University of the West of England
BRISTOL

Medicines for the future and today – from bench to bedside

UWe-book: Number One

Features in this publication

At UWE our research and development is real and dynamic, identifying problems and providing solutions to issues that really matter. UWE is also the partnership university, working with partners locally, nationally and internationally to deliver excellence in teaching and research.

Nowhere is this more evident than in our truly outstanding research and development in the area of health and well-being.

Working with a wide range of partners in the health services, industry and other universities, our research is making a real difference. Whether through improving the quality of life of those with long term conditions, or developing technologies and medicines that will lead to better treatments and save lives, our research puts people at its heart. None of our research takes place without a clear plan, and the right partnerships, to ensure that it has a route to impact, including the participation of those people we are aiming to benefit.

This is just a sample of the research in health and well-being at UWE but it gives a flavour of the work and the people who are striving to make a real difference to the quality of our lives. There can be no better ambition.

Professor Steve West
Vice Chancellor

Lighting up cancer cells

Professor Vyv Salisbury of UWE's Centre for Research in Biosciences, is using gene technology to develop a rapid predictive test to allow tailored chemotherapy for leukaemia patients.

"These biosensors use genetically modified bacteria that emit light when alive. They can be used to monitor the effectiveness of drugs and for rapidly predicting the effects of cancer chemotherapy on leukeamic cells".

The biosensor has been patented and is being used in a rapid assay that will be marketed by **Randox Laboratories.** Its application will allow patient-specific chemotherapy, initially for one drug used in the treatment of Acute Myeloid Leukaemia, but in future it could be used for combinations of drugs used in chemotherapy for a range of malignancies, including solid tumours.

"It is this area that excites me the most," says Vyv, "I am very keen to try and extend the research to see if we can design biosensors for predictive testing of chemotherapy for solid tumours such as breast and bowel cancer".

The development of bioluminescent bacterial biosensors requires multidisciplinary expertise and collaboration with a wide range of partners. Vyv appreciates that "the research programme has been helped immensely by being at UWE, and particularly having colleagues with expertise in optics, analytical chemistry, genetic engineering and haematology. The importance of good relationships with the health service and a strong commercial partner are also crucial for the successful development new healthcare devices."

UWE has been a centre of excellence in biosensor research since the 1990s, with its expertise being applied in a very wide range of areas, including food and environmental monitoring, and supplying biosensors to research groups worldwide.

Better treatment for diabetes

During meals our bodies break food down into a form of sugar called glucose which then moves from the bloodstream into cells to be utilised. This process requires insulin production by the pancreatic beta-cells. Impaired function of these cells leads to inadequate insulin output and elevated blood glucose level. The failure of beta-cells is responsible for the development of type 2 diabetes which affects ~2 million people in the UK. It consumes 10% of NHS expenditure, and is a major cause of illness and premature death.

Professor Aniko Varadi's research is looking at the mechanisms by which beta-cells respond to changes in blood glucose concentration. Identifying the mechanisms through which the healthy beta-cell responds to glucose is required for understanding the functional failure of the beta-cell in diabetes and for the development of new drugs to treat diabetes.

Type 2 diabetes is frequently associated with obesity and hyperlipidemia, as well as hyperglycaemia. There is ample evidence that fatty acids, which under normal circumstances are physiological fuels for the pancreatic beta-cell, become toxic when present at elevated concentrations for prolonged periods of time. In collaboration with AstraZeneca Aniko is investigating novel pathways by which fatty acids exert their cytotoxic effect on beta-cells.

We now have a better understanding of the biochemistry and cell biology of this fascinating cell type" says Aniko, "but there are still many functional aspects that we do not understand. Better understanding of beta-cell function will help us to develop anti- diabetic drugs for the treatment of the early stages of the disease that would focus on the prevention of beta-cell loss. The ultimate aim is to find a better treatment for Type 2 Diabetes.

Fighting Prostate Cancer and Breast Cancert

Working in close partnership with the Bristol Urological Institute at North Bristol NHS Trust, the Bristol Royal Infirmary and the University of Malaya Medical Centre, Professor Tony Rhodes of UWE's Centre for Research in Biosciences is undertaking crucial research that will improve the diagnosis and treatment of the more aggressive forms of prostate and breast cancer.

"With respect to prostate cancer one of the dilemmas with diagnosis is ascertaining which patients have the aggressive and potentially life threatening forms of the disease and which patients have the more indolent forms of cancer" he says. "As treatments are extremely invasive and can have a huge impact on quality of life, we are seeking to find a biomarker in cells of the aggressive form of the disease that can uniquely single out patients who need life-saving yet invasive treatment. Similarly, there are over 7,000 women diagnosed every year in the UK with a type of extremely aggressive breast cancer for which there is no known effective treatment other than surgery and traditional chemotherapeutic regimes."

Tony's research group focuses on the discovery, development and validation of prognostic and predictive cancer biomarkers and in particular ones related to perturbed metabolic pathways which are implicated in these aggressive forms of prostate and breast cancer. He is concerned to ensure that their leading-edge work is not confined to the laboratory but makes a real impact on people's lives.

"We also want to tell people about the exciting research being done in Bristol and elsewhere that will help improve the lives of men and women who are diagnosed with cancer and to clarify the complex issues surrounding diagnosis and treatment."

As a result, Tony and his collaborators have been working with **Bristol Rotary** and other local charities to include **The Friends of Bristol Haematology** and **Oncology Centre** and the **John James Bristol Foundation** on a mission to raise funds to both increase awareness and to conduct research into better testing methods for cancer. This has led to awareness-raising events such as the 5km 'Run for the Future' organised by **Bristol Rotary** and regular breast and prostate cancer symposiums held at UWE aimed to clarify and update patients, carers, health professionals and researchers on new and existing methods for the diagnosis, treatment and care of people with cancer.

Preventing the progression of Alzheimer's Disease

Researchers from UWE's Centre for Research in Biosciences are working with the charity BRACE on a project that may lead to earlier interventions that slow or even prevent the progression of Alzheimer's Disease.

Neurodegenerative diseases, such as Alzheimer's, are unforgiving conditions which strip people of their identity, with devastating consequences for their family and friends. By 2021 there will be an estimated 1 million people suffering from dementia within the UK, the mjority with Alzheimer's. The direct and indirect costs of caring for individuals with Alzheimer's runs into billions of pounds.

Dr Myra Conway from UWE's Centre for Research in Biosciences is working with UWE PhD student and **BRACE** scholar, **Jonathan Hull**, in collaboration with colleagues from the Dementia Research Group at the Institute of Clinical Neurosciences, University of Bristol, on a three year project that aims to identify how proteins control glutamate in the brain. Glutamate build-up can cause brain cell toxicity leading to neural degeneration.

"Pilot studies have established that there is a significant increase in the expression of brain specific enzymes, which regulate brain glutamate in patients with Alzheimer's disease (AD)" Myra explains. "This study provides an opportunity to improve our understanding of the biochemistry of cellular deterioration that can occur in the brains of people with AD in order to develop targeted and improved therapies".

In healthy individuals, the brain uses a chemical called glutamate to control memory and learning. If the glutamate reaches high levels, however, it becomes toxic to the brain cells that can contribute to the dementia process. A protein called the branched chain amniotransferase (BCAT) regulates brain glutamate and Myra's research aims to establish the reason why these proteins are so elevated in AD brain and if these elevations contribute to glutamate toxicity.

"It is critical that we gain better insights into the causes of Alzheimer's disease" she says "as it is estimated that there will be around 34 million people suffering from dementia worldwide by 2025. If we can ascertain how BCAT controls glutamate during disease conditions we will come closer to understanding how to develop treatments that may delay or even prevent the progression of AD. What drives me is not only the excitement of the scientific knowledge and its progression but also that the potential outcomes may impact hugely on people's lives".

Staff Profiles

Professor Vyv Salisbury of UWE's Centre for Research in Biosciences taught microbiology at UWE for many years before embarking on her successful research career. "As a relatively late starter in the field, I needed considerable help at the outset. I was encouraged and supported by more experienced academic colleagues at UWE and by experts in making funding applications and patents". As a result, Vyv has been awarded funding of more than £1m by the National Institute of Health Research, Natural Environment Research Council, European Commission, Biotechnology and Biological Sciences Research Council, Department of Trade and Industry, Wellcome Trust and a number of commercial partners.

http://hls.uwe.ac.uk/profiles/Profile.aspx?id=1420

Professor Aniko Varadi has worked with collaborators near and far in developing her research, from the University of Bristol to the University of Wollongong in Australia, and has been awarded more than £1m in research grants from the Medical Research Council, the European Commission, the Biotechnology and Biological Research Council and the Wellcome Trust. "Being at UWE has allowed me to obtain external research funding as an independent researcher and to build my research group," she says.

http://hls.uwe.ac.uk/profiles/Profile.aspx?id=2153602

Professor Anthony Rhodes taught Cellular Pathology at the University of Westminster and University College London for Medicine before he joint UWE.

His research group at UWE focuses on the discovery, development and validation of prognostic and predictive cancer biomarkers important in the field of breast cancer and prostate cancer. This has contributed to the evidence base and co-authorship of national and international guidelines for the clinical testing of breast cancer biomarkers

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Dr Myra Conway was educated at The University of Galway, Ireland and worked as a Research Fellow at Wake Forest University Medical Center, USA. At UWE her research focus is in understanding how changes in the redox environment can influence the structure/function relationships of proteins under both normal and pathophysiological conditions, in particular proteins with reactive thiol groups. Currently, her team is investigating the role of the branched chain aminotransferase (BCAT) proteins in glutamate toxicity, a key contributor to the pathogenesis of neurodegenerative disorders such as Alzheimer's Disease.

http://hls.uwe.ac.uk/profiles/Profile.aspx?id=2153601

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