REGIONAL CENTRE FOR BIOTECHNOLOGY
Seminar series

The RAGE axis: Novel Structural insights and key regulations in cardiovascular complication and tumorigenesis

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The immunoglobulin superfamily molecule RAGE (receptor for advanced glycation end product) transduces the effects of multiple ligands, including AGEs (advanced glycation end products), S100/calgranulins, high-mobility group box-1, amyloid-beta peptide, and beta-sheet fibrils. In diabetes, hyperglycemia likely stimulates the initial burst of production of ligands that interact with RAGE and activate signaling mechanisms. Consequently, increased generation of proinflammatory and prothrombotic molecules and reactive oxygen species trigger further cycles of oxidative stress via RAGE, thus setting the stage for augmented damage to diabetic tissues in the face of further insults. Many of the ligand families of RAGE have been identified in atherosclerotic plaques and in the infarcted heart. Our work suggests that RAGE-dependent acceleration of atherosclerosis in ApoE-null mice is dependent on the action of the ROCK1 branch of the transforming growth factor-beta pathway. Further, we discovered a novel ligand, lysophosphatidic acid for RAGE in vascular signaling and tumorigenesis. These findings identify novel roles for RAGE as a conduit for ligand signaling and indicate that therapeutic strategies to modify the pathological actions of LPA in vascular disease and tumorigenesis should include targeting the interaction of LPA with RAGE.