Investigating molecular mechanisms involved in Tissue Factor gene regulation

We are seeking a *highly motivated* student to do a Masters thesis project or equivalet in Molecular Genetics, starting in the autumn of 2011.
The project will be performed at the Department of Medical Sciences under the supervision of the post doc Jenny Alfredsson, PhD, in the Coagulation an Inflammation Science group headed by Prof. Agneta Siegbahn.

Background

The Tissue Factor gene (TF), or coagulation factor III, is the main initiator of blood coagulation *in vivo* (Rapaport and Rao, 1995). TF is constitutively expressed in most cells of the body, e.g. epithelial cells, lung and brain tissue, while in monocytes and vascular endothelial cells TF expression is only induced upon either stimulus by endotoxins, chemical cytokines or by rapture of the vascular cell wall. This induction then intitiates the blood coagulation cascade.
Blood clotting can also result in plaque formation and blockage of the vasculature leading to arterial disease. Furhermore, in many cancer cells TF expression is elevated and blood clotting is a major secondary problem in cancer suffering patients.

How the TF gene is activated under different conditions by a subset of alternative promoters is well documented (Mackman, 1995), while other molecular mechanisms governing TF gene regulation are still not well studied. However, the +5466 A>G SNP in intron 2 of the tissue factor gene is strongly associated with an increased risk of acute coronary syndrome (ACS) together with a higher procoagulant activity phenotype in heterozygotes (Malarstig et al., 2005). Other regulatory elements and factors such as enhancers, insulator regions and epigenetic mechanisms remain to be discovered.

Aims

The main aims of this study will be to identify novel mechanisms governing tissue factor gene regulation. These findings may be used in the future when searching for new ways of controlling TF gene expression thereby preventing coagulation and blood clotting in for example ACS and cancer patients.

Methods used in this project

- DNA and RNA extractions
- electrophoretic mobility shift assay (EMSA)
- PCR
- qRT-PCR (TaqMan)
- Chromatin Immunoprecipitation (ChIP)
- agarose gel electrophoresis
- cell culture work
- monocyte purification from venous blood
- Bioinformatics

Requirements

A successful candidate is a highly motivated student with a great interest in Molecular Genetics. It is *vital* that you posess experience from previous practical laboratory work and that you feel comfortable working both independently and as part of a group. It is also important that you are familiar with standard Bioinformatics applications, both web based and local software.
You also need to have a high level of english fluency.

If you want further information about the project please do not hesitate to contact Jenny Alfredsson, PhD:

jenny.alfredsson@medsci.uu.se

If you are interested in doing a project with us please send us a short description of yourself where you state your previous experience along with references to:

jenny.alfredsson@medsci.uu.se

For more information about the Research group in Coagulation and Inflammation Science

http://www.medsci.uu.se/coagulation/coagulation.htm

Supervisors

Agneta Siegbahn, Professor in Clinical Coagulation Science, MD, PhD
Jenny Alfredsson, post-doc, PhD, MSc, BSc

Department of Medical Sciences
Coagulation and Inflammation
Akademiska University Hospital
Clinical Chemistry
751 85 Uppsala