Project 1.2. Investigation of the impact of Protein Kinase D family members on the development of metabolic diseases.

Project description

Protein kinase D (PKD) family of serine/threonine kinases belongs to the Ca^{2+}/calmodulin-dependent protein kinase (CaMKs) superfamily and comprises of three isoforms in mammals encoded by three different genes, *Pkd1*, *Pkd2*, and *Pkd3*. All mammalian Pkd isoforms have two highly conserved cysteine-rich domains (C domain, C1a, and C1b), autoinhibitory pleckstrin homology (PH) domain, and a kinase segment at the C-terminus. Pkd isoforms are diacylglycerol (DAG) and protein kinase C effectors that integrate multiple nutritional and hormonal inputs. Our previous studies indicate that PKDs are central regulators of metabolic homeostasis. Particular members of the PKD family regulate different aspects of metabolism in different cell types. For example, PKD1 promotes lipid acquisition by adipocytes and suppresses energy dissipation driven by this cell type and therefore promotes obesity in diabetes. On the other hand, PKD3 suppresses hepatic insulin sensitivity and lipogenesis in the liver. However, determination of the functions of PKDs in other organs implicated in the regulation of metabolic homeostasis is required to determine if inhibition of PKDs or particular member of this family could develop into therapy against obesity and associated diseases.

Aim of the project

Obesity and associated diseases remain an epidemiological problem responsible for a large number of premature deaths. Currently, we are missing an effective, safe, and complex treatment against diseases caused by obesity or obesity itself. The aim of this project is to test, using genetic, cell biology, and biochemical approaches if inhibition of specific members of the PKD family might serve a treatment for obesity-associated disorders.