Deciphering heparin’s anti-inflammatory properties in cardiovascular disease

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Overall objective – Heparin is widely used clinically as an anti-clotting drug. Heparin is derived from animal sources, which makes it a highly heterogeneous drug with a range of clinically important properties. Since heparin is used in the treatment of clots, its anti-inflammatory properties became apparent. We have recently demonstrated that heparin’s anti-clotting activity can be removed (1, 2). In cardiovascular disease, heparin can alleviate inflammatory sites due to binding and removal of the protein myeloperoxidase (MPO) (2). Our aim is therefore to genetically engineer heparin variants that bind and remove MPO, but lack anti-clotting activity and explore if such heparin variants could be used to treat inflammation-induced tissue damage.

Aims:
1. To engineer cell-derived heparin designs with different desirable bioactivities.
2. To characterise the heparin binding motifs using the latest sequencing technology.
3. To test designed heparins on patient-derived cells with underlining cardiovascular disease.

Figure 1. The role of myeloperoxidase (MPO) in inflammation. (A) MPO plays a causative role in tissue damage following inflammation including in the heart and is implicated in the development of multiple cardiovascular diseases. Heparin is an inhibitor of MPO, however heparins potent anti-clotting properties prevents its long term use. (B) Neutrophil’s release MPO and MPO releases reactive oxidant species (ROS) resulting in extensive damage to the extracellular matrix. MPO is a highly positively charged protein that binds to negatively charged molecules in the extracellular matrix, mainly heparan sulfate (HS). An engineered heparin-variant has the potential to remove damaging MPO from the extracellular matrix at the site of inflammation.

Key References