Mycoses are quite common diseases of animals and humans. Several investigations indicate that over a billion people worldwide suffer from them. Among the pathogens causing mycoses, a significant place is occupied by yeast-like species responsible for many surface mycoses as well as systemic infections. Yeasts are the most often opportunists that cause disease symptoms when they get out of the host's immune system control. Despite this, mycoses in humans and animals are now being reported more and more frequently. Due to the fact that fungi are, as humans, eukaryotic organisms and display similar metabolism and cell structure, we have relatively limited defense options in the fight against mycoses. For this reason, drug resistance, increasingly common among yeast-like species, is a particularly dangerous phenomenon requiring cognition.

One of the most commonly used groups of antifungal drugs are polyenes, which have been present in medicine since the mid-twentieth century. These antimycotics are often used in the therapy of mycoses, primarily due to their wide spectrum of action. The mechanism of their action is based on the ability to damage the membranes of fungal cells and the acceleration of the free radicals generation. Data from Centers for Medicare & Medicaid Services show that in the years 1991–2009 polyenes were the second of the most commonly assigned group of antifungal drugs in the USA, and as much as 490 million USD was spent on their purchase. In the case of surface mycoses, nystatin and natamycin are the most commonly used in treatment, whereas systemic mycoses require the use of amphotericin B. There are many commercial preparations for the pharmaceutical market based on these polyenes that are widely available without a prescription. Widespread and uncontrolled access to these drugs can be a reason for resistant strains selection and for development of drug resistance. The issue among pathogens is a very important research problem in biology, medicine and veterinary. Among the potentially pathogenic fungi for humans and animals, an important position is occupied by yeasts-like species, especially from the *Candida* and *Malassezia* genera. *Malassezia pachydermatis* is a species that constitutes a significant part of the physiological biota of the skin and mucous membranes of most mammals and birds, but it can also cause an inflammation of the skin, mucous membranes and fungemia in warm-blood animals and even humans. The reasons for manifesting the symptoms of disease are mainly related to disorders of the functioning of the host's immune system. Recently, several authors, basing on research data proved high level of diversity among these fungi. However, strains causing disease symptoms probably may have specific features that distinguish them from typically commensal strains. Therefore, besides the status of the host’s immune system, the individual characteristics of the strain should be considered during the determination of the disease cause and etiology.

The planned research is based on our previous observations regarding high genetic variability among *M. pachydermatis* strains isolated from both, infected and healthy animals. A preliminary experiment conducted on a group of strains exposed to low concentrations of nystatin and natamycin indicated the possibility of resistance development in the case of selected strains. These results create the possibility of building a model for acquiring resistance to nystatin and natamycin in *M. pachydermatis* and tracking changes occurring during this process in individual strains in long time experiment. We assume that selection for specific point mutations could be followed by the changes in gene expression and the activity of enzymes involved in the organization of the fungal cell membrane structure. Consequently, genetically fixed-resistance may develop. Therefore, the aim of the project is to experimentally recreate the process of acquiring resistance to selected polyenes by *M. pachydermatis*. By the access to the initial strains and these obtained at subsequent stages of the experiment, it will be possible to compare selected features of strains at the genetic, biochemical and proteomic level. This will enable us to determine the sequence of events leading to the evolution of the resistance of the fungi to the studied antimycotics.

Until now, most researchers have based their research on drug resistance on a comparison of distinct strains with different sensitivity to each antimycotic. The current project involves the construction of an experimental model for the acquisition of drug resistance to polyenes as a result of multiple passages of selected *M. pachydermatis* strains on media containing subliminal concentrations of individual antibiotics. We will assess the process of acquiring drug resistance by following the changes in MIC (Minimal Inhibitory Concentration) values in relation to individual antimycotics in cultures of particular strains. The comparison of initial strain characteristics and their properties after the development of significant resistance will be used in order to explain the mechanism of this phenomenon on the genome, genetic and metabolic levels. In addition to cognitive value, planned research may have an application-related significance, especially in the context of the search for ways of counteracting this phenomenon. The advantage of this project is obtaining a specific model of acquiring resistance by fungi, which is unique at the moment and provides extensive opportunities to study the process of acquiring drug resistance among yeast-like species.