NUS National University of Singapore | Department of Anatomy, Yong Loo Lin School of Medicine

NUHS National University Health System

PhD Oral Defense

MS PUJA KHANNA

Graduate Student

Supervisor: Dr Baeg Gyeong Hun

24 April 2018, Tuesday
3pm – 4pm

MD10 Anatomy Museum
Level 2, Seminar Room

Gram Domain-Containing Protein 1B (GRAMD1B) as a Novel Regulator of JAK/STAT Signaling Mediated Tumorigenesis

Dysregulated JAK/STAT signaling has been implicated in tumorigenesis, but the mechanisms underlying it are poorly understood. We previously identified the Drosophila ortholog of GRAMD1B as a novel component of the JAK/STAT signaling pathway. In this study, we explored its role in JAK/STAT signaling-mediated tumorigenesis. In gastric cancer cells, GRAMD1B expression was found to be positively regulated by JAK/STAT signaling which conversely regulated STAT3 levels, suggesting a positive feedback loop mechanism. Consistently, GRAMD1B acted synergistically with the JAK/STAT circuitry to promote gastric cancer cell survival. Moreover, immunohistochemical analyses established a positive correlation between GRAMD1B and phospho-STAT3 expression in human gastric tissues, thereby confirming the existence of a close link between these two signaling molecules in vivo. Notably, GRAMD1B was also found to be regulated by JAK/STAT signaling in breast cancer cells. GRAMD1B knockdown caused morphological changes of the cells, characterized by the formation of membrane ruffling and protrusions, implicating GRAMD1B in cell migration. Consistently, GRAMD1B inhibition significantly enhanced breast cancer cell migration via activation of JAK2/STAT3 and Akt signaling. Taken together, this study has identified GRAMD1B as a novel regulator of JAK/STAT signaling-mediated tumorigenesis, and provided a foundation for its development as a cancer biomarker and/or therapeutic target.

Please contact **Dr Hu Qidong at 6601 3730** or **Ms Nuramalina at 6516 3200** for more queries. All are welcome.