Retinal and the optic nerve ischemia are one of the leading causes of visual impairment or loss of vision worldwide. Ischemia is also an important mechanism leading to the development of diseases of the retina, such as diabetic retinopathy, glaucoma, central retinal artery occlusion or central retinal vein occlusion. Ischemia develops due to insufficient blood flow to the retina in relation to the current metabolic needs. At the cellular level, ischemic damage to the retina primarily involves the triggering of a destructive cascade of reactions, led by the so-called oxidative stress associated with reduced oxygen availability to cells. In response to this process, reactive oxygen species appear in cells, possibly leading to proteins and other cellular elements damage and, at the same time, it stimulates cell death by activating programmed death, the so-called apoptosis. Currently, there are no available and effective neuroprotective therapies, i.e., those that protect nerve cells, including the retinal ganglion, bipolar and amacrine cells, against dying and that could be successfully used in retinal vascular diseases. Hence, it is so important to look for substances with neuroprotective and neuroregenerative effects, i.e., substances that additionally repair damage already done and stimulate cells to renew themselves.

The aim of our project is to evaluate the neuroprotective properties of Escitalopram, a drug from the group of serotonin reuptake inhibitors (SSRI) in a model of mouse retinal ischemia. Escitalopram belongs to the group of psychiatric drugs used successfully in the treatment of, among others, depression or anxiety disorders. Many studies describe the antioxidant (i.e., preventing the formation of reactive oxygen species) and neuroprotective effects of drugs from this group. In addition, these drugs reduce oxidative damage to neurons and additionally stimulate the secretion of natural neuroprotective substances, such as BDNF (brain-derived neurotrophic factor). Based on our pilot study, we also hypothesized that Escitalopram causes a reduction in the metabolic activity of the retina and therefore the demand for oxygen in the retina, making the retinal neurons less susceptible to ischemic damage. It can be said that Escitalopram in some way preconditions the cells of the retina to reduced availability of oxygen. Moreover, we suspect that Escitalopram influences the content of synaptic proteins and the conductivity of synapses, thus limiting the spread of apoptotic signals between cells under ischemic conditions. Electrical synapses and the associated connexin proteins seem to be of particular importance here. Appropriate experiments will be performed in mice treated orally with Escitalopram administered for 12 weeks. After this period, the animals will undergo retinal ischemia induction by increasing the intraocular pressure to the level that impairs the blood flow in the retinal vessels. At this stage of the study, we will evaluate the effect of Escitalopram treatment on survival and function of retinal ganglion cells and retinal interneurons, as well as BDNF and synaptic protein expression. For additional study, we will introduce BDNF knockout mice to assess the exact mechanism of Escitalopram on retinal ischemia and to evaluate the role of this protein in the neuroprotective effect of Escitalopram.

We expect that in our study we will confirm the positive effect of Escitalopram in the model of retinal ischemia and obtain a neuroprotective effect in the form of improved survival of retinal ganglion cells and retinal interneurons.