WINTER 2017

Researching New Potential Treatments for Unmet Medical and Veterinary Need

LIFE SCIENCES RESEARCH NETWORK WALES

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RHWYDWAITH GWYDDORAU BYWYD CYMRU

Cyngor Cyllido Addysg Uwch Cymru
Higher Education Funding Council for Wales

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Ariennir yn Rhannol gan **Lywodraeth Cymru**
Part Funded by **Welsh Government**

"As the international representative on the NRN Board since the start of the Network, I have been excited to see how the drug discovery program funded through the Welsh Government has grown to include the 4 different Universities and brought together chemists with molecular biologists and clinicians to form drug discovery teams. Our Board has not only provided the resources to seed these translational research programs but also core facilities to provide essential technology to facilitate the interactions. Whilst drug discovery programs have been financially supported at many Universities in the US, this special type of support is unique to Wales in the UK and will provide a special opportunity for Welsh Universities to be much more competitive in the broader European community."

Professor Laurence Hurley
University of Arizona, USA / NRN Management Board Member

"It is the collaborative and inspirational approach that Sêr Cymru provides that will help drive forward the next generation of talented researchers."

Vaughan Gething AM
Cabinet Secretary for Health, Well-being and Sport

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FOREWORD

Life Sciences Research Network Wales

Innovations in life sciences have resulted in dramatic changes in our ability to manage human disease and improve quality of life. However, with an increasingly aging population and a number of major drugs coming off patent, there is a pressing need to develop new drugs and therapeutic agents.

The Life Sciences Research Network was founded in 2013 with funding from the Welsh Government and the Higher Education Funding Council for Wales to enhance Wales' strength in research by developing new therapeutic treatments in areas of unmet medical and veterinary need.

As one of three Sêr Cymru National Research Networks, the Life Sciences Research Network is a pan-Wales initiative focused on drug discovery and development, anchored by our core academic partners at Aberystwyth, Bangor, Cardiff and Swansea Universities and actively engaged with partners in industry, the NHS and charities both nationally and abroad.

We fund a large portfolio of projects including PhD Studentships, Postdoctoral Research Projects and Platform Technologies with a focus (however, not exclusively) in the therapeutic areas of Oncology, Neuroscience and Infectious Disease.

The Network has helped to foster an improved understanding of translational research, highlighting areas of potential strength for innovation and commercialisation. Working in tandem with the Life Sciences Bridging Fund, 9 NRN projects have secured Bridging Fund awards to develop their translational potential.

The Network has committed £5.8 million towards life sciences drug discovery projects and has engaged with over 260 partners in collaborative research projects. Cumulatively, these partners have committed approximately £637,000 in co-funding and HEI partnerships within Wales have provided £2.7 million in additional co-funding, all directly in support of our projects.

By September 2017, Network projects had generated over £22.1m in additional research funding through competitive grant awards, leveraging over £2m funding from Research Councils and over £12m from EU H2020. Researchers had presented their work in over 220 conference presentations and had over 60 papers published in peer-reviewed journals. These levels of output highlight the quantity and quality of research being undertaken by Network projects.

We wish to pay special tribute to the late Professor Chris McGuigan, to whom we are indebted for both establishing and championing this flagship project in the life sciences in Wales.

Professor Andrea Brancale

Network Scientific Director

A TRIBUTE TO PROFESSOR CHRIS MCGUIGAN

On 17th June 2013, a press release indicated that I would be joining Cardiff University as the first appointment under the Welsh Government's £50M Sêr Cymru initiative. Ole Petersen, then Head of the School of Biosciences and the key operator of my move to Cardiff, explained to me that as part of the initiative, a Sêr Cymru Research Network was under discussion. It would focus on 'Drug Discovery and Development'. While the creation of this network was only officially approved by the end of the following month, a charming individual by the name of Chris McGuigan asked me the following day if I would be willing to join the Scientific Advisory Board of this still virtual network. This could be discussed at his home later in the day. In what I later realised was a typical McGuigan move, Chris had already prepared a brochure with the names and pictures of the Scientific Advisory Board members, including mine! He then explained to me during the course of a lovely summer evening that he had been confident that I would accept his invitation to join the Board. He was of course right and Chris documented this first encounter with the enclosed photograph he took in his garden. It also features Gary Baxter, Head of School of Pharmacy and Pharmaceutical Sciences where Chris was affiliated. This occasion was also made memorable by very interesting discussions with Chris's wife Maria, whose kindness and hospitality I discovered on this occasion. Like everyone who had the privilege to interact with Chris, I was greatly impressed by his energy and commitment to the goals he had set himself. Not only the creation of the Life Sciences Research Network, but also it's somewhat unusual initial phase following it's official approval further illustrate this point: for administrative reasons, the first call for PhD studentship applications could not be opened before September 2013. Because Chris had already prepared his colleagues at all major Universities in Wales, the Network received over 70 applications by the beginning of October. These were provisionally scored by remote correspondence and discussed at the first review meeting of the Scientific Advisory Board at the School of Pharmacy on 14th October 2013, with the result that newly recruited PhD students could start their work in January 2014! The successful completion of this first phase of the programme at such an extraordinary pace was entirely the result of Chris's exceptional dedication, and while he kept thanking the Board for its "heroic" work, an adjective Chris liked using when referring to the work of others, we of course all knew who was the sole hero of the story. Beyond the spectacular start of the Network, Chris's leadership remained remarkably effective and the Network continued to grow and prosper at an amazing pace, with Board meetings subsequently taking place at the Hub in Cardiff Bay which opened in March 2014 - another truly remarkable achievement driven by Chris, with the continued and very effective support of the Welsh Government.

Professor Chris McGuigan

L-R: Professor Yves Barde, Professor Gary Baxter

Chris was not just a very effective mover and shaker. His warmth, kindness and good humour made it a real delight to work with and for him – alas for a short period of time in my case. Little did I realise at the time that the pace at which the Network had been put together would turn out to be so critical. Chris left us at a time when the Network had just reached its cruising altitude and the Board is determined to keep it flying as it feels that Chris's vision to facilitate drug development in Wales is becoming a reality and will have a long term positive impact on the well-being of Wales.

Professor Yves Barde

Sêr Cymru Research Chair in Neurobiology

56

PhD Studentships

47 **Postdoctoral Projects**

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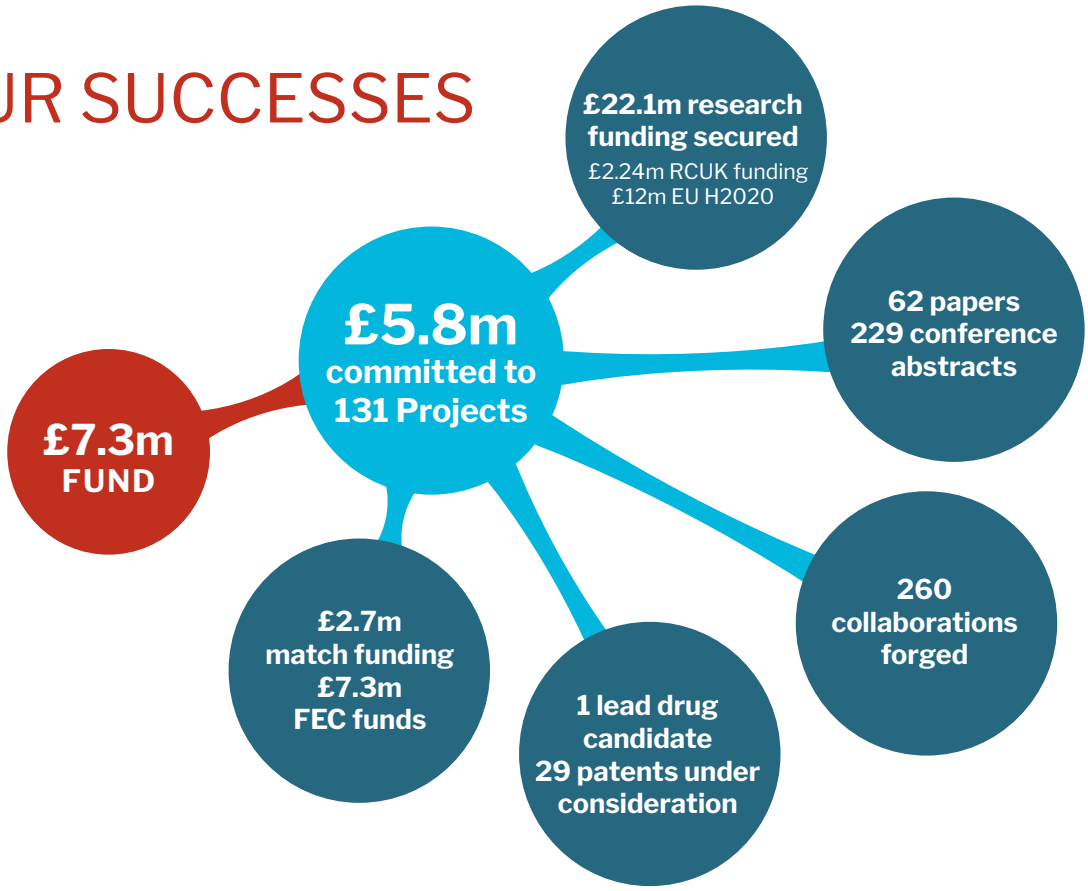
PLATFORM TECHNOLOGIES

£ ENDEAVOUR GRANTS

OUR SUCCESSES



OUR PROJECT PORTFOLIO

We have funded 131 projects across a wide range of therapeutic areas with a focus (although not exclusively) on Oncology, Neuroscience and Infectious Disease.

These are areas of unmet medical and veterinary need, requiring urgent, new treatments.

The key scientific questions addressed by our projects are:

- Novel target discovery and validation
- Finding new molecular entities as selective hits at these targets
- Developing hits at enzyme targets into viable drug like lead molecules
- Probing their mechanism of action
- Collaborative progression of leads towards being IND-ready clinical candidates

Our projects include PhD Studentships, Postdoctoral Projects, Research Impact Awards and Platform Technologies and are based in our core partner Universities at Aberystwyth, Bangor, Cardiff and Swansea.

All forms of collaboration are actively encouraged throughout our projects - across schools within one Higher Education Institute, across 2 or more of our partner HEIs, with Biotech and Pharma, with charities and Third Sector stakeholders.

"Our research group has benefited significantly from the support and guidance of the Network, securing over half a million pounds worth of funding which has allowed the group to undertake research aligned to meet the needs of local companies, secure Intellectual Property, and obtain additional funding from outside Wales. The Network is now at the heart of Welsh Life Sciences and has had a strong positive impact on both local science and student lives. The Network's Annual Congress, which brings all researchers together, has proved to be extremely beneficial for the Welsh Universities and our group, helping to establish strong collaborative links, share knowledge base and target resources more effectively."

Dr Chris Gwenin
Impact Award Holder, Bangor University

"My research focused on the development of novel antivirals to treat Dengue virus infection, an unmet medical need. The LSRNW not only allowed me to undertake my postgraduate studies but also provided me with the means to attend multiple national and international research conferences. I personally feel motivated and inspired by being part of this larger and multidisciplinary research community."

Cecilia Cima
PhD Studentship, Cardiff University

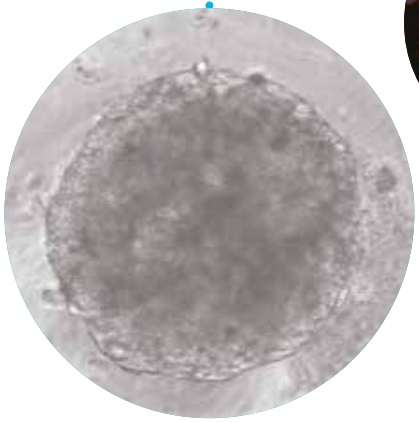
"It has been a great pleasure to serve on the Management Board of the Life Sciences Research Network, alongside so many highly experienced and talented colleagues. Academic research is becoming a more and more important source of new drugs. It is most pleasing to see the progress made by researchers in Welsh Universities and the consequent growth in the national drug discovery and development Ecosystem. A major highlight is the Annual Congress where the enthusiasm for their studies, on the part of PhD students and post-doctoral researchers, coupled with their evident talent, is inspiring. The next step is to have more of the successful projects advancing to support from the Wales Life Sciences Bridging Fund and / or other translational research funding schemes."

Dr David Owen OBE
NRN Management Board Member & Scientific Advisory Board Chair,
Life Sciences Bridging Fund

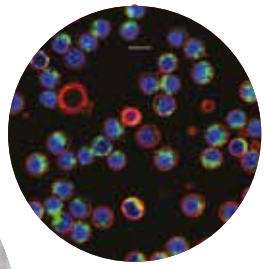
THERAPEUTIC AREAS

The Network Research Portfolio focuses on three main therapeutic areas and other diseases with unmet medical and veterinary need:

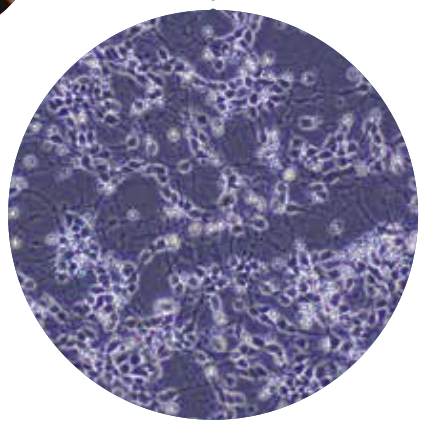
Oncology
48 Projects



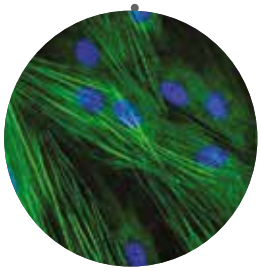
Infectious Disease
42 Projects



Neuroscience
22 Projects



Other Diseases
19 Projects

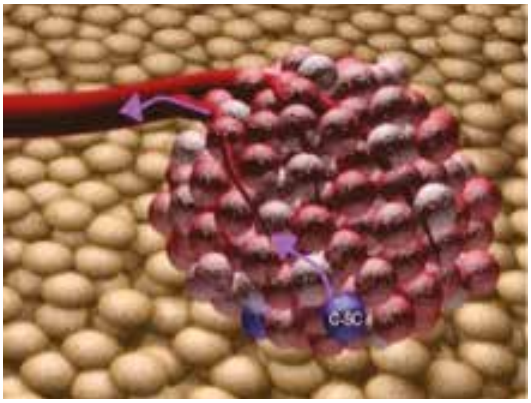


PROJECTS IN FOCUS

ONCOLOGY

Targeted cancer treatment: Optimising cellular uptake of enzyme/gold-coated magnetic nanoparticle conjugates; Dr Chris Gwenin, Bangor University, Postdoctoral Project in collaboration with University of Auckland, New Zealand

This project aimed to overcome some of the current limitations of treating certain types of cancer. Currently the targeting of tumours using chemotherapy does not specifically focus on the tumour itself but is delivered to the entire body, which means that healthy cells are also harmed, causing side effects. This new method delivers gold-coated magnetic nanoparticles directly into the tumour via a focussed magnetic beam. The nanoparticles contain enzymes that are capable of converting the low toxicity chemo agent into the chemo drug needed to kill cancerous cells. Network funding has helped the project to form strong collaborations with Swansea and Cardiff Universities and has led to further funding from the Knowledge Economy Skills Scholarships KESS II Scheme.



Bacterial-mediated RNA interference as a new therapy to target advanced prostate cancer; Professor Paul Dyson, Postdoctoral Project, Swansea University

Initial Network project funding has led to a major award by Cancer Research UK to develop novel therapies for the treatment of prostate cancer. This £180k award to Swansea University will support collaboration with Cardiff University, School of Biosciences in developing a new therapy to target any solid tumour, including late stage metastatic tumours. This patented technology delegates production and delivery of therapeutic molecules to tumour-targeting bacteria that are otherwise harmless to healthy tissue and has the potential to be developed into a new treatment for a wide range of cancers.

Role of DNA repair in resisting treatment with Gemcitabine and other nucleoside analogues; Lennart Boeckemeier, PhD Studentship, Bangor University

The cancer drug Gemcitabine, a nuceoside analogue, kills cancer cells by inhibiting their replication. The Hartsuiker laboratory at the Bangor North West Cancer Research Institute has identified and analysed various DNA repair pathways that resist Gemcitabine treatment by removing it from the DNA; these pathways are frequently inactivated in cancer cells. This research will allow us to tailor the choice of drugs to genetic defects in cancer cells and guide the use and development of small molecule inhibitors to exploit synthetic genetic interactions between redundant repair pathways.

"As Principal Investigators on a number of Network projects, and collaborators on projects with Cardiff and Bangor Universities, Network funding has enabled the Reproductive Biology and Gynaecological Oncology group at Swansea University Medical School to establish a wide research network in Wales. In addition, the support of the Network has enabled the accelerated development of Wales' first Antibody-Drug Conjugate (ADC) therapeutics research programme. The first ADC, RBGO 01, has proved successful during in vivo preclinical evaluation, sponsored by the Network. This major milestone opens a pathway for follow-on funding ahead of exploring commercial licensing opportunities."

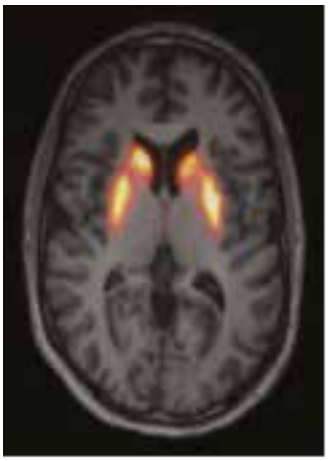
Professor Steve Conlan & Dr Deyarina Gonzalez
Impact & PhD Award Holders,
Swansea University Medical School

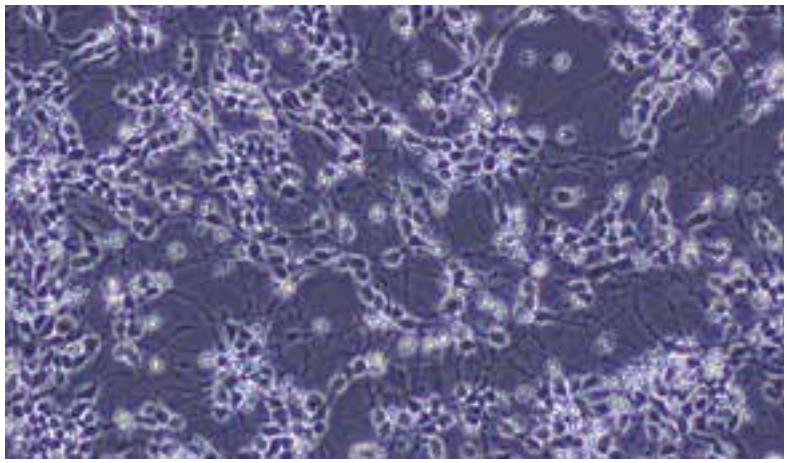
"Our Network award on the Wnt signalling pathway has directly led to the initiation of a new research collaboration with the pharmaceutical company, Merck. In the longer term, this research should benefit patients who have a particularly aggressive subtype of liver cancer."

Professor Trevor Dale
Postdoctoral Project, Cardiff University

"I am a PI on a Network funded grant. The original grant allowed us to test a new battery of oncolytic viral vectors to gauge activity in primary cancer cells, data that contributed to several peer-reviewed research outputs. We were also able to identify novel peptide agonists of folate receptor alpha, a molecular marker upregulated in ovarian cancers, which we are seeking to patent. The grant has allowed us to extend our collaborative network and we have secured an interdisciplinary research impact award to extend these findings into targeted delivery of drugs and virotherapies to cancer cells."

Dr Alan Parker
Impact Award Holder, Cardiff University





NEUROSCIENCE

Improved Fingolimods for Multiple Sclerosis; Dr Andrea Brancale, Postdoctoral Project, Cardiff University

An estimated 2,500,000 people in the world are diagnosed with Multiple Sclerosis (MS), where the immune system, which normally helps to fight off infections, mistakes myelin for a foreign body and attacks it. A recent breakthrough in Multiple Sclerosis treatment is fingolimod, which was approved by the FDA as the first oral disease-modifying agent for MS. The Protide approach, developed by Professor Chris McGuigan, has been very successful in the delivery of nucleoside monophosphate into the cell, thereby improving the activity of the parent drug. Network funding has enabled the successful synthesis of several examples of fingolimod ProTides (almost 50 different structures) and more importantly, to demonstrate that all our molecules are capable of delivering the fingolimod monophosphate when incubated with neuronal cell matrix. Another key achievement of this project is the stability of some of these compounds in human plasma. This is of pivotal importance in the design of an effective drug with a good chance to reach the market.

In Vivo Imaging of Tau Distribution in the Brain; Professor Chris Marshall, Platform Technologies Award, Cardiff University

The two biomarkers of Alzheimer's Disease are beta amyloid and tau. Until recently, the only way to measure the presence of these biomarkers was at post mortem. With the completion of this project, PETIC will have the capability to image, quantify and monitor the levels of these markers in the brain. This will be invaluable in enabling an earlier diagnosis than is currently possible, monitoring disease progression and assessing the effectiveness of novel therapies in this disease.

"The NRN allowed me to study in an exciting, fast evolving research environment and to learn from world-renowned scientists - A unique experience for which I'm very grateful for."

Katharina Sauerberli
PhD Studentship, Cardiff University

"My work focuses on a potential novel drug, an antibody called 2B3, which prevents the production and build up of beta-amyloid, one of the main pathological proteins causing Alzheimer's Disease. Funding from the Network has allowed this novel antibody therapy to be trialled in a mouse model of Alzheimer's Disease. This research has shown that 2B3 is able to prevent the onset of memory problems observed in this mouse model. Ongoing research now aims to show that this result is associated with reduced levels of the toxic beta-amyloid protein."

Charles Evans
Postdoctoral Project, Cardiff University

"With Network funding, we are developing a large animal model of Alzheimer's Disease, with the intention of establishing robust cognitive and physiological biomarkers that will track the progression of the disease as well as monitor the efficacy of putative therapeutic agents."

Dr Sebastian McBride
PhD Studentship, Aberystwyth University

INFECTIOUS DISEASE

Exploiting natural products from Hops (Humulus lupulus) to suppress tuberculosis; Rafael Baptista, PhD Studentship, Aberystwyth University

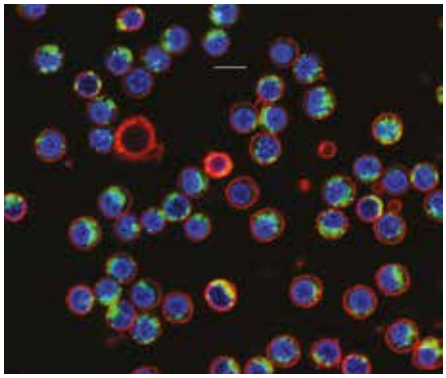
According to the World Health Organisation, Tuberculosis is the first leading cause of death from an infectious disease worldwide. Over the past 20 years there has been an emergence of extensive drug-resistant tuberculosis, which threatens global TB control. One metabolite from hops (H. lupulus) flowers, has been found to show significant activity against M. tuberculosis. This Network funded PhD project has constructed a library of promising metabolites with anti-mycobacterial activity from H. lupulus, and aims to discover a- and b-acid targets and mechanisms of action. This may aid the optimisation of anti-TB chemotherapy discovery, with further synthesis of new and more effective drugs against the disease.

Exploring the interaction of CD4+ T cells with influenza peptides derived from conserved viral proteins; Alex Greenshields-Watson, PhD Studentship, Cardiff University

Influenza is a recurrent and ever present threat to global health. The virus is highly variable and continuously evolves in order to escape control by the immune system. This Network funded PhD project has focused on the human immune response to the conserved elements of the influenza virus, specifically the response from a cell population that orchestrates multiple immune mechanisms that mediate symptom severity and facilitate protection. By identifying the conserved viral elements that these cells recognise, then characterising their presentation by X-Ray Crystallography and isolating the cells themselves in order to analyse their genetic information, we have been able to build a detailed picture of the immune responses that can be targeted by novel vaccination methods. Novel vaccines that boost the immune responses to such conserved elements may overcome the problem of viral variation and evolution, and help us to learn more about the cells that mediate severity during Influenza infection.

Lytic transglycosylases - a potential Achilles' heal for antibiotic-resistant bacteria?; Dr Joel Loveridge, Postdoctoral Project, Cardiff University

This project has led to the sequencing of the genome of a bacterium that produces antibacterial and antifungal compounds which has resulted in further successful funding to identify these compounds. The preliminary work, funded by the Network, is being further developed by an overseas-funded PhD student and a Network funded postdoctoral researcher.



"Support from the Network has allowed me to start my own research group and present our findings at international conferences, which in turn has led to new collaborations. The funding provided by the Network has been invaluable to me as an early career researcher looking to establish independence."

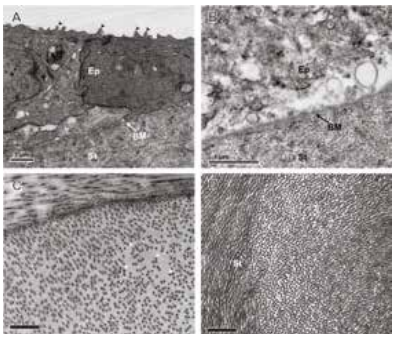
Dr Nigel Francis
Impact Award Holder, Swansea University

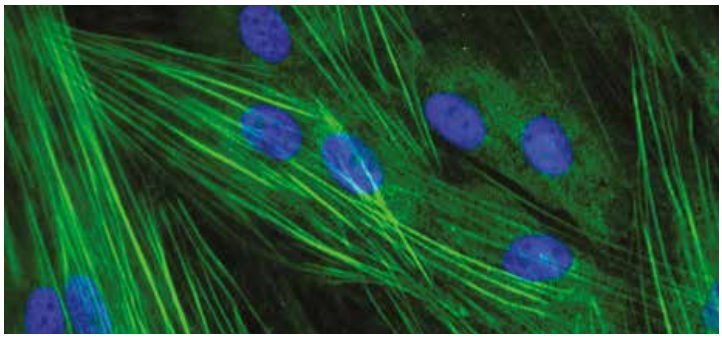
"Thanks to Network funding, I am part of an exciting PhD project about drug discovery for tropical diseases and I have the opportunity to collaborate with two universities, Aberystwyth and Cardiff, and a company, Phytoquest. Working in different environments will be a valuable experience for my future career."

Alessandra Crusco
PhD Studentship, Aberystwyth University

"My PhD project is based on finding antimicrobial compounds in invasive weed species to combat Methicillin-Resistant Staphylococcus Aureus (MRSA). These weeds could provide a plentiful source from which to harvest a compound. The project also aims to target bacterial communication as a non-lethal anti-virulence control for bacterial infections. Network funding has allowed me to develop my skills as a scientist in Aberystwyth University, and to collaborate with other Welsh universities as well as with Phytoquest, the company partner. The network has brought together many like-minded early career scientists into one group and provided an environment that encourages collaboration and teamwork. The free drug testing Platform technologies are world-class and would be impossible to gain access to without the Network."

David Fazakerley
PhD Studentship, Aberystwyth University





OTHER DISEASES OF UNMET NEED

Delivery of osteogenic molecules from acrylic bone cement to encourage regenerative bone repair around cemented joint replacements; Dr Wayne Nishio Ayre, Postdoctoral Project, Cardiff University

Approximately 180,000 hip and knee replacements are performed in the UK every year, of which a significant amount utilise cement to anchor the implant to bone. Unfortunately, around 10% of these implants fail after 10 years due to loosening which is linked to poor bone repair after surgery. Previous research at Cardiff University developed a patented method of delivering prolonged doses of antibiotics locally from the cement. Network funding has given researchers the opportunity to alter this delivery system to encourage bone growth around the cement by delivering a growth factor known as bone morphogenetic protein 2 (BMP-2). A further £86,000 research funding was leveraged from external sources to develop the system further. This has generated sufficient data to justify optimisation of the system, which has the potential to take the technology from lab-based experiments into animal and clinical trials.

Multimodal Theranostic (MMTs): A Diagnostic and Therapeutic Platform: Dr Ian Fallis, Postdoctoral Project, Cardiff University

Drugs, antibodies (Abs) and radio-isotopes have much potential, both individually and in combinations, as therapeutic entities in the treatment of a wide range of diseases. However, whilst their effectiveness and, equally importantly, their toxicity are established, their effects upon individuals remain difficult to predict. The project aimed to develop a new approach to personalised medicine by developing new long-lived radioisotopes and a nanoparticle carrier 'vehicle' in which their distribution in cells, animals and ultimately patients could be determined. This has facilitated the creation of a single entity with the potential to both diagnose and treat a disease. Further, in order to 'magic-bullet' the nanoparticles to the target site, new chemistries have been developed for the attachment of antibodies and other groups to aid the targeting of diseased tissue (e.g. cancer). This new technology is currently being developed with additional research funding, including the diagnosis of dementia, targeting of breast cancer and the development of stem cell therapy in wound healing. Network funding has directly enabled this research and ongoing projects and has had substantial indirect benefits by facilitating industrial investment in a related project to commercialise devices for the detection of supertoxic agents for military and first-responder medical triage applications. These projects have featured in several successful funding bids.

"My project focuses on the discovery of new ways to use anticancer drugs and the Network does not only support my own research, but also helps me to connect with fellow PhD students and senior researchers from my field and others. Notable here was a drug design workshop in Cardiff organised by the Network – a field I have little experience in but made accessible through the Network."

Lennart Boeckemeier
PhD Studentship, Bangor University

"As a direct result of Network funding, the project has discovered new insights into the role of Bcl-3 and breast cancer progression, including an interesting link between Bcl-3 suppression and cell senescence. This project has also helped contribute towards the identification of a novel Bcl-3 inhibitor which is showing very promising results in vivo and is being targeted towards human trials with the help of Tiziana Life Sciences, a collaboration which has been forged through NRN funding."

Daniel Turnham
PhD Studentship, Cardiff University

PROJECT OUTPUTS IN FOCUS

PHD STUDENTSHIP

Multiplexed in vitro assay for genetic toxicity screening. NRN PhD Project / Life Science Bridging Fund Award. Danielle Harte (PhD student), Dr George Johnson.

The Unmet Need

Genetic Toxicology is central to drug discovery and drug development. In vitro genetic toxicity tests are used during library screening, preclinical safety testing and often in order to address concerns at clinical trials and post-market stage. The in vitro micronucleus (MN) test is used to assess a chemicals ability to induce chromosome damage. These cells can be scored manually or by using flow cytometry or semi-automated microscopy based image classifiers. Manual scoring is laborious and the current high-throughput approaches lead to misleading positive or negative responses respectively. The aim of this project is to develop a new in vitro MN platform that has the precision of manual scoring, combined with the benefits of the high-throughput, high-content approaches. The commercial aspects include IP on the scoring algorithms, kit development and sales, consultancy, how-to workshops, contract work and the market report indicates the possibility of creating a contract research organisation in Swansea.

Research Progression

The NRN PhD project and Life Science Bridging Fund award are interlinked and focussed on the development of in vitro assays for detecting DNA damage using the ImageStream flow cytometer, along with machine learning algorithms.

There is an informal collaborative agreement with GlaxoSmithKline to develop the MN approach further. This interest and support from one of the largest pharmaceutical companies in the world shows the relevance of this project and it's major commercial potential.

A patent has been submitted which included a statement about future developments and this covers the NRN PhD studentship for combined DNA damage approaches and a deep learning scoring platform. This will potentially lead to commercialisation of kits and expertise in assessing novel molecular entities using a multiplex, automated, high-throughput high-content approach which could overtake the MN assay as the go-to screening assay. This assay will support many unmet needs and is of interest to industry, with an informal collaborative agreement with Pfizer in place, as well as being of interest to research councils, to which further funding applications will be made.

Research Impact

NRN and Bridging funding has:

- Resulted in a patent submission.
- Led to new collaborations with industrial partners to develop the approach further eg US-Litron and US-Pfizer; GSK, Astrazeneca, Janssen.
- Led to collaborative work with scientists from the Broad Institute (MIT and Harvard) around artificial intelligence work.
- Led to a funding application to NIEHS for development of the multiplex DNA damage assay and a travel award for the PhD student to present the work at the UKEMS Conference.

"The Bridging Fund enabled us to develop a highly improved version of the industry standard chromosome damage MN test, and the NRN funded project focusses on the next generation of test system to be used by industry, an automated multi-endpoint DNA damage assay."

Dr George Johnson

PHD STUDENTSHIP

Novel Bcl-3 Inhibitors – Target Validation and Anti-Metastatic Lead Optimization. Daniel Turnham (PhD student), Dr Richard Clarkson, School of Biosciences, Cardiff University.

The Unmet Need

The spread of tumours to vital organs (metastasis) is the principal cause of death in cancer patients and despite an improved understanding of the processes involved, therapeutics are notably slow to reach the clinic.

The Clarkson laboratory at the European Cancer Stem Cell Research Institute (ECSCRI) in collaboration with the School of Pharmacy at Cardiff University previously identified a gene (Bcl-3) responsible for the spread of breast cancer cells to vital organs and developed an anti-cancer drug to prevent tumour spread.

A patent and private investment had been secured to undertake further testing, but match funding was required to establish the role of Bcl-3 in breast cancer metastasis, the precise mode of action of the inhibitor and whether the inhibitor could work in other cancer types. Limited funding exists for this stage of research, which falls between basic research and further tests of the agent in new settings.

Research Progression

Match funding via an NRN Studentship plugged the funding gap and allowed the team to identify Bcl-3 as a key regulator of breast tumour cell migration and seeding.

The team developed a set of Bcl-3 inhibitors from which a lead compound showing promising results in breast cancer and other cancer types was identified. This compound is currently being developed for a phase one clinical trial and the study has generated further research questions to be explored.

Research Impact

NRN funding:

- Provided parity with the commercial partner.
- Bridged the funding gap between basic \ research and the establishment of mechanisms of action.
- Contributed toward the identification of a lead compound and the manufacture of a drug currently being prepared for clinical trials.
- Expanded the original remit of the project to encompass metastasis of other cancer types.
- Led to additional funding from Prostate Cancer UK to for the PhD student, Daniel Turnham, to secure a postdoctoral position to undertake related investigations for prostate cancer.

"The project has provided a valuable insight into the drug discovery pathway which has helped me secure a postdoctoral position with ECSCRI at Cardiff University. Moreover, the NRN Scientific Congress provided a means of building key collaborations, particularly with the NRN's Platform Technologies, which we were utilised for this project."

Daniel Turnham.

L-R: Tiziano Lazzaretti, Andrew Westwell, Andrea Brancale, Richard Clarkson; winning the Cardiff University Innovation Award

PAN-WALES PHD STUDENTSHIPS IN NOVEL ANTHELMINTICS

Two joint studentships between Aberystwyth and Cardiff Universities from collaborations forged during Scientific Congress.

Repositioning histone methyltransferase inhibitors as next generation anthelmintics; Gilda Padalino; Professor Karl Hoffman (Aberystwyth University), Professor Andrea Brancale (Cardiff University)

Increasing the selectivity and potency of a novel anthelmintic chemical entity; Alessandra Crusco; Professor Karl Hoffman (Aberystwyth University), Professor Andrew Westwell (Cardiff University), Phytoquest Limited

The Unmet Need

Both projects focus on the development of urgently-needed novel anthelmintics for the control of schistosomiasis, a neglected tropical disease. The global mass administration of a single chemotherapy drug is leading to drug failure and the spread of parasite resistance.

Research Progression

These interdisciplinary projects bring together biology and chemistry laboratories at Aberystwyth and Cardiff Universities, allowing the 2 students to dedicate 50:50 time at 2 institutions and develop expertise in:

L-R Gilda Padalino, Rafael Baptista, Alessandra Crusco, Andrea Brancale

Cross-lab training.

Medicinal chemistry, computational biology and automated screening.

Collaboration with additional external partners eg Phytoquest Limited.

Research Impact

NRN funding has:

- Enabled new collaborations forged via the NRN Scientific Congress.
- Enabled interdisciplinary research activity between 2 Welsh Universities.
- Provided PhD training at 2 institutions. with 50:50 student time at each institution.
- Secured external funding from Phytoquest Limited, a natural product company based in Aberystwyth.
- Provided enhanced opportunities for collaborations via 2 established laboratories and NRN Conferences and events

"The strength of this project is to be part of a collaboration among different institutions with diverse areas of expertise: the parasitology group in Aberystwyth University, the medicinal chemistry group in Cardiff University and the natural product company, Phytoquest."

Alessandra Crusco

"The poster presentation during the Annual Drug Discovery Congress gave me the opportunity to meet new collaborators and winning a prize was a strong stimulation for the progress of the project."

Gilda Padalino

PHD STUDENTSHIP

Prostate cancer cells require a Rab35-dependent exosome sub-population for stromal activation and tumour growth; Vincent Yeung, Dr Aled Clayton, Dr Jason Webber, School of Medicine, Cardiff University

The Unmet Need

Prostate cancer (PCa) is the most frequent male cancer, with around 40,000 new cases and 10,000 deaths annually in the UK. It is unclear why some prostate cancers are more aggressive than others. The team had however shown that the release of exosomes (complex fat-bubbles) from prostate cancer cells may be involved in enhancing tumour growth. Exosomes abnormally activate cells neighbouring the tumour, driving formation of blood vessels to feed and promote tumour growth. A molecule called TGFb which sits at the surface of exosomes is required for this activation.

This PhD studentship sought to validate exosomes as a target in prostate cancer.

Research Progression

The project resulted in the identification of components impacting exosome secretion and subsequent stromal activation capacity which could potentially be used as a therapeutic target in cancer and other diseases.

Additional funding has been secured to further explore the impact of the exosome-deficient Du145 cells on tumour growth and invasion in vivo, which will be key in supplementing the current data that prostate cancer exosomes act to progress disease in vivo. A new collaboration was forged at the NRN Congress with Axis Bioservices, to assist with in vivo experiments.

Research Impact

NRN funding has:

- Led to significant collaborations with academia and industry and the establishment of a new 'Tumour Microenvironment group' at Cardiff University.
- Led to the generation of some novel prostate cancer cells in which vesicle-production is attenuated, and the sharing of these to support researchers across Europe.
- Resulted in submission of a publication detailing project results.
- Generated additional funding from Welsh Crucible involving new multidisciplinary collaborations between Cardiff, Swansea and Aberystwyth Universities.
- Resulted in further funding applications (worldwide cancer research).
- Led to employment of Vincent Yeung as a researcher at Harvard Medical School to continue his work with vesicles.

"The funding has allowed me to learn new scientific techniques and expand my knowledge. Opportunities to present my research at international conferences, and subsequent awards has helped pursue my career goals. This has allowed my employment at Harvard Medical School as a Research Fellow."

Vincent Yeung

Vincent Yeung

PHD STUDENTSHIP

Exploring the interaction of CD4+ T Cells with influenza peptides derived from conserved viral proteins; Alex Greenshields-Watson, Dr David Cole; School of Medicine, Cardiff University

The Unmet Need

Influenza is a respiratory infection caused by an RNA virus that can cause serious illness in humans. Influenza vaccines are not universally effective, they do not work with all viral strains, and the protection they afford is short-lived. Thus, there is a pressing need for improved therapy. CD4+ T-cells, part of our immune system, play a key role in fighting off influenza infections.

This PhD studentship investigated CD4+ T-cell responses to peptides from conserved viral proteins. Such peptides may serve as targets for universal influenza vaccines and provide a platform for modified vaccination strategies that can generate highly effective immune responses.

Research Progression

This project worked to identify regions of the viral proteins which are presented to immune cells orchestrating the clearance and subsequent protection against infection. These regions were defined at the highest possible level of resolution, using X-ray crystallography. Definition at the highest level of resolution formed the basis for targeted modification of these "epitopes". Such modifications are aimed at enhancing their immunogenicity and ultimately improving the immune response to vaccination. The project successfully identified seven epitopes, four of which have been defined by x-ray crystallography. These epitopes will form the basis for later vaccine design and enhancement projects.

Research Impact

NRN funding has:

- Led to the submission of a publication based on project results.
- Led to further investigations to exploit the immunological findings of the project in the cancer setting.
- Resulted in a postdoctoral position for Alex with Profs Andrew Godkin and Awen Gallimore working on cancer-related work.

"My NRN PhD studentship was a fantastic experience. As well as being highly stimulating, it allowed me to explore multiple areas of cutting-edge immunology and develop essential skills for a career in scientific research."

Alex Greenshields-Watson

PHD STUDENTSHIP

Pharmaceutical evaluation of novel tiglianes as modulators of dermal fibroblast-myofibroblast differentiation, scar formation and fibrosis; and elucidation of their underlying mechanisms of action; Jordanna Dally (PhD student); Dr Ryan Moseley, School of Dentistry, Cardiff University

The Unmet Need

Chronic wounds and excessive scarring (fibrosis) in skin are major causes of disease, resulting in significant pain and debilitating shortening of muscles or joints, which can dramatically affect patients' physical and psychological quality of life. Existing therapies are largely unsatisfactory in treating these conditions.

Anti-cancer properties in seeds from Fontain's Blushwood trees in the Queensland Tropical Rainforest were previously identified by an Australian company who provided match studentship funding to a team at the Cardiff School of Dentistry to evaluate anti-scarring properties and the underlying mechanisms of action of the compounds.

Research Progression

Match funding via an NRN Studentship has allowed the team to confirm the underlying mechanisms of action of the compounds in the seeds to clarify how they have anti-scarring properties. This work has resulted in the filing of 6 patents and an additional 2 years postdoctoral funding at the School of Dentistry provided by the Australian commercial partner.

Research Impact

NRN funding has:

- Resulted in the filing of 6 patents with the PI as inventor.
- Secured an additional £251,706 postdoctoral research funding to develop therapies against abnormal wound healing and excessive skin scaring.

"NRN studentship funding has helped me become a more well-rounded researcher. Through various NRN workshops, I have learnt a lot about early career progression & the importance of exploring future career opportunities now. Furthermore, the NRN's PhD & Drug Discovery conferences have allowed me to network with other early-stage researchers, fostering the potential for future interdisciplinary collaborations. Post-PhD, I hope to stay in academia as a post-doctoral researcher; ideally, in my current research field & in continued collaboration with my Australian funders, QBiotics. Thanks to the NRN for match-funding my studentship - which has been the toughest, but most rewarding experience, of my academic life so far."

L-R: Dr Bob Steadman; Jordanna Dally; Dr Ryan Moseley

PHD & POSTDOCTORAL PROJECTS

TACKLING GYNAECOLOGICAL CANCERS

A precision medicine approach at Swansea University.

ADC targets from in-silico high-throughput screening identification into target validation; Dr Jetzabel Garcia Parra; Prof Steve Conlan & Dr Deyarina Gonzalez, Medical School, Swansea University, (Postdoctoral Impact Project)

Antibody-drug conjugates for gynaecological cancers; Belen Pan Castillo (PhD Studentship)

The Unmet Need

Antibody-drug conjugates (ADCs) are a new model for novel targeted cancer therapy in precision medicine. At present, there are no ADCs approved for the treatment of ovarian cancer, a malignant disease with poor prognosis that kills 12 women daily in the UK. Current anticancer treatments are problematic and often ineffective. There is therefore an urgent need for effective and targeted therapeutic approaches for ovarian cancer.

Research Progression

The NRN Impact project was based on 2 initial NRN projects, a PhD Studentship which established screening technology and expertise and a postdoctoral project which identified novel targets through in-silico screening.

The main objective of these projects was to develop an Antibody Drug Conjugate (ADC) as a targeted therapy for the treatment of ovarian and endometrial cancers.

Research Impact

NRN funding has generated:

- The identification of a target molecule that is druggable via ADC technology.
- Patent application.
- An ADC Development Programme.
- Additional research funding: Life Sciences Bridging Fund; Tenovus, A4B, Health & Care Research Wales, £397,000.
- New collaborations: with external partners (Axis Bioservices, ADC Biotechnology Limited, GE Biacore) and academic partners forged during Scientific Congress (Dr Chris Gwenin, Bangor University).

"This project has provided relevant results demonstrating ovarian and endometrial cancer as good candidates for SNIPER-TARGET therapy. The data obtained has been incorporated into a patent application and we are currently developing a multi-million pound bid for ADC therapeutics, which if successful will demonstrate the added value of NRN funding."

Belen Pan Castillo

Belen Pan Castillo

POSTDOCTORAL PROJECT

Delivery of osteogenic molecules from acrylic bone cement to encourage regenerative bone repair around cemented joint replacements.
Dr Wayne Nishio Ayre.

The Unmet Need

Joint related problems such as osteoarthritis are one of the most common conditions reported in elderly patients. The increase in the elderly population and a rise in obesity amongst the younger population in the UK poses significant problems for health care services to meet the increasing demand for treatments. Approximately 180,000 hip and knee replacements are performed in the UK every year, with a significant number using cement to anchor the implant to bone. Unfortunately, around 10% of these implants fail after 10 years, due to loosening of the cement related to poor bone repair after surgery.

Research Progression

Dr Wayne Nishio Ayre secured the NRN postdoctoral project funding at Cardiff University with the aim of enhancing an antibiotic delivery system to encourage bone growth around cemented joint replacements, by delivering a growth factor which would increase the rate that cells could create new bone material. The delivery system was originally developed and patented out of Wayne's PhD studentship at the School of Engineering and the School of Pharmacy & Pharmaceutical Sciences, Cardiff University.

Research Impact

NRN funding has generated:

- An additional £240,000 research funding, including a Life Sciences Bridging Fund award of £71,114 to further optimise the delivery system, scale up manufacturing processes, begin the process of regulatory approval and develop a protocol for an animal study that will significantly enhance the commercial potential of the system.
- Via the NRN Annual Scientific Congress, the formation of new collaborations with key investigators at the School of Biosciences and School of Medicine at Cardiff University; with research fellows and clinical orthopaedic leads at Velindre NHS Trust and Cardiff & Vale University Health Board.
- A prestigious Travelling Fellowship funded by the British Orthopaedic Research Society which led to new collaborations with orthopaedic centres of excellence and Universities in China, Singapore and Australia, where the NRN project was showcased.
- Strong commercial interest has been shown by global orthapaedic companies such as Zimmer-Biomet.
- Dr Nishio Ayre has secured a permanent lectureship in Biomaterials at Cardiff School of Dentistry as a direct result of the NRN postdoctoral project.

"Life Sciences Research Network funding has provided me with the opportunity to develop a track record in securing funding and undertaking interdisciplinary and translational research. It has greatly contributed to my recent appointment as a Lecturer in Biomaterials at the Cardiff School of Dentistry."

Dr Wayne Nishio Ayre

Dr Wayne Nishio-Ayre

POSTDOCTORAL PROJECT

The use of 3D culture to test the efficacy of a novel enzyme for cancer prodrug therapy; Dr Chris Gwenin, School of Chemistry, Bangor University.

The Unmet Need

Chemotherapy for cancer has evolved significantly, but most drugs in use today still cause severe side effects. Directing the therapeutic agent to the tumour is a way of avoiding these side effects.

This NRN Impact Project has built upon the Bangor group's original invention of gold-coated magnetic nanoparticles directing enzymes to solid tumours, by identifying a novel enzyme to be tested for efficacy against tumour types.

Research Progression

The project has resulted in the production of a purified protein and a purified enzyme.

Helped to secure a worldwide patent and secure additional funding into Wales.

Research Impact

NRN funding has:

- Generated new collaborations with: University of Auckland, New Zealand and with Professor Steven Conlan's and Professor Shareen Doak's group at Swansea University (also NRN award holders).
- Secured a KESS II Scholarship to further develop the project. To enable selective cellular uptake of the particles.
- Resulted in a paper in Biochemical Pharmacology.
- Generated research funding submissions eg BBSRC application for £156,349.
- Secured a worldwide patent.

"Our research group has benefitted significantly from the support and guidance of the Network, which has allowed the group to undertake research aligned to meet the needs of local companies, secure Intellectual property and obtain additional funding from outside Wales. The Network's Annual Congress has proved to be extremely beneficial for the Welsh Universities, helping to establish strong collaborative links, share knowledge base and target resources more effectively."

Dr Chris Gwenin

L-R: Patrick Ball; Dr Chris Gwenin

POSTDOCTORAL IMPACT PROJECT

Evaluation of Novel CD200:CD200R Blockade Cancer Immunotherapy; Dr Simone Lanfredini; Dr Girish Patel (PI), Cardiff University

The Unmet Need

A hallmark of cancer is the ability to avoid detection by the immune system.

Despite an advance in cancer therapies, current drugs have limited efficacy and most cancers fail to respond.

Research Progression

On-going research in the Patel lab at Cardiff University has demonstrated that acute myeloid leukaemia and basal cell carcinoma, including cancer stem cells, express the immune suppressive cell surface molecule CD200, a "do not kill me" molecule.

NRN impact project funding for Dr Girish Patel's lab has supported a drug discovery programme resulting in the identification of a compound capable of both blocking the CD200 signalling and inducing human cell killing of the molecule.

This programme has been assisted by the NRN-funded Welsh Computer Aided Drug Discovery Platform.

The team are carrying out safety and efficacy tests and will look at dosing and formulation to further develop the commercial potential of this NRN-funded research.

Research Impact

NRN funding has generated:

- An additional £101,000 research funding including a KESS 2 scholarship and further funding applications to progress testing.
- A patent application to protect the intellectual property of the lead compound.
- Spin-out option discussions with IP Fusion.
- Applications to CRUK, Wellcome and MRC for ADME and candidate drug development.

"What started as a dream, "to cure cancer", has been made closer each day by the funds from the LSRNW. Now with potential drugs in our hands, we hope to transform the dream into reality."

Dr Simone Lanfredini

POSTDOCTORAL IMPACT PROJECT

Discovery and development of a novel therapeutic for the treatment of inflammatory lung disorders; Dr Martin Schepelmann; Prof Andrea Brancale; School of Pharmacy & Pharmaceutical Sciences, Cardiff University, Prof Daniela Riccardi, School of Biosciences, Cardiff University.

The Unmet Need

Asthma and chronic obstructive pulmonary disease (COPD) are predicted to be the third most common cause of mortality worldwide by 2030 (WHO). The available treatments – corticosteroids and bronchodilators – only target the symptoms of disease and many patients suffering from asthma are resistant to this form of treatment. There is a clear need for a novel therapeutic approach able to halt disease progression and stop the decline of lung function.

Recently, a protein called Calcium-Sensing Receptor (CaSR) has been identified for being integral to the pathogenesis of inflammatory lung diseases. Drugs called "calcilytics" inhibit this protein and open-up a completely novel avenue for the treatment of these diseases by targeting one of their root causes (Yarova et al, Sci Tra Med 2015). This novel therapy has IP protection (owned jointly by Cardiff University and Kings College London).

To allow full commercial and therapeutic realisation of this new therapy, this NRN postdoctoral project and Impact project aimed to design and prepare a novel calcilytic for the treatment of asthma and chronic obstructive pulmonary disease.

Research Progression

The Postdoctoral project and Impact project, assisted by the NRN funded Welsh Computer Aided Modelling Platform, have led to the successful identification, synthesis, and biological evaluation of a novel calcilytic compound for the treatment of CaSR in inflammatory lung diseases. A patent application for the compound is being developed which should attract further investment and increase the therapy's commercial value to broaden the calcilytic application not only to asthma and COPD but to other incurable inflammatory lung diseases such as pulmonary fibrosis, pulmonary hypertension and interstitial lung disease.

Research Impact

NRN funding has:

- Enabled the successful scientific development of a novel compound to target the protein by: exploration of the molecule on the computer; development of a chemical synthetic strategy to prepare the compound and by deeper investigation of certain chemical properties of this molecule (stereochemistry).
- Allowed biological evaluation of the novel compound in cells and animal models of inflammatory lung disorders which showed that the novel compound successfully alleviates the symptoms of asthma.
- Led to a patent application being currently prepared to protect the IP.

Award winning presentation of this research at the 2nd Annual Drug Discovery Conference, Cardiff.

Added Value

The outcomes of these projects – a novel calcilytic compound for the treatment of inflammatory lung disorders – will substantially increase the commercial value of this novel therapeutic strategy. This will allow its effective further development in clinical investigation. A success in bringing such a calcilytic compound to the market could bring about a life altering new treatment for the millions of patients suffering from chronic inflammatory airway diseases in Wales, the UK and worldwide.

"Funding by the NRN has allowed me to successfully develop new skills and expertise in drug discovery and development. My research will allow us to develop new therapeutics to help the countless patients worldwide who are awaiting a real treatment for these life-changing diseases. The work on this project has made a profound impact on my research direction and career which is now leading me to continue my work on the CaSR as a target in other diseases."

PLATFORM TECHNOLOGY AWARD

In Silico platform to support drug discovery and development; Dr Salvatore Ferla (Postdoctoral researcher), Professor Andrea Brancale; School of Pharmacy & Pharmaceutical Sciences, Cardiff University

The Unmet Need

Drug discovery is a time-consuming and expensive process with 1 in 10,000 molecules developed reaching the market. The low rate of success and the elevated costs have led to a decrease in New Chemical Entities reaching the clinic. In silico techniques, such as virtual screening and computer aided drug design can offer an advantage over conventional lab approaches by being faster and cheaper speeding up the entire drug discovery process. However, because of the technical complexity of these methods, CADD techniques are often limited in the wider research community.

Research Progression

With expertise in this field, the School of Pharmacy and Pharmaceutical Sciences at Cardiff University was awarded an NRN Platform Technology grant to offer free support to a variety of drug discovery projects across Wales from different scientific backgrounds. The platform has been successful in helping develop current projects, generating preliminary data to support grant applications, producing intellectual property and fostering new collaborations across Wales and further afield.

Research Impact

NRN funding has:

- Resulted in 30 project collaborations across Wales, UK, USA, Europe and Australia (Including anti-cancer, anti-viral, hematology, parasitology, bacteriology, gastroenterology projects).
- Generated 8 publications with projects and presented at several international conferences.
- Led to the identification of hit compounds and 2 notable joint funding applications between the platform PI and 2 other NRN-funded PIs, to further develop these new molecules as anti-cancer agents.
- Demonstrated the viable commercial potential of the platform as a "fee for service" enterprise, collaborating with three small companies.

"The NRN funded platform gave me the invaluable opportunity to collaborate with several scientists from inside and outside Wales allowing to build a very large collaboration network which will be very useful for my career development. On top of that, the variety of project topics developed by the WCADD collaborations has had a positive impact on expanding my scientific knowledge and in developing and refining my research/project management skills."

Dr Salvatore Ferla

On left: Salvatore Ferla

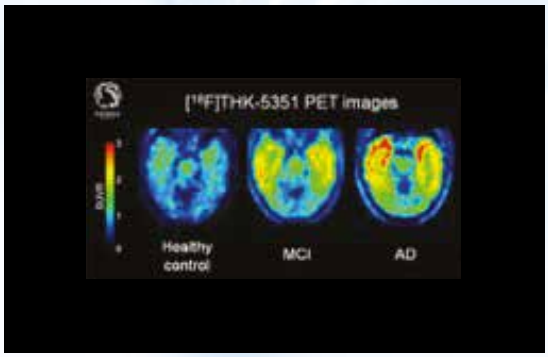
PLATFORM TECHNOLOGIES

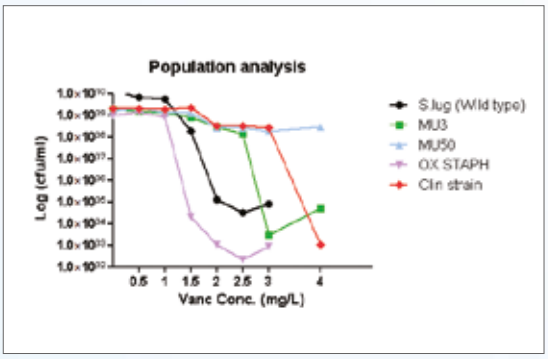
The Network has funded 13 Platform Technologies, enabling academics from across Wales to access free expertise and equipment at other institutions. These Platforms have proved to be highly successful and have led to a significant increase in the number of pan-Wales proposals submitted to the Network as well as collaborations with academia and industry.

In Vivo Imaging of Tau Distribution in the Brain

PET Tau imaging enables the assessment of Tau levels in the brain in order to facilitate drug development in the fields of Alzheimer's and other dementias involving Tau deposition. This technology could also be applied to the pharmacological assessment of anti-tau therapy, thereby allowing preventive interventions.

Contact: Professor Chris Marshall,
Cardiff University - marshallc3@cardiff.ac.uk





Novel Antimicrobial Evaluation Service

The Specialist Antimicrobial Chemotherapy Unit (SACU), Public Health Wales, provides a novel antimicrobial evaluation service for Welsh academics through it's Antimicrobial Chemotherapy Susceptibility Testing laboratory.

Contact: Dr Mandy Wootton, Public Health Wales
- mandy.wootton@wales.nhs.uk

Roboworm

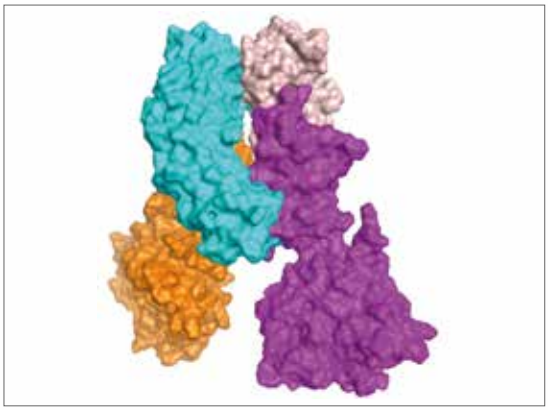
Roboworm is an automated high-content imaging platform for repositioning old drugs as next generation anthelmintics. Roboworm identifies potential new starting points for anthelmintic drug discovery programmes or new indications.

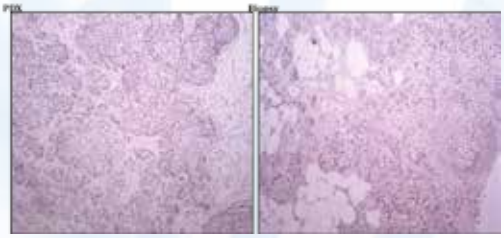
Contact: Professor Karl Hoffmann,
Aberystwyth University - krh@aber.ac.uk

Welsh Computer-aided Drug Design (CADD) Platform

CADD has often been indicated as a powerful tool to speed up the drug discovery process. In silico techniques, like molecular docking and de novo drug design, can offer advantages over lab based screening methods, being both faster and cheaper. This platform offers Welsh researchers access to a set of techniques, from hit identification to lead optimisation.

Contact: Prof A Brancale, Cardiff University - brancalea@cardiff.ac.uk





Development of a PDX platform for Drug Discovery and Studies of Disease Biology in Wales

The platform establishes PDX models across multiple cancer types through direct collaboration with Welsh-based researchers with expertise in these cancer fields. This will provide pre-clinical testing of putative therapies and biomarkers whilst also investigating biological mechanisms of cancer.

Contact: Dr Luke Piggott, Cardiff University - piggottl@cardiff.ac.uk

All Wales Cellular Bioenergetics Analysis Platform

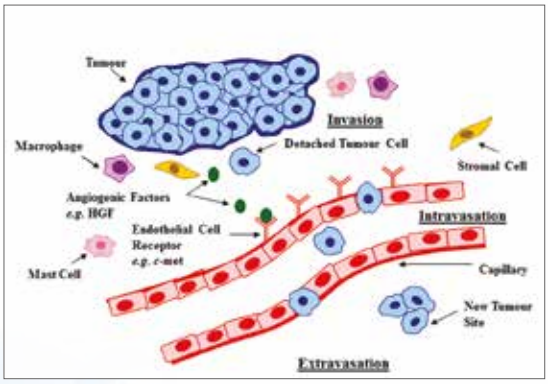
A real-time mitochondrial bioenergetics measuring system that can assess oxidative phosphorylation, glycolysis and fatty acid oxidation of any cell type. The platform measures oxygen consumption rate (OCR) and extracellular acidification rate (ECAR) from intact cells.

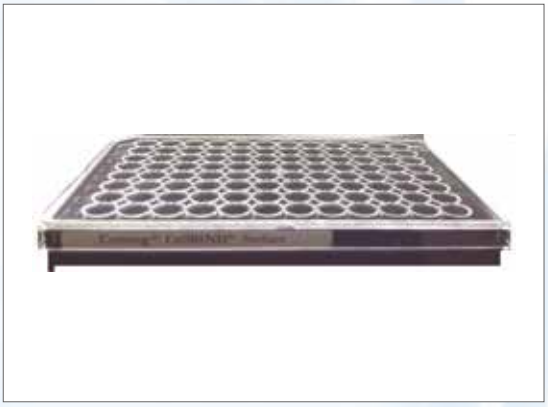
Contact: Professor Cathy Thornton, Swansea University - c.a.thornton@swansea.ac.uk

Cancer Metastasis Modelling Platform

Enables the testing and discovery of potential agents or molecules that are involved in metastasis. This involves an integrated programme of assays and tests, beginning with molecular discovery right up to in vivo testing. Researchers can benefit from excellent and one of a kind facilities by being able to test and evaluate their potential therapeutics or targets.

Contact: Professor Wen G. Jiang,
Cardiff University - jiangw@cardiff.ac.uk





Antivirals Discovery and Development

Offers high throughput analysis of antiviral candidate compounds.

The antivirals platform seeks to address the lack of effective antiviral drugs versus a number of viral pathogens with significant local and global health impact: measles virus, dengue virus, chikungunya virus and ebola virus.

Contact: Prof A Brancale, Cardiff University
- brancalea@cardiff.ac.uk

"The NRN funded platform gave me the invaluable opportunity to collaborate with several scientists from inside and outside Wales allowing to build a very large collaboration network which will be very useful for my career development. On top of that, the variety of project topics developed by the WCADD collaborations has had a positive impact on expanding my scientific knowledge and in developing and refining my research/project management skills."

Dr Salvatore Ferla
Welsh Computer-aided Drug Design Platform

"NRN funding has allowed us to increase our understanding of mechanisms which help cancer cells to resist treatment with DNA-damaging cancer drugs - this is a first step in improving cancer treatment. Also, NRN-sponsored meetings have brought me into contact and initiated new collaborations with other scientists in Wales."

Dr Edgar Hartsuiker
PI & Management Board Member,
Bangor University

TOWARDS COMMERCIALISATION

WORKING WITH THE LIFE SCIENCES BRIDGING FUND

The Network argued the case for a Bridging Fund to optimize the probability that successful research opportunities could be "advanced towards commercialisation". Since inception in September 2015, the Life Sciences Bridging Fund and the Network have worked in close collaboration – the Bridging Fund provides proof of concept funding to support the commercial development of academic research within Welsh Universities. This funding supports the translational research required to demonstrate the commercial potential of academic research conducive to realise economic and patient benefits - 9 NRN projects have secured Bridging Fund awards to develop their commercial potential.

"I was fortunate to be awarded a 12 month proof-of-concept grant, together with my colleague Dr Claire Morgan, to develop an idea to provide a new targeted therapy for solid tumours. The research was very successful, thanks to the skills of the post-doc, Laura Morris, who we appointed on this project. As a consequence we have rapidly moved forward and have obtained CRUK funding for translational research and collaboration with Dr Lee Parry at Cardiff University and a Life Sciences Bridging Fund Grant, so that the technology can be brought on for commercialisation."

Professor Paul Dyson
Network Postdoctoral Project & Bridging Fund Award Holder, Swansea University

Contact:
corinne.nguyen@lsbridgingfund.wales

"The Bridging Fund enabled us to develop a highly improved version of the industry standard chromosome damage MN test, and the NRN funded project focusses on the next generation of test system to be used by industry, an automated multi-endpoint DNA damage assay."

Dr George Johnson
Network PhD & Bridging Fund Award Holder, Swansea University

For more information on the Bridging Fund, contact: **Corinne.nguyen@lsbridgingfund.wales**

TIZIANA LIFESCIENCES

Network funding has helped to strengthen commercial endeavours:

"After founding Tiziana Lifesciences on the basis of our early drug development project, we sought Network funding to help support a PhD study jointly with the biotech company to investigate the molecular target of our novel agents in more detail. This was a key step in the drug development pipeline, which helped cement the relationship with Tiziana and strengthened our research portfolio in this area. This project, which is nearing completion, has been instrumental in the successful progression of the pipeline to its translational phase, with phase 1 clinical trials scheduled to begin in 2017."

Dr Richard Clarkson
Cardiff University

ANNUAL DRUG DISCOVERY CONGRESS

The Annual Scientific Congress takes place in the autumn and provides a key focal point for the drug development community in Wales, contributing to valuable exchanges and the formation of new relationships and research collaborations'

> "LSRNW funding is a great way to seed innovation and foster collaborations. The Annual Congress is one of the most fertile forums for interdisciplinary work that I have ever experienced. Long may it continue."
>
> **Dr Ian Fallis**
> Cardiff University

Julie James AM opening Congress 2016

ENDEAVOUR AWARDS

Network Endeavour funding provides a small amount of highly flexible funding to pump-prime research development activities.

The Network has funded an array of training events, workshops and meetings, focusing on a range of topics, from guidance in writing competitive funding proposals, to building effective consortia in advance of major funding calls.

Click on the link for more information:
www.lsrnw.ac.uk/what-we-fund/endeavour

ENGAGEMENT

The Network has engaged in a variety of STEM events where NRN researchers have interacted with members of the public through the demonstration of drug discovery activities.

Eisteddfod yr Urdd 2017

NRN PROJECTS CO-FUNDER CONTRIBUTORS **£2.7M**


GIG
CYMRU
NHS
WALES
Bwrdd Iechyd Prifysgol
Betsi Cadwaladr
University Health Board


INDOOR
biotechnologies


tenovus
cancer care
gofal canser


PRIFYSGOL
ABERYSTWYTH
UNIVERSITY


Eckert & Ziegler


BBSRC
20 Years of Pioneering
Great British Bioscience


北京大学
PEKING UNIVERSITY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PhytoQuest
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BIOVITAS
CAPITAL


RIDGEWAY
RESEARCH


UNIVERSITY OF
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Swansea University
Prifysgol Abertawe


Cardiff
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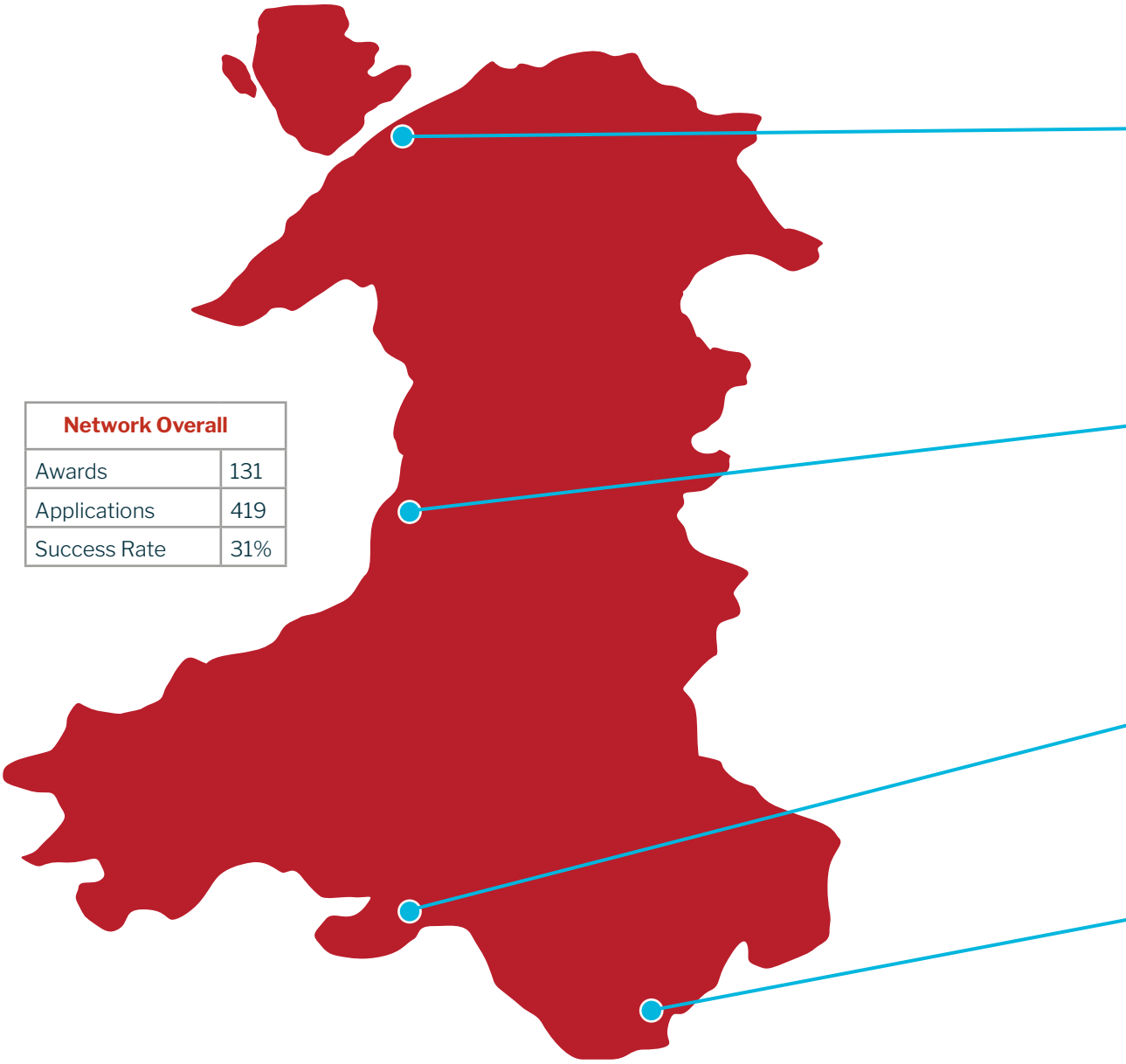
NUCANA
BIOMED

GEOGRAPHICAL DISTRIBUTION OF PROJECTS



Network Overall	
Awards	131
Applications	419
Success Rate	31%

Bangor University	
Awards	9
Applications	32
Success Rate	28%

Aberystwyth University	
Awards	13
Applications	35
Success Rate	37%

Swansea University	
Awards	24
Applications	72
Success Rate	33%

Cardiff University	
Awards	85
Applications	276
Success Rate	31%

RESEARCH PROJECTS

*Impact Award: These awards maximise the commercial, societal or scientific impact of previously funded Research Projects or PhD studentships

ONCOLOGY

PhD studentships

Novel Bcl3 Inhibitors – Target Validation and Anti-Metastatic Lead Optimisation; Daniel Turnham, Cardiff University; Supervisor: Dr R Clarkson

Targeting regulators of exosome secretion as a modality to attenuate cancer-associated stromal activation and disease progression; Vincent Yeung, Cardiff University; Supervisor: Dr A Clayton

Role of DNA repair in resisting treatment with Gemcitabine and other nucleoside analogues; Lennart Boeckemeier, Bangor University; Supervisor: Dr Hartsuiker

Antibody-drug conjugates for gynaecological cancers; Belen Pan Castillo, Swansea University; Supervisor: Dr D Gonzalez

Developing novel reagents to target the DNA damage signal associated with Wnt activated colorectal cancer; Maria Konstantinou, Cardiff University; Supervisor: Dr M Smalley

Characterisation and targeting of cancer stem cells in high-risk myelodyplastic syndrome that transforms to acute myeloid leukaemia; Juan Gonzalez, Cardiff University; Supervisor: Dr N Rodrigues

Diastereoselective synthesis of phosphoroamidate prodrugs; Elisa Pileggi, Cardiff University; Supervisor: Dr F Pertusati

Companion diagnostic development guides Antibody-Drug Conjugate formulation: Implications for patient stratification and precision medicine; Alice Luther, Swansea University; Supervisor: Dr R Del Sol

Combining carbon monoxide (CO)-releasing molecules with anti-VEGF therapy for triple-negative breast cancer therapy; Malamati Kourti, Cardiff University; Supervisor: Dr J Cai

Testing a novel chemotherapy delivery system using two dinitrobenzamide mustard prodrugs; Patrick Ball, Bangor University; Supervisor: Dr C Gwenin

Development of immune-modulators for preventing immune suppression by cancer-associated LAG3+CD4+ T-cells; Georgina Mason, Cardiff University; Supervisor: Prof A Godkin

Design and evaluation of an antibody-drug conjugate for prostate cancer treatment; Aimy Nguyen Chi, Swansea University; Supervisor: Prof S Doak

Targeting of interleukin-13 receptor (IL-13R)a2 expressing pancreatic cancer by a novel hybrid lytic peptide drug; Benjamin Skalkoyannis, Swansea University; Supervisor: Prof V Kanamarlapudi

Design and in vitro characterisation of a novel multimodular targeting platform for cancer treatment; Samuel Franklin, Cardiff University; Supervisor: Dr Y Tsai

Smart multifunctional nanocarriers with biodegradable and dual responsive (pH and temperature) properties from hyperbranched polymers for targeted cancer drug delivery; Chester Blackburn, Bangor University; Supervisor: Dr H Tai

Targeting zinc signalling to prevent cell division in cancer; Olivia Ogle, Cardiff University; Supervisor: Dr K Taylor

Development of artificially enhanced T cells for targeting cancer; Cardiff University; Supervisor: Prof A Sewell, PhD: Aaron Wall

Developing HCMV as a vaccine vector; Evelina Statkute, Cardiff University; Supervisor: Dr R Stanton

Postdoctoral Research Projects

Multi-Modal Theranostics (MMTs) - Towards personalized cancer therapies; Dr S Chanapaii, Cardiff University; PI: Dr Ian Fallis

Bacterial-mediated RNA interference as a new therapy to target advanced prostate cancer; Dr L Morris, Swansea University; PI: Prof P Dyson

Targeting αB-crystallin (CRYAB): A possible novel strategy to impede triple-negative breast cancer growth; Dr H Ping Weeks, Cardiff University; PI: Dr J Cai

Optimising cellular uptake of enzyme/gold-coated magnetic nanoparticle conjugates; Dr P Paramasivan, Bangor University; PI: Dr C Gwenin

⊛ The use of 3D culture to test the efficacy of a novel enzyme for cancer prodrug therapy; Dr R Beardmore, Bangor University; PI: Dr C Gwenin

Nanoparticle delivery of epigenetic modifiers: a targeted approach for endometrial cancer treatment; Dr K Brushafer, Swansea University; PI: Prof S Conlan

Developing a stem-cell containing 3D culture model for pre-clinical studies of colorectal cancer therapeutics; Dr K Ewan, Cardiff University; PI: Prof T Dale

Evaluation of Transglutaminase-4 as a therapeutic and target and diagnostic tool in human prostate cancer: Dr S Owen, Cardiff University; PI: Prof W G Jiang

⊛ Development of novel CD200:CD200R Blockade cancer immunotherapy; Dr S Lanfredini, Cardiff University; PI: Dr G Patel

Evaluation of Novel CD200:CD200R Blockade Cancer Immunotherapy; Dr S Lanfredini, Cardiff University; PI: Dr G Patel

Rational design of antibody drug conjugate targets – unlocking a goldmine and war chest; Dr Y Friedman, Swansea University; PI: Dr D Gonzalez

ADC targets from in-silico high-throughput screening identification into target validation; Dr J Garciaparra, Swansea University; PI: Dr D Gonzalez

Anti-inflammatory calpain inhibitor leads; Dr D Grundy, Cardiff University; PI: Prof R Allemann

Chimeric phosphoramidate ProTides as anticancer and antiviral agents with fluorescent probes; Dr S Kandil, Cardiff University; PI: Prof A Westwell

Optimisation of T-cell metabolism for anti-cancer vaccination; Swansea University; PI: Dr N Francis

⊛ Discovery of novel site-specific FAK inhibitors for potential treatment of metastatic breast cancer, Dr S Kandil; Cardiff University; PI: Prof A Westwell

Discovery of novel site-specific FAK inhibitors for potential treatment of metastatic breast cancer, Dr S Kandil; Cardiff University; PI: Prof A Westwell

Developing targeted virotherapies for advanced, platinum resistant ovarian cancer; Dr S Curtis, Cardiff University; PI: Dr A Parker

⊛ Evaluation of folate receptor α (FRα) binding oligopeptides for targeted gene and drug delivery; Dr S Curtis, Cardiff University; PI: Dr A Parker

Sensitizing to radiotherapy: pre-clinical evaluation of a novel indication for adjuvant bcl3i; Dr A Gruca, Cardiff University; PI: Dr R Clarkson

Advancing analogues of a novel cFLIP inhibitor which sensitises breast cancer cells and cancer stem cells to TRAIL; Dr O Hayward, Cardiff University; PI: Prof A Westwell



Establishing a screen for the WNT-STOP mitotic signalling pathway; Dr A Offergeld, Cardiff University; PI: Prof T Dale

The first preclinical analysis for a novel magnetically directed cancer treatment; Dr R Hobbs, Bangor University; PI: Dr C Gwenin

18F-Gemcitabine as diagnostic tool in personalised chemotherapy; Cardiff University; PI: Dr J Xiang Yin, Dr I Fallis

Targeting CtIP to sensitise cancer cells to DNA-damaging agents; Bangor University; PI: Dr R Beardmore, Dr C Staples

Developing next generation Bcl3 inhibitors as anti-metastatic drug candidates; Dr C Bordoni, Cardiff University; PI: Prof A Westwell

Targeting G-quadruplex nucleic acid structures with caffeine gold compounds for cancer treatment; Dr S Meier, Cardiff University; PI: Prof A Casini

⊛ Developing HCMV as a vaccine indicator; Evelina Statkute, Cardiff University; PI: Dr R Stanton

⊛ Small molecule inhibitors of Brachyury: addressing unmet clinical needs by targeting a sub-type of colorectal cancer with particularly poor patient-prognosis; Dr J Jezkova, Bangor University; PI: Dr J Wakeman

⊛ Identifying biomarkers to predict response to immunotherapies; Cardiff University, Prof A Godkin.

⊛ Development of novel GATA-2-specific inhibitors to target leukaemia stem cells (LSCs) in acute myeloid leukaemia; Dr Juan Bautista Menendez Gonzalez, Cardiff University; PI: Dr N Rodrigues

⊛ Small molecule inhibitors of CtIP to sensitise cancer cells to therapy; Dr S Ferla, Cardiff University; PI: Prof A Brancale

NEUROSCIENCE

PhD Studentships

Regulation of brain-derived neurotrophic factor levels by small molecules; Cardiff University; Katharina Saeuberli, Cardiff University; Supervisor: Prof Y Barde

Pharmacogenetic manipulations of cell signalling as therapeutic approaches for Huntington's Disease; Kyle Fears, Cardiff University; Supervisor: Prof R Brambilla

Fingolimod pro-drugs as a new therapeutic opportunity; Edward James, Cardiff University;

Supervisor: Prof A Brancale
Treating progressive Multiple Sclerosis using a novel neuroprotective and anti-inflammatory approach; Lewis Watkins, Swansea University; Supervisor: Dr O Howell

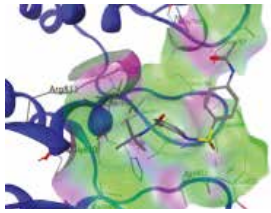
Investigating novel small molecule enzyme inhibitors for treating cognitive decline and dementia; Martina Sassi, Swansea University; Supervisor: Dr J S Davies

Developing new small molecule therapies for lysosomal diseases; Rafael Badell-Grau, Cardiff University; Supervisor: Dr E Lloyd-Evans

Novel drug therapy for Mitochondrial Optic Neuropathy and other mitochondrial diseases; Carmine Varrichio, Cardiff University; Supervisor: Dr M Rozanowska

Developing an ovine model of Alzheimer's Disease; Emma Davies, Aberystwyth University; Supervisor: Dr S McBride

Radiosynthesis of 18F-labelled pro-nucleotides (ProTides) for Positron Emission Tomography (PET) imaging; Alessandra Cavaliere, Cardiff University; Supervisor: Prof A Westwell



Postdoctoral Research Projects

Modelling motor neuron disease using patient derived iPS cells for novel therapeutic

discovery; Dr I Gilmore, Swansea University; PI: Dr Y Wang

The design, synthesis and evaluation of novel agents acting in the CNS; Pertusati / Prof A Brancale

⊛ Improved fingolimods for multiple sclerosis, Dr F Persuati; Cardiff University; Pertusati / Prof A Brancale

Investigating the potential of the sphingosine-1-phosphate receptor 1 modulators for the treatment of psychiatric disorders; Dr L Sykes, Cardiff University; PI: Prof J Hall

Investigating a novel therapy for Alzheimer's Disease in a mouse model of amyloid

pathology; Dr C Evans, Cardiff University; PI: Dr E Kidd

Long life imaging probes for Dementia Patient Stratification; Dr M Monti, Cardiff University; PI: Dr I Fallis

Validation in rodent models of a novel approach to treat mood disorders based on ERK signalling stimulation; Dr L Morella, Cardiff University; PI: Prof R Brambilla

Development of a drosophila melanogaster model for SGCE mutation positive Myoclonus Dystonia; Dr M Taylor, Cardiff University; PI: Dr K Peall

INFECTIOUS DISEASE

PhD Studentships

Exploring the interaction of CD4+ T Cells with influenza peptides derived from conserved viral proteins; Alex Greenshields-Watson, Cardiff University; Supervisor: Dr D Cole

Antisense peptide – PNA conjugates as novel antimicrobials for neutralising antibiotic resistance; Brekhna Hassan, Cardiff University; Supervisor: Prof T Walsh

Computer-aided design and synthesis of novel anti-DENV nucleoside analogues; Cecilia Cima, Cardiff University; Supervisor: Prof A Brancale

Evaluating small molecules to manipulate fungal development as a possible intervention target in controlling fungal growth; Hazel Sturt, Aberystwyth University; Supervisor: Dr G Griffith

Characterization of novel burkholderia antibiotic activity targeting mupirocin resistant Methicillin Resistant Staphylococcus Aureus (MRSA); Rachel Rowe, Cardiff University; Supervisor: Prof E Mahenthiralingam

Biological evaluation of dideoxy bicyclic nucleoside analogues with L-chirality as novel antiviral compounds; Rohan Narayan, Cardiff University; Supervisor: Prof A Jones

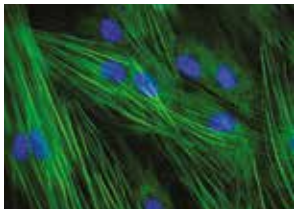
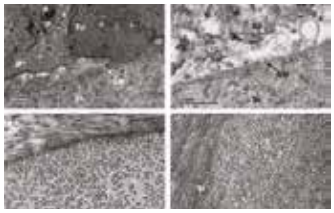
An innovative approach to new antimicrobial drugs; Robert Lloyd Hughes, Cardiff University; Supervisor: Prof R Allemann

Targeting natural products to counter the challenge of MRSA; David Fazakerley, Aberystwyth University; Supervisor: Prof L Mur

Increasing the selectivity and potency of a novel anthelmintic chemical entity; Alessandra Crusco, Aberystwyth University; Supervisor: Prof K Hoffman

Towards the repurposing of existing topical antimicrobials by ligand complexation; Hannah Bundy, Cardiff University; Supervisor: Dr C Heard

Repositioning histone methyltransferase inhibitors as next generation anthelmintics; Gilda Padalino, Aberystwyth University; Supervisor: Prof K Hoffman

Exploiting natural products from hops (Humulus Lupulus) to suppress tuberculosis; Rafael Baptista, Aberystwyth University; Supervisor: Prof L Mur

Manipulation of squalene synthase to limit bacterial infections; Mateusz Pospiech, Swansea University; Supervisor: Prof M Sheldon

Towards validation of an immune suppressor protein from liver fluke as a drug target; David Cutress, Aberystwyth University; Supervisor: Prof P Brophy

Computational approaches to mining the rumen microbiome for novel antimicrobials; Benjamin Thomas, Aberystwyth University; Supervisor: Dr C Creevey

Identifying new antimicrobial drugs in microbes from extreme environments, Aliyah Debbonaire; Aberystwyth University; Supervisor: Prof L Mur

Peptides derived from Yersinia Pestis V antigen as novel therapeutic interventions for sepsis; Cardiff University; Supervisor: Prof K Triantafilou, Jack Hale PhD

Targeting the terminal pathway in complement-driven disease; Wioleta Zelek, Cardiff University; Supervisor: Prof P Morgan

Inhibiting IL-17 production by blocking endogenous RORγt agonists for the treatment of autoimmune diseases; Daphne Davies; Swansea University; Supervisor: Dr Y Wang

Nanotechnology induced prolonged antimicrobial activity of antibiotic loaded PMMA bone cements; Silvia Latanza, Cardiff University; Supervisor: Dr P Prokopovich

Postdoctoral Research Projects

Mechanism of action of [L] ddBCNAs as novel cell-targeting antivirals; Dr L Farleigh, Cardiff University; PI: Dr J Bugert

Further prospecting and characterisation of novel antimicrobials from bovine metagenomes; Dr L Oyama, Aberystwyth University; PI: Dr S A Huws

Characterisation of novel antimicrobial peptides from the rumen eukaryotome; Dr L Akinmosin, Aberystwyth University; PI: Dr S A Huws

Lytic transglycosylases - a potential Achilles' heel for antibiotic-resistant bacteria?; Cardiff University; PI: Dr J Loveridge

Expression and activity determination of novel cloned antibiofilm peptides; Dr G Allen, Swansea University; PI: Dr T Wilkinson

⊛ Targeted metabolic inhibition of T-lymphocytes: directing immunity during human disease; Dr N Jones, Swansea University; PI: Dr N Francis

Anti-viral activity of ProTide derivatives on human T cells; Dr S Caucheteux, Cardiff University; PI: Prof V Piguet

A rapid point of care system to manage/monitor drug treatment in therapeutically relevant mycobacterial infections; PI: Dr C Gwenin

Development of new prothrombotic lipids for haemostatic applications; Dr A Watson, Cardiff University; PI: Prof V O'Donnell

Countering the unrestrained inflammation of sepsis by targeting the JAK-STAT pathway in human macrophages; Dr M Turner/Dr S E Owens, Swansea University; PI: Prof M Sheldon

Development of a safer method for corneal stromal photo-crosslinking to stop the progression of Keratoconus or to treat bacterial corneal infections; PI: Prof A Brancale

Development of Novel BMA-sulfobetaine Nanoparticle Delivery system to treat chronic wound; Dr M Al-Baldawi, Cardiff University; PI: Prof M Gumbleton

Novel antibacterial and antifungal natural products from Pseudomonas Mesoacidophila; Swansea University; PI: Dr S Moody, Dr J Loveridge

OTHER DISEASES OF UNMET MEDICAL NEED

PhD Studentships

Small molecule mediated enhancement of hematopoietic stem and progenitor cell function in transplantation; Lubaid Saleh, Cardiff University; Supervisor: Dr N Rodrigues

Positron Emission Tomography (PET) for therapeutic antibody discovery in personalised medicine; Geraint Roberts, Cardiff University; Supervisor: Dr I Fallis

Validation of nWASP (neuronal Wiskott-Aldrich Syndrome Protein) as a therapeutic target in chronic and non-healing human wounds; Bethan Frugtniet, Cardiff University; Supervisor: Prof W Jiang

Selective Rho Kinase Inhibitors for the treatment of corneal endothelial disease; Alina Akhbanbetova, Cardiff University; Supervisor: Prof A Quantock

Structure-based design of human P2X4-selective small-molecule modulators; Gaia Pasqualetto, Cardiff University; Supervisor: Dr M Young

Pharmaceutical evaluation of novel tiglianes as modulators of dermal fibroblast-myofibroblast differentiation, scar formation and fibrosis; and elucidation of their underlying mechanisms of action; Jordanna Dally, Cardiff University; Supervisor: Dr R Moseley

Using cytokines to define biomarkers and therapeutic targets in rheumatoid arthritis, Cardiff University; Supervisor Dr G Jones, David Hill PhD

Mechanistic evaluation of the impact of Superparamagnetic Iron Oxide Nanoparticles conjugated with drugs (SPIONd) on intracellular signalling/homeostatic mechanisms, Michael Theodoulides, Swansea University; Supervisor Prof S Doak

Multiplexed in vitro assay for genetic toxicity screening; Danielle Harte, Swansea University; Supervisor: Dr G Johnson

Postdoctoral Research Projects

A new angle to diagnosis and treatment of gluten related disorders; Dr R Griffiths, Cardiff University; PI: Prof D Aeschlimann

Development of human liver tissue models for drug safety assessment; Dr K Shah, Swansea University; PI: Prof G Jenkins

Delivery of osteogenic molecules from acrylic bone cement to encourage regenerative bone repair around cemented joint replacements; Cardiff University; PI: Dr W Nishio Ayre

Nanocarrier controlled delivery of antibiotics from acrylic bone cement; Dr E Preedy, Cardiff University; PI: Dr P Prokopovich

Discovery and development of a novel therapeutic for the treatment of inflammatory lung disorders; PI: Prof A Brancale

⊛ Addressing an unmet medical need: developing inhaled calcilytics for steroid-resistant asthma; Dr P Yarova, Cardiff University; PI: Prof D Riccardi

Novel modulators of the visual cycle for treatment of retinal degenerations; Dr M Bassetto, Cardiff University; PI: Dr M Rozanowska

⊛ Development of Novel BMA-sulfobetaine Nanoparticle Delivery system to treat chronic wound; Dr M Al-Baldawi, Cardiff University; PI: Prof M Gumbleton

LEGACY

WALES' LIFE SCIENCES SECTOR

The Life Sciences sector is one of Wales' fastest growing and most innovative industries, employing over 11,000 people in more than 350 companies and contributing around £2bn to the Welsh economy.

The Life Sciences Research Network supports the breadth of drug discovery and development and fosters the careers of the next generation of scientists in the field of Health & Life Sciences. The Network has helped launch the research careers of 56 PhD students and supported another 69 postdoctoral researchers in furthering their careers.

Unique investment has been provided to a number of Platform Technologies, enabling academics from across Wales to access equipment and expertise at other institutions, free of charge. These technologies have generated a volume of collaborative funding applications and demonstrate valuable commercial potential. The Network has provided the necessary infrastructure, environment and incentives to catalyse research collaborations, provide a stepping-stone to leverage further research funding, highlight areas of potential strength for innovation and ultimately develop the national and international reputation of Wales in this strategically important area.

SÊR CYMRU NATIONAL RESEARCH NETWORKS

The Sêr Cymru programme is supported by Welsh Government and the Higher Education Funding Council for Wales and aims to build upon and enhance research in Wales. Our endeavours focus on three Grand Challenge areas of scientific excellence which also have particular relevance to business and society. These are: Life sciences and health; Low carbon, energy and environment; and Advanced engineering and materials. The 3 NRNs support collaborative research across these topics to realise a Welsh research landscape that is truly integrative and able to fully develop the potential of its research talent.

The Networks have worked in close cooperation to deliver a variety of events, including an Annual Postgraduate Conference, as well as other joint endeavours including a Diversity in Science event.

Contact details:

Engineering Research Network Wales
ernw.ac.uk/en

Low Carbon, Energy and Environment Network
nrn-lcee.ac.uk

NRN Directors with key-note speaker Vaughan Gething AM at the Second Sêr Cymru Postgraduate Conference, September 2017

CONTACT

nrn@cardiff.ac.uk
www.lsrnw.ac.uk

02920 874 537
@LSRNW

Cardiff University Prifysgol Caerdydd

Swansea University Prifysgol Abertawe

Prifysgol Bangor University

Prifysgol Aberystwyth University