

Neuroblastoma tumor affects infants and young children. The goal of this project is to better understand this tumor and develop new treatment for it. However, our ultimate aim is to find a cure and to improve survival for all these kids.

It was shown, that neuroblastoma cancer cells produce on the surface a certain molecule called ganglioside. It seems to be an ideal target for us because it is in abundance on cancer cells. What is more it is absent in healthy cells of the body. Therefore, we may specifically attack cancer cells, with no risk of destroying healthy cells of our organism. The ganglioside molecule may be used as a landmark to deliver therapeutic agent specifically into cancer cells.

As a therapeutic agent, we use antibodies which identify cancer cells and induce yet not fully understood mechanisms to kill cancer cells. We know that one such mechanism is cancer cells death, a process called apoptosis. However, it seems that autophagy, another important process, might be at play here.

Autophagy is a process of self-cannibalization. Cells capture their own cytoplasm and organelles and consume them in structures called lysosomes. Autophagy preserves the health of cells and tissues by replacing outdated and damaged cellular components with fresh ones. In starvation, it provides an internal source of nutrients for energy generation and, thus survival. It does have a downside because cancer cells exploit this mechanism to survive in nutrient-poor tumors.

Autophagy has dual roles in cancer, acting as both a tumor suppressor by preventing the accumulation of damaged proteins and organelles and as a mechanism of cell survival that can promote the growth of established tumors. However, autophagy has been referred to as a double-edged sword because in certain cellular contexts, excessive or sustained autophagy may lead to death. Understanding the role of autophagy in cancer treatment is critical, because many anticancer therapies have been shown to activate autophagy. However, consequences of autophagy activation still remain unclear.

In this project, we address the question if autophagy is induced in neuroblastoma cells treated with antibodies recognizing the ganglioside. To do this, we will monitor production of proteins involved in autophagy, delivery of cell components to lysosomes and their degradation. We will also use electron microscopy to visualize autophagolysosome structures, in which autophagy is executed. We will investigate whether an inhibition of autophagy leads to enhancing tumor cell death. Additionally, we want to test if combination of autophagy inhibitors with targeted agents, in this case antibodies, will improve tumor killing.

Defining functions of autophagy would allow us to better understand cancer cells. Describe how they behave and escape treatment strategies. Most importantly, it will allow to propose new combinations of drugs for better cure of neuroblastoma patients.