

Protein modification in atherosclerosis

Background

Cardiovascular disease affects millions of people worldwide, with atherosclerosis being one of the leading causes of death. Atherosclerosis is characterised by chronic inflammation and formation of a fatty plaque, or lesion. During the progression of the disease, extensive damage is caused to proteins within the plaque and surrounding arterial wall. Large scale clinical studies support targeting these inflammatory processes as an effective therapy for the disease. There is a great need to understand how proteins become modified and the biological role of these changes in atherosclerosis.

Our recent work has shown that the inflammatory-enzyme myeloperoxidase (MPO) is a major contributor to protein damage in atherosclerosis, but the nature of the modifications and their role in the disease process is poorly understood.

The project

This work aims to determine the nature, extent and sites of modification on proteins in the diseased artery wall and the role of inflammation-induced damage in human atherosclerosis. Understanding the nature of the modifications, and how these are formed, should allow the development of novel therapeutic interventions that complement existing lipid-lowering strategies (e.g. statins) which treat the consequences of the disease but do not address the underlying causes. We will use a novel recently-developed approach to extract and identify modifications on arterial wall molecules, and particularly on extracellular matrix proteins. This will allow a detailed assessment of the biochemical, proteomic and metabolomic changes that occur during atherosclerotic plaque development. The studies will be carried out in collaboration with clinicians at Rigshospitalet.

Results from this study may validate protein modifications as a novel biomarker of arterial wall damage and disease development, with potential rapid translation to the clinic.

The team

You will become a member of the internationally and culturally-diverse Protein Oxidation group on floor 12.6 at the Panum Institute, and also collaborate with clinical staff at Rigshospitalet.

The candidate

You are interested in interdisciplinary science and exploring the molecular mechanisms behind disease. You are enthusiastic, curious and willing to learn. You are willing to work with human tissue samples.

We will guide you in developing new skills in state-of-the-art techniques such as immunoprecipitation, mass spectrometry (LC-MS), biochemical assays and the handling and processing of human tissue samples. We aim to provide you with the skills to become an independent scientist and develop your scientific career.

Contact

Michael Davies (davies@sund.ku.dk)