Anticoagulant Activity of Heparin used in Cardiovascular Disease

Supervisors: Prof. Michael Davies, Associate Prof. Rebecca Miller and Assistant Prof. Christine Chuang. Panum Building and Mæsk Tower.

Email: davies@sund.ku.dk, rmiller@sund.ku.dk, cchuang@sund.ku.dk

**Overall objective** – Heparins are widely used clinically in the prevention and treatment of blood clots. The heparin dose is often adjusted multiple times with protamine (a drug that reverses anticoagulation) to maintain activated partial thromboplastin time, which characterises coagulation in the blood. In thrombosis, myocardial infarction and unstable angina, the levels of reactive oxidant species (ROS) are highly upregulated, which results in damage and degradation of heparin (1, 2). It is currently unknown if heparin fragments degraded by ROS have a different anticoagulant activity compared with intact heparin. Our aim is to degrade heparin using ROS (hypochlorous acid and peroxynitrous acid reactive oxidants) and measure the anticoagulant activity of the ROS-degraded products in an anticoagulant assay used to defined anticoagulant activity (Figure 1).

**Aims:**

1. To degrade heparin using reactive oxidant species found in cardiovascular and general anti-inflammatory diseases.
2. Characterise heparin’s ROS degraded products using the latest sequencing technology
3. To define the anti-coagulant activity of the ROS degraded heparin fragments for improved clinical heparin dosing.

**Key References**