Department of Biomedical Sciences

presents the seminar series in Cancer Biology, Biotherapy and Nanomedicine

"Novel anticancer drug development candidates that target "undruggable" Ras or Wnt/β-catenin signaling pathways"

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Date : 3 December 2018
Time : 4:00pm - 5:30 pm
Venue : Meeting Room 2-130, 1/F, Block 2, To Yuen Building

Abstract

This presentation will describe the discovery, characterization, and development of novel small molecules that inhibit constitutively activated Ras- or Wnt/β-catenin mediated signaling pathways, which drive the growth of many human cancers but widely considered to be "undruggable". One subclass directly binds Ras to block Ras-effector interactions, thereby simultaneously inhibiting MAPK and Akt signaling to preferentially inhibit the growth of tumor cells harboring mutant or hyperactive Ras relative to cells with normal Ras. The other subclass targets phosphodiesterase 10A (PDE10), which we found is overexpressed in multiple cancer types. PDE10 inhibition activates cGMP/PKG signaling to induce β-catenin phosphorylation and proteosomal degradation, thereby suppressing Wnt-induced nuclear translocation of β-catenin and Tcf-mediated transcription of genes that encode for proteins necessary for tumor cell proliferation and survival. Both compound classes show high potency and selectivity to inhibit the growth of tumor cells expressing their respective target with minimal effects on normal cells. Both compounds classes also show strong *in vivo* antitumor activity in multiple mouse cancer models with no discernable toxicity.

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All are welcome!