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Sam-Pointed Domain Ets Transcription Factor-1 (SPDEF-1, a.k.a. PDEF-1) is a Tumor Metastasis Suppressor and its Mechanism(s) of Action

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Conventional therapies produce a high rate of cure for many patients with cancer, but there is, at present, limited effective treatments for intervention in metastatic cancer. Therefore, at present there is an urgent and unmet need for identifying new targets that could be exploited for intervention in metastatic disease. Progression of cancer from focal to metastatic cancer requires deregulation of growth control, invasiveness and cell motility. SPDEF/PDEF is the latest family member of the ETS transcription factor family, although it is unique in many aspects. PDEF was first discovered as an mRNA transcript highly expressed in prostate tumor cells where it regulates prostate-specific antigen (PSA) gene expression and is an androgen receptor co-regulator. SPDEF/PDEF expression is highly restricted to epithelial cells and has been found in prostate, breast, colon, ovary, stomach, and airway epithelium. Our recent studies demonstrated that SPDEF/PDEF is lost in a graded fashion as prostate cancer cells advance to aggressive stage (Molecular Cancer, 2010). Strong preclinical evidence is emerging that SPDEF/PDEF is a negative regulator of tumor progression and metastasis. PDEF expression is often lost in late-stage, advanced tumors. The induction of tumor aggressiveness in response to the loss of PDEF is thought to be due to the plethora of PDEF-regulated gene targets, many of which are known players in tumor progression including tumor cell invasion and metastasis (Cancer Letters 2011). Specifically our studies point to the direct regulation of MMP-9, a tumor progression associated MMP that is associated with cancer metastasis, by PDEF. These data lead us to the hypothesis that PDEF is a tumor metastasis suppressor protein. Current studies in our lab are aimed at understanding molecular mechanism/s involved in regulation of cancer cell metastasis by SPDEF/PDEF as well as mechanisms of SPDEF/PDEF silencing during cancer progression form indolent to aggressive metastatic phenotype.

Biography

Professor Hari K Koul is the founder Program Director of Urosciences Program and Cell Signaling and Molecular Urology Laboratory; Professor (with Tenure) and Director of Research, Department of Surgery-Division of Urology at The University of Colorado School of Medicine, Anschutz Medical Campus-Aurora-CO-USA; Research Biologist the Department of Veterans Administration Health Center-Denver-CO-USA; Professor Department of Bioengineering, and Program in reproductive Sciences; and Professor/ full member of the Developmental Therapeutics program at The University of Colorado Comprehensive Cancer Center Anschutz Medical Campus-Aurora-CO-USA. He is an internationally recognized researcher and over past two decades, Dr. Koul has greatly contributed to our understanding of molecular mechanisms, specifically signal transduction pathways in genitor-urinary disorders including prostate and bladder cancer. Dr. Koul's research is currently focused in understanding the role of Hypoxia/ re-oxygenation and the resulting ROS in mediating aggressive phenotypes in solid tumors in general and prostate, bladder and kidney cancer in particular. In addition his laboratory is engaged in deciphering the molecular signatures of aggressive renal and prostate tumors; and has recently identified MMP9 as a downstream target of Prostate Derived Ets transcription Factor (PDEF). Dr. Koul has been elected Fellow of the American Society of Nephrology (FASN: since 2004), and A Fellow of the American College of Nutrition (FACN; since 2002). Dr. Koul earned M.Sc. (Biochemistry-1986) from Kashmir University-Srinagar, J&K-India and Ph.D. (Biochemistry-1990) from PGI, Chandigarh, India. As a graduate student Dr. Koul was a recipient of prestigious fellowships from CSIR-India. Dr. Koul came to USA in 1991 on a NIH-post-doctoral fellowship and worked as a post-doctoral fellow (1991-1994) at the University of Massachusetts Medical School, in Worcester, MA. He was promoted to Jr. Faculty position at UMASS Medical School and continued to work there until 1996. Dr. Koul served as Sr. Staff Scientist and founding member of Urology Research team at Henry Ford Health Sciences Center/ Case Western University, Detroit MI from 1996-2003, when Dr. Koul was recruited to head the Urology Research Program at the University of Colorado Denver, School of Medicine.