

Alteration in effects of endoplasmic reticulum stressors induced by overexpression of P-glycoprotein in mouse leukemia cells L1210

Mário Šereš¹
Lucia Pavlíková¹
Viera Boháčová¹
Tomáš Kyca¹
Zdena Sulová¹
Albert Breier²

¹*Institute of Molecular Physiology and Genetics, Center of Bioscience, Slovak Academy of Sciences, Bratislava, mario.seres@savba.sk*

²*Institute of Biochemistry and Microbiology, Faculty of Chemical and Food Technology, Slovak University of Technology, Bratislava albert.breier@stuba.sk*

P-glycoprotein (P-gp) expression/efflux activity in cytoplasmic membrane can induced obstacles in the effective treatment of cancer by chemotherapy. Moreover, independently on its efflux activity, this protein can secure the resistance also to non-P-gp substrates and through affecting of several cell's regulatory processes (1). In previous paper, we have described a reduced sensitivity of P-gp positive variants of L1210 cells (R & T) to endoplasmic reticulum (ER) stressors thapsigargin and tunicamycin (Tun) as compared with P-gp negative parental L1210 cells (S). Here we have studied the mechanism of P-gp positive cell resistance against N-glycosylation inhibitor Tun. We found that Tun at 0.1 μ M induces an increase in expression of ER stress markers CHOP and spliced variant of XBP1 in S cells but not in R & T cells. Higher expressions of chaperones Hsp70 and Grp78/Bip were observed in R & T than in S cells. Transfection of S cells with the plasmid encoding Grp78/Bip, resulted in reduction of CHOP expression after ER stress induced with Tun. Therefore we suppose, that overexpression of Grp78/Bip is responsible for less response of R & T to ER stressor Tun. To understand this feature in details requires further investigation.

Keywords: MDR, ER stress, Grp78/Bip.

Article Information

Conference Proceedings: World Congress On Cancer Science and Therapy (Bangkok)

Conference date: 02-03 December, 2019

[Inovineconferences.com](http://inovineconferences.com)

***Corresponding author:** Mário Šereš, Institute of Molecular Physiology and Genetics, Center of Bioscience, Slovak Academy of Sciences, Bratislava, Email: mario.seres@savba.sk

Citation: Šereš M, Pavlíková L, Boháčová V, Kyca T, Sulová Z, et al (2019) Alteration in effects of endoplasmic reticulum stressors induced by overexpression of P-glycoprotein in mouse leukemia cells L1210. Int J Cancer Treat.

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