DukeNUS Medical School

Signature Seminar Series

Loss of ALK4 Function Promotes Cancer Progression Through Reprogramming of Receptor Glycosylation

ABOUT THE LECTURE

TGF-β superfamily signaling inhibits tumorigenesis while promoting metastasis during cancer progression. Activin receptor-like kinase 4 (ALK4) is a type I transforming growth factor-β (TGF-β) superfamily receptor that mediates signaling for several TGF-β superfamily ligands. While ALK4 is mutated in a broad spectrum of human cancers and has been identified in an unbiased screen as a gene whose disruption enhances Ras mediated pancreatic tumorigenesis in vivo, the role and mechanism of action of ALK4 in cancer progression is unknown. Here we demonstrate an unexpected role for loss of ALK4 function in promoting canonical TGF-β signaling to promote cancer progression. ALK4 expression is decreased in breast and pancreatic cancer, with loss correlating with poorer patient outcomes. Loss of ALK4 function increased TGF-β signaling, breast and pancreatic cancer cell migration and invasion, epithelial-mesenchymal transition and metastatic potential. Mechanistically, loss of ALK4 function promoted TGF-β signaling by altering Golgi morphology to promote TGF-β receptor glycosylation and cell surface stability. Thus, loss of ALK4 function is a frequent event in these human cancers that reprograms signaling via regulation of the Golgi and protein glycosylation.

Speaker: **Dr Gerard Blobe, MD, PhD**
Professor of Medicine
Professor of Pharmacology and Cancer Biology
Duke University School of Medicine

Host: **Dr Ong Sin Tiong**
Associate Professor
Cancer and Stem Cell Biology Programme
Duke-NUS Medical School

Date: **Tuesday, 16 July 2019**

Time: **12.00 PM - 1.00 PM**
(Light refreshments will be served at 11.30 AM)

Venue: **Duke-NUS Medical School**
Meeting Room 7C, Level 7

Contact Person: **Ms Serene Wie, Duke-NUS Research Affairs Department**
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ABOUT THE SPEAKER

Dr. Gerry Blobe is a Professor of Medicine, Pharmacology and Cancer Biology at Duke University School of Medicine. He is currently the Co-Director of the Solid Tumor Therapeutics Program and Associate Director of Training and Education for the Duke Cancer Institute. Dr. Blobe's laboratory at Duke University investigates the role of TGF-b superfamily signaling in cancer biology, focusing on mechanisms for their dichotomous tumor promoting and suppressing function, as well as investigating strategies for targeting these pathways. His research has established novel paradigms for TGF-b co-receptor function in regulating the trafficking and signaling of associated receptors, as well as the role of these TGF-b co-receptors in cancer biology. Clinically he specializes in treatment of patients with colorectal and pancreatic cancer, and in Phase I therapeutics. Dr. Blobe's lab has received peer-reviewed funding from the National Institutes of Health/National Cancer Institute, the Department of Defense, the American Cancer Society and the American Heart Association. Dr. Blobe currently serves on the editorial board for Breast Cancer Research, a Consulting Editor for JCI Insight and has served as an Associate Editor for The Journal of Clinical Investigation, on the editorial board for The Journal of Biological Chemistry, and as a standing member of the NIH Molecular Oncogenesis Study Section.



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