

Wednesday, October 31, 2012  
12:00 pm  
in LSC3

Life Sciences Centre  
2350 Health Sciences Mall



## Dr. Henning Stennicke

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### “Designing novel therapies for prophylaxis in haemophilia”

In search of a haemophilia therapy requiring fewer and less frequent infusions, focus has been on generating coagulation factors with an increased half-life. This has been achieved using either fusion or conjugation technologies. Generation of fusion proteins generally limits modifications to the N- or C-terminus of the protein of interest, while the use of chemical modification allows much broader scope of modification sites. However, there is a major challenge for chemical conjugation of large polymers in targeting a specific site on the protein to avoid interference with the functional properties of the target molecule. In our efforts to generate modified version of coagulation factors 7, 8 and 9 with improved pharmacokinetic properties, glycoPEGylation technology has proven highly suitable for targeting modifications to N- or O-glycans. Selectivity is generated through enzymatic conjugation of PEG-modified sialic acid to the target protein by specific sialyltransferases.

While long acting factors represents an obvious strategy toward improved prophylaxis, more recently alternative strategies have started to emerge. Among these is the Functional blocking of TFPI binding to FXa which can facilitate haemostasis initiated by FVIIa:TF hereby compensating for impaired FIX/FVIII-dependent coagulation. Using an antibody against we have been able to effectively prevent TFPI inhibition of both FXa and FVIIa/TF. The “dual mechanism of action” supports continuous generation of FXa in the absence of a functional FIXa/FVIIIa complex and thus may represent an alternative strategy in haemophilia treatment.

This Seminar is sponsored by:



Host: Dr. Chris Overall, Canada Research Chair in Metalloproteinase Proteomics and Systems Biology, Centre for Blood Research, UBC

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

