Wiskott-Aldrich syndrome is a rare genetic disease. It is a primary immunodeficiency disorder, which means that the immune system does not function properly and patients suffer from recurrent infections, eczema and are at an increased risk of malignancies and autoimmune diseases. Wiskott-Aldrich syndrome is caused by mutations in the *WAS* gene located on chromosome X, therefore mainly boys are affected with this disease. Undiagnosed disease leads to death at the age of several years.

The *WAS* gene encodes the protein WASP expressed exclusively in diverse blood cells (except red cells), where it is located in cortical actin patches, structures important for cytoskeleton functioning. WASP protein stimulates production of branched actin filaments and thereby organizes the cytoskeleton required for intracellular transport and cell division. A similar role is played by the orthologue of WASP in the budding yeast, the Las17 protein. Results obtained recently in our laboratory showed that besides the conventional localization to cortical actin patches, Las17 is also found in the nucleolus. Moreover, in yeast cells lacking Las17 the nucleolus does not function properly. We observed abnormalities of nucleolus morphology and division, and frequent nucleolus fragmentation. It has been shown that human WASP can complement the cytoplasmatic function of Las17 in yeast cells. In this project, we ask if WASP can also complement the nucleolar role of Las17. We will reveal what factors influence the nucleolar localization and functioning of Las17, uncover the functions of Las17 in the nucleolus, and identify the domains of Las17 critical for this functions. Finally, we plan to determine if mutations in *WAS* gene also cause nucleolar aberrations in human cells. To this end we will examine nucleolar morphology in cell lines derived from patients with Wiskott-Aldrich syndrome.

Realization of this project will help to uncover the previously unrecognized role of yeast Las17 and human WASP proteins in nucleolus organization and division in respective cells. The obtained results will not only expand the knowledge about the role of Las17, WASP and other factors promoting actin nucleation in organizing the cytoskeleton and likely also the nucleolus, but will also contribute to our understanding of the etiology of Wiskott-Aldrich syndrome. The results are also expected to help in elaborating novel, more effective therapies for patients with Wiskott-Aldrich syndrome to improve their quality of life.