Establishment of CML mouse model to examine the interactive role of normal hematopoietic system on the pathophysiology

Tomohisa Baba

Division of Molecular Bioregulation, Cancer Research Institute
Kanazawa University
Kakuma-machi, Kanazawa 920-1192, Japan

Chronic myeloid leukemia (CML) is a clonal myeloproliferative disorder resulting from the neoplastic transformation of hematopoietic stem cells (HSCs). This disease consists of triphasic process, a chronic phase, an accelerated phase, and a terminal blast crisis. More than 90 % of all CML cases are associated with the presence of the Philadelphia chromosome. This chromosome results from a reciprocal translocation between chromosomes 9 and 22, and forms the breakpoint cluster region with a constitutively activated tyrosine kinase, BCR-ABL fusion protein, the protein which is a pathogenic molecule in CML. Murine CML-like myeloproliferative disease can be induced by transferring primitive bone marrow (BM) cells, which are transduced with human-derived BCR-ABL oncogene, to lethally irradiated host. This experimental model has been generally used for the analysis of CML pathophysiology. However, in this model, when intravenously injected, donor BCR-ABL$^+$ leukemic cells home to devastating BM to grow and develop CML, because lethal irradiation breaks down completely normal hematopoietic system. Thus, this model is not helpful to elucidate the role of normal hematopoietic system in CML pathophysiology, especially in its initiation phase, when a small number of leukemia cells co-exist with normal hematopoietic cells in BM. In this study, we have succeeded in causing a marked leukocytosis resembling CML, in non-irradiated and BM-preserved host by direct transplantation of BCR-ABL$^+$ leukemic progenitor cells into BM cavity. This novel model will be useful to clarify the interaction between normal hematopoietic system and leukemic cells, particularly in the early phase of CML development.

EDUCATIONS AND POSITIONS

2003	Graduate School of Veterinary Medicine, Rakuno Gakuen University (DVM)
2003-2006	Doctoral Course, Department of Pathology/Pathophysiology, Hokkaido University (PhD)
2006-2007	Postdoc, Department of Pathology/Pathophysiology, Hokkaido University
2007-	Assistant Professor, Division of Molecular Bioregulation, Cancer Research Institute, Kanazawa University