YW1-09 Correlation between major histocompatibility complex class I (MHC-class I) molecules and CD8⁺ T lymphocytes and the effect of IFN-gamma on MHC-class I expression in prostate

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A better understanding of the immunology of prostate cancer is critical for developing immunotherapy against the disease. Increasing evidences suggest that the control of cancer growth is mediated by the interaction between growth-stimulatory and growth-inhibitory factors, which are released from either the cancer cells or tumor-infiltrating lymphocytes (TILs).

In the present study, we located CD8⁺ lymphocytes and assessed the correlation between the distribution of CD8⁺ lymphocytes and MHC class I expression in both benign and malignant prostates by immunohistochemical analysis. Secondary, the effect of IFN-gamma to the MHC-class I expression on prostate carcinoma was investigated using FCM.

There were significantly fewer CD8⁺ T lymphocytes in prostate carcinoma nests than in benign prostate. A significant correlation between the number of CD8⁺ T lymphocytes and MHC-class I expression in the prostate was revealed.

IFN-gamma stimulation could up-regulate MHC-class I expression on prostate cancer cells.

Reduced expression of MHC-class I was thought as one of the factor which is related to the reduced degree of TILs in prostate cancer. IFN-gamma which is secreted mainly from CTL (cytotoxic T lymphocytes) might increase the degree of TILs through up-regulated MHC-class I.

YW1-10 ¹⁸F-FLUOROTHYIMIDINE FOR MONITORING PROSTATE TUMOR RESPONSE TO THERAPY IN VITRO AND IN VIVO WITH PET

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¹⁸F-3'-deoxy-3'-fluorothymidine (FLT) has been recently described as a radiopharmaceutical for measuring cellular proliferation using PET imaging. This study was undertaken to determine whether the change of FLT uptake in tumor after initiation of androgen ablation therapy was correlated with the change of actual proliferative activity of the tumor cells determined by flowcytometric and immunohistochemical method. LAPC-4 cells were implanted in nude mice. Before and after the castration, the mice were imaged in a microPET scanner. The tumors were immunohistochemically assayed for proliferation (PCNA) and apoptosis (TUNEL). For cell study, LNCaP cells were treated FBS media with different concentration of dihydrotestosterone (DHT). The cells were incubated with FLT or FDG. MicroPET showed significant difference in FLT uptake in tumors between before and after castration. The changes of FLT uptake well correlated with those of cell proliferation. In vitro studies demonstrated that decrease of FLT uptake after incubation with low concentration of DHT correlated with the percentage of cells in S-phase fraction, while did not correlate with the number of apoptotic cells. These results indicate that FLT-microPET has a potential to visualize early-phase changes in proliferation activity of androgen dependent prostate cancer.

YW1-11 Retinoic acid in the male accessory sex organs

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Retinoids, analogs of vitamin A, play an essential role in epithelial proliferation and differentiation in a variety of tissues, including male accessory sex organs. In cancer cells, because retinoids induce terminal differentiation, they have been recognized as agents which could suppress tumorigenesis. Based upon the effects of retinoids in other systems, it would be expected that retinoids might affect development of male accessory sex organs and have a possibility of prostate cancer treatment. The actions of retinoids are mediated through nuclear retinoid receptor proteins that are members of the steroid/thyroid hormone superfamily of ligand-dependent transcription factors. Then, we examined the effects of retinoids on development of the organs *in vitro* and *in vivo*. Furthermore, we show the expression of retinoic acid receptor (RAR) proteins and mRNAs in the organs. We also mention the expression of RAR proteins and transcripts in human prostates, and the function of RARs in normal and cancerous prostates *in vivo*. The results indicate that retinoids reversibly inhibit androgen-dependent development of the organs, dose- or organ-dependently, both *in vitro* and *in vivo*. It would be mediated most likely through RARs. We show the expression of the proteins and transcripts in human prostates, too. The findings suggest that prostate cancer is a potential target of topical or systematic treatment with retinoids.

YW1-12 Possible involvement of reactive oxygen species in heat-induced germ cell apoptosis of testis

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Spermatogenic cells undergo apoptosis by various stimuli including heat stress. Since a mechanism of the heat stress-induced apoptosis in testicular cells is not fully understood, we investigated the apoptotic process *in vivo* and *in vitro* by heat stress. When lower abdomen of mice was immersed in hot water at 42°C for 15 min, cytochrome c (Cyt c) release from mitochondria to cytoplasm occurred within 45 min and DNA fragmentation, as judged by TUNEL staining, was observed within 3 hr in spermatogenic cells. Similarly, the Cyt c release was detected in spermatogenic cells that were isolated from rat and incubated at 42°C for 1 hr. Blockade of the Cyt c release by minocycline effectively suppressed the DNA fragmentation both *in vivo* and *in vitro*. Thus, the released Cyt c is responsible for apoptosis, and mitochondria are suspected to be a target organelle of the heat stress. Since tiron, a superoxide scavenger, suppressed the Cyt c release in culture, reactive oxygen species (ROS) would be responsible for the germ cell apoptosis. Among sources of ROS, mitochondrial respiratory chain would be a strong candidate because elevated temperature enhances metabolic use of oxygen molecule. (Supported by JSPS)