Mechanisms of chemotherapy resistance in human acute myelogenous leukemia (AML) stem cells

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【Outline of survey】

Acute myelogenous leukemia (AML) is one of the most common and intractable adult hematological malignancies that exhibits high relapse rate even following successful remission induction and hematopoietic stem cell transplantation. We have recently identified leukemic stem cells in AML that can self-renew, generate non-stem leukemic cells, and possess exclusive capacity to initiate leukemia in vivo. Transplantation of AML stem cells into NOD/SCID/IL2rgKO newborns successfully recapitulates human AML, which enables us to identify the role of leukemic stem cells in leukemogenesis and relapse. We aim to clarify the mechanisms of drug resistance underlying leukemia relapse by cell biological and global transcriptome analyses, with the ultimate goal of translating thus obtained research findings to the creation of novel therapeutic strategies for leukemia.

【Expected results】

The direct in vivo examination of stem cell properties such as stem-niche interaction, cell cycle quiescence, and drug efflux capacity as well as global gene expression profiling of leukemic stem cells enable us to identify the stem cell specific molecules and to develop therapeutic strategies to overcome AML relapse.

【References by the principal investigator】

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- Shultz LD, Ishikawa F, Greiner DL. Humanized mice in translational biomedical research. ***Nature Reviews Immunol*** , 7:118-130, 2007.
- Ishikawa F, et al. Development of functional human blood and immune systems in NOD/SCID/IL2rg chain null mice. ***Blood*** 106:1565-1573, 2005.

【Term of project】 FY2008－2012	【Budget allocation】 **65,700,000 yen** (direct cost)

【Homepage address】 http://web.rcai.riken.jp/en/labo/human/index.html