

Akt: Isoform-Specific Regulation of Cellular Signaling in Cancer

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Abstract : The serine/threonine protein kinase B (PKB) also known as Akt, is one of the multifaceted kinase in human kinome, existing in three isoforms. Akt plays a vital role in phosphoinositide 3-kinase (PI3K) mediated oncogenesis in various malignancies and is one of the attractive targets for cancer drug discovery. The functional significance of an individual isoform of Akt is not redundant in cancer cell proliferation and metastasis instead Akt isoforms play distinct roles during metastasis; thereby regulating EMT. This study aims to determine isoform specific functions of Akt in cancer. The results obtained suggest that Akt1 restrict tumor invasion, whereas Akt2 promotes cell migration and invasion by various techniques like MTT, wound healing and invasion assay. Similarly, qRT-PCR also revealed that Akt3 has shown promising results in promoting cancer cell migration. Contrary to pro-oncogenic properties attributed to Akt, it is to be understood how various isoforms of Akt compensates each other in the regulation of common pathways during cancer progression and drug resistance. In conclusion, this study aims to target selective isoforms which is essential to inhibit cancer. However, the question now is whether, and how much, Akt inhibition will be tolerated in the clinic remains to be answered and the experiments will have to address the question of which combinations of newly devised Akt isoform specific inhibitors exert a favourable therapeutic effect in in vivo models of cancer to provide the therapeutic window with minimal toxicity.

Keywords : Akt isoforms, cancer, drug resistance, epithelial mesenchymal transition

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