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Imura M[1], Kojima Y[2], Hamakawa T[2], Shibata Y[2], Hayase M[2], Kubota Y[2], Sasaki S[2], Kohri K[2]
1. *Department of Nephro-urology, Nagoya City University & Kamiida Hospital,* ***2.*** *Department of Nephro-urology, Nagoya City University*

FUNCTION OF KIT POSITIVE CELLS IN THE BENIGN PROSTATIC HYPERPLASIA

Hypothesis / aims of study

Interstitial cells of Cajal (ICC) are thought to be pacemaker cells for gastrointestinal motility. They express the proto-oncogene, c-kit, and signaling via the receptor tyrosin kinase gene product, KIT, is essential for development of the ICC phenotype and electrical rhythmicity.

Recently, spontaneous slow wave generation and contractile activity was reported in the guinea-pig prostate. At the same time, interstitial cells of the guinea-pig prostate were described. Gastrointestinal stromal tumors are KIT-expressing and KIT (tyrosine kinase receptor - CD117)-signaling driven mesenchymal tumors. Kit positive cells are pacemaker cells and are associated with the growth of stroma in the gut. Recently, KIT positive cells were recognized in human prostate, but the role of KIT positive cells is not clear. That is to say, it is suggested that KIT positive cells relate contraction and growth of prostate. We studied relations of KIT positive cells and benign prostatic hyperplasia.

Study design, materials and methods

Specimens were taken from patients with normal prostate, BPH and guinea-pig. Expression of c-kit and stem cell factor (SCF) which is KIT ligand was examined by immunostain and western blotting and PCR. In the functional experiments, prostate of guinea-pig was cut into longitudinal or spiral segments. One of these segments was suspended longitudinally in an organ bath containing Krebs solution gassed with a mixture 95% oxygen and 5% carbon dioxide at 37C. The tissue's response was measured by means of an isometric force-transducer. Effects of Imatinib mesylate were evaluated induced contraction, which was expressed as percentage of the maximal response.

Human prostate stromal cells (PrSC) were maintained using their respective medium kits. These cells were maintained at 37℃ in a humidified atmosphere of 95% air and 5% CO_2. The cell proliferation of PrSC treated with Imatinib mesylate or SCF was investigated by the WST-1 cell proliferation assay. Expression of c-kit in BPH patients (n=5) was compared to normal prostate patients (n=5) with immunostain and RT-PCR. RT-PCR for c-kit was performed by an Applied Biosystems PRISM 7700 sequence detection system.

Results

First, the expression of c-kit and SCF were recognized in the prostate by immunostain and western blotting and PCR. Second, the effects of Imatinib mesylate were evaluated induced contraction of guinea-pig. Imatinib mesylate administration inhibited contractions of guinea-pig dose-dependently. Third, cell proliferation of PrSC treated with Imatinib mesylate or SCF was investigated by the WST-1 cell proliferation assay. Interestingly, Imatinib mesylate administration inhibited cell proliferation dose-dependently for PrSC. On the other hand, SCF administration increased cell proliferation dose-dependently for PrSC. Finally, RT-PCR and immunostain were performed using prostate specimens from BPH and normal prostate patients to estimate c-kit expression level. The mean expression level of c-kit in the BPH was significantly higher than that in the normal prostate by RT-PCR ($p < 0.05$) The mean of KIT positive cells / prostate stromal cells by immunostain in the BPH was significantly higher than that in the normal prostate ($p < 0.005$)

Interpretation of results

Our results showed that the expression level of c-kit in the BPH patients is higher than normal prostate patients and KIT positive cells were possible to relate contraction and growth of prostate.

Concluding message

KIT positive cells were possible to relate contraction and growth of prostate.

Our study may lead to a greater understanding of the mechanisms of benign prostatic hyperplasia and provide a novel therapeutic target in the future.

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What were the subjects in the study?	**ANIMAL**
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	**Yes**
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