#29: Autophagy facilitates malignant transformation but not progression of acute myeloid leukemia in an MLL-AF9-driven mouse model

Qiang Liu, Longgui Chen, David F. Claxton, Hong-Gang Wang

Acute myeloid leukemia (AML) is a hierarchical hematopoietic malignancy originating from leukemic stem cells (LSCs). Autophagy is a lysosomal degradation pathway that is hypothesized to be important for the maintenance of AML as well as contribute to chemotherapy response. Here, we employ a mouse model of AML expressing the fusion oncogene MLL-AF9 and explore the effects of Atg5 deletion, a key autophagy protein, on the malignant transformation and progression of AML. The in vivo deletion of Atg5 during primary transplantation delayed the malignant transformation of MLL-AF9-transduced bone marrow cells to AML. However, Atg5 deletion in transformed AML cells during secondary transplantation did not affect the survival of leukemic mice. Surprisingly, deletion of Atg5 in malignant AML did not affect chemotherapy response or LSC viability. In contrast, autophagy was found to be involved in the survival of differentiated myeloid cells originating from MLL-AF9-driven LSCs. Taken together, our data suggests that autophagy contributes to MLL-AF9-driven malignant transformation of hematopoietic progenitors but is dispensable for the maintenance of LSCs.