CANCER RESEARCH

Tumor Biology

Abstract 1914: Acute myeloid leukemia cell and stem-progenitor cell behavior studied in mimetic bone marrow microenvironment

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Abstract

The bone marrow (BM) microenvironment plays a pivotal role in the survival and chemoresistance of leukemia stem cells (LSC) in acute myeloid leukemia (AML). However, conventional culture approaches do not reflect physiological conditions of crucial anatomical districts and signals of incubation-induced dysregulation may confound leukemic transcriptome results. *In vivo mimetic* cultures of the LSC districts will significantly aid in the disentanglement of LSC mechanisms and in the assessment of the therapy. We engineered Petri dishes able to mimic the “hypoxic” conditions found in the stem cell niches and in BM district. Our approach is based on a patented method which controls the physiological concentrations of oxygen, glucose and pH in the culture

apoptosis in the engineered device were investigated for OCI-AML3 and KG1 AML cell lines. We observed a slight but significant reduction in cell proliferation compared with control cells for OCI AML-3, which is in line with a more quiescent cell condition. No significant differences were obtained by culturing KG-1 cells, which are more resistant to low oxygen concentrations. We have analyzed the effects of cell culturing in the hypoxic dishes on the expression of MYC and p21. Immunofluorescence analysis of HIF-1α levels and HIF-1α nuclear localization as a function of oxygen concentration were determined. Time-lapse experiments of AML cell lines and primary BM cells were performed in the *in vivo mimetic* device to elucidate the response of $CD34^+$ AML cells to different oxygen concentrations. We tested an innovative cell culturing device able to mimic the dynamical conditions of oxygen content, which are found *in vivo*. Our results shed light on AML cells and progenitor-stem cells behavior in response to oxygen conditions in the BM niche and allow to disentangle the LSCs complex biology. This "*in vivo mimetic*" approach will generate crucial information on the molecular mechanisms preserving LSC in AML, thus providing novel potential therapeutic targets to eradicate leukemia initiating cells in their own microenvironment, contrasting therapy resistance.

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