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Regulation of tumor growth and metastasis through inhibition of laminin-10 degradation by Col4(α6)NC1

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Laminin-10 or 511 constituting the extracellular matrix (ECM) of tumors and basement membranes (BM) of blood capillaries promotes the cellular migration of tumoral and endothelial cells, thus enhancing tumor growth, metastasis and angiogenesis. Cellular survival or migration promoting activities of laminin-511 have been attributed to the EGF-like domains that are released from the laminin-511 by MT1-MMP cleavage which activate EGFR signaling in target cancer cells. We have identified that cleavage of laminin-10 into 310 kDa fragment by MT1-MMP was prevented by human type IV collagen alpha 6 chain derived non-collagenous domain [Col4(α6)NC1]. The inhibitory effect of Col4(α6)NC1 on laminin alpha 5 chain cleavage was also exhibited by this domain on cell mediated laminin-10 cleavage. Further, Col4(α6)NC1 inhibited migration of cells on laminn-10 coated plates, phosphorylation of EGFR in LLC and breast cancer tumor cells. Thus, the present study elucidates the novel inhibitory mechanism(s) of MT1-MMP mediated laminin cleavage by Col4(α6)NC1, which prevents tumor progression

Biography

Dr. Venugopal Gunda has completed his Ph.D in 2010 from Jawaharlal Nehru Technological University/Indian Institute of Chemical Technology, Hyderabad, AP, India and currently working as a Postdoctoral Associate at the Cell Signaling and Retinal Tumor Angiogenesis Laboratory, Department of Genetics, Boys Town National Research Hospital, Omaha, NE USA. He has more than 6 years of experience in research, 1 year teaching experience as Junior Lecturer, Zoology, SVSJ College, Nizamabad, AP, India. He was selected in top 20% in CSIR-UGC NET, and received CSIR (2005-2010) fellowships from Government of India for his graduation studies. He also received Cash prize for being topper in B.Sc (1999-2001). He has more than 10 publications in reputed journals and is also serving as AdHoc reviewer for many journals including: Circulation; Protein Expression and Purification; Current Eye Research; Journal of Cancer Science & Therapy; Journal of Bioanalysis & Biomedicine and Journal of Clinical & Experimental Ophthalmology.