TIFR Centre for Interdisciplinary Sciences, Narsingi, Hyderabad 500075

Seminar

The RAGE Axis: Novel Molecular and Structural Insights and Key Regulations in Diseases: Inflammation to Cancer

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Abstract: The immunoglobulin superfamily molecule RAGE (receptor for advanced glycation end product) transduces the effects of multiple ligands, including AGEs (advanced glycation end products), advanced oxidation protein products, S100/calgranulins, high-mobility group box-1, Mac-1, amyloid-beta peptide, and beta-sheet fibrils. Many important biochemical mechanisms are activated in the presence of high levels of glucose, which occur in diabetes. Elevated levels of glucose accelerate the formation of advanced glycation endproducts (AGEs). Via their chief signaling receptor—the AGE-specific receptor (RAGE)—AGEs generate reactive oxygen species and activate inflammatory signaling cascades. Consequently, AGEs have key roles in the pathogenesis of diabetic complications. Two discoveries have advanced our knowledge of the roles of RAGE in inflammation. First, this receptor has multiple ligands and binds not only AGEs but also proinflammatory, calcium-binding S100 proteins and nuclear HMGB-1. Second, RAGE is expressed on T lymphocytes, monocytes and macrophages; RAGE expression on T lymphocytes is essential for effective priming of immune responses *in vivo*. Our studies have shown, four novel findings. First, we have discovered LPA as a novel ligand of RAGE in vascular signaling and tumorigenesis., Second, chronicle roles for RAGE in the pathogenesis of diabetic complications and develop the hypothesis that, in addition to RAGE's central role in the inflammatory response, it is critically linked to the pathogenesis of types 1 diabetes. Third, Structural mechanism of the advanced glycated end products (AGEs) recognition by their receptor RAGE, and Fourth, Solution structure and amino acid residues of C-terminal RAGE (ctRAGE) involved in binding to Dia-1 FH1 and its signaling. These novel findings identify novel roles for RAGE as a conduit for ligand signaling and indicate that therapeutic strategies to modify the pathological actions with RAGE.

***Date*: Wednesday, February 06th 2013**

***Time*: 04:00PM (Tea/Coffee at 03:30PM)**

***Venue*: Conference Hall, TCIS**

All are cordially invited