required for definitive hematopoiesis, adult hematopoietic stem cell function and the maintenance of normal peripheral blood platelet numbers. However, the molecular details of how, ERG is involved in transcriptional regulation is not known. Our goal is to analyze the x-ray structure of ERG in native and complexed form and to develop potent inhibitors of ERG in order to cure prostate cancer disease.

We have cloned and expressed the four constructs of varying length of ERG in *E. coli* and all proteins have been purified by standard chromatographic techniques. Specific DNA binding assay with four ERG fragments have been done, which indicate longer fragments of ERG have decreased DNA binding. Combination of circular dichorism (CD) and molecular modeling data have yielded the structure of full length ERG.

In addition, we are also attempting crystallization and x-ray structure analysis of full length ERG & its fragments as well as their complexes with DNA. Crystals of ETS-DNA complex have been obtained, which diffracted to 3.0-Å resolution. All these results will be discussed in detail in the meeting.

Biography

Dr. Ajay K. Saxena has completed his Ph.D. in 1995 from AIIMS, Delhi and postdoctoral studies from Austrian Academy of Sciences in Europe during 1996-1998 and NIAID, National Institutes of Health, Maryland in USA during 1998-2005. Since 2005, He has been working as Associate Professor at Structural Biology Section of School of Life Sciences, Jawaharlal Nehru University in Delhi, a premier university of India. He has published more than 23 papers in reputed journals and reviewer of several national and international journals. He has obtained national and international research funding and awards for his excellent research performance.