

Characterization of methionine oxidized human recombinant erythropoietin by nano LC-ESI-MS/MS; Isoform distribution and biological activity

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Methionine (Met) oxidation is a significant form of protein damage caused by endogenous or environmental oxidizing agents. In this study we examined the effect of increasing levels of Methionine-54 oxidation on the isoform distribution and biological activity of the human recombinant erythropoietin. Mass spectrometry was applied to determine and compare the Met oxidation level of three batches of human recombinant erythropoietin. Isoform distribution of the analyzed products was assessed by capillary zone electrophoresis (CZE) method. The calculated area percent of isoforms 2-4 which belongs to more acidic glycoforms, were decreased with increasing the level of methionine oxidation in all samples. Also, the results showed that the percent of isoforms 5-8 (more basic) were increased in all samples along with the elevating Met

oxidation level. The *in vivo* biological activity of proteins was decreased by increasing the level of oxidation. In conclusion, Met oxidation level in human recombinant erythropoietin showed significant association with the net charge and isoform distribution of the glycoprotein and could be applied for monitoring and validation of production processes and quality control assessments.

Speaker Biography

M Reza Khorramizadeh, is a full Professor at Tehran University of Medical Sciences (TUMS), directs Biosensor Research Center and newly instituted Zebra Fish Core Lab at Endocrinology and Metabolic Molecular-Cellular Sciences Institute. Concurrently, he is a 2nd affiliation to the Dept. of Medical Biotechnology, School of Advanced Technology in Medicine, TUMS.

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