Title: Study of transport systems of microorganisms

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Abstract: Overexpression of drug efflux pumps is responsible for a multidrug resistance (MDR). We used the potentiometric fluorescent probe diS-C_3(3), which is a substrate of major MDR pumps in three yeast species, *Saccharomyces cerevisiae* (*Sc*Pdr5p, *Sc*Snq2p), *Kluyveromyces lactis* (*Kl*Pdr5p) and *Candida albicans* (*Ca*Cdr1p, *Ca*Cdr2p), to monitor inhibition of selected membrane transporters caused by various chemical stressors (diS-C_3(3) assay). The extent of inhibition of probe transport points to a tighter arrangement of the *K1*Pdr5p binding pocket compared to that of *Sc*Pdr5p. Furthermore, we discovered that while deletion of the *KlPDR16* gene does not affect *K1*Pdr5p activity, it only caused cell hyperpolarization, deletion of the *KlERG6* gene results in both change in membrane potential and in a suppression of the pump´s activity. We developed an effective method to search for inhibitors of MDR proteins of. *C. albicans*, which is based on pre-screening their potential to block the probe efflux from *S. cerevisiae* cells. Using this method we identified the substance H, derivative of 1,4-dihydropyridine, which efficiently inhibits the activity of the *Ca*Cdr1p pump. Moreover, we have shown that stressors that block the activity of both the *Ca*Cdr1p and the *Ca*Cdr2p pumps can completely inhibit the probe export from the resistant clinical isolates of *C. albicans*.

Keywords: multidrug resistance, fluorescence probe diS-C_3(3), MDR pump, inhibitor, substrate