Characterization of a zebrafish model of MYC-driven acute myeloid leukemia

Anna M. Luciano1,2,3, Juan-Francisco Rodríguez-Vidal1,2,3, Alba Jiménez-Blaya1,2,3, Miriam Fernández-Lajarín1,2,3,4, María L. Cayuela2,3,4, Diana García-Moreno2,3, Victoriano Mulero1,2,3

INTRODUCTION

Acute myeloid leukemia (AML) is a clonal malignancy of the stem cell precursors of the myeloid lineage associated with uncontrolled proliferation and impaired differentiation of hematopoietic stem and progenitor cells. The main causes are genetic and epigenetic changes that lead to neoplastic changes and clonal proliferation. Among the different genes found amplified in AML, the oncogene MYC is one of the prognostic factors with an impact of AML and several type of cancer. Albeit MYC is a well known factor associated with the uncontrolled proliferation of AML, the mechanism that led to the oncogenesis established by MYC are not well known. In the last years zebrafish has emerged as an attractive model organism for studying cancer development because of its genetic accessibility.

RESULTS: HsMYC fish reflects patient with poor prognosis and early death

A) Kaplan–Meier representation of the survival of WT and Lyz:HsMYC transgenic line, underlying the poor prognosis of the transgenic line Lyz:HsMYC
B) IVIS acquisition of WT and Lyz:HsMYC. This image reveals the infiltration of HMYC positive cells into different organs

RESULTS: HsMYC fish exhibit a similar hematopoietic population to AML patients

A) Representative flow cytometry density plots of WKM or WT and Lyz:HsMYC suspensions. B) Percentages of each cell population in WT and Lyz:HsMYC. A significant reduction of erythroid cells and an increase of the myeloid can be observed

RESULTS: HsMYC fish exhibit immune cell proliferation and infiltration into specific organs

A) IHC staining of kidney and liver with L-plastin and mpx antibody on paraffin section of Lys: HsMYC revealed infiltration of immune cells both in the liver and in the kidney. B) qPCR analysis of human(Hs_MYC) and endogenous myc (Zf_myc) in liver and kidney.

RESULTS: Gut microbiota analysis revealed a similar pattern of HsMYC fish with AML patients

A) IHC staining of gut with anti L-plastin antibody on paraffin section of WT and Lys: HsMYC fish revealed a complete disruption of the intestinal villi in the transgenic line overexpressing HsMYC
B) Pie charts showing the bacterial relative abundance at the phyla level, confirming relevant data obtained in patients with AML

CONCLUSION

The model developed here is an excellent tool to further understand the mechanisms involved in MYC-induced AML and the relevance of the gut microbiota on this disease.