Can marine microorganism extracts prevent heart attacks?

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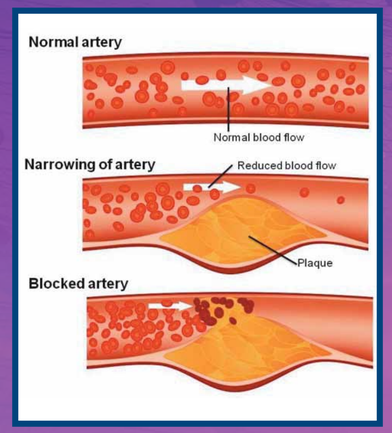
What is the problem?

Coronary Heart Disease (CHD) is the most common cause of death in the UK and worldwide – causing 74,000 deaths each year in the UK.

In CHD your heart's blood supply is interrupted by a build-up of fatty substances in arteries. Over time these fatty deposits form plaques that harden or rupture or can become so large that they block the artery and stop the blood flow. This can cause a heart attack. Current treatments for this are not particularly effective and better ones need to be developed.



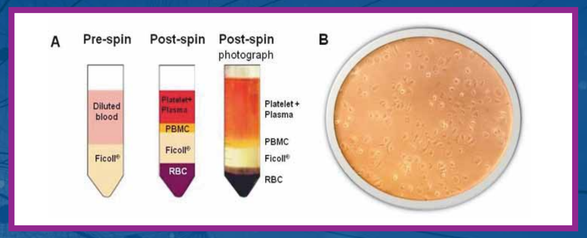
What are we interested in?

The fatty deposits leading to plaques are built by a type of white blood cells called macrophages. These macrophages take up oxidised low density lipoproteins (oxLDL), the 'bad' cholesterol in your bloodstream and form lipid-loaded foam cells in artery walls. During that process reactive oxygen species (ROS) and chemical pro-inflammatory substances (cytokines) are produced in the surrounding tissue, which damage the innermost artery layer and enable plaque build-up by activating and recruiting more macrophages.

Together with our industrial collaborator (Smith & Nephew Ltd) we have identified a novel chemical compound (AQP) from deep-sea microorganisms and determined if it would be a suitable and more effective drug treatment for CHD. Another compound, chemical name BG12, is already used clinically for Multiple Sclerosis, a nerve-destructive disease and it acts on the same 'master' regulator to down-regulate inflammation as our novel AQP. We determined if BG12 could also be used to treat CHD.

What did we do?

Macrophages were isolated from human blood by gradient centrifugation and used for our experiments



A: Blood before (pre-spin) and after (post-spin) centrifugation. We separated red blood cells (RBC) from white blood cells (PBMC) and then isolated macrophages from other PBMCs.

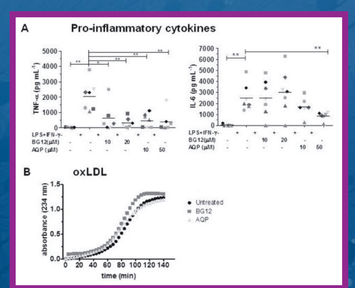
B: Human macrophages.

Macrophages were stimulated with lipopolysaccharide (LPS), a bacterial cell wall and treated with AQP or BG12 to compare efficacy in down-regulating pro-inflammatory cytokines (IL-6 and TNF-α).

Human LDL was isolated and exposed to AQP or BG12 to determine if AQP or BG12 can prevent the formation of oxLDL.

What did we find?

- AQP reduced both pro-inflammatory cytokines
- BG12 reduced only one pro-inflammatory cytokine
- Neither AQP nor BG12 prevented the formation of oxLDL



What does it mean?

- Both drugs reduced inflammatory responses. The reduction of pro-inflammatory cytokines was more effective in macrophages treated with AQP than with BG12.
- Both compounds target more specific pathways to down-regulate inflammation although they do not 'catch' ROS and prevent the formation of oxLDL.
- AQP could be developed as a novel and more effective drug for the treatment of atherosclerosis.

Who am I?

I am a PhD student at the University of Aberdeen. My project is to characterise the novel AQP molecule as a new therapeutic drug and investigate whether it is more effective than BG12 to treat inflammatory diseases such as atherosclerosis. I gratefully acknowledge the funding support from Medical Research Scotland. Additional thanks to my supervisors Heather, Elaina and Tim.

Miriam Obliers started her PhD project, *"Novel small molecule modulators of the antioxidant response pathway: potential for therapy in cancer/inflammatory disease"*, under the supervision of Dr Heather Wilson in 2011 and while principally based at Aberdeen University, she is also working closely with Smith & Nephew Ltd.