## Reg. No: 2020/37/B/NZ6/00457; Principal Investigator: prof. dr hab. in . Jarosław Feliks Kaba

One of the most serious problems that is currently faced by medicine and veterinary medicine is increasing resistance to certain drugs used to fight with them. This issue mainly concerns antibacterial antibiotics, and in veterinary medicine also anthelmintics. In all over the world, parasitic invasions, especially those caused by gastro-intestinal nematodes, are one of the main problems associated with health disorders in goat herds. Treatment and prevention of these invasions is mainly based on the use of antiparasitic drugs. We talk about drug resistance when a specific parasite population ceases to be sensitive to a drug or similar group of drugs. Nowadays, not only resistance to single drugs (chemical groups) is more and more often found, but also to many drugs at the same time (several chemical groups - multidrug resistance). The issue of multidrug resistance of parasites, especially gastrointestinal nematodes in some countries has already led to the necessity of liquidation of whole herds of goats. In the absence of alternative, equally effective methods of prevention and treatment of parasitic invasions, this problem becomes now a huge threat to goat breeding in the world. In Poland, for the first time the resistance of gastrointestinal nematodes to drugs from the group of benzimidazoles has been found and described in goats by the authors of this project in 2017. Ongoing in our laboratory research on anthelmintic resistance confirm that multi-drug resistance of gastrointestinal nematodes is also present in goat herds in Poland. Our research confirms that this phenomenon is just emerging. In this epidemiological situation, early detection of drug resistance in individual herd is very important. The basic method for confirming the drug resistance and assess it intensity degree is a *in vivo* faecal egg count reduction test performed from goats faecal samples. Unfortunately, this test is labour-intensive, expensive because requires the examination of many animals twice times. Therefore the result of the test may led to data of poor quality with many errors caused by natural variability in the number of eggs excrete by parasites in individual animals over time, as well as high inter-individual variability of animals within the examined herd or herds. A cheaper and less labour-intensive method, an alternative to drug resistance diagnosis carried out on live animals, are in vitro carried out tests (egg hatch test, larval development test). These tests are performed from pooled faecal samples from animals from the examined herd. Unfortunately, the results of these tests only provide qualitative information on the presence of drug resistance. They do not give quantitative information about the percentage reduction of the effectiveness of a given drug, which is the main factor influencing decisions regarding the further prophylaxis and antiparasitic treatment used. These tests do not take into account the impact of individual animals on the overall outcome of the examination, as well as many risk factors predisposing to the development of drug-resistant gastrointestinal nematodes in individual individuals. The aim of the proposed project will be to develop a multivariable biostatistical model which will allow obtaining information provided so far only by testing live animals, based on much less labour-intensive and cost-intensive in vitro methods. This is a new, interdisciplinary approach to the problem. There are no such publications in the world literature. Created biostatistical model will provide quantitative information on degree of anthelmintic resistance at an early stage of its development, and also will allow make quick and accurate decisions regarding the prophylaxis and the fight against anthelmintic resistance.

Since 2016, as part of a screening of parasitological survey (conducted by the authors of the project), 153 goat herds from all over Poland have been examined. On the basis of the obtained data, goat herds will be selected, in which there is a suspicion of drug resistance of gastrointestinal nematodes. In these herds the faecal egg count reduction test will be carried out with use drugs from the most common used in goats three groups of anthelmintics (benzimidazoles, imidazothiazoles and macrocyclic lactones). This test will allow to confirm or rule out the occurrence of drug resistance linked to each drug (chemical group) and provide data on the reduction of the effectiveness of a given drug (chemical group) in individual animals, as well as the entire herd. At the same time, tests using in vitro methods: egg hatch test and larval development test will be performed from faecal samples collected from individual animals before and after treatment as well as pooled faeces samples from whole flocks. Species or genus of nematodes present before and after the treatment will be obtained with use of faecal culturing methods and differentiation of morphological features of the invasive larvae of a given species. Information about risk factors related to the emergence of anthelmintic resistance will be obtained from the owners of the flocks in a questionnaire survey. The collected data will be used to conduct statistical analysis and create a biostatistical model.

The conclusions from such studies will be the basis for the future development of recommendations for prevention of spreading and combating anthelmintic resistance in gastrointestinal nematodes in goats in Poland. If the developed model proves to be highly accurate, we will undertake further work to create in the future a commercially available test for early diagnosis of the occurrence of the resistance of parasites.