Title: Analysis of the arrangement of the binding pocket of the MDR pump Cdr1p of the pathogenic yeast *Candida albicans* - a major contributor to clinical drug resistance.

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Abstract: Candida infections are becoming an increasing cause of death in hospitalized patients. The main reason for drug resistance in the most common yeast pathogen *Candida albicans* is an increased production of transport proteins, which are removing the drug from the cell cytosol and thus producing the phenomenon called multidrug resistance – MDR. The goal of this thesis was to verify the suitability of the yeast strain *Saccharomyces cerevisiae* with heterologously expressed MDR pumps from the pathogenic yeast *Candida albicans* and comparison to the results from *C. albicans* with homologous expression. The results that the azole drugs miconazole, bifonazole, and ketoconazole, together with potentiometric fluorescent probe diS-C_3(3), are substrates of the *Ca*Cdr1p and *Ca*Cdr2p pumps, but not, or minimally, of the pump *Ca*Mdr1p, are consistent with the previously published work. The binding pocket of *Ca*Cdr1p was explored using the disc diffusion assay and the diS-C_3(3) fluorescent probe method, with the help of structurally similar molecules voriconazole, fluconazole, and ravuconazole, and its intermediates. It revealed that all the azoles, together with the fluorescent probe *Ca*Cdr1p, compete with each other for the transport out of the cell. Ravuconazole, the only one with benzonitrile group, is the most potent pump inhibitor. Furthermore, the azoles without the benzonitrile group do not compete with the benzonitrile group itself and therefore, it could be asserted that there are at least two different binding sites in the *Ca*Cdr1p binding pocket. The results contribute to a better understanding of the MDR pump substrate specificity.

Keywords: multidrug resistance, MDR, Candida albicans, Cdr1p, diS-C_3(3) fluorescent probe