

FUNDING PROGRAM FOR NEXT GENERATION WORLD-LEADING RESEARCHERS

Project Title: Creating therapeutic strategies targeting chemotherapy-resistant acute myeloid leukemia stem cells

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1. Background of research

Acute myeloid leukemia (AML) is a hematological malignancy common in adults. Development of various chemotherapeutic agents have allowed many AML patients to achieve complete remission. However, AML patients with poor prognostic factors experience relapse. It is essential to understand why relapse occurs in AML patients to improve clinical outcomes.

2. Research objectives

We therefore aim to identify human AML cells that are resistant to conventional therapy and are responsible for relapse. Through investigation of chemotherapy-resistant human AML cells, we further aim to identify therapeutic targets expressed by chemotherapy-resistant AML cells for future drug development.

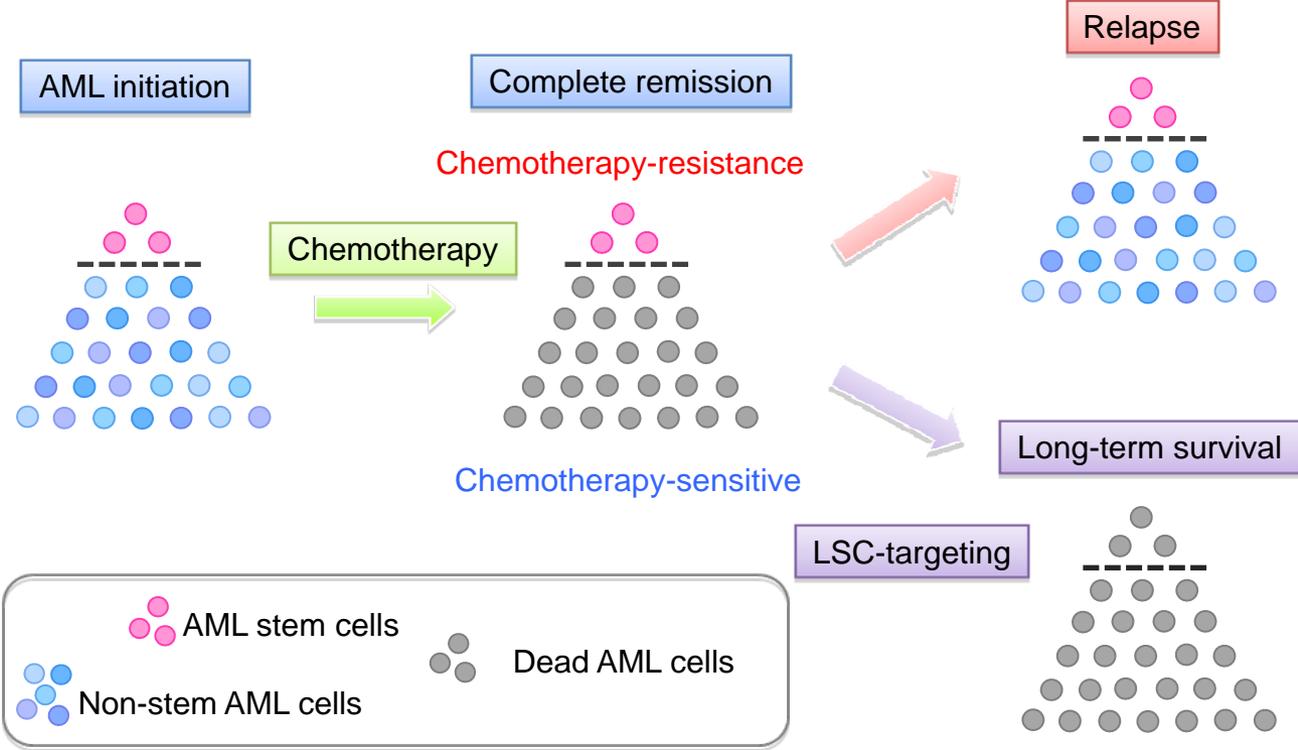
3. Research characteristics (incl. originality and creativity)

In vivo investigation into biology of human diseases has been difficult. In vivo reconstitution of normal human hematopoiesis and immunity and recapitulation of human leukemia in our mouse models help overcome limitations associated with human research. In particular, by creating in vivo therapeutic models, direct assessment of the location, cellular properties and drug resistance of human AML cells has become possible.

4. Anticipated effects and future applications of research

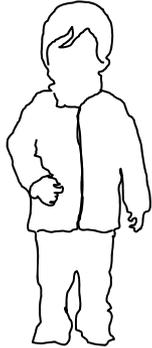
By directly investigating AML stem cells present in patient-derived samples, we anticipate our findings can potentially lead to development of antibody drugs, small molecule inhibitors and immune-therapy. Building upon the successes of current treatments for AML, we seek to overcome relapse and to achieve long-term survival in AML patients by eliminating chemotherapy-resistant AML stem cells.

AML stem cells exhibit chemotherapy-resistance and possibly cause relapse



Humanized mouse model recapitulating human acute myeloid leukemia

Patient

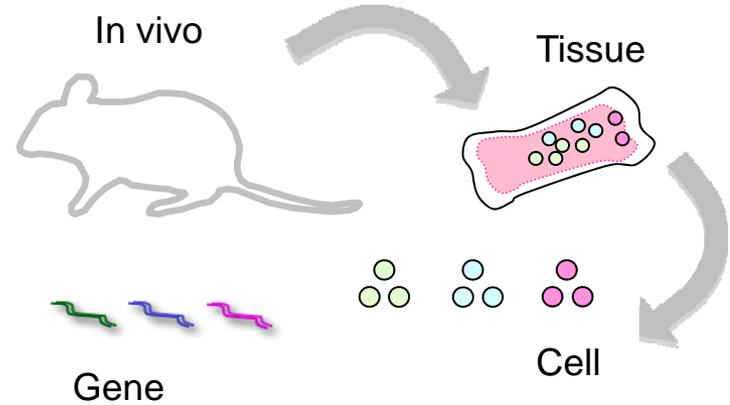


Recapitulating AML



Translation into medicine

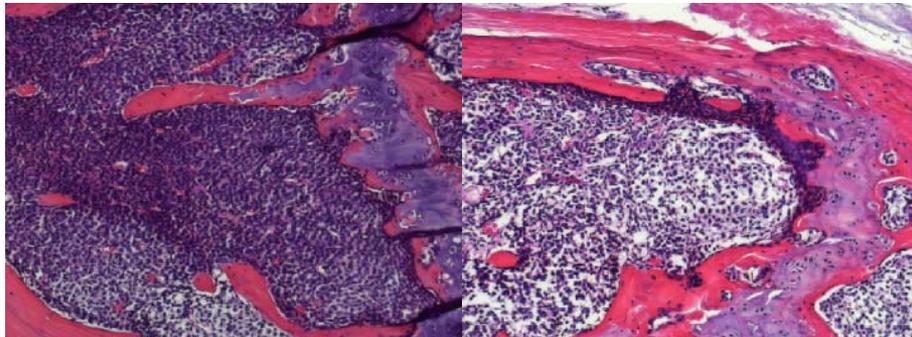
Understanding human AML



Location of chemotherapy-resistant AML cells

Therapy (-)

Therapy (+)



Targeting stem-niche interaction

Steady state

Cytokine(+)

