Project no. **037740**

Project acronym: ***PRISM***

Project title:

__P__hospholipid and Glycolipid __R__ecognition, __I__nteractions and __S__tructures by __M__agnetic Resonance

Instrument: STREP

Thematic Priority: LSH-2005-1.2.5-4

Publishable Executive Summary

Period covered: from 1/5/2007 to 31/10/2010

Date of preparation: 15/12/2010

Start date of project: 1st May 2007

Duration: 42 months

Project coordinator name:
Professor Michael Overduin

Project coordinator organisation name
The University of Birmingham

Summary Description of Project Objectives

The overriding objectives have been to:

1. Form experimentally useful and physiologically realistic mimics of cellular membranes,
2. Profile and model molecular specificities of proteins for diverse membrane compositions,
3. Progress the field of NMR spectroscopy for broader utility in lipid and protein research by boosting experimental sensitivity and resolution
4. Develop tools to produce and apply labelled proteins and lipids to better understand membrane trafficking and signalling pathways
5. Develop, test and validate software tools to extend knowledge of protein:membrane interactions from experimental to virtual applications.

Contractors

The *PRISM* project includes the following participants as coordinators and contractors, with PhosPhoenix SARL also being involved as a subcontractor.

Participant Role	Participant Name	Short Name	Country	Leader
Coordinator	University of Birmingham	UB	UK	Michael Overduin
Contractor	Johann Wolfgang Goethe-Universität BMRZ	JWGU-BMRZ	DE	Harald Schwalbe & Clemens Glaubitz
Contractor	Max Planck Institute CBG	MPG	DE	Kai Simons
Contractor	University of Geneva	UG	CH	Jean Gruenberg
Contractor	Utrecht University	UU	NL	Gerrit van Meer
Contractor	Oxford Instruments Molecular Biotools Ltd	OIMBL	UK	Andrew Sowerby

Coordinator Contact Details: Professor Michael Overduin
Institute of Cancer Studies
The University of Birmingham
Edgbaston
Birmingham B15 2TT
Tel: 00-44 121 414 3802
Email: m.overduin@bham.ac.uk

Project web site: http://www.lipidprism.org/

Project Logo:

Work Performed

The overall objective of the *PRISM* project is to understand how membranes are specifically recognized and modulate protein function. The underlying goal is to help bridge the technical and knowledge divide between proteomics and lipidomics using key functional paradigms.

The PRISM project is an integrated program which brings together a number of different biological disciplines and NMR technologies through the following workpackages:

WP0: Coordination and management

WP1: NMR methods to obtain structural parameters

WP2: Membrane models

WP3: Protein production

WP4: NMR structures of protein lipid complexes

WP5: Functional NMR

WP6: Software tools

WP7: Exploitation and dissemination

The development of multidisciplinary studies and versatile tools to connect these fields was intended to enable translation of discoveries of lipid functions and associated protein mechanisms into exploitable insights, with most drug targets being proteins residing in lipid environments. It was felt that the European pharmaceutical and biotechnology sectors in particular would benefit from technological advances that make accessible new membrane associated targets for therapeutic development. We recognized that the EU has entered a period of unprecedented economic opportunity due to biomedical advances and the wealth of 'omics' knowledge. However moving beyond this realization requires intensified communication and skills exchange between fields as well as overcoming technical barriers including sample production, handling, screening and analysis. PRISM brought leading experts in membrane biology and biochemistry together with NMR spectroscopists in order to focus on key problems in the field of membrane protein research and supercede rate-limiting barriers.

Highlights of results achieved

- Novel amphipathic polymer-based nanoparticles designed to solubilise and study membrane proteins from cellular material.
- Development of a dynamic nuclear polarization NMR probe
- Synthesis and testing of new radicals for enhanced polarization of biomolecular samples
- Novel sample dissolution methods to boost DNP sensitivity

- Analysis of the network of specific and nonspecific structural interactions of peripheral membrane proteins.
- Characterization of protein domains that recognize PI(4)P and Golgi membrane
- Development of modelling approaches to calculate 3D structures of protein – lipid – micelle complexes.
- Over 50 papers published in scientific journals including EMBO, Nature, PNAS USA, and Science, and over 100 conference presentations given

Expected End Results

The achievements from the *PRISM* project include development of novel tools and methods for membrane protein analysis, new structures and dynamical features of membrane proteins, and software tools for predicting membrane protein assembly structures and binding sites.

The products of the *PRISM* consortium include four patents, over fifty publications, and over one hundred conference presentations. The consortium has taken advice on exploitation routes, and has a set of licensing agreements in place to distribute new products to global markets. The PRISM External Advisory Group includes SME directors and industry representatives and along with university technology transfer offices will continue to provide guidance on exploitation.

Intentions for Use and Impact

PRISM has developed a range of experimental and computational tools for understanding protein structures in terms of the lipids they recognize and for calculating protein-lipid-micelle structures. In addition to providing a novel computational approach illuminating protein-lipid interactions at the atomic level, PRISM has yielded multistep binding mechanisms for biomolecular systems that adapt and respond to their molecular environments. This has long-term potential for applications such as drugs that act specifically on protein-lipid interfaces, and biochemicals agents which regulate the assembly and subcellular localization of proteins *in vivo*.