The Prognostic and Therapeutic Potential of AMP-activated Protein Kinase in Ovarian Cancer

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Ovarian cancer is one of the leading causes of cancer-associated death in women. The high mortality is due to its poor prognosis as most cases are found in late stages. Therefore, searching reliable tumor markers is urgently needed for clinical management of this disease. Altered cellular metabolism is a crucial phenomenon for the development and progression of ovarian cancer. AMP-activated protein kinase (AMPK) acts as a key intracellular energy sensor and regulator for governing energy balance homeostasis. It also closely links with cancer cell metabolism. Others and we have reported that the activation of AMPK by pharmacological agents shows cytotoxicity to cancer cells, indicating that targeting AMPK could be a promising therapeutic approach. On the other hand, our study also demonstrated that the AMPK activity had an inversely correlation between tumor stage and/or high grade ovarian cancer. Importantly, the reduced AMPK activity was associated with the increased ERK/FOXM1 signaling cascade in advanced ovarian cancers. The ERK/FOXM1 signaling pathway has been shown to possess oncogenic effects on promoting oncogenesis in numerous human cancers and showed a progressive increased pattern from low- to high-grade tumor. In fact, using ovarian cancer cell models, we showed that the activation of AMPK by pharmaceutical or natural AMPK activators could inhibit not only ERK/FOXM1 activity but also the tumor growth. The suppressive functions were equivalent to ERK or FOXM1 inhibitors in ovarian cancer cells or other gynecological carcinoma cell lines. Taken together, these findings suggest that the decreased AMPK activity may act as a prognostic marker in ovarian cancer because it is significantly correlated with the increased ERK/FOXM1 signaling cascade and the advanced stage ovarian cancers. Moreover, targeting AMPK by either pharmaceutical or natural AMPK activators may be explored as an alternative therapeutic regimen in the treatment of this disease.

Curriculum Vitae

Academic Qualifications: BSc. (Hons) (HKBU) 1992, MPhil (HKU) 1996, PhD (Monash) 2002

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2001-2003	Research Officer, Peter MacCallum Cancer Institute, Uni. of Melbourne.
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