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ATHEROTHROMBOSIS AND VASCULAR

Research Brief

The laboratory is driven by the clinical objective to prevent and to improve treatment of myocardial infarction, which is the most frequent cause of death worldwide. A broad range of methods and approaches are undertaken. Members of the group investigate the mechanisms that cause the rupture of atherosclerotic plaques, causing clot formation, vessel occlusion and ultimately loss of myocardial tissue. Based on computational flow modelling, we have developed a unique plaque rupture model that is instrumental in defining genes and microRNA involved in plaque rupture. We are developing tests to identify patients at risk of plaque rupture that are based on characterising the urine proteome, microparticle and microRNA composition in blood. We have also developed molecular imaging tools to identify (and consequently treat) plaques that are prone to rupture using an extensive set of laboratory-made targeted nanoparticles that can be used as contrast reagent in various imaging modalities such as ultrasound, MRI, CT and PET. Our work in identifying mechanisms of plaque rupture is focusing on mediators of inflammation such as CRP and CD40L, with the particular focus of developing novel recombinant therapies that will prevent plaque rupture. Interestingly, we found that similar mechanisms of inflammation are active in diseases such as Alzheimer disease and MS. Treatment and prevention of myocardial infarction is very much focused on antiplatelet therapy, which currently unfortunately causes major bleeding problems in patients. We have described and are currently developing a number of novel biotechnological approaches that allow effective anti-thrombotic treatment without bleeding complications.

Methodologies

- Recombinant single-chain antibody generation (phage display) and production
- Flow cytometry
- Intravital microscopy
- Molecular imaging (using ultrasound, MRI, CT, PET)
- Targeted drug and cell delivery
- Thrombosis models and platelet function tests

Selected Publications

- Wolf D et al., Binding of CD40L to Mac-1’s I-domain involves the EQLKKSKTL motif and mediates leukocyte recruitment and atherosclerosis—but does not affect immunity and thrombosis in mice. Circ Res. 2011;109:1269-79.
Role of C-Reactive Protein (CRP) in atherosclerosis

Targets of recombinant lab tools for therapeutic and diagnostic targeting of thrombosis, inflammation and atherosclerotic plaques

Mouse model of unstable, vulnerable, rupture-prone atherosclerotic plaque