The Centre for Blood Research

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Wednesday, March 16th, 2011
12:00pm
in LSC3

Life Sciences Centre
2350 Health Sciences Mall

Characteristics and applications of a new mouse model of hemolytic hereditary

Hereditary spherocytosis (HS) is genetic disease that can range from very mild, subclinical cases to severe and life threatening. The gene lesion passed on from parents, or arising spontaneously, often affects the function of red cell proteins that assemble the RBC membranous cytoskeletal network. These structural complexes are required to support the distinctive shape and deformability of red cells. HS patients frequently have a mutation in one or more of the key structural components: Ankyrin-1, Band 3, Spectrin α, Spectrin β and protein 4.2. A mutation in Ankyrin-1 (Ank1) is accounts for approximately 50% of all mapped cases. Ankryin is the "linch-pin" linking the integral membrane protein Band 3 to the Spectrin-$\alpha 2\beta 2$ tetramer scaffold that underlies the plasma membrane inner leaflet.

Using an ENU-mutagenesis strategy to generate mouse models of human blood disease, we created a novel mouse strain that models ankyrin-deficient HS. Heterozygous mice closely resemble cases of mild HS, whereas homozygous are severely anemic. These mice (Ank1E794X) have an in-frame nonsense mutation that results in a severely truncated ankyrin-1 consisting of only the Band 3 binding domain but not a spectrin-binding or regulatory domain. We will discuss the generation and characterization of this novel mouse strain and how this mouse disease model, together with other mouse models of ankyrin-deficient HS, can be used to understand RBC membrane structure, hereditary spherocytosis, diseases secondary to hemolytic anemia, and malaria infection.

This Seminar is sponsored by:

MacoPharma

Host: Dr. Kelly McNagny, Professor, Medical Genetics, Biomedical Research Centre, UBC

Refreshments will be served 10 minutes before the seminar
Seminar information: 604 822 7407