DUKE NUS
GRADUATE MEDICAL SCHOOL SINGAPORE

Signature Seminar Series

Pericytes, the blood-brain barrier, and brain diseases

ABOUT THE LECTURE

Our previous work identified platelet-derived growth factor B-chain (PDGF-B) signaling through PDGF receptor beta (PDGF-Rb) as a major mechanism in pericyte recruitment during normal and pathological blood vessel formation. Mice with null or hypomorphic mutations in *Pdgfb* show pericyte hypoplasia and display an impaired maturation of blood-brain barrier (BBB) through a combination of activated endothelial transcytosis and abnormal astrocyte end-foot polarization. Until recently, this phenotype was not connected to any specific CNS pathology. However, we have now found that loss-of-function mutations in PDGF-B in humans and mice cause idiopathic basal ganglia calcification (IBGC). Calcifications in the basal ganglia are a common incidental finding but sometimes inherited as an autosomal dominant trait (IBGC). In collaboration with a consortium of clinical geneticists, we identified six families of different ancestry with nonsense and missense mutations in the *PDGFB* gene. We also found that mice carrying hypomorphic *Pdgfb* alleles developed brain calcifications with similar composition, regional distribution and age-related expansion as human IBGC. These calcium depositions depend on the loss of endothelial PDGF-B, and correlate with the degree of pericyte and blood-brain barrier deficiency. Our data show that loss-of-function mutations in the gene for PDGF-B cause IBGC and IBGC-like disease in humans and mice, respectively. Somatic gain-of-function mutations in PDGF and PDGF-receptor genes have previously been connected to various types of cancers, but this is the first case where a human disease has been connected to an inherited loss of PDGF or PDGF-receptor function.

Speaker: **Prof Christer Betsholtz**
Professor of Tumor Biology, Uppsala University
Professor of Vascular Biology, Karolinska Institutet

Host: **Prof Karl Tryggvason**
Professor, Cardiovascular and Metabolic Disorders Program
Duke-NUS Graduate Medical School

Date: **Wednesday, 8 January 2014**

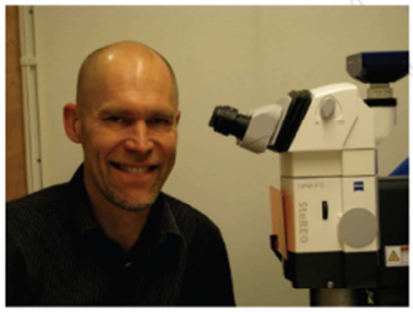
Time: **4:00 PM — 5:00 PM**
(Light refreshments will be served at 3:30 PM)

Venue: **Duke-NUS Graduate Medical School**
Amphitheatre, Level 2

Contact Person: **Ms Cynthia Lim, Duke-NUS Research Affairs Department**
Tel: 6601 2275 or Email: Cynthia.lim@duke-nus.edu.sg

ABOUT THE SPEAKER

Christer Betsholtz is professor of Vascular and Tumor Biology at Uppsala University and professor of Vascular Biology at Karolinska Institutet. His research deals with the role of growth factors in blood vessel formation and function. Betsholtz work has elucidated mechanisms of angiogenic sprouting, recruitment of pericytes and the role of these cells in vascular morphogenesis and function. A current interest concerns how pericytes regulate the blood-brain barrier, and how this regulation may impinge on diseases in, and the delivery of drugs to, the brain.



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