Oral presentations

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Assessment of hematopoietic stem cells in norma and pathology in cell culture *in vitro* and *in vivo*

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Background. Chronic myeloid leukemia (CML), originated from leukemia stem cell, was the first oncological disease whose cause was clearly associated with the target molecule, tyrosine kinase BCR-ABL. This led to the discovery of targeted drugs – tyrosine kinase inhibitors (TICs), which provide selective action only on cells of the leukemic clone. Identification of the effectiveness of targeted therapy drugs criteria for leukemic clone cells in chronic myeloid leukemia is a current issue of modern hematology, cell biology and medicine. It was established that cells of leukemic clone are capable of differentiating into hematopoietic cells, including erythroid lineage. However, there is a large number of controversial data regarding the role of the erythroid progenitor cells in the pathogenesis of CML.

Aim. The aim of the current study was to to determine the role of erythroid lineage of differentiation side by side with granulocyte-macrophage progenitor cell in the mechanism of resistance for TICs therapy.

Methods. Hematopoietic progenitor cells obtained from bone marrow of 32 patients with CML were studied in semisolid agar culture *in vitro* and *in vivo* (in diffusion chambers). Cultured cells were analyzed regarding their phenotypes and functions using flow cytometry, colony-forming unit (CFU) assay and long-term culture-initiating cells (LTC-IC) assay.

Results. With the application of the original model for determination of hematopoietic progenitor cells in gel diffusion chambers *in vivo*, the influence of soluble microenvironment factors on the erythroid progenitor cells in CML was detected. Correlative relationship was found between the number of erythroid colonies and the number of leukemic cells in the patient's bone marrow. It was established that the acquisition of resistance by leukemic clone cells to TKI is characterized by increased proliferative activity and insensitivity to the presence or absence of soluble microenvironmental factors, granulocyte-macrophage colony stimulating factor and erythropoietin in the culture medium.

Conclusion. The role of erythroid lineage of hematopoiesis in the mechanism of leukaemia process was shown. It was proved that prognostic value of patient's bone marrow cells functional activity is comparable with a recognized prognostic factor – Sokal index.

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