SMALP technology: unlocking membrane proteins for drug discovery

The Challenge

Over the past 60 years our world has been revolutionised by the continued development of new medicines to treat a wide range of debilitating and life threatening diseases. The process of developing these new drugs often starts with gaining a detailed understanding of the disease itself. This leads to the identification of various target proteins within the body that play an important part in the progression of disease. For example, in cancer a protein may be identified that is responsible for the uncontrolled growth of the tumour. Pharmaceutical companies would then examine a wide range of potential drugs to see if any of them can turn this protein off thereby preventing the growth of the tumour.

A central part of realising this ambition has been the development of a set of methods to first isolate biomolecules and a second set of methods to study their structures and interactions. Unfortunately the lack of a single effective method for extracting membrane proteins from living tissues has meant that our knowledge of these important molecules has lagged far behind their soluble counterparts. This is particularly problematic as membrane proteins are essential to our understanding of life and represent more than 50% of pharmaceutical targets.

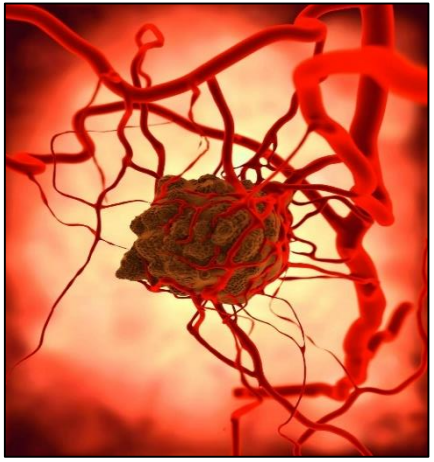
The Research

Professor Tim Dafforn at the University of Birmingham has developed a new method that for the first time allowed an auto-assembled nanoparticle (SMALP) to encapsulate membrane proteins complete with their supporting lipid membrane. Most importantly the method can be used to directly extract membrane proteins from the biological tissue preserving the activity of the protein.

MedImmune is a leading global biologics R&D company, focusing on three core therapeutic areas: Oncology; Respiratory, Inflammation and Autoimmune; and Cardiovascular and Metabolic Disease.

Professor Dafforn applied for a CBMNet Business Interaction Voucher with MedImmune to develop a collaborative partnership and produce preliminary data that could be built on in future funded projects.

The aim of the project was to investigate whether Professor Dafforn's method can be used to make proteins of interested to drug discovery. If this is so, then this would revolutionise the MedImmune business.



CBMNet Business Interaction Voucher

The Result

Medimmune supplied Professor Dafforn with 2 membrane proteins that were expressed in SF9 cells. Professor Dafforn developed two protocols for solubilising the protein using the SMALP protocol

A joint one day meeting was held in May at the University of Birmingham. Results from both sides of the project were reported in a confidential meeting and protocols were shared.

The results showed that the SMALP method was effective producing proteins in a form that was complementary to drug discovery methods.

The method was quicker and more reproducible than existing methods and provided a material that was more stable.

The Future

The collaboration has provided data that has laid the foundations for future projects exploring the wider use of SMALP technology in drug discovery.

The PDRA (Dr Ian Cadby) has now moved to a different project in an adjoining laboratory which has allowed him to continue to support Medimmune with protocols.

Medimmune have agreed to support a CASE Industrial Strategy Studentship at the University of Birmingham to enable the continued development of the project.

In addition Professor Dafforn is in discussions with Medimmune regarding partnership in an EPSRC Senior Fellowship application.

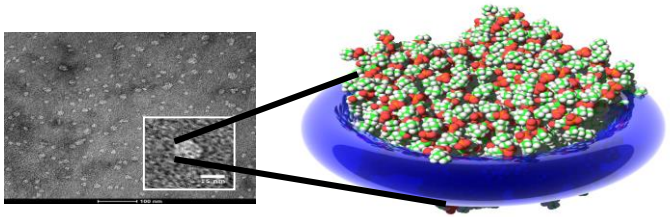


Figure shows a styrene maleic acid lipid particle that can stabilise active drug targets for drug discover

"Often the hardest part of a project with industry is getting the funds for the initial exploratory experiments. This CBMNet Business Interaction Voucher has helped us to get valuable data which will help us grow a productive collaboration with Medimmune"

Professor Tim Dafforn
University of Birmingham

"Having recently become an Industrial member of CBMNet we became aware of the innovative funding opportunities that the network provides. This enabled us to very rapidly set up a collaboration with Professor Dafforn following the award of a Business Interaction Voucher.

This collaboration helped to rapidly achieve proof of concept work and has acted as a springboard for a longer term collaboration. This has been instrumental in opening up an exciting new avenue for working with complex membrane protein targets."

Trevor Wilkinson
Associate Director, Protein Sciences MedImmune

This project was funded through the Crossing Biological Membranes Network (CBMNet) by the Biotechnology and Biological Sciences Research Council (BBSRC)

Email: cbm@sheffield.ac.uk
Telephone: 0114 222 9766

Website: www.cbmnetnibb.net
Twitter: @CBMNet_NIBB