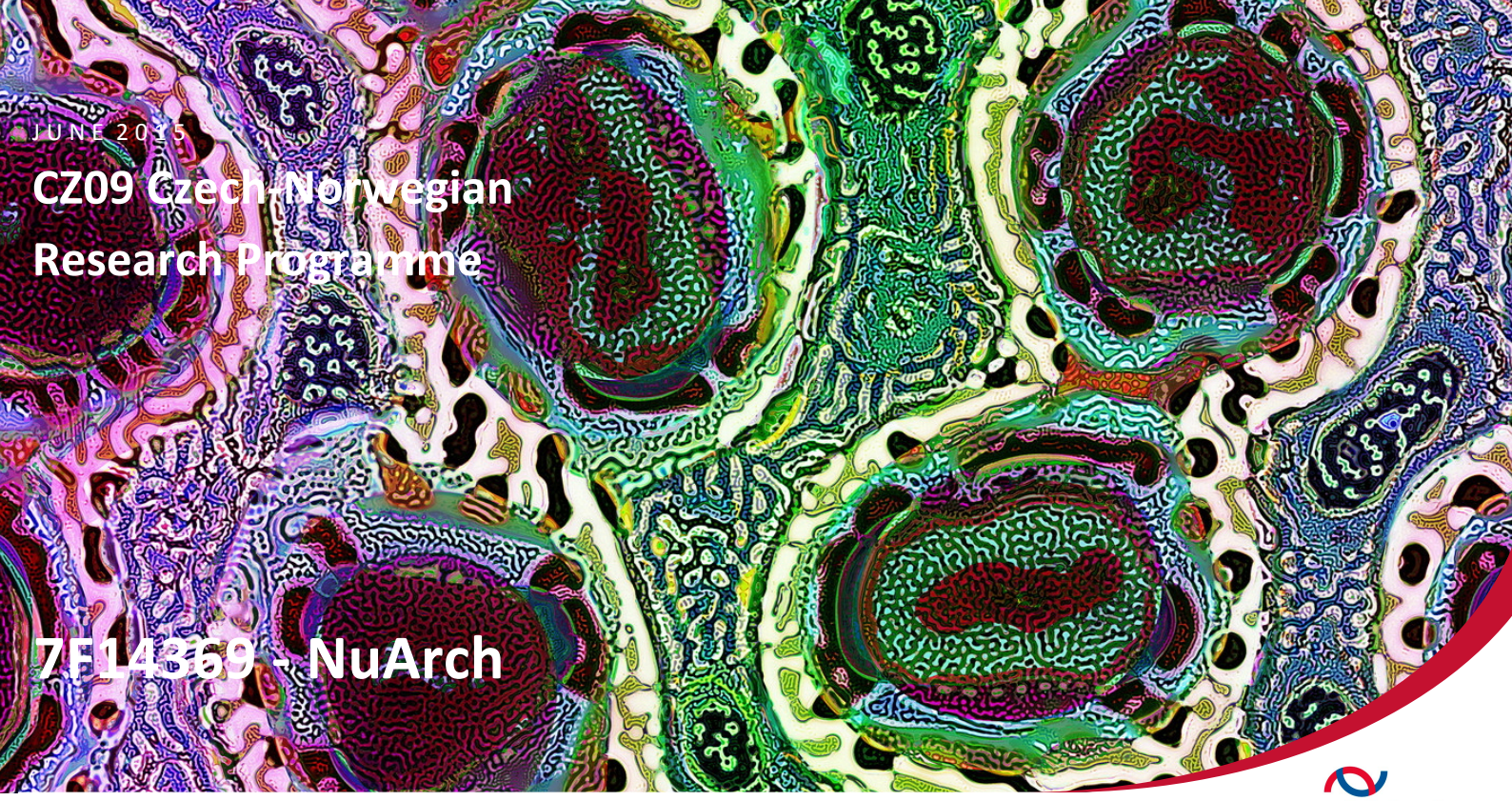

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CZ09 Czech-Norwegian Research Programme

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EVA BÁRTOVÁ, Institute of Biophysics, AS CR

Nuclear Architecture in the Regulation of Autophagy, DNA Repair and Gene Expression

Proteins with known structural roles in the architecture of the eukaryotic cell nucleus are increasingly shown to play additional functional roles in chromatin organization and orchestration of key nuclear processes such as DNA replication, transcription and repair. The importance of the functional roles played by these proteins is evidenced by the number and variety of rare diseases collectively referred to as nuclear envelopathies (including dystrophies affecting several tissues, premature aging syndromes and dystonia) that result from mutations in corresponding genes. The DNA damage response (DDR) and autophagy are key processes that can be viewed as an elaborate two-tiered quality control system to repair or eliminate essential macromolecules that have become non-functional. NuArch is based on the hypothesis that nuclear structural proteins, in addition to their roles in gene expression regulation, are also implicated in autophagy and DNA damage repair. Defects in these proteins are likely results in defective autophagy and DDR signaling, with important implications for cellular homeostasis and the regulation of cell and tissue growth. We propose to test this hypothesis through a series of specific objectives: 1) implicating the nuclear protein ALFY in a nuclear aggregate clearance mechanism; 2) examine how the dynamics of chromatin proteins recruited to DNA damage sites is affected by nuclear lamins. dynamics of chromatin proteins recruited to DNA damage sites is affected by nuclear lamins. A potential crosstalk between autophagy and DDR will be studied. 3) investigate the roles of the AKAP95-TPR anchoring complex in chromatin organization and dynamics at the nuclear periphery. NuArch is expected to establish new roles for known nuclear structural proteins and link them to key nuclear processes critical for cellular homeostasis and regulation of cell and tissue growth. It will also shed a new light on several nuclear proteins known to be implicated in a variety of rare diseases collectively referred to as “nuclear envelopathies”.

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"Participation on NuArch project brings us direct communication with The Institute of Basic Medical Sciences at Oslo University in Norway. Collaboration with Norwegian colleagues, at NuArch project, would allow us gain more unique knowledge and expertise in the biology of the nuclear envelope, chromatin and DNA damage. It will be useful for better understanding roles of known nuclear structural proteins and nuclear process."

Soňa Legertová, researcher

Programme operator: Ministry of Education, Youth and Sports of Czech Republic
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