



## Redox Status of a Metastatic Microenvironment in the Liver of Patients with Colorectal Cancer from EPR

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### Abstract

Colorectal cancer is the third most common cancer with the predominant metastases (Mts) into the liver. Metastases, tissues adjacent to Mts (AMT) and remote tissues (RMT, taken at the distance of 5 cm from Mts) from 25 patients with metachronous liver Mts after the liver resection as well as blood and urine were studied by electron paramagnetic resonance (EPR) including the spin-trapping EPR for the detection and quantification of the activity of N<sub>2</sub> iron-sulfur proteins, levels of NO-N<sub>2</sub> complexes, labile iron pool (LIP), lactoferrin (Lf), superoxide and NO radicals. Activity of metalloproteinase MMP-2 and MMP-9 were determined. In adjacent and remote liver tissues low activity of N<sub>2</sub> in mitochondrial electron transport chain (EPR signal with  $g=1.94$ ), loss of functions of detoxification system (cytochrome P450,  $g=2.25$ ), appearance and growth of NO-N<sub>2</sub> complexes ( $g=2.007$ ) are obtained. Intensive EPR signals from LIP ( $g=2.2-2.4$ ) and Lf ( $g=4.3$ ) are registered. Superoxide generation rates in liver tissues and blood are of up to 6 times higher than for the control group ( $p<0.001$ ). NO levels are of 1.7 times higher for the AMT compared to RMT ( $p<0.05$ ) while being 15 times higher for blood comparing to the reference species ( $p<0.001$ ). Activity of MMP-2 and MMP-9 was registered both in AMT and RMT and is in 1.7 times higher in AMT ( $p<0.05$ ). The obtained results can be used to estimate the functional state of organs and tissues with distant metastases, the risk of recurrence, to correct the antitumor therapeutic procedures.

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