

## ABSTRACT (ENGLISH)

Phosphoinositides (PIs) are negatively charged glycerol-based phospholipids with inositol head (ring) which can be phosphorylated. Inositol ring phosphorylation yields in seven different PIs species which can be mono-, bis-, or tris-phosphorylated. Roles of cytoplasmic PIs have been extensively studied in for membrane and cytoskeletal dynamics, vesicular trafficking, ion channels and transporters and generating of second messengers. Nuclear PIs have been implicated in posttranscriptional processing of pre-mRNA, DNA transcription and chromatin remodelling. While cytoplasmic functions are very well described, the molecular mechanism of their nuclear functions are still poorly understood. In this study we focus on description of localization of nuclear PIs in particular functional nuclear compartments, which enable us to reveal PIs involvement in nuclear processes. We also focused on identification of nuclear PIs involved in the regulation of genes transcription and revealed detailed mechanism of PI(4,5)P2 a PHF8 interaction in the regulation of ribosomal genes transcription.

By two independent approaches, we have described PIs localization to the nuclear membrane, nuclear speckles, small foci in the nucleoplasm, and the nucleolus. This spread nuclear localization suggests and confirms PI's involvement in various processes such as signalling, production of secondary messengers, splicing and transcription.

Known PI(4,5)P2 binding protein involved in the regulation of transcription is actin which can be present in the cell in two forms, as monomeric or filamentous. However, the presence of filamentous actin in the cell nucleus is not well described. Here we show that actin can form filaments in the cell nucleus and these filaments col-localize with known actin binding proteins, such as cofilin and actin related protein 3 (Arp3). The presence of nuclear filamentous actin increases transcription in S-phase and on the other hand decreases cell proliferation and aberrant mitosis.

Moreover, we demonstrated a direct interaction of PI(4,5)P2 with histone lysine demethylase PHF8 (PHF8), enzyme that demethylates H3K9me2/1, H3K27me2, H4K20me1. Through this interaction PI(4,5)P2 represses PHF8 function as rRNA genes transcription activator. Therefore, is PI(4,5)P2 an important regulator at the epigenetic level and contributes to the fine-tuning of rRNA genes expression.

Using *Caenorhabditis elegans* as a model organism, we showed that PI(4,5)P2 itself is involved in various nuclear processes such as chromosome pairing, DNA-damage driven apoptosis or chromatin shape in germ cells.