

Pro-inflammatory mediators in cancer development and progression

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Chronic or acute inflammatory conditions together with genetic and epigenetic changes in various organs are believed to trigger cancer genesis and progression. These conditions promote an increase in cytokines that activate a variety of pro-tumorigenic activities, such as stimulation of alternate proliferative pathway, chemotactic motility, increased survival and increased invasive potential. In prostate cancer, for example, chronic infection and/or altered fatty acid metabolism are known to trigger carcinogenesis and progression. Interleukins and members of TGF- β family are linked to such conditions.

We and others reported recently that constitutive activation of a pro-inflammatory chemokine, IL-8 promotes androgen-independent prostate tumor growth, motility, invasion, and angiogenesis. This was further demonstrated by the depletion of IL-8 expression in tumor cells significantly reduced their proliferation (>60%), growth arrest at G0/G1 phase, invasion and increased sensitivity (>50%) to docetaxel. Further, we showed increased IL-8 transregulates other, unrelated CXC-chemokine receptors, CXCR4 and CXCR7 in prostate cells, which are over-expressed and implicated in metastasis. Moreover, we reported that CXCR1, the co-receptor for IL-8 and CXCR7 also control proliferation by activating ERK1/2 MAP kinase and epidermal growth factor receptor through direct or indirect (G-protein coupled receptor activation) pathways. In addition, our work suggests, the early carcinogenesis is also regulated by IL-8 that triggers classic and non-canonical signaling via Nuclear Factor- κ B, resulting in rapid cancer progression. The presentation will be focused on an overview of the cellular determinants of inflammatory process and mechanism of regulation of pro-inflammatory factors in prostate and other related malignancy for advancement of novel therapeutic strategies.

Biography

Dr. Rajendra K Singh received his Ph.D from Avadh University, India in Biochemistry and Molecular Toxicology. He did his postdoctoral training in Environmental Carcinogenesis and Molecular Cancer Biology from reputed laboratories in USA. Currently, he is working at University of Miami, Miller School of Medicine, Miami-Florida. His major research interest is to understand mechanism by which environmental factors cause malignant transformation in mammalian cells and examine the patho-physiology of pro-inflammatory mediators in oncogenic transformation and progression. He has published several papers in high impact journals. He is Editorial board of Journal of Cancer Science and Therapy and Journal of Carcinogenesis and Mutagenesis. He is also an ad hoc reviewer for several reputed journals in Molecular Carcinogenesis and Toxicology research areas.