The maintenance of genome integrity is essential for proper functioning and survival of organisms. Cells are constantly exposed to several endo- and exogenous factors causing DNA damage. To prevent the harmful effects of DNA damage, cells have developed several efficient mechanisms for detection and repair of DNA lesions. Improper functioning of these mechanisms leads to genomic instability, and in consequence, to malignant transformation. Several proteins are involved in the cellular response to DNA damage. Among them, the ATM kinase (ataxia-telangiectasia mutated) plays a crucial role. The ATM kinase is encoded by a gene located on the long arm of chromosome 11 (11q22.3). Mutations in both alleles of the *ATM* gene lead to the genetic disorder ataxia-telangiectasia (AT). The most characteristic manifestations of AT are neurological dysfunction (ataxia) and dilated blood vessels (telangiectasia). Additional AT features are immunodeficiency, genomic instability, and cancer predisposition. ATM deficient cells demonstrate hypersensitivity to ionizing radiation. AT patients have a 100-fold increased risk of cancer compared with the general population, and are most commonly diagnosed with lymphoid malignancies.

Despite a substantial knowledge of DNA repair processes, still several aspects of DNA damage detection and signaling are not fully understood. Recent studies have suggested that long non-coding RNAs (lncRNA) are an important player in the cellular response to DNA damage. LncRNAs are a class of regulatory RNAs, longer than 200 nucleotides, that do not encode for proteins. Among over 15 thousands of known lncRNAs, so far only a few have been implied in the DNA damage repair. **In this project we aim to verify the hypothesis that ATM-dependent lncRNAs are essential molecules involved in the DNA damage detection and repair.** The study will fullfill three objectives: **identification of ionizing radiation-induced lncRNAs, identification of ATM-interacting lncRNAs, and functional characterization of selected lncRNAs in the context of DNA damage response.** Studies will be performed in immortalized lymphoblastoid cell lines (LCLs) derived from 4 patients with AT and 4 healthy donors. DNA damage will be induced by ionizing radiation (IR). Cells will be collected 1 h and 8 h after IR to allow identification of lncRNAs involved in the early and late response to DNA damage. For selected lncRNAs induced after IR in the ATM-dependent manner and lncRNAs interacting with ATM we will perform functional assays allowing to assess their role in DNA damage response.

Our approach, utilizing immortalized cell lines derived from ataxia-telangiectasia patients with mutated *ATM*, offers the possibility for a comprehensive identification of the ATM-dependent lncRNAs with crucial role in the DNA damage response. **Results obtained in this project will broaden the knowledge about lncRNAs involved in the detection and repair of DNA damage and will help to better understand the mechanisms of DNA damage response.** Moreover, **results of functional assays can also indicate lncRNAs as novel factors modulating cells sensitivity to radiotherapy,** which may be useful for further applied research.