DOCTORAL CANDIDATE:	Tianzhou Zhang
DEGREE:	Philosophiae Doctor
FACULTY:	Faculty of Mathematics and Natural Sciences
DEPARTMENT:	Bioscience
AREA OF EXPERTISE:	Molecular Genetics
SUPERVISORS:	Michael Leitges
DATE OF DISPUTATION:	3rd of May 2016

DISSERTATION TITLE: *Analysis of isoform specific functions of PKD1 and PKD3*

In the thesis we studied two PKD (PKD1, PKD2 and PKD3) isoforms—PKD1 and PKD3. Although PKD1 and PKD3 are homologous and were reported to participate in some signaling pathways together, we were able to show PKD1 has distinct anti-apoptotic functions while PKD3 involves in mitosis and cytokinesis regulation.

Protein kinase D (PKD) is a group of protein kinase that involve in mitochondrial mediated apoptosis, cell cycle and cytokinesis, cytoskeleton remodeling and cell motility, trans Golgi network related vesicular fission and transport, and type II HDAC nuclear export. PKDs were discovered at the end of last century and their basic function is phosphorylating serine/threonine and exerting activation or inhibition influence on their substrates. Novel PKCs (nPKC) are classic activators of PKD via phosphorylation on the “activation loop”. So PKDs are involved in PKC participated pathways.

PKD1 was shown to involve in upregulating reactive oxidative species induced anti-apoptotic protein expression. In this thesis for the first time we showed that PKD1 also has anti-apoptotic functions in ROS induced; mitochondria dependent apoptosis initiation via influencing Bax dependent mitochondrial apoptosis induced channel (MAC) formation in a PKC delta dependent manner.

We also showed PKC epsilon promotes the abscission step of cytokinesis through the activation of PKD3. Moreover, we identified a possible PKD3 substrate—ARHGAP11a (MPGAP) which is responsible for regulation of RhoAGTP hydrolysis to RhoAGDP and further promotes the completion of cytokinesis. Besides the function in cytokinesis, PKD3 also regulates the spindle apparatus assembly in mitotic metaphase. The PKD3 deficient immortalized mouse embryonic fibroblast cells have low proliferation rate due to spindle assembly checkpoint blockage which led to high tetraploid population. So for the first time we revealed the PKD3 has positive effects on mitosis and cytokinesis.