第 430 回つくば分子生命科学セミナー

TSUKUBA MOLECULAR LIFE SCIENCE SEMINAR

Title : Generation of human T cell acute lymphoblastic leukemia by de novo transformation of human cord blood progenitors with a 4-oncogene cocktail.

Speaker : Dr. Manabu Kusakabe

Postdoctoral fellow at Terry Fox Laboratory, British Columbia Cancer Agency, Vancouver, Canada

Data : October 18, 2016　17:00-18:30

Venue : Seminar Room 483 (Igakukei-tou 4th floor)

Abstract :

T-cell acute lymphoblastic leukemia (T-ALL) is an aggressive form of blood cancer that affects both children and adults. Numerous studies have explored the effects of putative T-ALL oncogenes in mouse models and have contributed to our understanding of disease pathogenesis. Nonetheless, it is clear there are important differences between mouse and human cells, particularly with respect to cellular transformation. In this study, we sought to create human T-ALL in the lab from normal cord blood (CB) progenitors by lentiviral transduction with a combination of known T-ALL oncogenes. Transduced cells were cultured on OP9-DL1 stromal feeders to study their behaviour in vitro. Also, we performed transplantation into NOD/SCID-IL2Rg-null (NSG) mice to assess leukemogenesis in vivo. Non-transduced cells stopped expanding within the first few weeks, however T-ALL oncogenes transduced cells continue to expand for over 60 days in vitro. The recipients of T-ALL oncogene transduced cell developed clinically morbid disease and showed splenomegaly, lymphadenopathy, and enlarged thymus. Transduced cells were infiltrated into these organs and expressed CD2, CD3, CD7 and CD38 supporting acute T-cell leukemia. Importantly, these cells were serially transplantable into NSG mice. Our *in vitro* and *in vivo* results suggest that the 4 T-ALL oncogenes are sufficient to transform normal human blood cells into clonal T-ALL-like malignant cells. This model provides a significant step forward to reveal the mechanisms involved in human T-ALL pathogenesis.

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