

Nijmegen breakage syndrome (NBS) is a genetic defect of DNA breaks repair, which used to appear either during physiological processes or due to harmful external factors. Lack of effective repair of such mistakes leads to severe clinical consequences observed in NBS patients like an extremely high risk for developing lymphoid malignancies. Although clinical course of lymphomas in NBS is frequently aggressive and recurrent, more intensive chemotherapy is not applicable in these patients because of severe side effects of oncologic treatment that they develop. The main objective of the project is to expand the knowledge about specific for NBS genetic lesions resulting in aggressive biological features of cancer such as chemoresistance or fast proliferation of lymphoma cells. We plan to gain this knowledge through the analysis of thousands different types of defects in the whole genome of cancer cells and through the assessment of their impact on the activity of metabolic pathways involved in the cell function. We also plan to investigate whether and in which mechanism development of lymphoma depends on the integration of Epstein-Barr (EBV) genome into the host genome. We know that at least in some NBS patients active replication of the virus precedes cancer transformation. We believe that more precise molecular knowledge about tumorigenesis in NBS resulting from of this project will contribute in future to the creation of innovative therapy of lymphoma in DNA repair disorders.