

シグナル伝達医学講演会

日時

平成28年8月4日(木)

17:00~18:30

場所

研究棟B 2F 共同会議室

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Light and Dark Sides of aPKC; aPKC controls endothelial growth by modulating FoxO1 DNA binding ability

Cell proliferation is tightly controlled during development and in tissue homeostasis. Conversely unrestrained cell division is a hallmark of cancer. Atypical protein kinase C (aPKC) is a key regulator in various cell polarization events from worms to mammals and it is often overexpressed in multiple malignant tumors. In endothelial cells (ECs), suppression of PKCI, one of isoforms of aPKC, impairs proliferation, meanwhile it paradoxically leads to hyper-activation of growth factor signaling (Nakayama et, al. 2013 Nat Cell Biol). Here we discover that aPKC directly phosphorylates the FoxO transcription factor thereby preventing downstream gene transcription selectively. Although FoxO1 localization is crucial for the activity and is known as a strong growth suppressor, inhibition of FoxO1 phosphorylation by aPKC does not affect its localization. Additionally, we find that this factor is highly expressed in the patients suffering from angiosarcoma, a malignant EC-derived tumor. Intensive phosphorylation of FoxO1 by aPKC and high levels of aPKC expression are also present. Moreover, suppression of aPKC activity reduces proliferation in patient-derived angiosarcoma cells. Our study uncovers how aPKC controls physiological and pathological EC growth.

Reference

Nakayama M*, Nakayama A, Van Lessen M, Yamamoto H, Hoffmann S, Drexler HCA, Itoh N, Hirose T, Cooper JA, Ohno S, Kaibuchi K, Adams RH*. Spatial regulation of VEGFR endocytosis in angiogenesis (2013) *Nat Cell Biol* 15: 249-60

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