

Wednesday, March 26th, 2014

LSC 3 - Life Sciences Centre

2350 Health Sciences Mall

12-1pm



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“RasGRPs: Important Regulators of Ras in Lymphocytes and Potential Drug Targets in Mantle Cell Lymphoma ”

The small GTPase Ras plays a key role in governing cell proliferation, differentiation and viability. In lymphocytes, Ras is regulated by two types of Ras guanyl exchange factors: Sos and RasGRP. RasGRP family members have a catalytic domain similar to Sos. They also have calcium-binding EF hands and diacylglycerol (DAG)-binding C1 domains. In T cells and B cells, RasGRPs act to couple immune receptor signaling, phospholipase C activation and DAG/calcium messengers to Ras signaling.

RasGRPs in lymphocytes are potently activated by DAG analogues. Non-tumor promoting DAG analogues have been investigated as possible anti-cancer agents. Accordingly, we used a “disease discovery” approach to identify lymphocyte malignancies that might respond to DAG analogue stimulation of RasGRP pathways linked to cell death. Although our studies are limited by the use of cell lines, results indicate that certain cases of B non-Hodgkin’s lymphoma, including mantle cell lymphoma, might benefit from DAG analogue therapy.

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