The interconnection between cells in all living creatures is complicated. To maintain normal functioning of the whole organism, billions of molecules and cells should work harmoniously. If some molecular pathways are impaired or even slightly changed, it will affect many other functions of the organism.

The eye is a sophisticatedly organized sensory organ that perceives light stimuli from outside and transmits them into the brain. Different species perceive different spectrums of light – some of them can discriminate only darkness and light, some of them are able to see even ultraviolet light, such as zebrafish. Zebrafish (Danio rerio) is a small fish that was originally found in Eastern India's Ganges River and currently serves as a model object for a variety of experiments due to relatively high genetic similarity to humans – more than 70% and other features including larvae transparency. Zebrafish is especially useful in investigation of various mechanisms of eye functioning, because it has well developed eye structures from early stages that are highly similar to those in humans.

To maintain the complexity of an eye, a large number of cell types are involved – from cells that are directly involved in transmitting the information, such as photoreceptors, bipolar cells, horizontal cells, amacrine cells, ganglion cells, to cells that help them to perform all the necessary processes – Muller cells, astroglia, microglia. Microglia is a special type of cells that work as a guardian and help to repair other cells in case of their damage, simultaneously signalizing to attract more immune cells to the site of damage.

The majority of microglial functions are regulated by changing the level of calcium in the different parts of the cell. In that process many proteins are involved, among them is STIM2. This protein is located in endoplasmic reticulum (ER) and senses Ca^{2+} level in it. When Ca^{2+} level in ER is decreased, STIM2 changes its conformation and interacts with calcium channel in the plasma membrane. This leads to Ca^{2+} influx from the external medium into the cell cytosol. This process is called store-operated calcium entry (SOCE).

It has been shown in our laboratory that when *stim2* gene is not active in zebrafish (*stim2* knocked out, KO) they have vision problem and various changes in morphology of eyes: the layers of particular types of cells in retina are thinner, the structure of mitochondria in photoreceptors is altered and level of expression of selected genes is changed. Among them is *anxa3a* gene which is overexpressed when *stim2* is knocked out. Anxa3a protein is considered to be a marker of activated microglia. Therefore, based on the facts that Stim2 is important for the function of microglia, and its knockout leads to changes in the structure of the eye, I suppose that some of these changes may be caused by microglia, since the expression of *anxa3a* indicates that these cells are activated in *stim2* KO. One of the layer that is affected is retinal ganglion cell layer. In *stim2* mutants we observe thinning of this layer, therefore it is supposed that the number of retinal ganglion cells (RGCs) is decreased. Retinal ganglion cells collect the visual information from other retinal cells by dendrites and transmit it to the particular brain region via the optic nerve. I hypothesize that lack of Stim2 dysregulates calcium homeostasis what activates microglia and causes loss of RGCs.

The investigation of possible mechanisms of RGCs loss is important because the changes in *stim2* mutants eyes are similar to some of glaucoma manifestations. Therefore, it might be a good model to study the features of glaucoma.

I am going to investigate the possible mechanisms by which active microglia influence RGCs loss. First, I want to determine how microglia behave when *stim2* is knocked out. Due to the fact that active microglia can behave differently – produce molecules that cause inflammation, change morphology and engulf other cells, or excrete substances that are able to affect other cells, I hope to find out what properties of microglia are changed that in consequence lead to abnormalities present in zebrafish stim2 KO. Second, using established research models having fluorescently labeled microglia and RGC cells I hope to determine the interaction between these two types of cells.

I believe that new knowledge of microglia and RGCs features in *stim2* KO zebrafish will allow us to better understand the mechanisms of abnormal eye function in this mutant. This may also underlie some features of glaucoma in humans.