



Free radical research

The Free Radical Research Facility was established as the foundation for the Department of Diabetes and Cardiovascular Science.

Free radicals play crucial roles in human physiology and disease progression. The free radical research team is focusing on nitric oxide (NO), a potentially protective agent when produced in the correct quantities in the right place and at the right time, and oxygen-centred radicals that are generally regarded to be damaging and cytotoxic. In healthy individuals, the potentially toxic effects of oxygen-centred radicals are countered by a battery of antioxidant defences.

Imbalance in free radical production in favour of harmful radicals is a feature of diabetes that might be fundamental in many of the worst aspects of the disease.

The team is currently involved in a number of projects to investigate the cellular mechanisms that underlie free radical production, the link to inflammatory processes that exacerbate the harmful effects, and antioxidant and nutritional interventions that might help to manage these consequences. Ongoing projects link closely with the Genetics and Immunology Group and the Lipidomics Research Facility, and those that require input from patients utilise the adjacent Highland Clinical Research Facility.

Ongoing contract research is centred on measurement of a wide range of metabolites and markers in biological samples, with a special focus on those associated with oxidative stress and inflammation. The laboratories host the latest technology for measuring free radicals and their characteristic cellular 'footprints'.

Researchers are also conducting functional studies *in vitro* and *in vivo* to establish the impact of new therapeutics at both the cellular level and in terms of clinical measures.



Case study: Free radical research

Aquapharm Biodiscovery

The core focus of Aquapharm is the development of novel pharmaceutical compounds leading to the development of novel antibiotics, targeting both Gram negative and Gram positive infections. In addition, Aquapharm's development pipeline is also fed by an active discovery portfolio of anti-oxidants, anti-inflammatories and novel biocatalysts.

Aquapharm has an ongoing collaboration with the Department of Diabetes and Cardiovascular Science at the University of the Highlands and Islands to help screen marine extracts for biological activity to determine the mechanism by which active extracts exert their effects in cell culture assays.

"The work to date has been instrumental in identifying lead compounds for further analysis and we look forward to an ongoing collaboration with the team at the University of the Highlands and Islands."

Andrew Mearns Spragg

Chief Technical Officer and Founder, Aquapharm Biodiscovery Ltd





Genetics and immunology

The Genetics and Immunology Group has a background in the mental health arena and is using molecular genetics, molecular biology, epigenetics and immunological techniques to investigate pathways common to schizophrenia, diabetes and the impact of medication on metabolism.

The group is investigating these diverse conditions through two main avenues. Firstly, in the biology of lipid-based signalling and inflammation. Secondly, investigating the interplay between environment and disease, particularly through adverse immune responses to diet. For example, some types of wheat gluten proteins may be involved in type-1 diabetes and schizophrenia.

This latter field, known as nutrigenomics, involves the study of the interaction between our genetic make-up and our diet. Researchers within the group strongly believe that the immune system plays a central role in bridging the link between our genes and toxic proteins from foods.

Identification of susceptibility genes and risk factors, as well as simple tests (biomarkers) that measure these traits will allow for prediction, treatment and prevention of conditions such as type-1 diabetes and schizophrenia.

The implications of this research work have the potential to be of benefit to people all over the world and to influence agricultural and food industries.

The Genetics and Immunology Group can work with your organisation on bespoke research projects, or in a consultative capacity, to enhance your research and development activities in the field of genetics, immunology and nutrition.



Case study: Genetics and immunology

Glory Biomedical Co Ltd, Taiwan, is a company that has been developing novel immunotherapies of cancer, with a major focus on propagation of particular white blood cells from healthy people for use in cancer therapy.

Glory Biomedical has collaborated with the University of the Highlands and Islands to develop a technology to rapidly propagate a specific white blood cell population, and the team has now opened trials in China and India to test the therapy in cancer patients. In addition, the company is working with the university to develop an in-house test for identification of blood samples rich in a factor that could work in concert with white blood cells to further enhance cancer treatment in patients receiving chemotherapy.





Lipidomics

Lipidomics involves the large-scale characterisation of molecular species of lipids produced by cells, tissues and organisms. Our understanding of the importance of lipids in physiological processes and as indicators of disease status is only just emerging. To date the discipline of lipidomics has been adopted by only a few institutions worldwide, one of which is the University of the Highlands and Islands.

The Lipidomics Research Facility combines in-depth expertise with cutting-edge instrumentation for the global and targeted analysis of lipids. The main thrust of the research carried out by the team is focused on investigating the key role that lipids play in health and disease. The highly skilled research team has considerable knowledge of the development, validation and application of lipidomic approaches, as well as practical experience of the identification and quantification of a wide variety of lipids in biological matrices. This breadth of expertise allows the team to provide lipidomic investigations ranging from in vitro experiments in cells through to clinical studies with body fluids.

The Lipidomics Research Facility is located in purpose-built laboratories, which house a modern and well-equipped mass spectrometry suite for lipid analysis. A full range of bioinformatic and statistical tools are also available for the processing of lipidomic data sets.



Lipidomics Research Facility: Equipment and software

- Thermo Scientific LTQ-Orbitrap XL LC-MSn
- Thermo Scientific Exactive LC-MS
- Thermo Scientific TSQ Quantum Ultra LC-MS/MS
- Electrospray, nanospray and APCI sources
- All LC-MS platforms can be interfaced with Thermo Scientific Accela UPLC, Waters nanoAcquity UPLC and Proxeon EASY-nLC II systems
- Advion Triversa Nanomate with LESA
- Thermo Scientific ISQ GC-MS with EI and CI sources
- The GC-MS system can be configured for liquid, headspace and SPME analysis
- Bioinformatic software
- Univariate and multivariate statistical software





Proteomics

Proteomics seeks to provide a functional link between gene expression and phenotypic outcomes and is a key technology used to study the biology of living systems.

The proteome is not a pre-determined, static entity and the concentration and location of a protein within a cell or organism can change depending on physiological or environmental conditions. Proteomics is able to define changes in protein expression by employing a combination of efficient separation techniques, high-resolution mass spectrometry and bioinformatics.

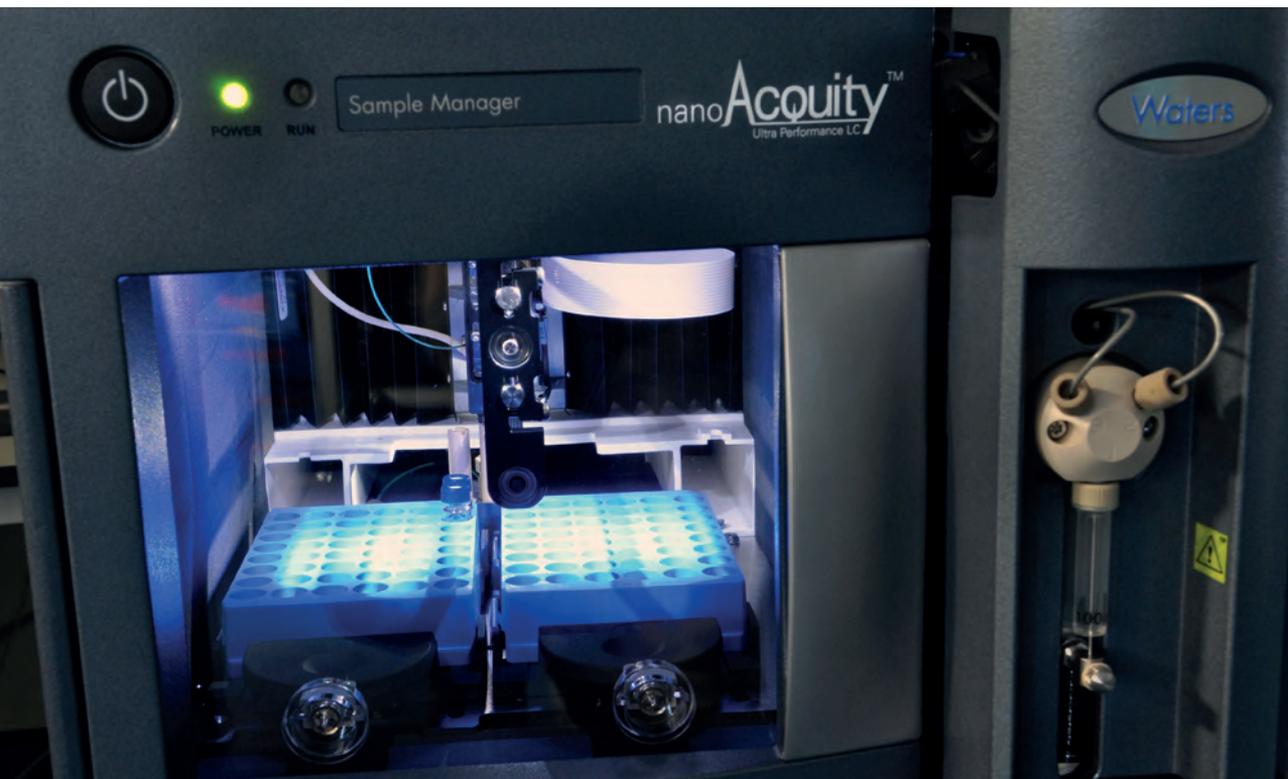
The Proteome Analysis Facility has a highly skilled research team with a strong background in protein chemistry. Services range from standard protein identifications to the characterisation of post-translational modifications and high-throughput quantification of large cohorts of proteins, including label-free, iTRAQ and SILAC approaches. There is also expertise in stable isotope labelling strategies to measure the turnover rates of individual proteins in biological systems. Ongoing studies are focused on proteomic analyses of human cells in culture and model organisms such as *C. elegans* and zebrafish.

The Proteome Analysis Facility is based in purpose-built laboratories, which house a modern and well-equipped mass spectrometry suite for protein analysis. Bioinformatic tools, including locally hosted servers with the capability of searching standard or custom protein databases, are also available for the processing of proteomic data sets.



Proteome Analysis Facility: Equipment and software

- Thermo Scientific LTQ-Orbitrap XL LC-MSn
- Thermo Scientific Exactive LC-MS
- Thermo Scientific TSQ Quantum Ultra LC-MS/MS
- All LC-MS platforms have nanospray sources and can be interfaced with Waters nanoAcquity UPLC and Proxeon EASY-nLC II systems
- Advion Triversa Nanomate with LESA
- Agilent OFFGel system
- BioRad GS-800 calibrated densitometer
- Bioinformatic software
- Univariate and multivariate statistical software





Case study: Centre for Rural Health

Remote Service Futures

The Remote Services Futures project was a response to the challenges of engaging rural communities and healthcare providers in collaborative planning for future service needs.

Funded by the Knowledge Transfer Scheme, NHS Highland and Highlands and Islands Enterprise, the project took place in four remote communities in the NHS Highland area. Through the trialling of different methods of participation, information sharing and needs identification, a method for co-planning service delivery with community members was developed. This method forms the basis of the Remote Service Futures toolkit and Co-Planning Game which is featured in the Scottish Health Council's Participation Toolkit.

The project won the Knowledge Transfer Partnership Best Scottish Partnership Award and is an exemplar of how researchers, practitioners and community members can work together to develop locally appropriate service delivery solutions.





Case study: Centre for Rural Health

Virtual diabetes clinic

In January 2013 a pilot virtual diabetes clinic was launched to support people with type-1 diabetes, living at a distance from specialist services across the Highlands and Islands of Scotland.

The year-long pilot study will involve around 20 patients who have difficulty controlling their disease, something common to two-thirds of Scots with type-1 diabetes. Led by Professor Sandra MacRury, Professor of Clinical Diabetes at the University of the Highlands and Islands, the virtual clinic project aims to reduce the distances travelled by patients and staff to make face-to-face appointments, while maintaining a high quality service.

In 2011 the diabetes service started using video conferencing to reach patients in remote areas, enabling them to attend peripheral clinics and have an appointment with a consultant based in Inverness. This increases capacity within the health service so that clinicians can see more patients and waiting lists can be reduced.

The second stage involves the creation of virtual clinics whereby patients will be able to choose the best way for them to interact with a clinician, which could be by email, text, phone call or video conference, as well as directly to patients' homes. The team is looking at a more structured email and SMS system where clinicians can take questions from patients and respond with clinical decision support and for that engagement to be logged in the patient record.

This pilot project is designed as an add-on to face-to-face support, but the team believes that some patients may choose to have all their care provided remotely once they have their condition well controlled.

The goal is to reduce unplanned admissions and interactions with the health service by "trouble shooting issues" before a patient's problem becomes too serious. If the pilot is successful, virtual clinics could become embedded into routine care for all diabetes patients.



Case study: Highland Clinical Research Facility

Facilitating a specialist study: TEMPO trial

The Highland Clinical Research Facility was invited by a renal consultant at Raigmore Hospital in Inverness to host an Otsuka Pharmaceutical Development and Commercialisation Inc (TEMPO) trial.

This was a phase 3 study to determine the long-term safety and efficacy of oral Tovaptan regimens in adults with autosomal dominant polycystic kidney disease. The study lasted 36 months with regular research assessments scheduled at four monthly intervals.

Following patient recruitment in the renal department, the facility was the base for all further trial work, clinic visits and management of study files and folders. This ensured that the study could proceed efficiently and with limited disruption to the clinical activities in the renal unit.





Case study: Highland Clinical Research Facility

Recruitment and data management: Novo Nordisk 3770 study

The Highland Clinical Research Facility hosted the Novo Nordisk 3770 study, which investigated the efficacy of a new insulin for type-1 diabetes. Treatment was prescribed in flexible or fixed dosing regimens to control glycaemia after a 26-week treatment for type-1 diabetic patients.

This was an intense interventional study in which timely recruitment was a key requirement. A recruitment plan was implemented to make use of the diabetes research register and to engage with those patients attending the NHS Diabetes Clinic to meet recruitment targets.

The research nurse built up strong relationships with patients and provided them with an excellent standard of healthcare. Compliance with treatment regimens and study activities was optimised ensuring complete data sets were provided by the facility.





Health research collaborations

UK academic collaborations

James Hutton Institute

- Dr Derek Stewart: Health benefits of soft fruit extracts

The Robert Gordon University

- Prof Cherry Wainwright: Endocannabinoids and vascular function

University of Aberdeen

- Dr Gary Small: Cardiology – Nitrite in cardiac rehabilitation
- Dr Roy Soiza: Nitrite and geriatric vascular health
- Dr Gerald Lobely: Rowett Institute – Oats in diabetes
- Dr Gary Duthie: Rowett Institute – Oats in diabetes
- Prof David St Clair: Autoimmune mechanism of schizophrenia
- Prof Duncan Shaw: Genetic studies in diabetes and schizophrenia

University of Edinburgh

- Prof Nick Bateman: Toxicology – N-acetylcysteine in contrast-induced nephropathy
- Prof Ken Donaldson: Centre for Inflammation Research – Nanotoxicology
- Prof David Newby: Centre for Cardiovascular Science – Pollution and cardiovascular health
- Prof Adriano Rossi: Centre for Inflammation Research – Inflammation in cardiovascular disease and diabetes

University of Liverpool

- Dr. Iain Young: Protein turnover in zebrafish

Institute of Child Health, University College London

- Dr. Kevin Mills: Diabetes and inherited metabolic disorders

University of St Andrews

- Prof Russell Morris: Chemistry – High capacity gas storage materials for health applications



European collaborations

Turin University

- Prof Alberto Gasco: Medicinal Chemistry – Nitric oxide hybrid drugs for diabetes and cardiovascular disease

United States of America collaborations

The University of Rochester

- Dr Irfan Rahman: Antioxidant effects of curcumin in diabetes

The University of California (Santa Barbara)

- Prof Peter Ford: Quantum dot technology for cardiovascular and cancer therapeutics

China collaborations

Chinese Academy of Medical Sciences and Peking Union Medical College

- Prof Qi Xu: Immunogenetic mechanism of schizophrenia and diabetes

Jilin University

- Prof Jian Wu: Genetic mechanism of ischemic stroke