Abstract

Oxidative stress is an important factor in carcinogenesis of oncohematological diseases. However its role in the pathogenesis of myelodysplastic syndromes (MDS) remains unclear. In this study, we have determined the oxidative status and evaluated proteomic changes in plasma of MDS patients as a consequence of oxidative dysbalance (oxidative modifications, protein-protein interaction and complex forming).

We measured the levels of total cysteine, homocysteine, cysteinylglycine, glutathione, nitrites and nitrates in the plasma from 61 MDS patients and 23 healthy donors using high performance liquid chromatography. Glutathione and nitrites levels reduced significantly while other aminothiols levels increased significantly in plasma of MDS patients. This association with oxidative stress did not correlate with iron overload. We also found enhanced levels of asymmetric dimethylarginine in serums of middle aged patients with MDS that correlate to posttranslational modifications of proteins arginyl residues. Furthermore, carbonylated proteins level was significantly elevated in MDS patients compared to healthy donors. Using mass spectrometry, 5 S-nitrosylated blood platelets proteins were identified in plasma and blood platelets of MDS patients and set of 16 plasma proteins with high probability of carbonylation has been suggested. The surface plasmon resonance (SPR) biosensor system for the direct and label-free detection of a soluble vascular endothelial growth factor receptor (sVEGFR-1) which takes advantage of a high affinity interaction between VEGFR-1 and its ligand vascular endothelial growth factor A has been developed. We designed a SPR protein chip allowing us to identify proteins forming complex with key molecules of MDS disease. We identified possible key proteins in MDS pathophysiology, which could be elucidated by further studies.

This study presents oxidative processes in MDS as an important cause proteomic changes and its significant role in the pathophysiology of MDS.

Key words: myelodysplastic syndromes, oxidative stress, SPR, posttranslational modification, protein-protein interaction.