Organ Specific *Gst-pi* Expression in New Metastatic Androgen-Independent Prostate Cancer Animal Model

Introduction and Objective: Elucidating the mechanisms of metastasis in prostate cancer, particularly to the bone, is a major issue for treatment of this malignancy. We previously reported that an androgen-independent variant had higher expression of glutathione S-transferase pi (*Gst-pi*) compared with a parent androgen-dependent transplantable rat prostate carcinoma which was established from the transgenic rat for adenocarcinoma of the prostate (TRAP).
Materials and Methods: A new cell line, PCai1, was established from the androgen-independent prostate tumor and used to investigate its metastatic potential in nude mice. PCai1 had strong expression of *Gst-pi* as well as androgen-independent prostate tumor, therefore we knocked-down *Gst-pi* in PCai1 by iRNA strategy to examine the roles of *Gst-pi* on androgen-independency, cell proliferation, and oxidative stress.
Results: It was clearly demonstrated that PCai1 frequently formed metastatic lesions in the lung and lymph nodes after orthotopic implantation in the prostate, and in the lung and bone after intravenous injections. Immunohistochemically, *Gst-pi* expressions were demonstrated in prostate tumors derived from orthotopically implanted PCai1 cells, and metastasis to bone resulting from tail vein injections, but not in lung and lymph nodes. Attenuation of *Gst-pi* expression by *Gst-pi*-siRNA *in vitro* significantly suppressed cell proliferation rate and increased levels of intracellular reactive oxygen species (ROS) in androgen depleted condition.
Conclusions: These results suggest that *Gst-pi* has an important role in adapting prostate cancer for growth and metastasis involving an alteration of ROS signaling, and that *Gst-pi* expressions of the prostate cancers are dependent on metastatic sites.