LABORATORY OF

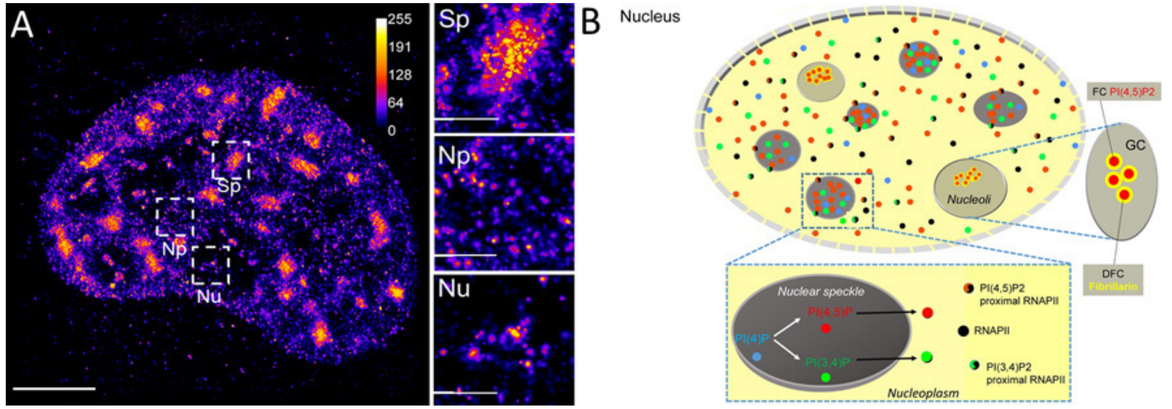
BIOLOGY OF THE CELL NUCLEUS

Nuclear lipids, phosphatidylinositol phosphates, nucleoskeleton, transcription, subnuclear compartments

Pavel Hozák

In the picture: 1. Antiga Ludovica | 2. Jelínková Iva | 3. Pišlová Lenkam | 4. Filimonenko Vláda | 5. Miladinović Ana | 6. Kříž Pavel | 7. Hoboth Peter | 8. Hozák Pavel | 9. Sztacho Martin

Functional nuclear sub-compartments linked with the crucial cellular processes, such as gene expression, contain phosphoinositides in the form of small foci (Fig. 1). Nevertheless, current models of gene expression largely omit the roles of nuclear lipids and amongst them nuclear phosphatidylinositol phosphates. We aim to fill this gap, and to this end, we use a combination of advanced light and electron microscopy (Fig. 2) together with biochemistry and molecular biology. These approaches allow us to gain insight into the role of nuclear phosphatidylinositol phosphates in the regulation of gene expression and push the boundaries of the field. We identified a novel type of nuclear structures – nuclear lipid islets – that contain phospholipids, proteins, and nucleic acids and serve as platforms for efficient transcription (Sobol et al., 2018). Our efforts continue to systematically unravel the phospholipid identity of the gene expression compartments (Hoboth et al., 2021), and we are testing the idea that PIs and their interactors regulate, at the molecular level, subsequent stages of RNAPII transcription (Sztacho et al., 2021). Moreover, our group has identified nuclear myosin I as a novel transcription factor (Philimonenko et al., 2004) and also contributed to understanding the role of nuclear actin and actin-related proteins in the establishment of functional nuclear architecture and regulation of gene expression (Balaban et al., 2021). Our research centred on the role of nuclear lipids in the formation of lipo-ribonucleoprotein transcription hubs is important for better understanding the role of functional nuclear architecture, nucleoskeleton, and nuclear lipids in the gene expression in health and disease.



Left: Fluorescent super-resolution imaging of nuclear phosphatidylinositol 4,5-bisphosphate. Selected regions show a specific pattern of PIP2 associated with nuclear speckles (Sp), nucleoplasm (Np) and nucleolus (Nu). © Hoboth et al. Int. J. Mol. Sci. 2021. Right: Detailed map of the sub-nuclear localization of PI(4,5)P2, PI(3,4)P2 and PI(4)P within nuclear speckles, in the proximity of a subset of RNAPII in the nucleoplasm and within the nucleolus. © Hoboth et al. BBA – Mol. Cell. Biol. Lipids 2021.

Selected publications:

1. Petrusová J, Havalda R, Flachs P, Venit T, Darášová A, Hůlková L, Sztacho M, Hozák P*: Focal Adhesion Protein Vinculin Is Required for Proper Meiotic Progression during Mouse Spermatogenesis. Cells 2022 11(13).
2. Balaban C, Sztacho M, Blažíková M, Hozák P*: The F-Actin-Binding MPRIP Forms Phase-Separated Condensates and Associates with PI(4,5)P2 and Active RNA Polymerase II in the Cell Nucleus. Cells 2021 10(4).
3. Hoboth P, Sztacho M, Šebesta O, Schätz M, Castano E, Hozák P*: Nanoscale mapping of nuclear phosphatidylinositol phosphate landscape by dual-color dSTORM. Biochim Biophys Acta Mol Cell Biol Lipids 2021 1866(5): 158890.
4. Sztacho M, Šalovská B, Červenka J, Balaban C, Hoboth P, Hozák P*: Limited Proteolysis-Coupled Mass Spectrometry Identifies Phosphatidylinositol 4,5-Bisphosphate Effectors in Human Nuclear Proteome. Cells 2021 10(1).
5. Fáberová V, Kalasová I, Krausová A, Hozák P*: Super-Resolution Localisation of Nuclear PI(4)P and Identification of Its Interacting Proteome. Cells 2020 9(5).