CASE Award; Polymeric Coating to Inhibit In-Stent Restenosis

Chemistry Innovation Case Study no 35, 2010

Knowledge Transfer Network

Chemistry Innovation

Coronary Artery Disease (CAD) is the major cause of illness, disability and death, worldwide. It is responsible for the deaths of 3.8 million men and 3.4 million women annually worldwide.

This Case Study resulted from a CASE project awarded by Chemistry Innovation. It strongly aligns with Chemistry Innovation's 'Sustainable Chemistry' priority area and was completed by associate Katie Nickson, supervised by Dr Rachel Williams. Please contact Dr Stephen Hillier for further information on this project or Case Awards in general.

The Problem

CAD occurs when the arteries supplying blood to the heart muscle harden and narrow, due to the accumulation of atherosclerotic plaque on the lumen wall. Narrowing of the vessel reduces blood flow, causing depletion in oxygen and nutrients supply, which results in symptoms such as chest pain and shortness of breath (angina pectoris) which if left untreated may lead to a heart attack (myocardial infarction). Percutaneous Coronary Intervention (PCI) is a therapeutic procedure used to treat CAD by physically remodeling the vessel using an angioplasty balloon and in most cases insertion of a metallic (wire mesh) stent. Reocclusion of the vessel (restenosis) following PCI is a considerable problem in the long-term clinical performance of cardiovascular stents. This results from a cell response to the surgery in which the vascular endothelium is damaged and the underlying smooth muscle cells are stimulated to proliferate. It has long been hypothesised that the re-growth of a functional endothelial cell monolayer is important in the prevention of restenosis.

The Challenge

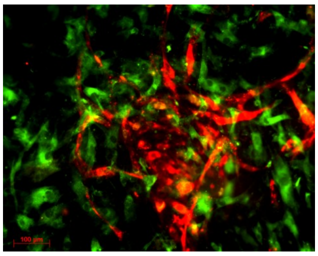
Biomer Technology Limited (BTL) has developed a range of complex synthetic polymers displaying novel surface chemistry and wished to study the interaction of these surfaces with human cells to determine the optimum candidate material for future pre-clinical and clinical studies. The optimum material would support the rapid attachment and proliferation of endothelial cells while limiting the stimulation of smooth muscle cells which theoretically would result in the rapid, re-endothelialisation of the endothelium post stenting and thereby lower the risk of restenosis.

Collaboration

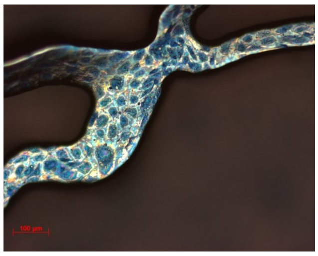
The project followed on from a previous KTP collaboration between BTL and the University of Liverpool resulting in a successful bid for an Industrial CASE Award in Chemistry Innovation's 2007 call. Scientists from the University are internationally renowned for their expertise in the evaluation of biomaterials and, in particular, the biointeractions at the cell/ material interface and their influence on biocompatibility.

The Solution

The project required a multidisciplinary approach involving polymer chemistry, surface analysis, biointeractions and in depth *in vitro* cell culture testing to develop the robust testing protocols required to identify optimised surface chemistries. During the CASE studentship the Associate has worked closely with BTL and developed *in vitro* cell culture methodology to evaluate the human vascular endothelial and smooth muscle cell response to the BTL polymers. Using these methods has helped BTL to identify an optimal polymer coating which they are taking forward through clinical trials.



Human endothelial and smooth muscle cells in co-culture



Human endothelial cells growing on a BTL polymer coated stent strut

Benefits

- The project has identified candidate polymers which have subsequently entered pre-clinical and clinical testing
- The Associate has developed her expertise in this cross-disciplinary research field
- The collaboration has lead to other joint projects in parallel areas
- Applications have been submitted for further major funding to design an ethically favourable *in vitro* test method to evaluate coronary stents using a 3-D dynamic flow model

biomer technology

UNIVERSITY OF LIVERPOOL

Biomer Technology Limited

BTL is a UK based biomaterials company specialising in the design, development and manufacture of high performance polymers, process technology, components and products for the medical device industry. The Company works in partnership with leading academic, clinical and commercial organisations in the UK, Europe and USA to evaluate its materials and ultimately to ensure commercialisation of its broad based technology platform.