

## **Project 9.2. Identification of novel vulnerabilities of VPS4B-deficient cancer cells (NCN/OPUS)**

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**www:** <https://www.iimcb.gov.pl/en/research/laboratories/4-laboratory-of-cell-biology-miaczynska-laboratory>

### **Background:**

One of the key challenges in oncology is to effectively kill cancer cells while leaving healthy cells intact. To meet this goal, precision oncology aims to tailor anti-tumor therapies to individual genetic changes in cancer cells of a given patient. To provide new targets for precision oncology we need to understand the relationship between the genetic alterations of cancer cells and the dependencies (vulnerabilities) they cause. VPS4A and VPS4B enzymes together with the Endosomal Sorting Complex Required for Transport (ESCRT) machinery are involved in membrane remodeling during e.g. endocytosis, cell division, and plasma membrane repair. In our previous project, we identified VPS4B deficiency as a selective weakness of colorectal cancer cells with chromosome 18q deletion. We also demonstrated that survival of VPS4B-depleted cancer cells depends on the presence of VPS4A and characterized the molecular consequences of simultaneous depletion of VPS4 proteins that lead to cell death (more details in Szymańska et al, EMBO Mol Med, 2020). Very probably, VPS4B deficiency makes cancer cells more vulnerable not only to VPS4A loss but also to other perturbations affecting gene(s) cooperating with VPS4B in cellular processes essential for life.

### **Aim:**

We aim to identify and characterize novel vulnerabilities of VPS4B-deficient cancer cells among candidates selected from datasets of the Cancer Dependency Map Project (Broad Institute). To this end, we will examine the impact of simultaneous depletion of VPS4B and a selected candidate on in vitro and in vivo growth of cancer cells. Further, we will elucidate the consequences of depletion of VPS4B and a candidate for cancer-relevant cellular processes, e.g. endocytosis, cytokinesis and migration.

### **Requirements:**

- master's degree in biology, biochemistry or related field,
- solid understanding of the principles of cell and molecular biology,
- previous experience in laboratory work and familiarity with basic molecular biology techniques,
- written and spoken fluency in English,
- good interpersonal skills and a collaborative attitude,