1040 / 13 - Patient derived xenografts of hematologic malignancies for translational research

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Presenter/Authors

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Abstract

Acute leukemias and lymphomas represent a very heterogeneous group of hematologic malignancies and pose an important challenge in the clinical routine. They frequently develop resistance to the treatment with standard-of-care (SoC) drugs and have a high incidence of disease recurrence. Recent progress in molecular profiling has helped to identify new potential drivers for the different leukemia and lymphoma subtypes, with some of them being potential therapeutic targets. Further target validation and drug development projects are highly dependent on corresponding preclinical models representing the different clinical subtypes. Therefore, we started to establish and characterize new patient derived xenografts (PDX) of AML, ALL and lymphomas for drug development and translational research.

AML- and ALL-PDX were derived from bone marrow aspirates or peripheral blood samples, from primary or relapsed acute leukemia patients. Purified cells were transplanted either intravenously (i.v.) and/or subcutaneously (s.c.) into immunodeficient mice. Some mice developed a systemic AML, which was monitored by flow cytometric analysis of blood samples. Non-Hodgkin- or Hodgkin lymphoma-PDX were derived from peripheral blood, lymph node extirpations or core needle biopsies, and were usually transplanted subcutaneously into immunodeficient mice.

For further characterization, established PDX models were treated with SoC and investigational drugs. In parallel, gene expression profiles as well as mutations were analyzed within the first in vivo passages.

More than 20 new PDX models from AML, ALL, NHL and HL have been successfully established and characterized. Highly individual response to the treatments were observed, correlation analyses with mutations and gene expression are ongoing.

Our newly and extensively characterized PDX models from hematologic malignancies are suitable tools for preclinical drug development. They provide an exceptional platform for the identification and validation of new targets and allow the preclinical screening of new compounds and combinations for translational research projects.