

Interplay between P-glycoprotein mediated multidrug resistance and intracellular calcium homeostasis

Albert Breier, Mário Šereš, Lenka Gibalová, Branislav Uhrík, Zdenka Sulová

Laboratory of Biochemistry and Cytochemistry, Institute of Molecular Physiology and Genetics, SAS, Vlárská 5, 83334 Bratislava, Slovakia. E-mail: albert.breier@savba.sk

Multidrug resistance (MDR) of neoplastic tissue represents real obstacle in effective chemotherapy of cancer. Several mechanisms of MDR were identified, from which overexpression and efflux activity of P-glycoprotein (P-gp) – plasma membrane ATPase (ABCB1 member of ABC transporter family) – represent the most common observed reason of neoplastic diseases chemotherapy misfunction.

Process of P-gp mediated MDR seems to be related to intracellular calcium homeostasis at least indirectly because: i. substances blocking calcium influx through L-type of calcium channels like verapamil were often found to antagonize P-gp mediated MDR; ii. calcium signal abnormalities were observed in cells overexpressing P-gp; iii. cells with P-gp mediated MDR were often resistant to thapsigargin; iv. several differences in intracellular calcium localization were observed when P-gp negative and P-gp positive cells were compared; v. differences in contents of several proteins of endoplasmic reticulum involved in calcium homeostasis were observed to be associated with P-gp overexpression. The current study represents an attempt to summarize knowledge about possible relations between P-gp mediated MRD and intracellular calcium homeostasis.