1. Record Nr. TD18003119

Autore	DE CONTI, GIULIA
Titolo	IN VIVO SHRNA SCREENING TO IDENTIFY QUIESCENCE-RELATED GENES REQUIRED FOR AML GROWTH [Tesi di dottorato]
Editore	Università degli Studi di Milano, 2018-03-26
Lingua di pubblicazione	Inglese
Formato	Tesi di dottorato
Livello bibliografico	Monografia
Note	diritti: info:eu-repo/semantics/openAccess In relazione con info:eu-repo/semantics/altIdentifier/hdl/2434/556139
Sommario	AML is hierarchically organized with at the apex Leukemia Stem Cells (LSCs), a rare cell population able to initiate and sustain the tumor growth. LSCs share many functional properties with normal Hematopoietic Stem Cells (HSCs) including self-renewal capacity and quiescence. Quiescent LSCs can survive to radiation and chemotherapy acting as a reservoir for leukemia relapse, the major cause of death for AML patients. Therefore, LSCs quiescence is critical for leukemia maintenance and few evidences suggest that quiescence regulation in pre-leukemic phase plays a pivotal role for leukemogenic process as well. In this work, we demonstrated that the expression of NPMc+ or PML-RAR? in HSCs is sufficient to enforce a quiescent stem cell gene expression profile. Therefore, we hypothesized that enhancement of the quiescent phenotype in HSCs could be a shared mechanism for leukemia development and maintenance. As an approach to examine the contribution of representative quiescence related genes in AML, we exploited RNA interference technology to perform in vivo screening. Among the target genes we found depleted during the screening, silencing of Stat1 or Sytl4 in AML blasts was sufficient to significantly decrease in vitro self-renewal and delay leukemia growth in vivo.