Characterization of Lamin A / Phosphatidylinositol-4,5-bisphosphate complex

Sara Escudeiro-Lopes, Vlada V. Philimonenko, Lenka Jarolimová, and Pavel Hozák

Department of Biology of the Cell Nucleus, Institute of Molecular Genetics ASCR v.v.i. Vídeňská 1083, 142 20, Prague 4, Czech Republic

Lamins, the intermediate nuclear filaments, are important regulators of nuclear structural integrity as well as DNA transcription, replication and repair, and epigenetic regulation. Mutations in the LMNA gene, which encodes for lamin A protein, cause a large variety of human diseases, known as laminopathies, including muscular dystrophies and progeroid syndromes. Phosphorylable serines in lamin A may play important roles in different cell processes. Our data demonstrate that lamin A forms a complex with nuclear myosin I (NM1) in a phosphatidylinositol 4,5-bisphosphate (PIP2) – dependent manner, and the formation of the complex might be modulated by lamin A phosphorylation status. Therefore, we used expression vectors for GFP-tagged lamin A with mutations (phosphomimetics and phosphorylation-deficient) of selected high-turnover phosphorylation sites and analysed the patterns of mutated lamin A separated with 2D-electrophoresis. To understand the influence of these phosphorylations in the formation of lamin A complexes, we investigated the differences of protein binding partners that bound to lamin A compared to lamin A phospho-mutants. This revealed that some proteins bind to lamin A independently of phosphorylation on studied sites, while others require specific phosphorylations for the binding. We conclude that some phosphorylation sites might be crucial for PIP2-dependent interactions of lamin A, important for nuclear functions.

Acknowledgements: We would like to thank to the COST Action (CA15214) and to the Grant Agency of the Czech Republic (17-09103S, 16-03346S and 15-08738S) for their financial support. We would also like to thank for the institutional support due to the long-term conceptual development of the scientific organization (RVO: 68378050). The microscopy work was performed at the Microscopy Centre, Institute of Molecular Genetics AS CR, supported by the MEYS CR (LM2015062 Czech Bioimaging).