Candida albicans is one of the fungi naturally occurring in human organism microflora. It lives in the gastrointestinal tract, on mucosal membranes and skin and usually does not cause infections. However, when an organism is immunocompromised, e.g., by surgeries, long antibiotic therapy or long illness (e.g. AIDS) *Candida* becomes virulent and causes a disease called candidiasis. Fungal infections may occur on skin and mucosal membranes, causing surface infections but, more importantly, the fungi may attack internal organs and spread in blood. In this cases infection may prove to be deadly.

Fungal infections caused by *Candida* are difficult to treat since both fungi as well as humans belong to eukaryotes and because of that the structure and functions of both cells are similar. It is difficult to find the drug that will damage fungus and at the same time be safe for humans. This is the reason why there are only a few known and used antifungal drugs. Furthermore, *Candida* developed many mechanisms of resistance against them. One of the mechanisms is active export of drugs out of the cells. It is accomplished by cell membrane transporters. Only a few inhibitors are known for drug transporters but they are toxic for humans and cannot be used in clinical treatment.

Candida can change its morphological form depending on ambient temperature and in presence of different stimulating factors, e.g. serum. In human blood and in temperature of our bodies round yeast cells change to virulent filaments which, in turn, change into hyphae. Hyphae can mechanically damage and penetrate tissues, simultaneously releasing enzymes that can break down our cells. Taking it all together, a new therapy has to be found that will lower resilience and virulence of *Candida*, helping the activity of antifungal drugs.

Our goal is to investigate the influence of different carbon sources on *Candida* activity and their synergism with most commonly used antifungal drug – fluconazole. The main carbon source used by *Candida* is glucose, whose excess in diabetic patients often increases incidence of fungal infections. On the other hand, not much is known about the influence on the fungus of non-fermentable carbon sources, i.e. lactic acid, which is produced by *Lactobacillus* – a bacterium living in some of the niches in the human organism and capric acid produced by some of the probiotics.

In the proposed project we want to investigate the influence of the above carbon sources on the activity of drug transporters, using a fluorescent method measuring their activity in real time as well as at specific time points of incubation. By tagging drug pumps with fluorescent protein GFP we want to study their localization in membrane and beyond it, and using a novel spectroscopic correlation of fluorescence (svFCS) technique we want to demonstrate specific localization of drug transporters in ergosterol-rich domains, which has yet to be proven. We want to demonstrate that carbon source not only causes changes in how the fungus obtains energy but also influences membrane structure, especially its ergosterol domains which will affect membrane function, namely e.g. its fluidity. We will construct *Candida* mutants that will not produce ergosterol or produce it in a lower quantity. Changes in fluidity in mutant membrane should, according to our assumptions, change the activity of drug transporters. We plan to monitor physicochemical properties of membrane in various conditions using *in vivo* fluorescent methods, measuring it directly on fungal cells. We will also isolate cell membranes, and from them extract ergosterol so we can measure its quantity using analytical chemistry methods (HPLC), depending on culture growing conditions. All the above studies we also want to carry on pathogenic *Candida* form, i.e. filamentous form.

Our project belongs to the field of basic research and its main goal is better understanding of mechanisms governing *C. albicans* cells, but the results may have importance for practical applications. Better insight into drug transporters activity under various conditions and cellular processes may provide useful clues in the search for ways to combat fungal infections caused by this pathogen.