Regulation of Cell Proliferation Through a KIT-Mediated Mechanism in Benign Prostatic Hyperplasia

Introduction and Objective: We investigated the role of the KIT-mediated mechanism in benign prostatic hyperplasia (BPH), and discuss the pathophysiology of BPH and a candidate target of BPH medical therapy.
Materials and Methods: First, we performed immunohistochemical analysis to examine the localization of KIT and KIT ligand, stem cell factor (SCF) in the prostate. Second, cell proliferation of a human prostate stromal cell line (PrSC) treated with SCF or imatinib mesylate was investigated by the WST-1 cell proliferation assay to investigate the pathophysiological function of KIT. Third, the expression levels of JAK2 and STAT1 protein of PrSCs treated with SCF or imatinib mesylate were also investigated by Western blotting to confirm their effect on cell proliferation because JAK2/STAT1 is one of the main pathways downstream of cytokine receptors and growth factor receptors by transducing signals from the cell surface to the nucleus. Finally, we compared the expression level and distribution of KIT in normal prostate and BPH of human to clarify the contribution of KIT to the pathogenesis of BPH.
Results: Immunohistochemical analysis demonstrated that KIT was localized in interstitial cells (ICs) of the stromal component in human prostate. On the other hand, SCF was found in basal cells of prostate epithelium. SCF administration increased cell proliferation dose-dependently for PrSC. In addition, Imatinib mesylate administration inhibited cell proliferation dose-dependently. Treatment with SCF increased the expression of JAK2 and STAT1 dose-dependently in PrSCs. On the other hand, treatment with imatinib mesylate inhibited the expression of JAK2 and STAT1 dose-dependently. The mean expression level of c-kit and SCF mRNA in BPH was significantly higher than in normal prostate as determined by RT-PCR ($p < 0.05$). The number of KIT-positive ICs/total prostate stromal cells in BPH was also significantly higher than in normal prostate ($p < 0.005$).
Conclusions: The role of KIT and KIT-positive cells may be related to the regulation of cell proliferation. The JAK-STAT signaling pathway appears to be involved in the prostate growth mechanism. Inhibition of KIT in the prostate induces an antiproliferation effect on the prostate. Our study may lead to provide a novel therapeutic target in the future.