J Appl Bioinforma Comput Biol 2018, Volume 7
DOI: 10.4172/2329-9533-C1-006

Calcium-mediated KRAS allosteric modulation: Implications in cancer drug discovery

Patrick DePaolo
Stevens Institute of Technology, USA

For decades, KRAS, a small GTPase, has been implicated in cancer research. Many have attempted to synthesize small-molecule inhibitors that have the capacity to interrupt the constitutively active, GTP-bound state of KRAS which causes an overstimulated oncogenic pathway. Burhman (2015) solved the KRAS X-ray structure in the presence of calcium, a breakthrough suggesting the existence of allosterically-mediated changes not previously hypothesized. Recent *in vitro* assays that will be presented reveal calcium-mediated structural stability changes, the facilitation of SOS-catalyzed nucleotide exchange, and the facilitation of KRASGTP intrinsic and GAP-catalyzed hydrolysis. KRAS-calcium structural and functional modulation is a novel finding that can contribute to the elucidation of the true intracellular behavior of KRAS, presenting new potential in cancer drug discovery by the synthesis of high-affinity KRAS-binding compounds that promote active site inhibition of calcium-mediated KRAS, which is highly present in the cell.

patdepaolo@gmail.com

Notes: