Oncogenic mechanisms of DIS3 mutations

Tumors arise as a result of mutations that occur in somatic cells. Usually this is a multistep process and tumor formation requires several mutations that increase the cell division rate (proto-oncogenes) or inactivate control mechanisms that normally lead to controlled cell death (tumor suppressors). There are also mutations that have a so-called mutator effect - they facilitate occurrence of other mutations.

In recent years technical development has allowed for identification of all mutations found in many cancer types. As a result, a number of genes were identified, mutations in which can be associated with tumorigenesis. Interestingly, it appears that different genes are mutated in various types of tumors.

Multiple myeloma is one of the most frequent hematologic neoplasms that – unlike most leukemias – develops in the bone marrow. Multiple myeloma is an incurable disease that for the most part affects elderly people.

One of the most frequently mutated genes in multiple myeloma is DIS3, but the role of these mutations in cancer progression remains unknown. Our unpublished results strongly suggest that mutations in DIS3 have a mutator effect specific to antibody-producing B cells, from which multiple myeloma originates. The aim of this project is to understand how mutations in DIS3 promote tumor formation.