Rheumatology 2012, 2:3
http://dx.doi.org/10.4172/2161-1149.S1.010

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference and Exhibition on
Orthopedics & Rheumatology

August 13-15, 2012 Hilton Chicago/Northbrook, USA

Deregulation of NF-κB signal transduction is involved in the Sjögren's syndrome inflammatory process

Massimo Amore
University of Bari Medical School, Italy

Background: Chronic inflammatory diseases are caused by prolonged production of pro-inflammatory cytokines and many pro-inflammatory cytokines are involved in the inflammatory process of primary Sjögren's syndrome. The transcription factor nuclear factor-κB (NFκB) is related to the transcription of these pro-inflammatory cytokines. Therefore, NFκB plays an important role in inflammatory diseases and in the development of autoimmunity. We analyzed the importance of IκBα (inhibitor of κB alpha) as NF-κB signal transduction inhibitor in monocytes from Sjögren's syndrome (SS) patients versus healthy controls.

Methods: Monocytes were obtained from the peripheral blood of 30 SS patients and 23 healthy subjects. IκBα expression was studied by semi quantitative RT-PCR, Real-Time PCR, immunoblotting, flow cytometry and ELISA.

Results: Analysis of the gene and protein expression profiles of SS monocytes revealed a down-regulation of IκBα and, all the Sjögren's syndrome cases examined, serum IκBα levels were significantly decreased in comparison with controls.

Conclusions: our findings clearly demonstrate changes in the levels of IκBα in SS monocytes, suggesting that the attenuated expression of IκBα could contribute to the deregulation of NF-κB pathways in the SS pathogenesis. Decreased expression of IκBα may specifically amplify cytokines production and inflammatory response linked to Sjögren's syndrome.

m1damore@libero.it

Advances in structure-based drug design – Lessons to design robust drugs to inactivate targets that exhibit poor specificity

Moses Prabu
Commonwealth Medical College, USA

The ability to design chemical agents that specifically block a target is assessed by how well the natural activity of the target is blocked. Inhibition of protein-protein/protein-ligand interactions for drug therapy can be achieved by designing inhibitors that mimic several molecular features of the natural interaction. However, drug targets that engage in interactions with no apparent specificity for other proteins/ligands often exhibit high variability in the primary structural composition at the binding interface. HIV-1 protease is a highly suitable example of such a promiscuous target which specifically proteolyzes at cleavage sequences that share poor similarity. A combined investigation that involved X-ray crystallography, biocalorimetry and molecular modeling conclusively revealed the presence of a consensus structural motif that is assumed by variable substrate sequences. This motif, also called as substrate-envelope, is crucial for molecular specificity and it also elucidates the structural correlation between drug resistance and substrate co-evolution. In this presentation, the factors intrinsic to substrate recognition and a method to incorporate them in drug development to facilitate the design of novel potent drugs which will be discussed. Our ongoing effort on other such enzymes with promiscuous recognition sites, such as human cathepsin D and malarial plasmepsins, will also be presented.

Biography

Dr. Moses Mohandas Prabu,PhD., is an Assistant Professor of Molecular, Leader of the Crystallography Laboratory, Division of Basic Sciences, The Commonwealth Medical College, USA. He received his B.Sc. & M.Sc. degrees in Physics with specialty in Optics. Dr. Prabu's graduate work includes the structure function of plant lectins (Thesis mentors: Professors K. Suguna, Ph.D. and M. Vijayan, Molecular Biophysics Unit, Indian Institute of Science, India). He subsequently joined Dr. C. Schiffer at University of Massachusetts Medical School, USA, where he elucidated the structural consequences of molecular recognition and drug resistance of HIV-1 protease and the co-evolution of its substrates in response to drug therapy. Dr. Prabu's current research focus is in determining the rationale for molecular recognition of enzymes that proteolyze multiple amino acid sequences that share poor similarity. Specifically, his laboratory investigates the aspartyl proteases Plasmodium falciparum plasmepsins and human cathepsin D. In addition, Dr. Prabu's research also includes the determination of the structural consequences of cell-trafficking and activation of cathepsin D.

moses.prabu@gmail.com