

## Hycult Biotech participates in study on novel biomarker detection for vascular inflammation

Marie Curie Initial Training Network (ITN): Assessing biomarkers for multi-system inflammatory disease



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Project name: Translational Science for Vascular Inflammation and Repair

Project acronym: TransSVIR

December 2009, Hycult Biotech (HB) has started participating in a translational European study on vascular inflammation. The study will help to facilitate the development of new drugs that can reduce vascular inflammation. The European Commission has supported the study with in total 11 Early Stage Researchers (ESR) and 1 Experienced Researcher. It is a collaborative project including 6 centres from 4 European countries and is coordinated by the Medical University in Vienna, Austria. Within Hycult Biotech one ESR has been recruited who has started January 2011 for a period of 3 years.

**TransSVIR** will establish an Initial Training Network (ITN) in vascular inflammation and remodeling - an area of Translational Science where Europe can provide leadership on an internationally competitive level. The need for a training programme on vascular inflammation and remodelling is dictated by their pervasive roles in maintaining tissue integrity. The molecular processes involved are central to the pathogenesis of most severe inflammatory and malignant neoplastic diseases currently requiring more effective treatments. Rapid advances in basic science have identified numerous molecules as potential therapeutic targets for these conditions and developments in biotechnology and medicinal chemistry have produced potential therapies that await detailed evaluation.

### Summary of the project

The immune system has a central pathogenetic role in an increasing number of diseases including many not usually considered "inflammatory" (such as diabetes or cancer). In some settings, autoimmunity initiates a cascade of pathogenic events responsible for tissue destruction while in other situations involvement of the immune system is secondary. Intimate and reciprocal interactions between microvascular endothelium and circulating leucocytes are an essential feature of all types of inflammation: for example, endothelial cell activation not only facilitates localization of leucocytes to the injured tissue but the nature of the activation influences the properties of the recruited leukocytes; endothelium is the target of autoimmune attack by antibodies and leucocytes in systemic small vessel vasculitis; appropriately activated infiltrating macrophages induce capillary involution after injury but when activated differently they induce angiogenesis and lymphangiogenesis at chronically inflamed tissues and in tumours. Recent studies emphasise the critical links between immune mediated disease and infection and the multiple levels on which they operate. These document clearly the compromises that organisms have to make to balance between destructive immune responses against invading micro-organisms whilst simultaneously preserving host tolerance to self-antigens. They also highlight the role of the innate immune system and specifically the ways in which macrophages and dendritic cells maintain the balance between immune activation and immune tolerance and between destructive and reparative immune responses. Some of the receptors that control this balance have been identified: these include toll-like receptors (TLRs) and complement molecules. Currently, standard treatments for inflammatory diseases are based on the use of non-specific immunosuppressive drug regimens that are associated with severe toxicity in at least 25% of the patients. Many would be helped by more targeted therapies designed to correct the specific abnormalities in the innate immune system that fail in a particular disease. However this requires a deeper understanding of the control of the immune response and of the pathogenesis of the diseases it causes. This is illustrated by the clinical use of anti-angiogenic therapy after

successful trials in rodents was expected to circumvent the problem drug resistance whereas the opposite proved to be the case. Accordingly, **TranSVIR** will mount a comprehensive research programme designed to identify better ways to target key processes responsible diseases involving for acute vascular inflammation and remodelling.

### **Contribution Hycult Biotech**

Hycult Biotech is a company specialized in biomarker assay development in innate immunity, inflammation and tissue damage with particular expertise in assays for complement. Complement activation is important for many types of human disease including those with acute vascular inflammation, such as systemic lupus erythematosus (SLE) and possibly AASV. Despite the ubiquity of murine models of vascular inflammation there are no robust assays for measuring mouse complement activation. Consequently, analysis of the role of complement has not been feasible. The purpose of the proposed PhD project is to develop novel assays for measuring mouse complement and to use them to delineate pathways of complement activation in various mouse models of experimental disease such as autoimmune MLB/LPR mice but also in mice with renal Ischemia/reperfusion and anti-glomerular basement membrane disease. The specific aims of the project are to: (i) develop and characterize monoclonal antibodies against all relevant mouse complement proteins, including C1q, C3, C9 and the complex of C5b-C9; (ii) develop and standardize a method for the full measurement of the classical-, alternative- and lectin pathway of complement for the analysis of mouse complement activity; (iii) to delineate the pathways of complement activation in various mouse models of experimental disease including autoimmune MLB/LPR mice but also in mice with renal Ischemia/reperfusion and anti-glomerular basement membrane disease, (iv) Assess the quantitative levels of the lectin-, classical- and alternative pathways in different strains of mice, and (v) Apply the developed assays to mice with different types of autoimmune disease and to the renal diseases.

Updates on the TranSVIR project activities will be available on website [www.transvir.org](http://www.transvir.org).

Contract number: 238765.

### **List of Participants**

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