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Superoxide- and NO-dependent mechanisms of the reprogramming of bone marrow cells by tumor cells

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Abstract

© Springer-Verlag Wien 2014. Electron paramagnetic resonance (EPR) experiments in vitro; spin trapping of the reactive oxygen/nitrogen species (superoxide radicals and nitric oxide, NO); gel zymography measurements in the tumor tissues, in the healthy and tumor-affected bone marrow (BM) samples of rats are carried out. The superoxide and NO generation rates are derived; matrix metalloproteinases (MMP-2 and MMP-9) concentrations are measured. Their changes after the incubation of BM samples with Guérin carcinoma cells at 37 °C are defined. It is shown that the impact of tumor cells on BM manifests in the metabolic disorder, increased concentrations of active forms of MMP-2 and MMP-9, increased production of superoxide and NO radicals. Correlation between the appearance and intensity of the broad EPR signal at $g = 2.2-2.4$ with the concentrations of active forms of MMP-2 and MMP-9, NO and superoxide radicals' rates is observed. The obtained spatial and temporal changes of the measured parameters demonstrate the usefulness of the potential application of EPR imaging to study the mechanisms of tumor invasion. The EPR signal may indicate the presence of distant metastases, may become a part of diagnostics and used for the estimation of the therapeutic treatments in the preclinical studies. It is proposed that labile iron pool is responsible for the appearance of the EPR signal in tumor and BM samples.

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