CENTRE FOR CANCER BIOMEDICINE

CCB welcomes you to seminar by

Angela Oppelt and Kay Oliver Schink

Tuesday the 13th of December at 13:00 hrs

The Auditorium in the Research Building, the Norwegian Radium Hospital

Refreshments are served in the lobby after the seminar

At 13:00 hrs: Angela Oppelt, PhD student – Department of Biochemistry, Institute for Cancer Research, The Norwegian Radium Hospital

Production of phosphatidylinositol 5-phosphate via PIKfyve and MTMR3 regulates cell migration

Phosphoinositides are an important group of membrane lipids that reversibly anchor cytosolic proteins to cellular membranes, thereby modulating their localization and activity. The last identified phosphoinositide, phosphatidylinositol 5-phosphate (PtdIns5P), is present in many cell types, but its precise cellular function remains elusive. Here we show that PtdIns5P levels increase when cells are stimulated to move and we identify PtdIns5P to promote cell migration in tissue culture and in a Drosophila in vivo model. First, class III phosphatidylinositol 3-kinase, which produces PtdIns3P, was shown to be involved in migration of fibroblasts. In a subsequent cell migration screen for proteins containing PtdIns3P-binding motifs, we identified the phosphoinositide 5-kinase PIKfyve and the phosphoinositide 3-phosphatase MTMR3, which together constitute a phosphoinositide loop that produces PtdIns5P via PtdIns(3,5)P2. We also identified FGD1, a Cdc42 activator that is known to bind both PtdIns3P and PtdIns5P. The ability of PtdIns5P to stimulate cell migration was demonstrated directly with exogenous PtdIns5P and a PtdIns5P-producing bacterial enzyme. Thus, the identified phosphoinositide loop defines a novel role for PtdIns5P in cell migration.

At 13:35 hrs: Kay Oliver Schink, Postdoc – Department of Biochemistry, Institute for Cancer Research, The Norwegian Radium Hospital

Tracking of phosphoinositide dynamics during cell division

Phosphoinositites, phosphorylated derivatives of phosphatidylinositol, play a critical role in the regulation of membrane trafficking and cytoskeletal organization. The phosphoinositide PtdIns(3)P has been shown to be a key regulator of endosomal trafficking, membrane sorting and autophagy. Recently, a novel role for PtdIns(3)P during cell division has emerged.

Several PtdIns(3)P-binding proteins have been identified that play a role during cytokinesis, the final step of cell division that leads to the physical separation of the dividing cells. Defects in cytokinesis can lead do aneuploidy, which is one of potential causes for malignant transformation.

In order to elucidate the role of PtdIns(3)P during mitosis, we have analysed the distribution of PtdIns(3)P and its effector proteins in dividing cells. Time lapse imaging revealed that PtdIns(3)P-positive structures undergo rapid reorganization in dividing cells. During mitosis, PtdIns(3)P-positive structures accumulate at the cleavage furrow and to the intercellular bridge between the two dividing cells, possibly providing membrane material necessary for the physical separation of the two cells. PtdIns(3)P accumulates next to the midbody of dividing cells directly prior to abscission. This localization suggests that specific effector proteins of PtdIns(3)P are recruited to the midbody and coordinate cytokinesis.