



CDB SEMINAR

Masanori Nakayama

Max Planck Institute for Heart and Lung Research, Germany

Thursday, July 20, 2017

14:00-15:00 Seminar Room A7F

Light and Dark sides of aPKC

Summary

Cell polarity is critical for tissue and organ architecture and its loss is frequently associated with overproliferation and tissue expansion. The polarity protein atypical protein kinase C lambda/iota (aPKC λ) is an oncogene and is associated with cell proliferation through unknown mechanisms. In endothelial cells, suppression of aPKC λ impairs proliferation despite hyperactivated vascular endothelial growth factor (VEGF) signaling. Here we show that aPKC λ phosphorylates the DNA binding domain of forkhead box O1 (FoxO1) transcription factor, a gatekeeper of endothelial growth. Although VEGF signaling is known to exclude FoxO1 from the nucleus, consequently increasing c-Myc abundance and proliferation, aPKC λ controls c-Myc expression via the FoxO1/miR-34c signaling axis without affecting its localization. We find this pathway is strongly activated in the malignant vascular sarcoma, angiosarcoma, and aPKC inhibition reduces c-Myc expression and proliferation of angiosarcoma cells. Moreover, FoxO1 phosphorylation by aPKC and aPKC expression correlates with poor patient prognosis. Our findings may provide a new therapeutic strategy for treatment of malignant cancers, such as angiosarcoma.

Host:

Li-Kun Phng

Vascular

Morphogenesis, CDB

likun.phng@riken.jp

Tel:078-306-3196

(ext:3196)

RIKEN CENTER for DEVELOPMENTAL BIOLOGY (CDB)