NUS National University of Singapore | Department of Biological Sciences Faculty of Science

SEMINAR

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AMPK and Oncogenic Signaling in Cancer Metastasis

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Activation of phosphatidylinositol 3 kinase (PI3K), Ras, and Her2 signaling plays a critical role in cancer development. We demonstrate that hotspot oncogenic mutations on PIK3CA and RAS inhibit p53-related p63 expression via Akt-FOXO3a signaling, resulting in increased cell motility and tumor metastasis. Expression of ΔNp63α effectively reversed p110αH1047R-, K-RasG12V–, H-RasG12V–, or Her2-induced cell motility in vitro and tumor metastasis in mouse models. Furthermore, expression of FOXO3a and ΔNp63α is closely correlated in human cancer biopsy samples.

AMP-activated protein kinase (AMPK) functions as an energy sensor and plays a pivotal role in maintaining cell metabolism homeostasis. We show that expression of AMPK catalytic subunit AMPKa1 is dramatically decreased in advanced human breast cancer samples. Knockdown of AMPKa1 promotes EMT and cell mobility in vitro and cancer metastasis in vivo. Oncogenic Ras inhibits AMPKa1 expression, resulting in disrupted cell-cell adhesion and increased cell motility, In addition, we show that ΔNp63α transactivates AMPKa1 expression. These results indicate that AMPK plays an important role in oncogenic signaling-induced cancer metastasis.

Artwork by Ann Nee, DBS, NUS