IT Tralee Masters by Research Programme Details

Title of Project: Biomimetic Cell Membranes as Skin Barrier Models (SkinArt-M)

Name of Principle Supervisor: Dr. Joanna Tierney

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Brief Biography of Principle Supervisor: Dr. Tierney has specific expertise in skin cell health research in the context of cosmetic product support. Her research experience encompasses the fields of cell biology, immunology, infection and disease with applications in biopharmaceutical, medicine and veterinary sciences and she has completed a number of postdoctoral positions both in academia and industry. She is a Principal Investigator with Shannon Applied Biotechnology Centre on several applied research projects for industry, has a wide ranging funding portfolio (Enterprise Ireland, European Union, and Science Foundation Ireland) and currently supervises students to Masters and PhD level. Relevant to this project, her vast experience in mammalian cell culture applications for SMEs including current projects on skin cell analysis of skincare formulations for cosmetic companies.

Recent Publications:

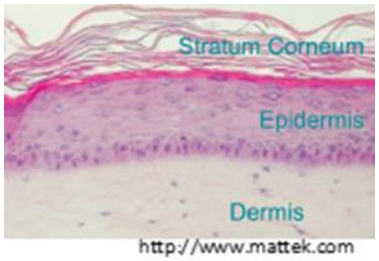
- Islam N, Whitehouse M, Mehendale S, Hall M, Tierney J, O'Connell E, Blom A, Bannister G, Hinde J, Ceredig R, Bradley BA (2014). Post-traumatic immunosuppression is reversed by anti-coagulated salvaged blood transfusion: deductions from studying immune status after knee arthroplasty. Clin Exp Immunol. Aug:177(2):509-20.
- Islam N, Whitehouse M, Tierney JB, Mehandale S, Hall M, Blom A, Bannister G, Ceredig R & Bradley B (2012). Biomarkers for post-traumatic immunosuppression. Network for the Advancement of Transfusion Alternatives, Copenhagen, Denmark.
- Islam N, Whitehouse M, Tierney JB, Mehandale S, Hall M, Blom, A, Bannister G, Ceredig R & Bradley B (2011). Post-traumatic immunosuppression syndrome and its reversal by salvaged blood transfusion. British Society for Immunology, Liverpool, UK.
- McCarron C & Tierney JB (2011). Metabolic characterisation of macrophage activation by phenotype microarrays. Irish Society for Immunology Galway, Ireland
- Keating P, O'Sullivan D, Tierney JB, Kenwright D, Miromoeini S, Mawasse L, Brombacher F & La Flamme AC (2009). Protection from EAE by IL-4Ralpha (-/-) macrophages depends upon T regulatory cell involvement. Immunol Cell Biol. 87 (7) : 534-45
- Godber B, O'Reilly F, White A, Donovan C, Tierney JB & Cusker MD (2008). New and Improved Immunoglobulin assays on the Olympus AU400/400eTM, AU640/640eTM, AU2700/5400TM, and AU680TM chemistry immunoanalysers. American Association for Clinical Chemistry, Washington, USA.

Research Project Abstract

Human skin is the largest organ in the body and serves as a protective barrier against the outside environment. Skin is composed of three primary layers, with the upper outer layer contributing to its formidable protective barrier functions. Compounds applied on to skin must pass through this outer layer with human (in-vivo) studies, the optimal method for assessing the absorption of test compounds for dermatology industry needs of evaluating new formulations. However due to ethical and economic considerations associated with in-vivo testing, a laboratory (in-vitro) based approach to measure skin absorption is often preferred and is routinely used as an alternative. Today, a variety of skin models are available for evaluation of compounds. As these cell models vary in their sensitivity, technical difficulty and cost, great interest in the development of artificial membrane platforms to predict compound absorption has evolved in recent times. These membranes can be created artificially in the lab and the **main goal of this project is to employ artificial biomimetic lipid bilayer cell membranes as non-cell based skin barrier models to predict percutaneous (skin) absorption** amenable to high throughput approaches in compound formulation development for a variety of industries including the cosmetic sector.

Research Context (Technical Merit & Impact)

Human skin is composed of three primary layers and within each layer are mixtures of unique cells that provide skin with structure and function. The upper epidermis is responsible for the skin's barrier properties and is highly cellular. The absorption of compounds occurs primarily by passive diffusion through the skin's outer layer, the stratum corneum. This process can be slow and dependent on the permeability coefficient of the compound, applied concentration and surface area which is influenced by many factors including skin thickness and lipid composition. The solvent system used in compound formulations also has a controlling influence over the rate and extent of active ingredient absorption. Percutaneous permeation experiments using excised mammalian skin employing diffusion cell systems (e.g. Franz cell or flow through cell) are routinely used to assess absorption of compounds across skin.



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The stratum corneum is a bio-membrane and is less permeable to lipophilic compounds which pass through its protein/lipid domains. Great interest in the development of model membrane platforms that enhance membrane biology understanding, especially the lipid bilayer environment has evolved due to potential applications as tools to investigate cellular and molecular interactions. Lipid bilayers can be created artificially in the lab to enable experiments that cannot be done with natural bilayers. These synthetic systems are called biomimetic lipid bilayer models which aim to encompass lipid complexity, asymmetry, stability and high lateral fluidity.

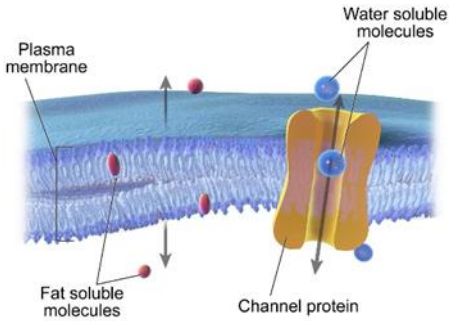

Diagram courtesy of Blausen.com staff. "Blausen gallery 2014"

The research proposed in this project is to investigate the use of a biomimetic membrane platform to predict percutaneous absorption in human skin as an early stage, low-cost alternative test to existing cellular models. In-vivo studies are the optimal approach for assessing absorption through skin even though there are several ethical and economic considerations associated with this form of testing. An in-vitro approach is often preferred with the predominant cell forms employed for percutaneous absorption being that of excised mammalian skin including pig which

has relevant physiology to that of human skin and monolayer cultures of human keratinocytes the predominant cell type in the epidermis. A high throughput alternative is desirable to avoid the cost and time exhaustive measures of current testing practices in industry.

Research Methodology

Research Location:
The research programme will be based in IT Tralee. As the project is in collaboration with the National Biophotonics and Imaging Platform Ireland, Dublin City University (DCU), secondments to perform comparative studies on the biomimetic platform in DCU will be required.

Research objectives:
Investigate the use of a biomimetic membrane platform to predict percutaneous absorption as an early stage alternative test to existing cellular models;

- Establish and optimise cultures of human keratinocyte cells for barrier formation.
- Generate characterised skin barrier equivalents that represent stratum corneum epidermis by fabrication on artificial membranes in Franz Diffusion cell or cell culture Transwells.
- Compare an artificial lipid bilayer cell membrane model with a stratum corneum lipid model to predict percutaneous absorption of model compounds.

Discipline-specific training:

- Knowledge of cellular biology and processes in skin health.
- Understanding of cell interactions within skin and the different in-vitro methods used in cosmetic testing methods.
- Understanding of biomimetic artificial membranes for their ability to predict percutaneous absorption.
- Knowledge of the factors influencing the absorption process for each membrane through the use of quantitative structure-permeability relationships.

Other Core training benefits:

- Good Laboratory Practice in class II facilities set to international best practice.
- Cell culture: Primary cell culture (keratinocyte cells), cryopreservation and cell proliferation assays. Biochemical analysis: enzyme assays, protein assays, protein purification, spectrophotometry, ELISA, Flow cytometry, DNA, RNA extraction, PCR, real time PCR.
- Biomimetic membrane with Langmuir Blodgett methods, microfabrication, electrochemical impedance and fluorescence correlation spectroscopy.
- Educational development; statistical and graphic packages for analysis and dissemination for publications/reports.

Project Schedule- Gantt chart