

## Abstract (English)

Phosphoinositides (PIs) are glycerophospholipids with a negative charge. As components of cell membranes, PIs are involved in membrane and cytoskeletal dynamics, cell movement and signalling, and the modulation of ion channels and transporters. Apart from the cytoplasm, phosphoinositides also localise to the cell nucleus. PIs play a role in crucial nuclear processes, such as DNA transcription, pre-rRNA and pre-mRNA processing, cell differentiation, DNA damage response, or apoptosis. Phosphatidylinositol 4-phosphate (PI(4)P) and phosphatidylinositol 4,5-bisphosphate (PI(4,5)P<sub>2</sub>) are the most abundant phosphoinositides in the cell. However, their exact localisation and function in the nucleus are largely unknown. Here, we describe their localisation at super-resolution level and their involvement in some nuclear processes.

PI(4)P is present in nuclear lamina, nuclear speckles and nucleoli, and it forms small foci in nucleoplasm. The majority of nuclear PI(4)P localises to the nucleoplasm, whereas almost 16 % is present in nuclear speckles. On the other hand, the majority of nuclear PI(4,5)P<sub>2</sub> localises to nuclear speckles, almost 30 % localises to nucleoplasm and the lesser portion to nucleoli. In the nucleoplasm, PI(4,5)P<sub>2</sub> forms small foci called nuclear lipid islets (NLIs). Their core is rich in lipids and is surrounded by proteins, RNA and DNA. The NLIs' periphery is associated with RNA polymerase II (RNA pol II) transcription machinery. In addition, nuclear myosin 1 (NM1) localises to the NLIs' periphery. NM1 interacts with PI(4,5)P<sub>2</sub> directly and this interaction is required for RNA pol II transcription. The levels of active RNA polymerase II transcription are dependent on the levels of PI(4,5)P<sub>2</sub>. Therefore, NLIs provide a structural platform promoting the formation of RNA pol II transcription factories.

Mass spectrometry analysis of immunoprecipitated PI(4)P lipid-protein complexes revealed almost 100 nuclear proteins participating in essential nuclear processes such as pre-mRNA processing, transcription or nuclear transport indicating the role of PI(4)P as an important player in the cell nucleus.

Furthermore, we show that lysine-specific histone demethylase 1 (LSD1) interacts with PI(4)P and PI(4,5)P<sub>2</sub> directly. LSD1 demethylates H3K4me<sub>2</sub> active histone mark and thus represses transcription. The binding of PI(4)P to LSD1 inhibits its activity, on the contrary, the binding of PI(4,5)P<sub>2</sub> to LSD1 stimulates its activity in vitro. Phosphorylation of PI(4)P or dephosphorylation of PI(4,5)P<sub>2</sub> might also have a quick regulatory effect on LSD1 function in vivo.