



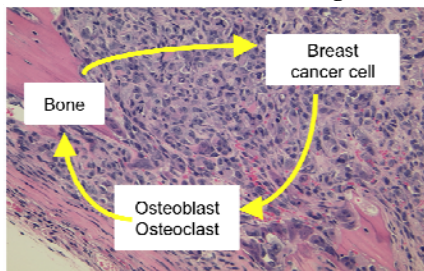
Title of Project : Integrative Research on Cancer Microenvironment Network

Term of Project : FY2010-2014

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【Purpose of the Research Project】

In 1889, Stephen Paget proposed the seed and soil hypothesis for the mechanism of cancer metastasis, in which he described the biological importance of cancer cells (“seed”) and appropriate microenvironment (“soil”) for cancer metastasis. Since then, critical roles of cancer microenvironment (CME) in the progression of cancer have been reported by numerous investigators. Growth, invasion, and metastasis of cancer are often regulated by the action of CME; however, integrated studies on CME from different aspects have not been conducted in Japan. In this research project, researchers on various scientific backgrounds will join in the program, and study various aspects of CME.



【Content of the Research Project】

Dynamism of CME: CME is not static. Characteristics of CME may dramatically change during the progression of cancer. We will study the genetic and epigenetic changes of CME during the progression of cancer, using latest genome research technologies. Also, using biomaterial technologies, we will generate artificial CME, and study the interaction of cancer cells and CME.

Cancer Stem Cells and CME: Cancer Stem cells have self-renewal activity as well as the ability to differentiate into their daughter cells, and show resistance to conventional chemotherapy and radiotherapy. In this project, we will study the mechanisms of maintenance of stemness of cancer stem cells from various types of cancer, and investigate the functional relation to CME.

Novel Approach to Angiogenesis and Lymphangiogenesis: Angiogenesis and lymphangiogenesis play pivotal roles in

invasion and metastasis of cancer. Cancer treatment targeting VEGF has already been established; however, new strategies for therapy targeting other angiogenic factors may be needed. In this project, we will study the roles of tumor angiogenesis and lymphangiogenesis, focusing on some angiogenic inhibitors, transcription factors, and plasmin proteolytic factors.

Mechanisms of Metastasis and Molecular Target Therapies: We will isolate novel metastasis-related genes using a spontaneous cancer metastasis model using mice. We will also investigate responses to hypoxia in tumor tissues using bioimaging techniques, and establish a new strategy for treatment of cancer. In addition, we will study the phenotypic change of CME cells during the acquirement of resistance to chemotherapy using human lung cancer cells, and develop a new method for regulation of resistance to chemotherapy.

These studies will be carried out in close collaboration with the “Scientific Support Programs for Cancer Research”, Grant-in-Aid for Scientific Research on Innovative Areas, MEXT.

【Expected Research Achievements】

Findings obtained by the project will be useful for development of the strategies for novel cancer therapy targeting CME and cancer stem cells. They will also be valuable for understanding the roles of microenvironment of normal tissues in morphogenesis during development.

【Key Words】

Cancer microenvironment, cancer stem cell, angiogenesis and lymphangiogenesis, invasion and metastasis

【Homepage Address】

<http://cancer-microenvironment.jp/>