Department of Cell Fate Dynamics and Therapeutics

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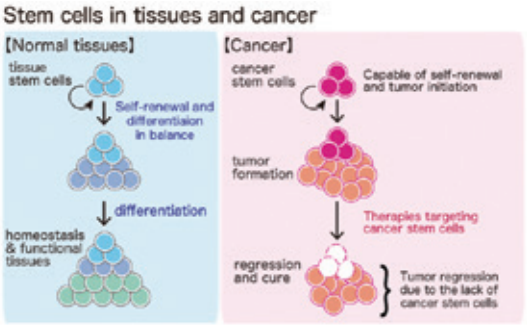
Research Projects:

What determines how stem cells and cancer behave?

My laboratory studies the molecular basis of cell fate regulation in normal and malignant stem cells. We are currently investigating several pathways of hematopoiesis and skeletal muscle systems in mice and human. Stem cells have a remarkable ability to propagate themselves, which is called "self-renewal". It allows tissue regeneration and repair after injury. But this ability is a double-edged sword; the same mechanism of self-renewal can be a target of malignant transformation and lead to cancer development. In the past decades, we have learned a great deal about the mechanisms of cancer-causing transformation, and yet finding effective ways to eradicate cancer cells has remained an elusive goal in many types of cancers. This is partly because tumors are often complex and heterogeneous mixtures of neoplastic cells with different self-renewal and differentiation abilities. Unlike many differentiated cells within a tumor, some cancer cells are capable of self-renewal. These self-renewing cancer cells, or cancer stem cells, are therapy-resistant and can drive tumor relapse and metastasis following treatment cessation. Recent studies, including our own work, suggest that the normal and malignant stem cells operate on cell fate regulatory signals that are common or specific to each population.

The primary goal of our research is to understand the molecular basis of self-renewal and differentiation in stem cells and cancer, i.e. cell fates. Specifically, we study hematopoiesis and myogenesis to identify cellular machinery that regulates tissue homeostasis and regeneration as well as molecular drivers of transformation that lead to human malignancies such as leukemia. We are particularly interested in the stem cell regulatory circuits governed by RNA binding proteins and cellular metabolism. Recent studies from our lab and others have demonstrated that understanding molecular machineries operating in stem cells and cancer could help us to develop new effective approaches to treat human diseases including cancers. Our research program seeks to improve our understanding of stem cell and cancer biology, and to apply this knowledge to the development of novel and effective approaches to treat human disease and cancer.



Recent publications

- Hattori A *et al.*, Cancer progression by reprogrammed BCAA metabolism in myeloid leukemia. ***Nature*** 545:500-504 (2017).
- Hattori A *et al.*, RNA binding protein MSI2 positively regulates FLT3 expression in myeloid leukemia. ***Leuk Res*** 54:47-54 (2017).
- Hattori A *et al.*, Regulation of stem cell self-renewal and oncogenesis by RNA-binding proteins. ***Adv Exp Med Biol*** 907:153-88 (2016).
- Fox RG *et al.*, Image-based detection and targeting of therapy resistance in pancreatic adenocarcinoma. ***Nature*** 534:407-11 (2016).
- Zimdahl B, Ito T, *et al.* Lis1 regulates asymmetric division in hematopoietic stem cells and in leukemia. ***Nat Genet*** 46:245-52 (2014).