



# Regulation and molecular analysis of cancer stem cells in the tumor

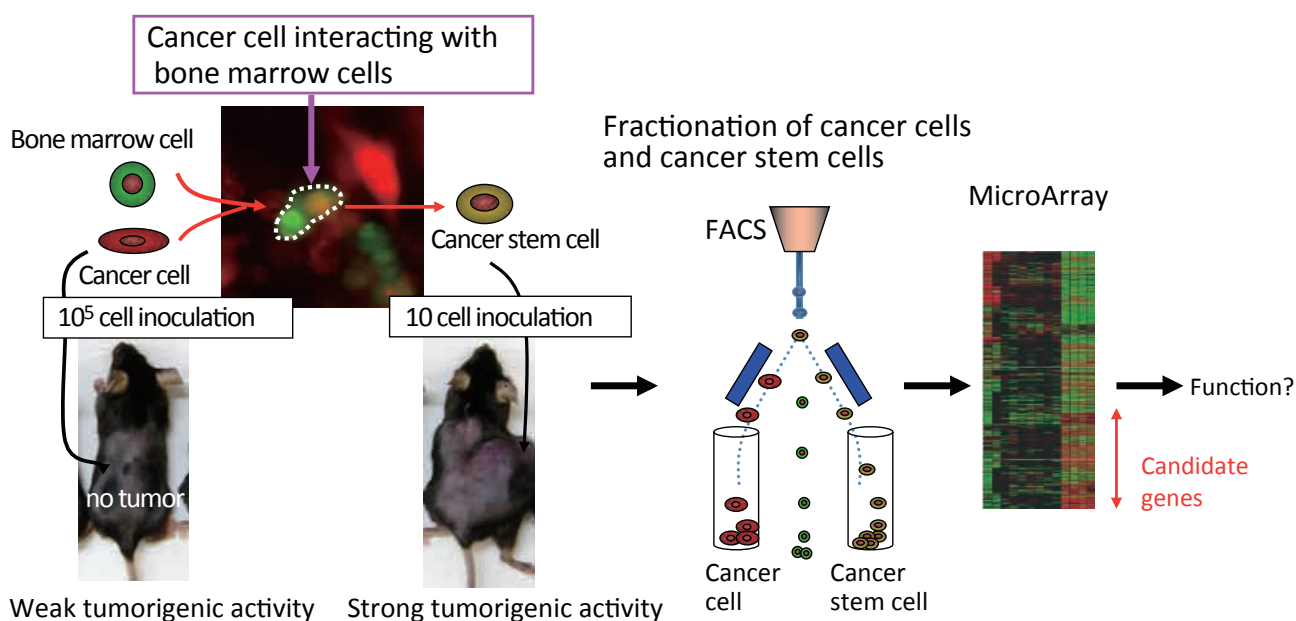
## Outline

Cancer stem/initiating cells (CSCs/CICs), which show resistance against anti-cancer drugs and irradiation and are responsible for tumor growth, have been implicated in hematological and solid cancers. Identification of these cells and their niche is critical for elucidating molecular targets to inhibit their growth and to destroy their niche. For this purpose, sorting of living CSCs/CICs is required to monitor their presence in the presumptive niche in order to establish whether a CSC candidate actually shows malignant features. We will visualize CSCs by using specific molecules expressed on CSCs and will obtain a method to destroy CSC niche.

## Expected Outcome

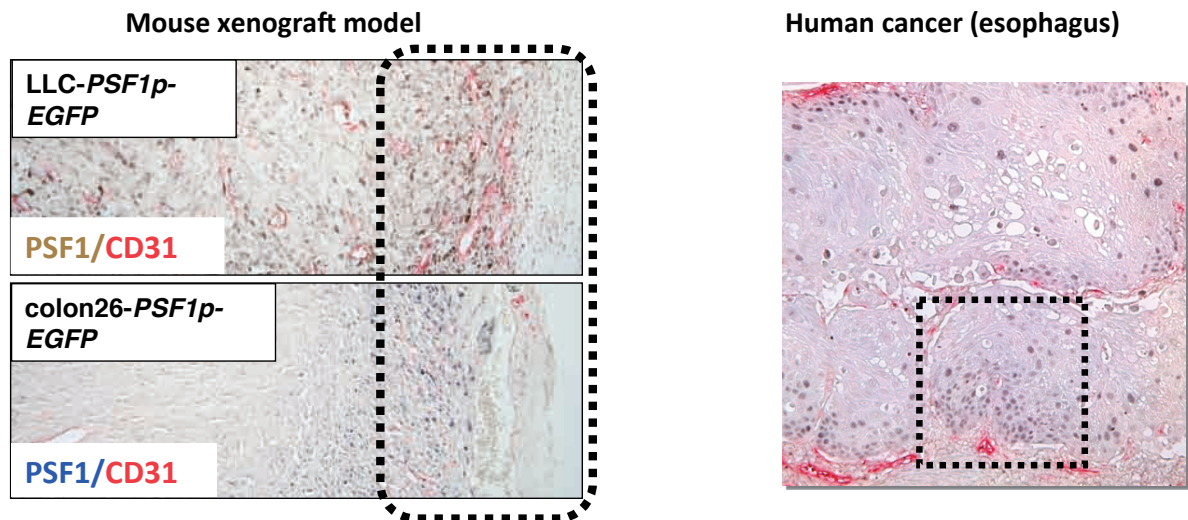
It has been indicated that proliferation of CSCs is induced around blood vessels and has been expected the effect of anti-angiogenic drugs for destroying vascular niche for CSCs. However, present strategy using such drugs has difficulties in destroying it because blood vessels are already matured in vascular niche. Our studies will be able to visualize CSCs exactly and develop a new strategy to destroy vascular niche based on the molecular analysis of vascular niche formation, resulted in obtaining a treatment which is sure to effect a cure.

## Profiling and functional analysis of genes associating with induction of cancer stem cells



By the interaction with bone marrow cells, cancer cells change their character into more aggressive ones like cancer stem cells. We have isolated several genes from cancer stem cells affected by this interaction. We will analyze the function of those genes to get more information of generation of cancer stem cells.

## Visualization of cancer stem cells by using DNA replication factors, GINS component

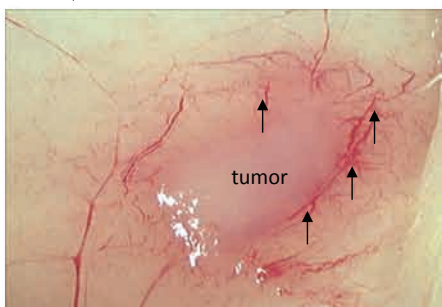


We succeeded in detection of cancer stem cell population by visualizing PSF1, a member of GINS component regulating DNA replication, in cancer. Cancer stem cells are self-renewing in the perivascular region of tumor edge. We will further analyze the cancer stem cells niche in tumor precisely by using other GINS component.

## Disruption of cancer stem cell niche

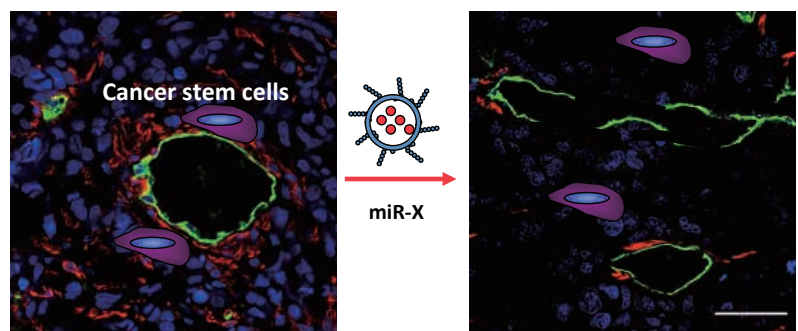


Injection of angiogenesis inhibitor



Remaining mature blood vessels (↑)

Disruption of tube formation in blood vessels



Blood vessels supporting stemness of cancer stem cells are mature ones and show resistance against present angiogenesis inhibitors. We isolated microRNA that can inhibit translation of VE-cadherin involved in tube formation of endothelial cells and have developed methods to disrupt vascular niche by using this microRNA.