

Structure and function of mammalian scavenger receptors

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Introduction

Atherosclerosis and vascular disease is responsible for 50% of the mortality in the UK and industrialised nations. Scavenger receptors are integral membrane proteins that bind modified low-density lipoproteins that are implicated in atherosclerotic plaque formation. A model protein that is the current focus of our efforts is the LOX-1 scavenger receptor that is found on vascular tissues especially endothelial cells. Increasingly, this receptor has also been reported to be expressed on other cell types including monocytes and macrophages that play a key role in the inflammatory response leading to atherosclerosis.

We are testing various bacterial, insect and mammalian expression systems to generate recombinant LOX-1 for biophysical, biochemical and cell biological studies. Structural approaches including NMR and X-ray crystallography are being investigated. Purified proteins are being tested for their ability to bind different ligands. Cell biological studies on the localisation and trafficking of LOX-1 allow us to reconcile how LOX-1 structure and function is linked to its temporal and spatial distribution within a cell. How such properties are altered in vascular disease states are an obvious area of interest.

Publications

Murphy, J.E., Tedbury, P., Homer-Vanniasinkam, S., Walker, J.H. and Ponnambalam, S. (2005) Biochemistry and cell biology of mammalian scavenger receptors. *Atherosclerosis*, In press.

Cobbold, C., Monaco, A.P., Sivaprasadarao, A. and Ponnambalam, S. (2003) Aberrant trafficking of transmembrane proteins in human diseases. *Trends Cell Biol* **13**, 639-647.

Funding

This work was supported by the BBSRC and The Wellcome Trust.

Collaborations

We collaborate with Dr. John Walker (BMB, Leeds) Prof. Simon Phillips (BMB, Leeds) and Prof. Shervanthi Homer-Vanniasinkam (Vascular Surgery, Leeds General Infirmary) on this project.