Epilepsy is an example of neurological disorder, about which little is said in the public space and around which many myths have arisen since antiquity. At present, we do not think that seizures are the result of possession, however, epilepsy patients are still kept at a distance by other people. Well-controlled seizures, as it is in 70-75% of cases, allow patients to live a full-fledged life. Some famous people suffered from epilepsy, e.g. Fyodor Dostoevsky, Vincent van Gogh, and nowadays Melanie Griffith. The problem is the remaining 25-30% of the so called drug-resistant epilepsy diagnosed when correctly conducted therapy with 2-3 drugs remains ineffective. Unfortunately, gradual introduction of 2nd and 3rd generation antiepileptic drugs (AEDs) since the 1990s did not bring the expected breakthrough. The quality of life of patients suffering from drug-resistant epilepsy is severely limited. They usually cannot conduct normal professional, social and even family life. Antiepileptic treatment is a long-term process, therefore chronic application of AEDs in experimental studies corresponds more closely to clinical practice. Due to the time□consuming and cost-consuming nature of this research, such studies are rarely undertaken. In the previous project, we found that 14-day treatment with LTG resulted in the potentiation of the antielectroshock effect and motor impairment. Pharmacokinetic interactions could only partially contribute to the obtained results. We assumed that chronic application of LTG may changes expression of genes (and their protein products) regulating the processes of neural excitation and inhibition. The available literature does not provide any data on this subject. In the presented project, we plan to examine the influence of chronic treatment with LTG on expression of 5 selected genes. For this purpose LTG will be administered to mice twice a day for 14 days. Then the brain structures involved in seizure processes (hippocampi, frontal cortex, thalami) will be isolated. Due to similarity between neurons and cardiomyocytes (both types of cells are excitable, generate an action potential and have almost identical ion channels) as well as co-existence of epilepsy and cardiac arrhythmias, gene expression will be also detected in the mouse hearts.

Genetic material (mRNA) will be isolated from sequestered brain structures and hearts. Then the reverse transcription and cDNA synthesis will be performed. The cDNA preparations will be amplified using the technique of RQ PCR (real time polymerase chain reaction) and analyzed for the expression of selected genes. If significant differences in gene expression are found, protein expression will also be investigated by the immunoenzymatic method. Results of the study will answer the question of whether changes in expression of genes related to generation and spread of electrical impulses in the nervous tissue are correlated with changes in therapeutic and undesired effects induced by LTG. This will hopefully contribute to better understanding of the mechanisms of drug-resistant epilepsy and perhaps the nature of cardiac arrhythmias in the course of epilepsy. It may also be a step forward in the development of personalized epilepsy therapy – knowledge of the gene expression profile will allow predicting the range of efficacy of a given drug in a particular patient.