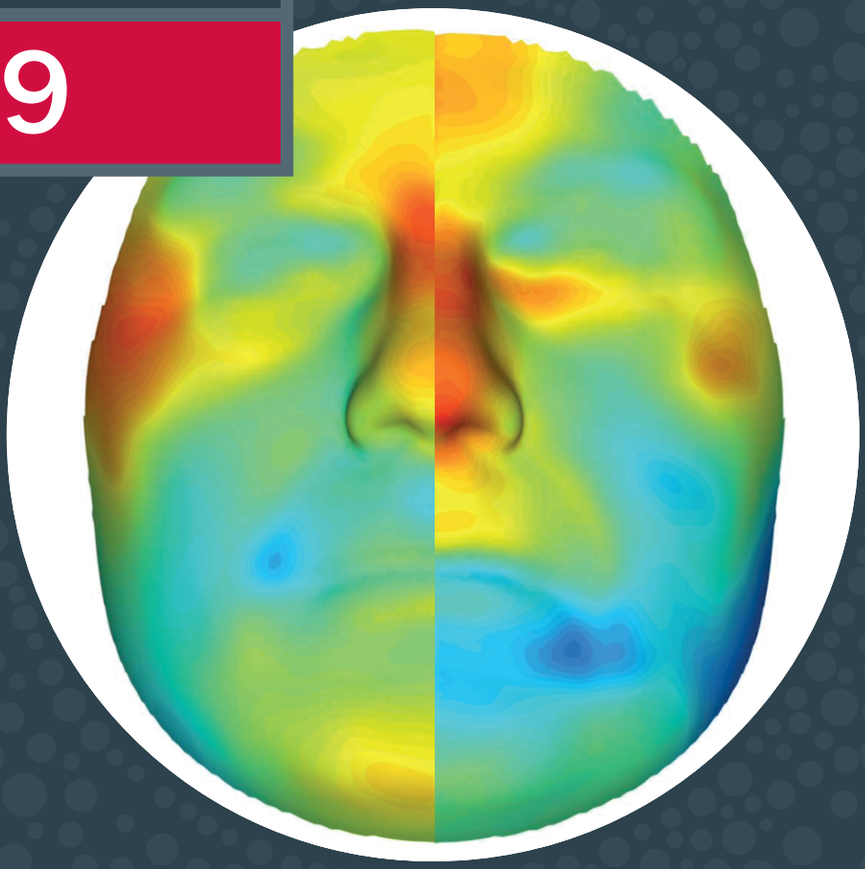
CARDIFF UNIVERSITY
PRIFYSGOL CAERDYDD

School of Dentistry
Ysgol Deintyddiaeth

ANNUAL RESEARCH REPORT

for 2019



Contents

Cover image: The Orthodontic and 3D imaging group led by Professor Stephen Richmond is investigating the genetic determinants guiding facial shape, based on a novel approach employing spatially dense multivariate analysis of the facial heritability and coheritability. The image shows facial heritability maps for sons on the right side and daugthers on the left side given as offspring 3D landmark heritability (%) as obtained from the regression on fathers. The maximum value for heritability was set to 80% for visualization purposes, and the areas of lowest and highest heritability are reflected by blue and red colours in the spectrum, respectively. Regions in the face with the greatest heritability included the areas encompassing the nasion and zygomas, as well as the nose and forehead. Differences between male and female offspring were primarily found in the lower part of the face. For example, higher estimates of heritability were obtained in the chin area for daughters, while sons displayed apparent greater heritability in the philtrum area. (Hoskens H et al, 2018. Front Genet 9:554)

Foreword

Professor Daniel Aeschlimann
Director of Research

It is my pleasure to introduce the 2019 edition of the Cardiff University School of Dentistry Annual Research Report. This report outlines the emphasis and important discoveries of our research programmes over the last year and highlights the breadth and depth of the research conducted in our School. Participation in national and international research consortia is central to the success of our research programmes as this offers the necessary research power and interdisciplinary state-of-the-art expertise to address key challenges.

Research in the School embraces a wide range of topics, and organisationally, is conducted in focused groupings. These are clustered into two major interacting themes, essentially constituting the biomedical sciences and public health-related research, which share some of their technical capabilities. The emphasis of our research is on addressing key questions relevant to dentistry and oral health, but with a focus on fundamental topics including microbiology, cell biology, genetics, structural biology, bioinformatics, behavioural science and other aspects of biology. Through this focus on the general principles underlying complex biological systems and their dynamic interactions, our research programmes reach beyond the specialty and impact on many different aspects of clinical medicine. Additionally, broad societal impacts, reaching beyond the UK, are delivered through our evaluation studies and leadership in health policy development. To this end, research from our Violence Research Group that is seeking to reduce alcohol related violence has gained international acclaim and adoption as “the Cardiff Model”, and has led to changes in alcohol pricing policy in Wales and beyond, and improved service effectiveness through redirection of patients with alcohol intoxication from Emergency Departments (EDARA project).

Among the notable publications for this period were the following studies:

- In Frontiers in Genetics by Stephen Richmond and colleagues in Leuven, Belgium who applied a new approach to investigating heritability of craniofacial parameters and defined 63 modules of co-inheritance, which when analyzed as groups, provided a multivariate estimation of heritability for various facial segments, ranging from the full face (global) to smaller facial regions (local);
- A study by Elaine Ferguson and colleagues published in Molecular Pharmaceutics investigating biopolymer conjugation as a mechanism for targeted antibiotic delivery (dextrin-colistin) that related biological activity of the different drug derivatives released following unmasking of the conjugates by glycoside hydrolases to their structural composition, and identified drug species with enhanced efficacy and reduced systemic toxicity;
- In Scientific Reports by Vera Knäuper and colleagues showed that early effector CD8+ T cells re-express L-selectin before lymph node egress and used L-selectin to relocate to virus-infected tissues whereby shedding of L-selectin controlled early cytotoxic T cell expansion and should therefore be considered a regulator of T cell activation at sites of immune activity, a new paradigm in the research field;
- An article published in Clinical Gastroenterology and Hepatology from my group with collaborators in Sheffield reporting on the Coeliac UK funded prospective study investigating patients with Coeliac disease at time of diagnosis for neurological deficits and identified a correlation between structural changes affecting specific brain regions and autoimmunity to TG6.

The School’s annual one-day research conference took place in May 2019, with sessions on New approaches to treat complex infections, Regulation of immune cell responses in tissue repair, and New approaches to tackling public health issues. A particular highlight among the many outstanding presentations was from the guest speaker Professor David Price from Cardiff University Medical School who discussed how chronic inflammation driven by repeated antigen-stimulation in Coeliac disease patients permanently reshaped their tissue-resident TCR + intraepithelial lymphocyte compartment, with profound implications for organ-specific immunity. Special congratulations go to our junior researchers Drs Matthieu Varache and Jordanna Dally, who won prizes for their excellent contributions on ‘re-engineering’ an existing drug (colistin) to great effect and combatting fibrosis with a plant derived protein kinase C modulator (epoxytigliane), respectively.

Besides our contributions to the research base and collaborations and partnerships with research users, our researchers are also involved in many public engagement activities be it educational programmes for prospective students of STEM disciplines or dental, medical, or allied health professions, or interactions with patients directly or networks that foster wellbeing of people living with a disabling condition, or even international outreach. To **highlight our activities in this space we have introduced a special section in this report that provides a glimpse of the broad range of activities currently undertaken.**

Looking to 2020 and beyond, later this year we will make our submission to the periodic assessment of research in the UK (REF2021) and are in the final stages of preparation. Summarising the achievements over the 6-year period evidently provides an opportunity to reflect about the trajectory of development. The integration of the Life Sciences, Medical, and Allied Health Schools within a College of Biomedical and Life Sciences has brought about increasing alignment of research programmes across Schools and also enhanced collaboration with University Research Institutes. Embedding of research groups within research clusters has maximized benefits of expertise base, allowed establishment of core areas of strength and building of capacity, but most importantly, allowed us, using a team approach, to start to tackle challenges of global significance. This is clearly evident from the increasingly collaborative nature of our research and participation in national and international research networks. This approach has not only enhanced the quality of our research programmes further, but also their reach in terms of health and socio-economic impacts. It has also raised our standing internationally, with Cardiff University School of Dentistry featuring among the top 50 in QS University World Ranking in 2019. Finally, the start of 2020 saw Professor Alastair Sloan move to Australia to become Head of the School of Dentistry at the University of Melbourne. We are grateful to Alastair for his leadership in different roles during his tenure in Cardiff, most recently as Head of School, and wish him all the best with this new challenge. A search is currently underway to identify the individual from an international field of applicants that can take a School focused on high quality research programmes and delivering a research-inspired curriculum to the next level.

Professor Alastair J Sloan
Head of School

I am pleased to introduce our Annual Research Report for 2019 from Cardiff University School of Dentistry. Over the past 12 months, the School has continued to build on its research strengths, increasing its success in winning competitive research funding and seeing further achievements from our academic staff and students. The School of Dentistry is proud to have a strong national and international reach and we engage in world leading translational research which aligns not only with Welsh and UK Government policy of integrating health and social care but with global research challenges. By working closely with our collaborators and partners we continue to undertake truly interdisciplinary studies and our researchers are able to build strong relationships with Universities, Research Institutions and Businesses across the globe. I am proud of what we at the School of Dentistry continue to achieve during my time as Head of School and I must thank our Director of Research, Professor Daniel Aeschlimann for his leadership across the research agenda over the past 3 years and also the highly talented researchers we have in the School. I hope you enjoy reading this latest report and learning more about the current research activity in the School.

Our **World-Leading Research** has **impact**

The School of Dentistry is involved in world-leading research programs aimed at improving human health and welfare. Our research directly influences public policy and clinical practice in a number of key areas, and generates health, socio-economic and commercial impacts.

www.cardiff.ac.uk/dentistry/research/impact-and-translational-research

Our research is built on partnerships with national bodies and Government, and some of the World's leading organisations, as well as interdisciplinary collaboration across our institution and with other universities, and contributes to major projects. As a result, our research has a wide reach and makes a real difference to people's lives.

Case study 1: Implementing strategies to reduce the harm from excessive alcohol consumption

Alcohol contributes to 3.3 million deaths globally and accounts for 5.1% of the global burden of disease each year. Research from the Violence Research Group (VRG) at Cardiff University has informed policy and legislation and caused a change in practice to help mitigate the harmful effects of alcohol abuse.

The VRG have tackled this problem with 3 strands of research and influence on policy and legislation. Their work has provided evidence to back up a new law in Wales for the minimum pricing of alcohol at 50p per unit, anticipated to come into force in 2020. They developed a motivational tool – Have a Word – to reduce risky consumption as part of routine interventions which has been adopted by Public Health Wales, Public Health England, The Ministry of Defence and Police.

The team's contribution and evaluation of the Cardiff Alcohol Treatment Centre meant this service became a fixture in Cardiff city centre on weekend nights. Building on the Cardiff pilot work, EDARA (a large mixed-method multicentre study funded by NIHR) was established in January 2016 to evaluate the impact of UK alcohol intoxication management services (AIMS) by non-randomised comparison of six towns/cities with AIMS with six towns/cities without. In collaboration with the VRG, the CEO of NHS England funded a number of AIMs in England over Christmas 2018. This research indicates that AIMs address previously unmet demand for a place of safety in the night-time environment, in addition to their stated purpose of diverting the intoxicated (those who require monitoring for acute alcohol intoxication, treatment of minor injury, or simply a safe place) away from A&E.

www.cardiff.ac.uk/violence-research-group/research-projects/an-evaluation-of-alcohol-treatment-centres

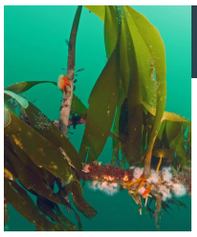
Case study 2: New diagnostic assay for patients with neurological dysfunction due to gluten-mediated autoimmunity

Celiac disease is an autoimmune disease caused by intolerance to gluten (found in wheat, barley and rye). As much as 1% of the population in Western Europe and the US may be affected by gluten sensitivity but only 1 in 8 of those present with gastrointestinal symptoms. Patients developing neurological dysfunction are a particular problem as not only are the consequences of continued gluten exposure severe and the damage irreversible but such patients often do not present with overt gastrointestinal symptoms and hence commonly present to the Neurologist at an advanced stage. The inability of the clinician to link the neurological problem to gluten sensitivity results in unnecessary extensive investigations of such patients in search of an alternative cause. Collaborative research between Cardiff and Sheffield University has provided molecular evidence that confirms that neurological dysfunction is a distinct form of presentation of gluten sensitivity that is associated with the development of an autoimmune response to transglutaminase 6 (TG6). This follows on from seminal studies of Professor Aeschlimann's team which discovered the role of this enzyme in central nervous system development and more specifically in differentiation of a subset of cortical and cerebellar neurons. The team entered into a cooperation with Zedira, a market leader in the race to develop therapies for Celiac disease, to develop a commercial diagnostic test - based on proof-of-principle findings from the Cardiff team - that allows for rapid and accurate diagnosis of these patients with gluten sensitivity that previously were difficult to diagnose due to the absence of enteropathy. This led to the development of ELISA kits (zedira.com/Celiac-disease-products/Neuronal-TGase-TG6-ELISA) to detect anti-TG6 autoantibodies in serum for human diagnostic purposes according to the European iVD directive (98/79/EG). The format of the ELISA assays has since been adapted for use on platforms used in clinical diagnostics, and the assay is now for the first time offered as a service by a diagnostic laboratory in the UK (in Sheffield led by Dr Wild: www.immqas.org.uk/pru.asp?S=611185631&C=1252&CID=1) and in Germany (in Heidelberg led by Professor Kramer: transglutaminase-immunpathologie-labor.de/).

The concept of neurological manifestations of gluten-sensitivity is gaining broad recognition and is now being accepted internationally as evidenced through recent consensus reports on gluten related disorders. This is largely due to these advances in serological testing alongside the identification of imaging biomarkers which have for the first time enabled the identification of such patients through linking features of clinical presentation to underlying molecular mechanisms. A recent prospective study assessing Celiac disease patients at diagnosis identified that central nervous system involvement is much more prevalent than previously anticipated (see page 8), further highlighting the need for effective intervention. Accordingly, understanding neurological forms of Celiac disease was identified as 1 of the 10 top research priorities by Coeliac UK in 2019 (www.coeliac.org.uk/research/our-approach/research-priorities/).

Other highlights of our influential research:

Our researchers made significant progress this year in a wide range of areas.



Treatment of antibiotic resistant infections:

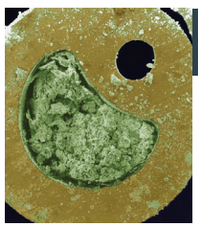
With €6 million funding from the European Union's Horizon 2020 Research and Innovation programme and $11 million from the US Cystic Fibrosis Foundation, recruitment into the pivotal Phase 2b clinical trial for OligoG (AlgiPharma's lead drug candidate for cystic fibrosis) has started in December 2019, with the studies being performed at 49 clinical sites, in 11 countries.

Improving children's oral health:

The Dental Public Health Unit as part of its remit for monitoring the impact of "Designed to Smile" programme has reported that the number of General Anaesthetics administered for tooth extraction in children in Wales has fallen from 9,306 in 2011/12 to 6,582 in 2018/19. Although in parts likely attributable to changes in availability of services, it also reflects the significant improvements in oral health in children in Wales over the past decade.

Informing national care home policy and action on oral hygiene:

This research acted as a catalyst for the introduction of "Gwen Am Byth – Everlasting Smile" programme. With cross-disciplinary action from the Welsh Government to support oral health in care homes, this new intervention has been implemented in 340 care homes in Wales.



Commercialisation of early warning sensor for catheter blockage:

In 2019, a worldwide licence to manufacture and sell the early warning sensor for urinary catheter blockage, developed by Professors Waters, Stickler and Williams, has been granted to a major Chinese manufacturer of medical devices.

Further details at: www.cardiff.ac.uk/dentistry/research/impact-and-translational-research

Research **summary**

Core competencies in Oral and Biomedical Sciences:

Advanced Therapies

- Novel antimicrobial therapies
- Polymer therapeutics
- Bacterial biofilms
- Treatment of chronic infections

Regenerative Biology Group

- Repair and regeneration mechanisms for oral, dermal and neural tissues
- Dental pulp, oral mucosal & bone marrow stem cells
- Orthopaedic/dental biomaterials
- Drug discovery for wound repair.

Matrix Biology & Tissue Repair

- Stem cell driven synovial joint engineering
- Organotypic tissue & disease models
- Imaging of cellular processes at molecular level
- Protein structure, modification & function analysis

Microbial Diseases

- 3D models of infection
- Biofilms & defence mechanisms
- Candida pathogenicity
- Microbiome

Core competencies in Applied Clinical Research and Public Health:

Orthodontics & 3D Imaging

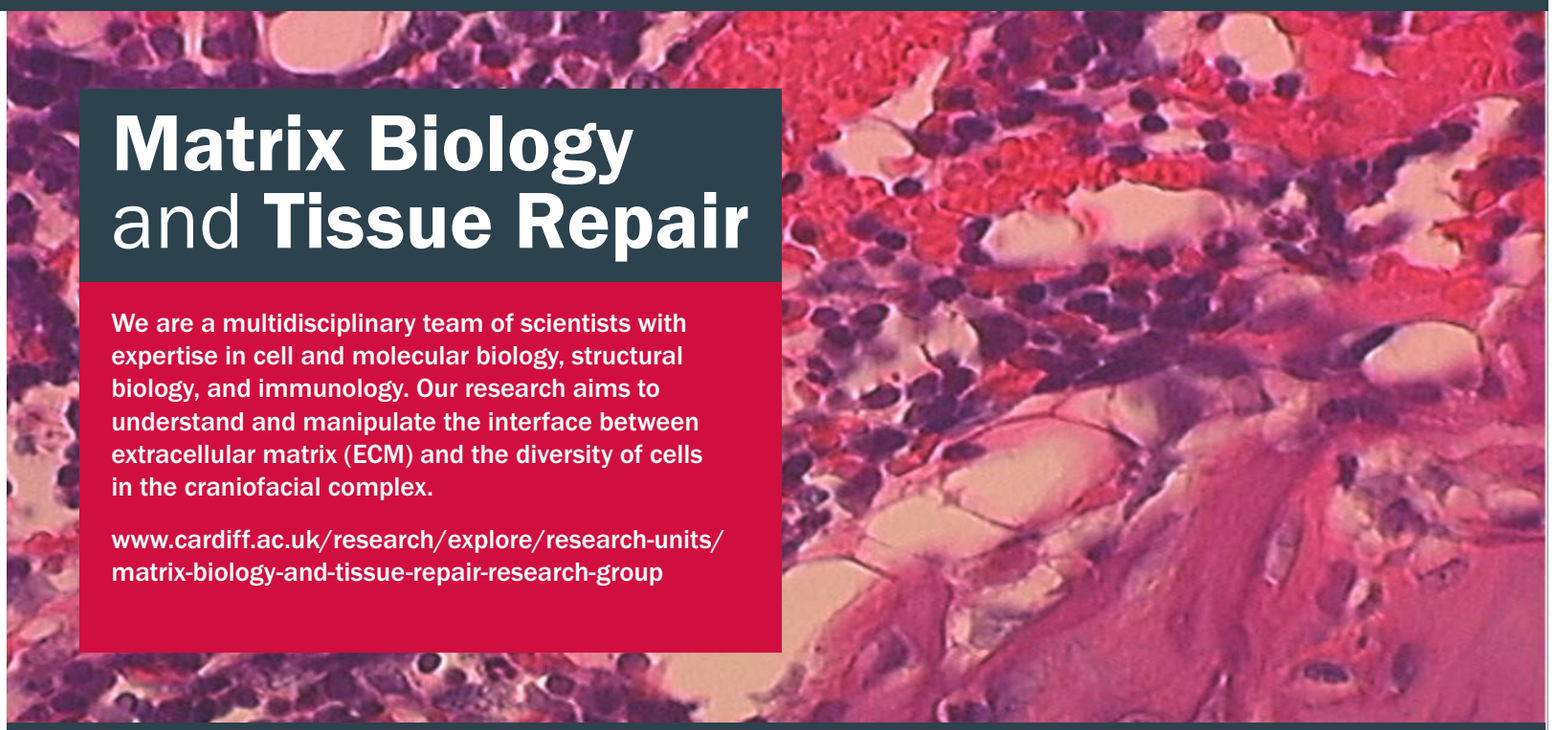
- Craniofacial imaging
- Mathematical modelling
- Genetic determinants for craniofacial shape
- Correlation of pathology with facial shape

Dental Public Health

- Epidemiology of dentally-related diseases
- Oral health assessment & improvement
- Preventative intervention strategies & technologies
- Antimicrobial therapies

Alcohol & Violence Research

- Alcohol-related violence
- Policy informing violence prevention, anti violence partnerships
- Understanding life-course effects of alcohol use/misuse
- Strategies preventing alcohol abuse and misuse



Matrix Biology and Tissue Repair

We are a multidisciplinary team of scientists with expertise in cell and molecular biology, structural biology, and immunology. Our research aims to understand and manipulate the interface between extracellular matrix (ECM) and the diversity of cells in the craniofacial complex.

www.cardiff.ac.uk/research/explore/research-units/matrix-biology-and-tissue-repair-research-group

Our goals are:

- to elucidate and counteract pathological processes leading to tissue destruction in inflammation, cancer and ageing
- to create functional tissue through application of life science principles.

The ECM and its interaction with various cells are critically important to regulate inflammation, repair/regenerative processes and invasive cancers. Connective tissue cells control migration, survival and proliferation of endothelial and epithelial cells as well as recruitment and activation of antigen presenting cells that orchestrate the inflammatory response. Altered connective tissue cell responses are associated with many diseases, because of either direct involvement in the aetiology or because of fibrosis, which accompanies the tissue damage. Experimental models have been established within the group to decipher cellular interactions regulating distinct aspects of the repair and disease process. These relate to inflammation, angiogenesis, re-epithelialisation, cancer stromal cell interactions and ECM changes occurring with ageing. The emphasis is to gain a molecular understanding of the role of post-translational modifications of proteins in organ system function, and how aberrant protein modifications or proteolysis contributes to pathogenesis.

Highlights of 2019:

- Professor Aeschlimann presented an invited lecture on the role of transglutaminases in neurodegeneration at the 10th International Symposium of the Society for Research on the Cerebellum and Ataxias (SRCA).
- Autoimmune diagnostic assay detecting TG6 antibodies attained CE mark to verify compliance with European In-Vitro Diagnostic Devices Directive (98/79/EC) (https://zedira.com/Celiac-disease-products).
- Collaborative work led by Dr Knäuper and Prof Ager (MEDIC, Cardiff University) demonstrated a non-redundant ADAM-17 function in TCR-induced proteolysis of L-selectin in T cells that plays a role in early clonal expansion of cytotoxic T cells following viral infection. Therefore, L-selection has critical functions not only in extravasation of naïve and central memory cells for homing to lymph nodes but also as a regulator of T cell activation at sites of immune defense upon infection. (Mohammed R et al., 2019. Sci Rep 9: 5487).
- Collaborative work by Dr Beck with the groups of Drs Vladena Bauerová-Hlinková and Marcela Kúdelová from the Slovak Academy of Sciences, Bratislava, revealed that mutating two key residues of the murine gamma herpesvirus-68 protein M3 impact its ability to bind specific chemokines. This opens the way for the development of new therapeutic chemokine blockers and sheds light on the myriad evasion strategies of viruses. (Šebová R et al, 2019. Front Cell Infect Micrbiol 9: 210).

Linked Research Centres:

Professor Aeschlimann is a founding member of the Centre of Excellence for Biomechanics and Bioengineering Versus Arthritis, where he is the lead for the osteoarthritis biomarker development programme. Organotypic *in vitro* human cartilage osteoarthritis models were developed and employed in biomarker discovery.

www.cardiff.ac.uk/arthritis-biomechanics-bioengineering-centre/

He is also a founding member of the Sheffield Institute of Gluten-Related Disorders (SIGReD) and associated with the respective Theme of the NIHR-funded Biomedical Research Centre, which brings together interdisciplinary experts to develop new strategies for effective diagnosis of gluten-related disorders. The work here focuses on the gut-brain axis of the immune system and how this links to autoimmune ataxia.

www.sheffield.ac.uk/news/nr/gluten-related-diseases-1.259247

Key project summary:

Neurological symptoms and pathology in patients with newly-diagnosed, “classical” Celiac disease

Hadjivassiliou M et al, 2016. Am J Gastroenterol 111(4): 561-567.
De Leo L et al, 2018. J Pediatr Gastroenterol Nutr 66(1): 64-68.
Hadjivassiliou M et al, 2019. Clin Gastroenterol Hepatol 17(13): 2678-2686.

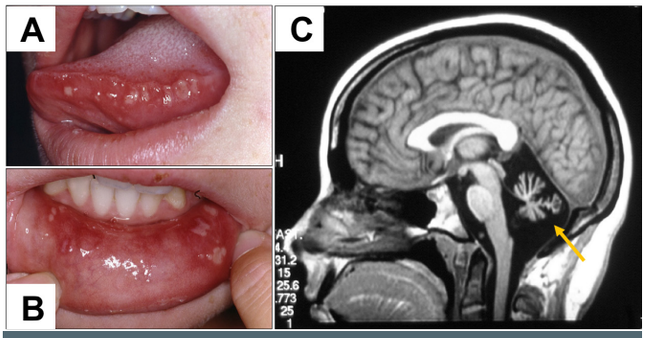


Fig 1. CD is a systemic autoimmune disease that manifests in different organ systems. Oral examination revealing aphthous stomatitis in a CD patient, involving both lining mucosa of the tongue (A) and lower lip (B). Nervous system involvement due to gluten sensitivity most commonly presents as pure cerebellar ataxia; sagittal MR image showing extensive degenerative changes in cerebellum of a patient with gluten ataxia (C, arrow image courtesy of Prof M Hadjivassiliou).

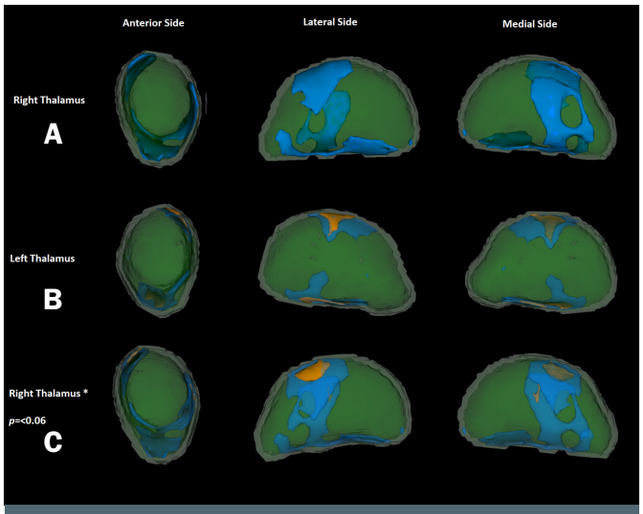


Fig 2. Visualization of TG6 autoantibody-related atrophy in the thalamus. T1-weighted MR images were processed to generate normalized brain volume data sets of CD patients stratified for anti-TG6 antibodies (pos vs neg). Comparative volumetric analysis of gray matter brain subregions revealed significant differences in the thalamus, here visualized using threshold-free cluster enhancement corrected “vertex” shape analysis from FIRST. These models control for age, and hence the differences in ‘shape’ between the two groups reflects the overall pattern of atrophy associated with the presence of TG6 autoantibodies. Significantly ($p \leq 0.05$) altered locations are highlighted in orange, whereas locations where $p \leq 0.1$ are shown in blue for reference (A,B); though results reached significance only for the left thalamus, a very similar pattern is revealed for the right thalamus when the threshold is set to $p \leq 0.06$ (C; orange).

Background: Gluten-related disorders represent a spectrum of diverse clinical manifestations that share a common trigger, polypeptides derived from certain grains and collectively referred to as ‘gluten’. The best characterized disease within this spectrum is Celiac disease (CD), a common (1% of Western population) T cell-driven autoimmune disease that classically presents with intestinal problems including diarrhea, malabsorption and anemia in susceptible individuals (carrying HLA DQ2 or DQ8). However, it is now recognized that patients can present with minimal or no gastrointestinal symptoms and diverse extra-intestinal manifestations affecting other organ systems including the nervous system (Fig 1). A B cell response not only to gluten-derived peptides (antigen) but also the autoantigen transglutaminase 2 is a hallmark of active CD. Moreover, targeting of other transglutaminase isozymes by the immune system has been implicated in extra-intestinal disease, notably we have previously linked autoantibodies to transglutaminase 6 (TG6) to neurological dysfunction.

Discovery: Although patients with neurological presentation due to gluten sensitivity are on average diagnosed significantly later than those presenting with the classical gastroenterological symptoms (53 vs 42 years) (Hadjivassiliou et al, 2016), this is not due to progressive expansion of the autoimmune repertoire with continued gluten stimulation as we have recently shown that TG6 autoantibodies can be detected in young children at time of presentation with considerable frequency (De Leo et al, 2018). Therefore, these autoantibodies are not a late stage disease sequelae. This raises the question as to whether patients with acquired TG6 autoimmunity are susceptible to the development of neurological problems with continued dietary gluten exposure or indeed, whether such patients have subtle pre-existing neurological dysfunction that was missed due to lack of neurological assessment. To address this we performed a prospective cohort study at a secondary-care gastroenterology Center of 100 consecutive patients that received a new diagnosis of CD based on gastroscopy and duodenal biopsy analysis (mean age ±SD at diagnosis, 43±15 years; range, 19-77 years) (Hadjivassiliou et al, 2019). Clinical examination revealed neurological deficits at high frequency, with gait ataxia evident in 29% of patients, nystagmus in 11%, and distal sensory loss in 10%. Unexpectedly, 60% of patients also had abnormal magnetic resonance (MR) brain imaging results, with 47% having functional deficits in the cerebellum as indicated by abnormal cerebellar N-aspartyl acetate / creatine ratio in MR spectroscopy. Circulating anti-TG6 antibodies were detected in 40% of CD patients, and based on detailed morphometric assessment from MR imaging data, these anti-TG6 antibody positive patients displayed significant atrophy of subcortical brain regions, particularly in the thalamus and cerebellum. In the thalamus, a broad pattern of gray matter loss with relative sparing of anterior and pulvinar nuclei was identified, and following application of age correction, focal atrophy around the lateral/ventral posterior nulcei became apparent as a significant finding (Fig 2). The thalamus is involved in motor control in terms of acting as a relay center between the cerebellum and the motor cortex. Taken together, our MR imaging analysis and functional deficits in patients could be consistent with loss or impairment of a group of TG6 positive thalamic neurons, affecting GABA-ergic inhibitory pathways.

Importance: In patients presenting with classical CD, neurological deficits are common at CD diagnosis but are often overlooked. TG6-specific autoantibodies signify neurological involvement, and are prevalent among patients with newly diagnosed CD. Here, we observed a significant reduction in volume of specific brain regions in patients with circulating TG6 autoantibodies, providing evidence for a link between autoimmunity to TG6 and brain atrophy. Given the severity and irreversibility of the consequences of disease progression, there is a need for neurological assessment and early diagnosis, and reinforcement of importance of adherence to a strict gluten free diet by such patients to avoid permanent neurological disability.

Professor Daniel Aeschlimann

AeschlimannDP@cardiff.ac.uk
+44 (0)29 2074 4240

MSc (Biochemistry, Biophysical Chemistry, Cell Biology and Molecular Genetics), 1990, Biocenter, University of Basel, Basel, Switzerland. PhD (Biochemistry), 1993, University of Basel, Basel, Switzerland. Fellowships from EMBO and Swiss National Science Foundation. Various academic positions in Switzerland, USA and UK. Since 2001, Professor of Biological Sciences, Cardiff University, UK. Head of Matrix Biology & Tissue Repair Research Unit and Director of Research for School of Dentistry.

The function of transglutaminases and protein crosslinking in physiological processes and also in disease has been a central theme of my research. Current research focuses on the role of transglutaminase enzymes in innate immunity and in the development of autoimmune disease in the context of gluten sensitivity and arthritis.

Key Publication:

Hadjivassiliou M, et al (2019). Neurological deficits in patients with newly diagnosed Coeliac Disease are frequent and linked with autoimmunity to transglutaminase 6. Clin Gastroenterol Hepatol 17(3):2678-2686.

Full list at: www.cardiff.ac.uk/people/view/39472-aeschlimann-daniel

Dr Konrad Beck

BeckK@cardiff.ac.uk

Diploma in Physics, 1981 JWG University Frankfurt a. M., Germany. PhD. in Biology, 1984, MPI Biophysics, Frankfurt a. M., Germany. Habilitation (DSc) in Biophysics, 1990, University Linz, Austria; various academic positions and fellowships in Basel, Switzerland; Linz, Austria; Portland OR, USA; Piscataway NJ, USA; Nagoya, Japan; Lyon, France; since 2004 Lecturer in Protein Biophysics, Cardiff University, UK.

My main work relates to the structure, folding and assembly of multidomain proteins especially those of the extracellular matrix. Collaborations with the groups of F.A. Lai (School of Biosciences) and M. Nomikos (College of Medicine, Qatar University) focus on the effect of mutations in the cardiac calcium release channel (RyR2), phospholipase C zeta, and calmodulin. Work together with the groups of AK Sewell and DK Cole (School of Medicine) aims to determine the molecular mechanism of immunological escape by SL9, a well-known HIV epitope restricted by HLA-A2.

Key Publication:

Šebová R, et al (2019). Residue mutations in murine herpesvirus 68 immunomodulatory protein M3 reveal specific modulation of chemokine binding. Front Cell Infect Microbiol 9: 210.

Full list at: www.cardiff.ac.uk/people/view/39468-beck-konrad

Dr Sharon Dewitt

Dewitt@cardiff.ac.uk
+44 (0)29 2251 0665

BSc (Pharmacology, University of Wales College of Medicine), PhD (Cell Biology & Immunology, Cardiff University), Wellcome Trust funded postdoctoral researcher (Cardiff University, 2003-2010), Cardiff Academic Fellow (Arthritis Research UK, 2010-2014), Since 2014 Lecturer at Cardiff University School of Dentistry..

The focus of my research is to identify the early cellular events that occur in disease processes such as arthritis. These early events can then be exploited as indicators of disease to enable early diagnosis and treatment; or as a means of manipulation and modification of the disease process. Areas of expertise include Ca^{2+} imaging, confocal and single cell microscopy.

Key Publication:

Al Jumaa MA, et al (2017). Topographical interrogation of the living cell surface reveals its role in rapid cell shape changes during phagocytosis and spreading. Sci Rep 7(1): 9790.

Full list at: www.cardiff.ac.uk/people/view/39492-dewitt-sharon

Dr Vera Knäuper

KnauperV@cardiff.ac.uk
+44 (0)29 2074 2595

Diploma in Chemistry (University of Bielefeld, Germany), Dr rer. nat. (equivalent PhD in Biochemistry, University of Bielefeld, Germany), 1993-1995 Wellcome Trust Travelling fellow (Strangeways Research, Cambridge), 1995-2000 Post-doctoral fellow (University of East Anglia, Norwich), 2001-2006 Lecturer (University of York, York). Since 2006 Senior Lecturer (Cardiff University).

Major research interests in my group focus on the understanding of metalloproteinase function in the arthritic diseases and cancer. The groups main focus is to understand the role of metalloproteinases in cellular signalling at the molecular level and to design novel therapeutic regimens to combat arthritic disease and cancer as well as to discover biomarkers.

Key Publication:

Mohammed R, et al (2019). ADAM17-dependent proteolysis of L-selectin promotes early clonal expansion of cytotoxic T cells. Sci Rep 9: 5487.

Full list at: www.cardiff.ac.uk/people/view/39462-knauper-vera

Advanced Therapies

We are a multidisciplinary team of clinicians, microbiologists, pharmacists and engineers whose research aims are to apply our knowledge of the molecular and cellular control of human disease processes to inform the design, development and testing of novel therapies.

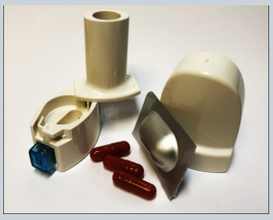
www.cardiff.ac.uk/research/explore/research-units/advanced-therapies-group

Working with our academic and industrial partners around the world, we are using our expertise in the design and delivery of novel therapeutic interventions, to target a range of, often life-threatening, infective and chronic inflammatory conditions including multi-drug resistance, cystic fibrosis, chronic skin wounds and peri-implantitis.

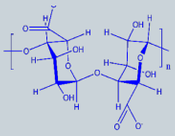
Our goals are:

- to translate our findings, from the laboratory to the clinic, to improve the treatment of patients
- to develop treatment strategies (both topical and intravenous) to improve current treatment efficacy/efficiency and inform the design of entirely novel polymer therapeutics
- to utilise the toolkit our experienced inter-disciplinary team has developed, to analyse anti-biofilm therapeutic interventions against bacterial biofilms and surfaces (at the cellular, protein and gene levels).

Highlights of 2018:



- Research translation from laboratory to patients: commencement of a phase 2b randomised, double-blind, dose-finding study of inhaled oligosaccharide (OligoG) vs placebo in patients with cystic fibrosis (ClinicalTrials.gov Identifier: NCT03698448).
- Industrial collaborations: commencement of an industrially-funded PhD studentship with QBiotics Ltd, a new KESS PhD studentship with AlgiPharma AS and completion of a KESS studentship with Cultech Ltd.
- Joana Stokniene successfully completed her PhD; Dr Katja Hill was promoted to Senior Lecturer.



OligoG

Linked Research Centres:

Dr Anne Tøndervik & Dr Havard Sletta, Biotechnology and Nanomedicine, SINFEF, Trondheim, Norway. **www.sintef.no/en/industry/biotech-and-nanomedicine**

Prof. Tim Walsh & Dr Brad Spiller, Infection & Immunity, School of Medicine, Cardiff University. **www.cardiff.ac.uk/medicine/research/divisions/infection-and-immunity**

Prof. Paul Lewis, School of Management, Swansea University. **www.swansea.ac.uk/som**

Prof. Thorsten Wohland, Centre for Bio-Imaging Sciences, National University of Singapore, Singapore. **www.dbs.nus.edu.sg/lab/BFL/index.html**

Prof. Mark Gumbleton, School of Pharmacy and Pharmaceutical Sciences, Cardiff University. **www.cardiff.ac.uk/pharmacy-pharmaceutical-sciences**

Prof. Peter Parsons, Drug Discovery Group, QIMR, Brisbane

Dr Niklaas Buurma, Physical Organic Chemistry, School of Chemistry, Cardiff University. **www.cardiff.ac.uk/study/postgraduate/research/programmes/area/physical-organic-chemistry**

Dr Gary Chinga-Carrasco, Paper & Fibre Research Institute, Trondheim, Norway. **www.rise-pfi.no**

Prof. Peter Griffiths, Pharmaceutical, Chemical & Environmental Sciences, Faculty of Engineering & Science, Greenwich University. **www.gre.ac.uk/engsci/study/pharchemenv**

Prof. Finn Aachmann, Department of Biotechnology and Food Science, NTNU Norwegian University of Science and Technology, Trondheim, Norway. **www.ntnu.edu/ibt/research/biopol**

EUNCL **www.euncl.eu**

Key project summary:

Cellulose nanofibril formulations incorporating a low-molecular-weight alginate oligosaccharide modify bacterial biofilm development

Jack A et al, 2019. *Biomacromolecules* 20: 2953−61.

Background: Due to their customisable porosity, mechanical strength, translucency, and environmental biodegradability, cellulose nanofibrils (CNFs) derived from wood pulp are a renewable material possessing considerable uses for biomedical applications. Here, we investigated the growth of multi-species wound biofilms on CNF formulated as aerogels and films incorporating the low-molecular-weight alginate oligosaccharide OligoG CF-5/20 to evaluate the structural and antimicrobial properties of these materials.

Discovery: In Jack et al (2019), using scanning electron microscopy (SEM), we demonstrated distinct differences between different formulations; the aerogel- OligoG bionanocomposite formulations had a more open three-dimensional structure, whereas laser profilometry (LP) showed that film formulations coated with OligoG were significantly smoother than untreated films or films incorporating PEG400 as a plasticiser (Fig 1). The OligoG−CNF formulations as aerogels or films both inhibited pyocyanin production (Fig 2). Confocal laser scanning microscopy (CLSM) of biofilms grown on films incorporating OligoG demonstrated altered biofilm architecture, with reduced biomass and decreased cell viability (Fig 3). Cross sectional analysis of the aerogels showed gross changes in the CNF material following incorporation of OligoG (Fig 4).

Importance: These novel CNF bionanocomposites were able to modify bacterial growth, biofilm development, and virulence factor production *in vitro*. These data support the potential of OligoG and CNF bionano-composites for use in biomedical applications where prevention of infection or biofilm growth is required.

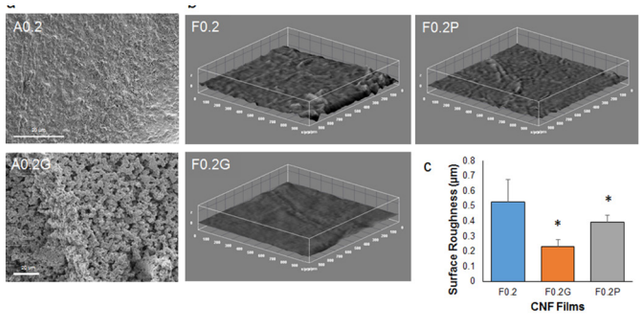


Fig 1. Structural characterisation of CNF formulations. SEM of (a) aerogels A0.2 and A0.2G. (b) LP of films F0.2, F0.2G, and F0.2P. (c) Corresponding surface roughness measurements (from LP only) (*significantly different compared to the F0.2 control; n = 3; P < 0.05).

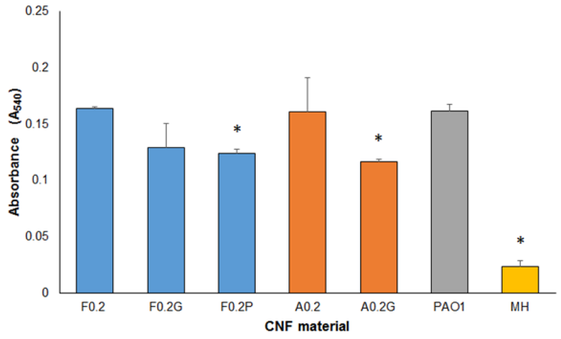


Fig 2. Effect of the different CNF formulations on pyocyanin production by *P. aeruginosa* PAO1. PAO1 and MH broth only were positive and negative controls, respectively (*significantly different compared to the PAO1 control; n = 3; P < 0.05).

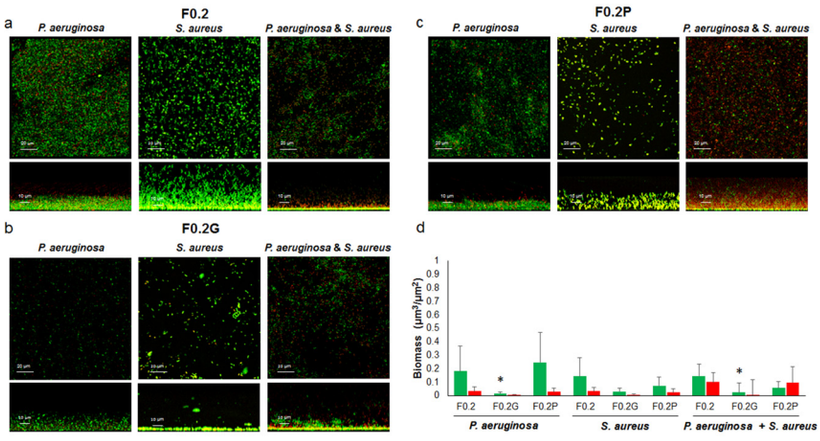


Fig 3. CLSM showing the effect of OligoG (0.5%, 2% & 6%) on EPS components of mucoid *P. aeruginosa* biofilms stained with ConA (EPS polysaccharides, red) and TOTO-1 (eDNA, green) in biofilm formation and disruption assays.

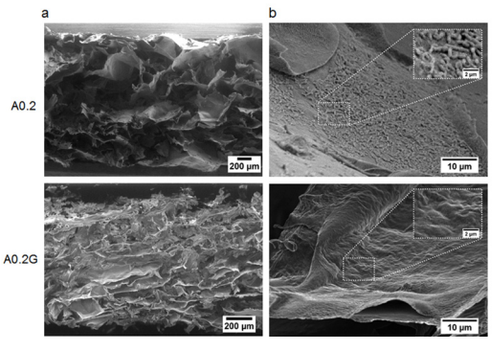


Fig 4. SEM of mixed *P. aeruginosa* and *S. aureus* biofilms growing on un-treated aerogels A0.2 or the OligoG bionanocomposite A0.2G. (a) Cross-sectional view following ion milling. (b) Aerial view with inset-magnified to show biofilm growth.

Professor David W Thomas

ThomasDW2@cardiff.ac.uk
+44 (0)29 2074 4873

A clinician with a background in studying the role of microbial biofilms in human disease states to improve their management and diagnosis, I lead the Advanced Therapies Group. I am a previous Wellcome Trust Clinical fellow (Bristol University) and currently Professor/ Hon. Consultant in Oral and Maxillofacial Surgery at the University Hospital of Wales.

Key Publication:

Jack A, et al. (2019). Cellulose nanofibril formulations incorporating a low molecular weight alginate oligosaccharide modify bacterial biofilm development. Biomacromolecules 20(8): 2953-2961.

Full list at: www.cardiff.ac.uk/people/view/39420-thomas-dave-w

Dr Katja E Hill

HillKE1@cardiff.ac.uk
+44 (0)29 2074 4252

With a background in microbial ecology and molecular biology, I am interested in the mechanisms of gene regulation and control in bacterial biofilms. My current research involves translation to clinical practice through the testing of novel compounds (from e.g. seaweed and the Australian rainforest) for the management of human chronic diseases such as cystic fibrosis and wound healing of 'difficult to treat' wounds, to characterise their antibacterial/anti-biofilm properties.

Key Publication:

Jack A, et al. (2019). Cellulose nanofibril formulations incorporating a low molecular weight alginate oligosaccharide modify bacterial biofilm development. Biomacromolecules 20(8): 2953-2961.

Full list at: www.cardiff.ac.uk/people/view/39529-hill-katja

Dr Elaine L Ferguson

FergusonEL@cardiff.ac.uk
+44 (0)29 2251 0663

My translational research in polymer therapeutics focuses on optimising drug release by attachment of biodegradable polymers, to target proteins, peptides and drugs to sites of inflammation, thereby minimising toxicity, overcoming resistance and increasing bioavailability. Funded by an MRC New Investigator Research Award, I am currently investigating the accumulation and nephrotoxicity of dextrin-colistin conjugates and, in collaboration with AlgiPharma AS, investigating novel combinations of polymers and antibiotics.

Key Publication:

Varache M, et al. (2019). Polymer masked-unmasked protein therapy: Identification of the active species after amylase-activation of dextrin-colistin conjugates. Mol Pharmaceut 16(7): 3199-3207.

Full list at: www.cardiff.ac.uk/people/view/39401-ferguson-elaine

Dr Manon F Pritchard

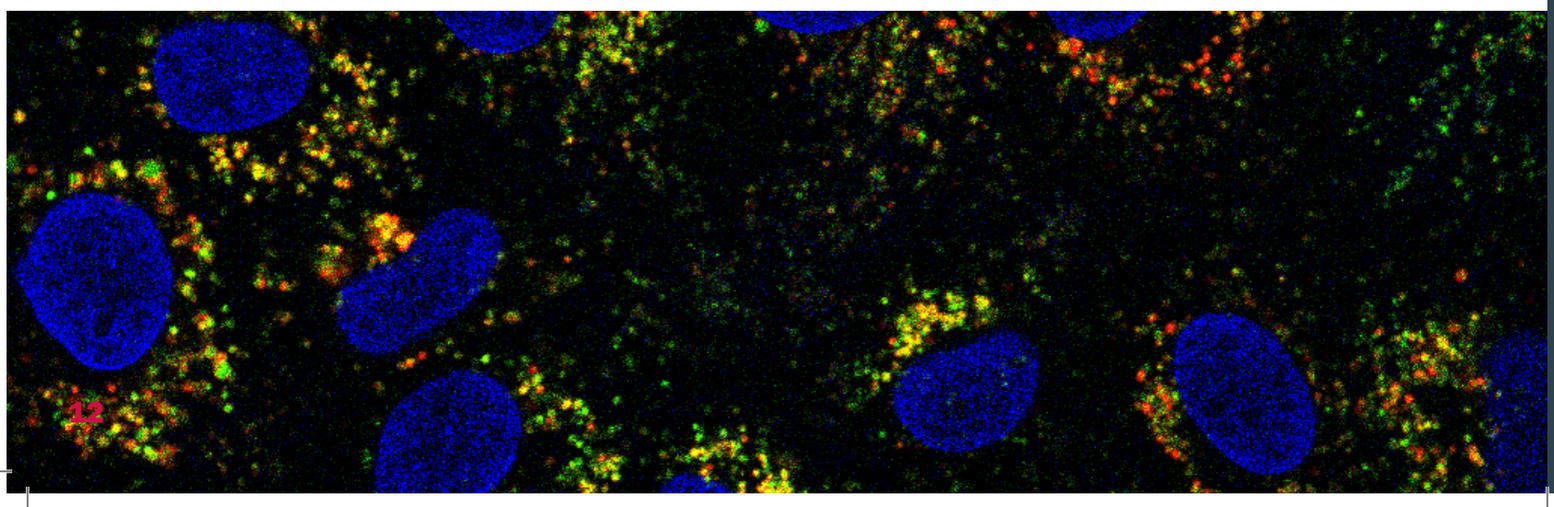
PritchardMF@cardiff.ac.uk
+44 (0)29 2251 0659

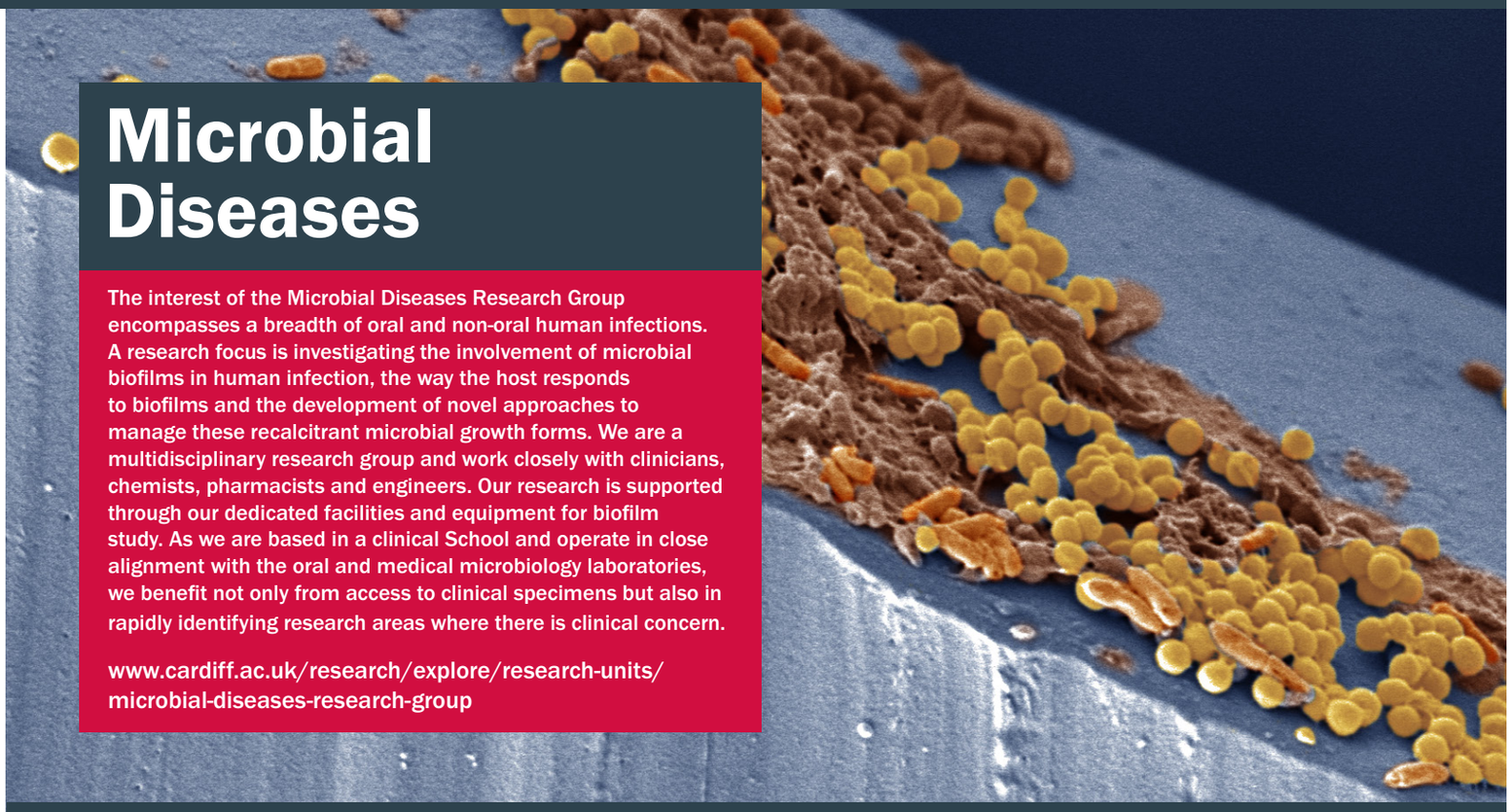
Following completion of my dental clinical foundation years and PhD in microbiology, I have successfully published a series of papers and been awarded several prizes in recognition of my work. I am currently developing therapeutic nanomedicines for the treatment of multi-drug resistant bacterial biofilm infections. My research is consolidated by my successfully obtaining a Precision Medicine Fellowship from the Welsh European Funding Office (WEFO).

Key Publication:

Pritchard M, et al. (2019). Mucin structural interactions with an alginate oligomer mucolytic in cystic fibrosis sputum. Vib Spectrosc 103: 102932.

Full list at: www.cardiff.ac.uk/people/view/178890-pritchard-manon





Microbial Diseases

The interest of the Microbial Diseases Research Group encompasses a breadth of oral and non-oral human infections. A research focus is investigating the involvement of microbial biofilms in human infection, the way the host responds to biofilms and the development of novel approaches to manage these recalcitrant microbial growth forms. We are a multidisciplinary research group and work closely with clinicians, chemists, pharmacists and engineers. Our research is supported through our dedicated facilities and equipment for biofilm study. As we are based in a clinical School and operate in close alignment with the oral and medical microbiology laboratories, we benefit not only from access to clinical specimens but also in rapidly identifying research areas where there is clinical concern.

www.cardiff.ac.uk/research/explore/research-units/microbial-diseases-research-group

Our research aims are:

- to develop novel approaches in the management of biofilm-mediated human infections
- to characterise biofilm communities, the relationships between associated microorganisms and the way the local environment influences biofilm behaviour
- to explore how the host responds to infection, with the aim of developing diagnostics and immunotherapies.

Previously, the study of microorganisms in human infection primarily focused on monotypic species grown in broth culture. Furthermore, the assessment of antimicrobial susceptibility also is predominantly based on testing microorganisms in liquid culture. What is now increasingly evident is that infections most frequently involve microorganisms attached to a surface and encased within protective extracellular matrices. These growth forms are referred to as biofilms and are responsible for an estimated 65% of human infections. Dental plaque is the most widely studied biofilm as it is the cause of both caries and periodontal disease which are amongst the most prevalent of human infections. Biofilms are highly resilient and can exhibit a 1000-fold greater tolerance to administered antimicrobials compared to the same microorganisms grown in broth culture. Exploring strategies to eradicate biofilms where they are causing infection therefore represents an extremely challenging and important area of study.

Highlights of 2019:

- Establishment of an exciting research collaboration with Destiny Pharma PLC (UK), Shenzhen Kangzhe Pharmaceutical Co. Ltd (China), and Tianjin Medical University (China) on the evaluation of novel XF drugs as bacterial resistance breakers. This research is supported by the UK-China AMR programme: ktn-uk.co.uk/news/uk-and-china-to-fund-new-collaborative-projects-to-tackle-antimicrobial-resistance

Linked Research Centres:

The research group is linked with the University Research Network: CURE-Infection (Cardiff University Antimicrobial Resistance and Infection Biology Network). CURE-Infection network addresses fundamental questions about infection biology - how pathogens are acquired, transmitted and evolve in an era of increasingly mobile human population, drug dependency and antimicrobial resistance. It aims to enhance research on the interlinked themes of antimicrobial resistance, antimicrobial discovery, and infection biology.

Key project summary:

Metataxonomic sequencing reveals compositional shifts within the denture-associated microbiome in pneumonia

Background: Lower respiratory tract infections, including pneumonia, are the fourth leading cause of death worldwide. In the United Kingdom pneumonia cases are ten-fold higher in patients over 65 years of age.

A growing body of evidence indicates an association between changes in the oral microbial communities and respiratory infection in susceptible individuals. This is most evident in ventilator-associated pneumonia where we have previously demonstrated an increase in the relative abundance of putative respiratory pathogens in dental plaque during intubation of patients. Respiratory pathogens have similarly been recovered from denture surfaces and enhanced oral care shown to reduce the incidence of pneumonia. That a relationship appears to exist between the denture-associated oral microbiota and respiratory infection suggests that the presence of an artificial biomaterial surface may itself promote a pathogenic reservoir that can seed infection of the respiratory tissues in susceptible individuals.

This project sought to analyse the bacterial community of the denture-associated biofilms in patients with and without pneumonia, and to determine whether microbial changes could be indicative of pneumonia occurrence. In addition, the antibiotic resistance profiles of target bacterial species was established. Salivary cytokines were also analysed to explore the host response to infection and to the presence of respective biofilm communities.

Discovery: This study characterised denture-associated oral bacterial communities by metataxonomic sequencing of 16S rRNA genes. The prevalence of antimicrobial resistance among two representative pathogenic species, *Staphylococcus aureus* and *Pseudomonas aeruginosa*, was also assessed.

Significant shifts were observed in microbial species composition, diversity and richness in the denture-associated microbiome of pneumonia patients. Importantly, the relative abundance of putative respiratory pathogens in the denture-associated microbiota of pneumonia patients was significantly higher than in respiratory-healthy individuals (Fig 1) and the extent of this increase was approximately three-fold greater in denture-associated bacterial communities compared with other oral sites. Antimicrobial resistance profile was similar between microbes isolated from both participant cohorts, highlighting the potential for oral biofilms to protect microbes from systemic antimicrobial therapy. While salivary cytokine profiles did not correlate with pneumonia status, the concentration of IL-6 and IL-8 was positively correlated with the relative abundance of putative respiratory pathogens on denture surfaces.

Importance: This is the first study to directly examine compositional shifts in the denture-associated oral microbiome in respiratory infection, providing a basis for disentangling potential causal relationships.

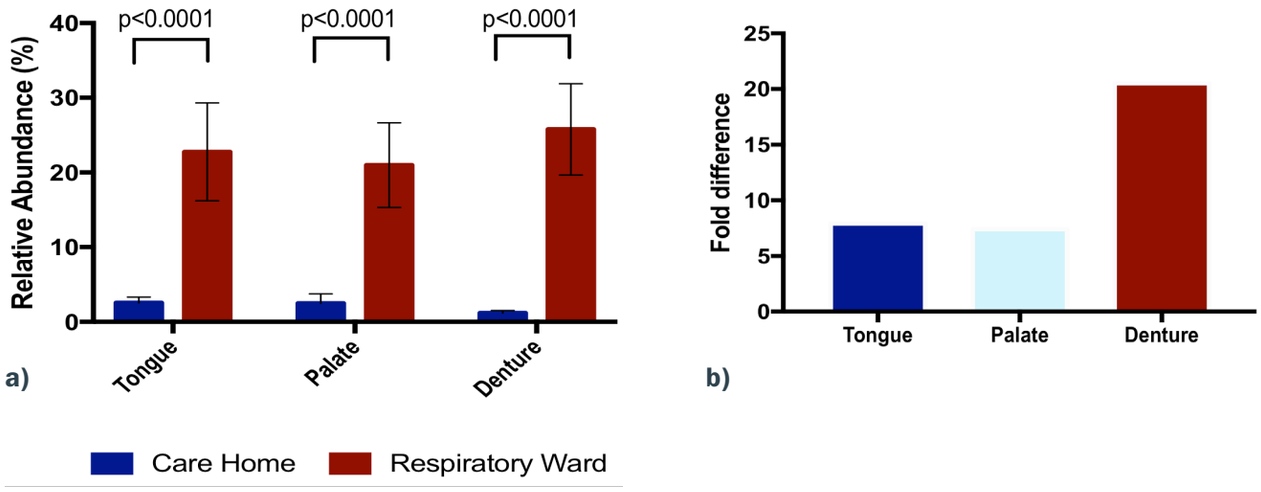


Fig. 1: Cumulative relative abundance (%) of respiratory pathogens identified in respiratory healthy (care home) and pneumonia patients (respiratory ward) (a; mean values are shown, error bars represent 95% confidence intervals.) Cumulative relative abundance of respiratory pathogens in pneumonia patients, compared to respiratory healthy individuals (b; fold difference calculated using mean values reported in panel a)

Professor David W Williams

WilliamsDD@cardiff.ac.uk
+44 (0)29 2251 0654

Professor Williams leads the Oral and Biomedical Sciences research theme and is a principle investigator within the Microbial Diseases research group.

His research interests primarily focus on microbial biofilms and human infection. Over 65% of hospital infections have a biofilm origin and their treatment is highly problematic given their high resistance to antimicrobials. Unsurprisingly, biofilm research is highly important and timely given global concerns over the emergence of antimicrobial resistance. On-going projects are studying biofilms in ventilator-associated pneumonia, catheter associated urinary tract infection, and denture stomatitis. He has access to a dedicated biofilm research laboratory which houses a range of flow cells and bioreactors to enable biofilm study.

Key Publication:

Morse D, et al. (2019). Molecular community profiling of the bacterial microbiota associated with denture-related stomatitis. Sci Rep 9(1): 10228.

Full list at: www.cardiff.ac.uk/people/view/39506-williams-david

Professor Mike Lewis

LewisMAO@cardiff.ac.uk
+44 (0)29 2074 2541

Professor Lewis is Professor of Oral Medicine in the School of Dentistry. He served as Dean of Dentistry and Head of the School of Dentistry (2010-2017). He is Director of the Clinical Board for Dentistry of Cardiff & Vale University Health Board. He holds an honorary NHS position as Consultant in Oral Medicine.

His research interests for more than 30 years have involved clinical and laboratory based aspects of orofacial bacterial, candidal and viral infections. He has on-going research projects in the involvement of biofilms in ventilator-associated pneumonia and denture stomatitis (erythematous candidosis). In addition, he presently has active studies exploring the appropriate usage of antimicrobial agents in primary dental care practices within Wales and the antibiotic prescribing for treatment or prophylaxis of dental infections in the secondary care dental hospital in the UK. He is presently developing a quality improvement tool for management of mouth cancer in primary care in Wales.

Key Publication:

Lins R, et al. (2019). Comparison of genotypes, antimicrobial resistance and virulence profiles of oral and non oral *Enterococcus faecalis* from Brazil, Japan and the United Kingdom. J Dent 84: 49-54.

Full list at: www.cardiff.ac.uk/people/view/39465-lewis-michael

Professor Mark Waters

WatersMG@cardiff.ac.uk

Mark Waters is Professor of Biomaterials and a Director of MBI (Wales) Ltd, an R&D led University spin-out company specializing in the formulation of custom silicone elastomers.

He has over 25 years' experience in the area of biomaterials and in particular in the development of novel silicone elastomeric materials. Recent research has focussed on the development of antimicrobial silicone materials and biosensors for detecting the early onset of bacterial infection. This work has led to a patented sensor which gives an early warning of impending urinary catheter blockage caused by the prevalence of urease producing bacteria in the bladder.

Key Publication:

Jindal S, et al. (2018). Development of a 3D printable maxillofacial silicone. Part II: Optimization of moderator and thixotropic agent. J Prosthet Dent 119(2): 299-304.

Full list at: www.cardiff.ac.uk/people/view/183030-waters-mark

Dr Xiao-Qing Wei

WeiX1@cardiff.ac.uk
+44 (0)29 2074 4529

Dr Xiao-Qing Wei is a Senior Lecturer. He has a Medical degree from the School of Medicine of Peking University in Beijing, China, and worked in Beijing Youan Hospital as a clinician. He subsequently received a PhD in Immunology from the University of Glasgow, UK, where he remained as a postdoctoral research fellow until moving to Cardiff in 2004.

Cytokines play a pivotal role in controlling the outcome of infectious and inflammatory diseases by regulation of host innate and adaptive immunity. My research has focused on understanding the role of some important pro-inflammatory cytokines, such as IL-18, IL-12, IL-23, IL-27 and a novel anti-inflammatory cytokine, IL-35, in the disease process in order to find practical ways to regulate host immune responses for disease treatment.

Key Publication:

Wang X, et al. (2019). A generic coordination assembly-enabled nanocoating of individual tumor cells for personalized immunotherapy. Adv Healthc Mater 8(17): 1900474.

Full list at: www.cardiff.ac.uk/people/view/39509-wei-xiao-qing

Dr Melanie Wilson

WilsonMJ@cardiff.ac.uk
+44 (0)29 2074 2548

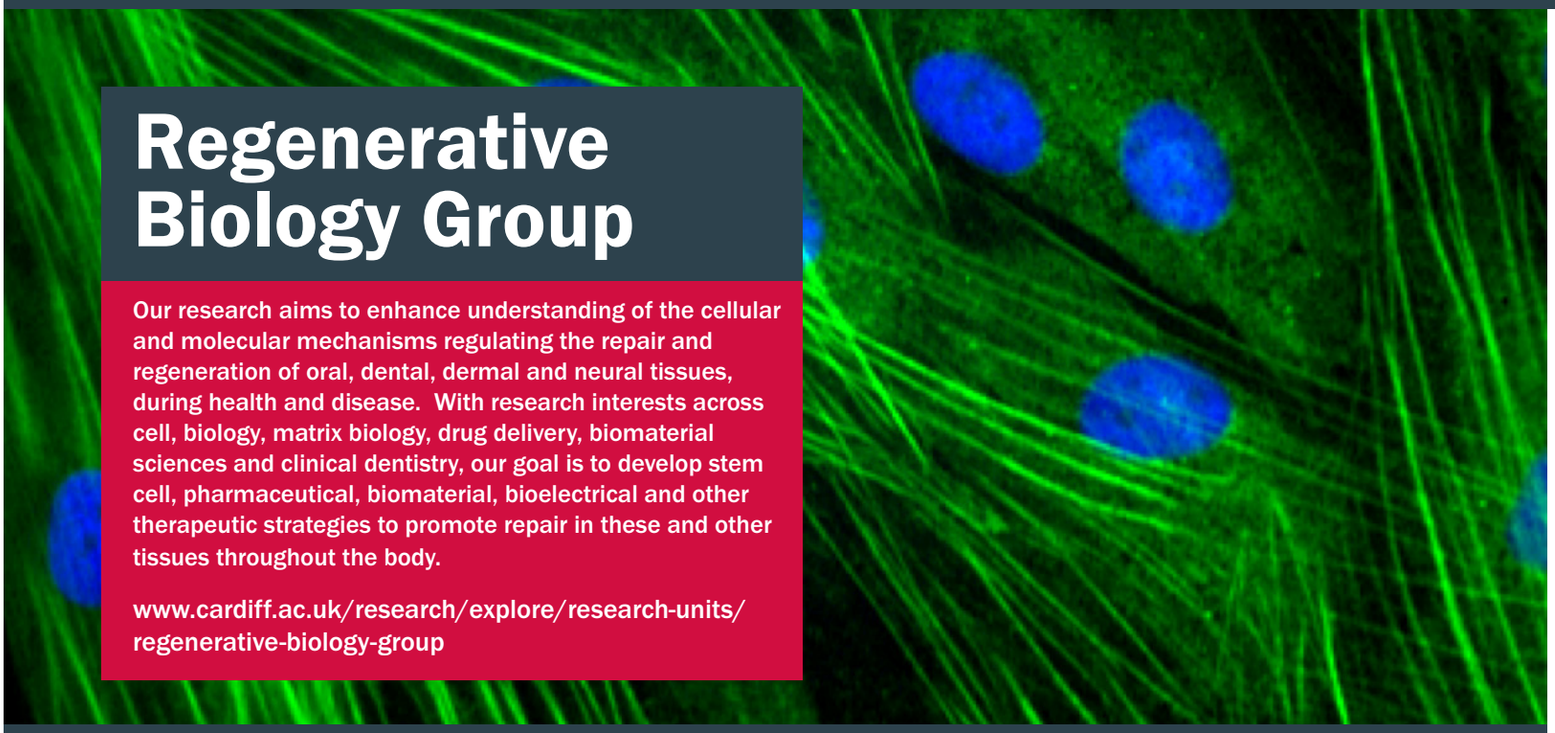
BDS Queens University Belfast (QUB); BSc (Hons) Medical Microbiology, QUB; Fellowship in Dental Surgery, London; PhD University of Wales College of Medicine; Fellowship Royal College of Pathologists. MRC Clinical Fellowship; currently Senior Lecturer and Honorary Consultant in Oral Microbiology.

The main focus of her research has been the application of molecular methods to the study of complex microbial communities, including dental plaque, the chronic wound microbiota, bacteria associated with oral cancer and, more recently, the biofilms involved in community and ventilator associated pneumonia. Other research interests relate to antimicrobial resistance in orofacial infection, the antimicrobial and antibiofilm effects of probiotics and their products, and host pathogen interactions, for example the interaction of microaerophilic *streptococci* with extracellular matrix components and *Candida* species with host tissues.

Key Publication:

Morse D, et al. (2019). Modulation of *Candida albicans* virulence in *in vitro* biofilms by oral bacteria. Lett App Micriobiol 68(4): 337-343.

Full list at: www.cardiff.ac.uk/people/view/39519-wilson-melanie



Regenerative Biology Group

Our research aims to enhance understanding of the cellular and molecular mechanisms regulating the repair and regeneration of oral, dental, dermal and neural tissues, during health and disease. With research interests across cell, biology, matrix biology, drug delivery, biomaterial sciences and clinical dentistry, our goal is to develop stem cell, pharmaceutical, biomaterial, bioelectrical and other therapeutic strategies to promote repair in these and other tissues throughout the body.

www.cardiff.ac.uk/research/explore/research-units/regenerative-biology-group

Our goals are:

- to understand the mechanisms underlying the repair and regeneration of oral, dermal and neural tissues, during health and disease
- to develop novel targeted technologies to promote tissue repair and regeneration in oral and non-oral tissues.

Despite significant medical advances in recent years, clinical conditions associated with impaired or dysfunctional healing remain a major healthcare challenge; especially with the rising incidence of these conditions due to ageing populations, diabetes, antimicrobial resistance and the acknowledged inadequacies in current treatment options.

Research within the Regenerative Biology Group is particularly focussed on the role of tissue-intrinsic mesenchymal stromal cells (isolated from dental pulp, bone marrow, oral mucosa) in driving tissue repair processes.

We aim to achieve impact on patient health and well-being, by continuing our research advances in developing stem cell technologies with pharmaceutical, biomaterial, bioelectrical and other therapeutic approaches for the treatment of diseases and conditions affecting dental, maxillofacial and orthopaedic functioning; impaired dermal wound healing and organ fibrosis; and spinal cord repair. A further focus of our research is the development of novel antimicrobial delivery and release technology for the elimination of bacterial infections that can hamper repair processes.

Through academic, clinical and industrial collaborations, we aim to facilitate the advancement of novel and more effective repair and regenerative therapies to drive improvements in patient quality of life.

Highlights of 2019:

- Recruitment of three International PhD students for cross-collaborative studies with the Schools of Pharmacy, Optometry, Biosciences and the Royal Botanical Gardens Kew, to investigate the potential of plant derived compounds for enhanced wound healing in skin and cornea.
- Award for Dr Ayre from the EPSRC ECR Institutional Equipment fund for a contact angle goniometer and quartz crystal microbalance. The equipment will be used in the development of novel antimicrobials and osteogenic implant coatings in collaboration with academics across the University and externally.
- Successful award of PhD degree for three postgraduate researchers working in the field of developing novel targeted technologies for enhancing wound healing and minimising infection.

Linked Research Centres:

All members of the group belong to the Cardiff Institute for Tissue Engineering and Repair (CITER), Cardiff University's internationally recognised centre in the field of tissue repair, regeneration and rehabilitation, focusing on interdisciplinary research, education and clinical practice.

Dr Nishio Ayre and Professors Sloan and Waddington are members of the Cardiff University Nanosome network and Materials network

www.cardiff.ac.uk/cardiff-institute-tissue-engineering-repair

Key project summary:

An intelligent neural stem cell delivery system for treatment of neurodegenerative diseases:

Qiao S et al, 2018. Adv Healthc Mater. 7(12): 1800080.

Background: Stem cell replacement therapy constitutes a promising approach in treatment of neurological disorders. Emerging evidence indicates that a "negative" microenvironment caused by acute inflammation or immune responses can severely affect the survival of grafted stem cells. We designed an intelligent, double-layer, alginate hydrogel delivery system to protect grafted cells. This system fosters reaction of the MMP secreted by transplanted stem cells with MMP peptide grafted on to the inner layer and destroys the structure of the inner hydrogel layer during the inflammatory storm. Meanwhile, having an optimum concentration of RGD peptide (which reportedly promotes stem cell adhesion and proliferation) immobilized to the inner hydrogel layers is crucial to obtain a critical number of stem cells before enabling this interaction with the Cripto-1 antibody immobilised to the outer hydrogel layer (Fig 1). Extracellular matrix interaction (initiated by RGD) is essential for neuronal survival and differentiation, and facilitates treatment of neurodegenerative diseases.

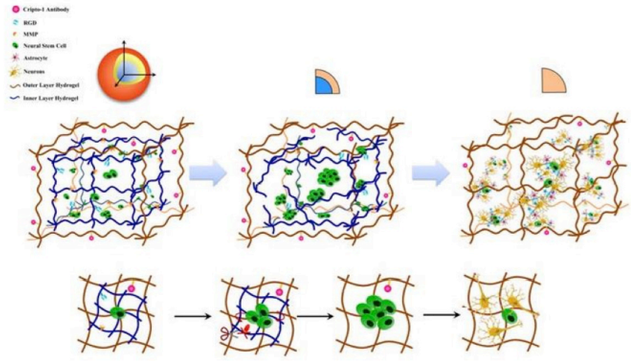


Fig 1: Schematic outlining the principle of our intelligent, double-layer, alginate hydrogel for neural stem cells transplantation to achieve better therapeutic efficacy in Parkinson's disease treatment.

Discovery: We demonstrate that blocking Cripto-1, which was known to promote differentiation of embryonic stem cells into dopaminergic neurons, also stimulates/accelerates this process in neural stem cells (NSCs). Excitingly, we also discovered a novel link between Cripto-1 inhibition of neuronal differentiation and bias in NSCs. By default, 90% of NSCs will differentiate into astrocytes in astrocyte-differentiation medium. Here, we reported for the first time, that NSCs / dopaminergic neuron differentiation can be conducted in astrocyte-differentiation medium when conducted in the context of Cripto-1-neutralization both *in vitro* (Fig 2), and *in vivo* (Fig 3).

Importance: The novel design of our double-layered hydrogel system, containing an inner layer comprised of alginate hydrogel-grafted MMP target on the RGD peptides (promoting NSC proliferation, and subsequent delayed release of cells), and an outer layer of alginate hydrogel-grafted Cripto-1 antibodies (to promote neural differentiation) can successfully support lineage-specific neuronal differentiation. This novel system can be easily adjusted to the different parameters required for differentiation of transplanted stem cells to support the clinical application of stem cells as a replacement therapy in treating different progressive neurological disorders, for example Parkinson's disease, as we demonstrated in this study substantially enhanced dopaminergic differentiation using our system.

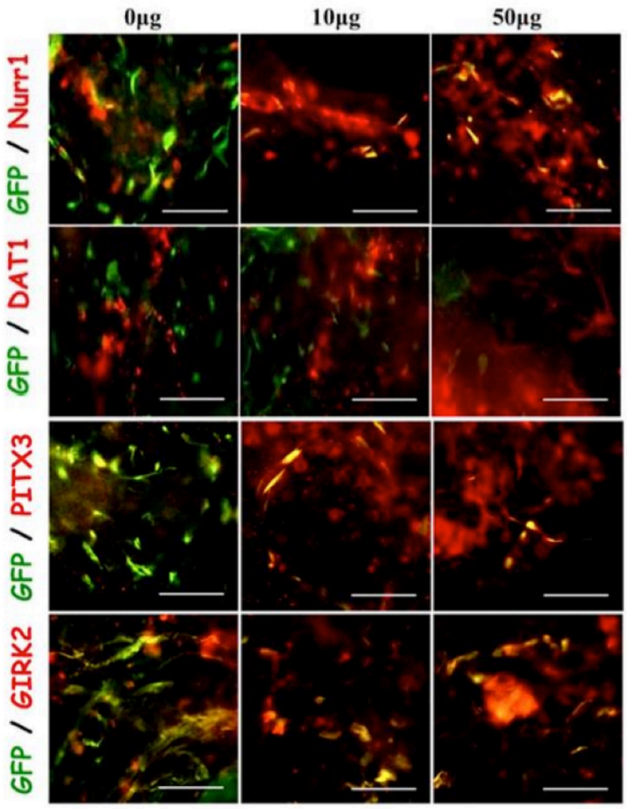


Fig 2: Immunocytochemistry analyses of NSCs cultured in hydrogel delivery system for 14 days for the A9 dopaminergic differentiation marker (PITX-3/GIRK2, in red) confirms desired lineage-specific differentiation.

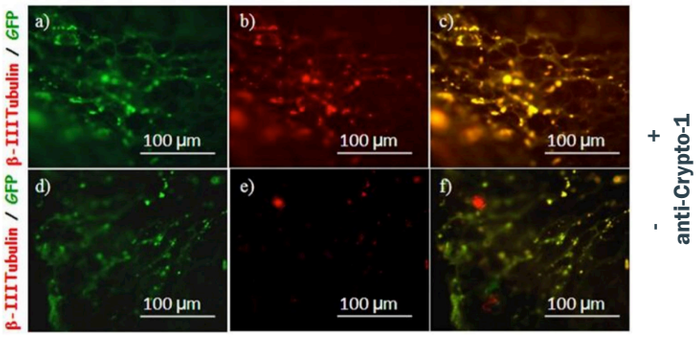


Fig 3: Correct differentiation of transplanted NSCs through our intelligent, double-layer, alginate hydrogel system is confirmed *in vivo*. A rat brain injury model was employed, and equivalent defects in the two hemispheres treated with NSCs in the presence or absence of antibodies to Crypto-1. After 14 days, repair tissue was examined for neurogenesis (β-III tubulin).

Professor Bing Song

SongB3@cardiff.ac.uk
+44 (0)29 2074 4182

MD, China Medical University, China (1995). PhD, School of Medical Sciences, University of Aberdeen, UK (2004). University Research Fellow, the Royal Society, UK (2005). Since 2009, Professor of Regenerative Medicine, Cardiff University. British Council Global Innovation Initiative award (2014). Since 2017, Director of International, School of Dentistry, Cardiff University. Co-lead of the Regenerative Biology Group.

His research interests are electric signals regulated stem cell biology (migration, proliferation, differentiation); electric signals promoted neural regeneration and repair (spinal cord injury, Parkinson's disease); remyelination of regenerated neuron with oligodendrocyte progenitor cells; dental pulp stem cells based bioengineered nanoscaffold assisted tissue engineering; stem cell encapsulation; cornea and retina regeneration; electric signals regulated immunisation and wound repair.

Key Publication:

Jiang W, et al (2019). Wnt-GSK3ß/ß-catenin regulates the differentiation of dental pulp stem cells into bladder smooth muscle cells. Stem Cells Int 2019: 8907570.

Full list at: www.cardiff.ac.uk/people/view/39415-song-bing

Professor Alastair Sloan

SloanAJ@cardiff.ac.uk
+44 (0)29 2251 0650

PhD (Cell Biology), Faculty of Medicine & Dentistry, University of Birmingham (1997); BSc (Hons) Biomedical Sciences; University of Wales (1993); Postgrad. Cert. Teaching in Higher Education, University of Birmingham, (2002). He is a Fellow of the Higher Education Academy (FHEA) and was elected a Fellow of the Royal Society for Biology (FRSB).Winner of International Association Dental Research Distinguished Scientist Young Investigators Award 2011; British Society Oral and Dental Research MINTIG Research Travel Award (1998). Visiting Professor, 4th Military Medical University, Xi'an, China and China Medical University, Shenyang, China. Currently non-clinical professor of Bone Biology & Tissue Engineering and Head of School of Dentistry. Co-lead of the Regenerative Biology Group.

Professor Sloan's research is multi-disciplinary and focussed on the repair and regeneration of mineralised tissues through study of the behaviour and therapeutic use of dental pulp stem cells, *ex vivo* organotypic culture models and to control infection within these tissues.

Key Publication:

Rivera M, et al (2019). Anti-inflammatory drug-eluting implant model system to prevent wear particles induced periprosthetic osteolysis. Int J Nanomed 14: 1069-1084..

Full list at: www.cardiff.ac.uk/people/view/39434-sloan-alastair-j

Professor Phil Stephens

StephensP@cardiff.ac.uk
+44 (0)29 2074 2529

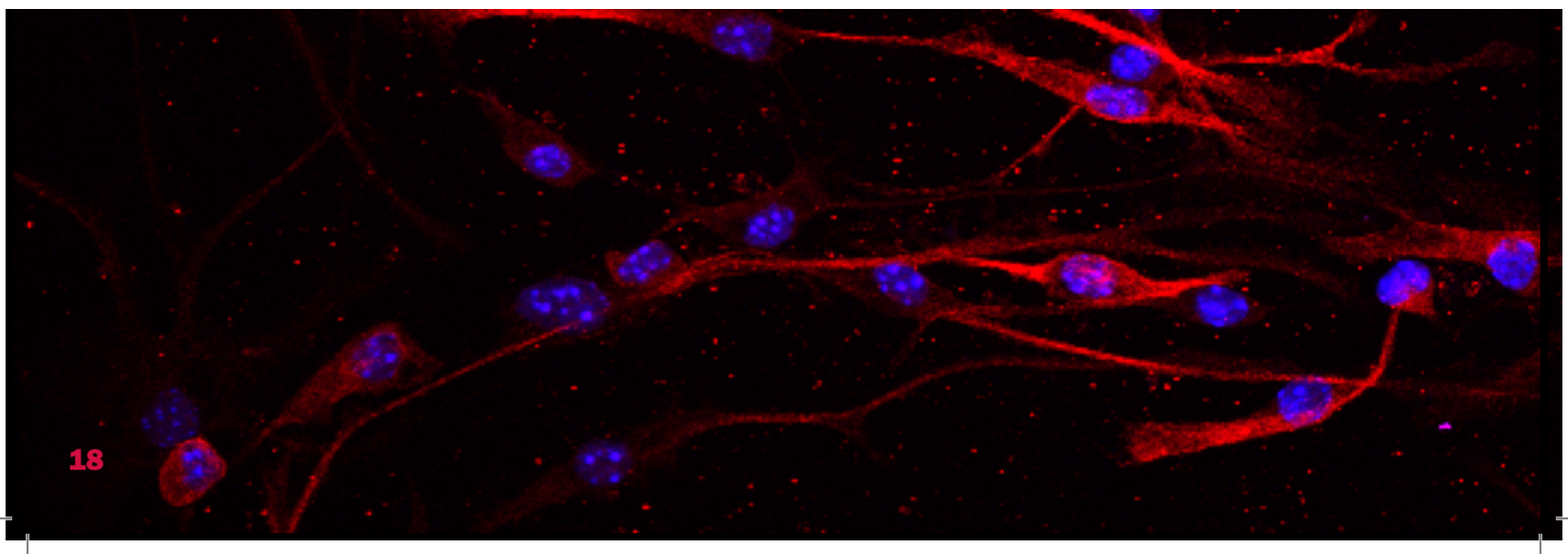
BSc (Hons) Biochemistry and Cell Biology, University of Leeds; PhD Biochemistry and Cell Biology, University of Leeds. Since 2008, Professor of Cell Biology, Cardiff University. Since 2013, Designated Individual HTA Research Licence, Cardiff University. Since 2015, Academic Lead for Cardiff University Biobank. Since 2016, Dean of International & Engagement, College of Biomedical and Life Sciences, Cardiff University. Since 2017, President of the European Tissue Repair Society (ETRS).

His research interests are oral progenitor cell biology (lineage development/control, immunosuppression, bacterial suppression, tissue healing); dysfunctional (chronic skin wound) biology; development of *in vitro* systems to replace animals in experimentation; live cell imaging (*in vitro* and *in vivo*).

Key Publication:

Masia F, et al. (2018). Label-free quantitative chemical imaging and classification analysis of adipogenesis using mouse embryonic stem cells. J Biophotonics 11:e201700219.

Full list at: www.cardiff.ac.uk/people/view/39411-stephens-phil



Professor Rachel Waddington

WaddingtonRJ@cardiff.ac.uk
+44 (0)29 2251 0647

PhD Faculty of Medicine, University of Liverpool 1988; BSc (Hons), Biochemistry, University of Birmingham 1984. Winner of Senior Colgate prize (1990) and the MINTIG Mineralised tissue Research Travel Award (1996), both awarded by the British Society for Dental and Oral Research. Currently professor in Oral Biochemistry and Associate Director for Engagement, Enterprise and Innovation.

Professor Waddington has more than 30 years' experience of research in bone and dentine biology and the role of the extracellular matrix environment in driving repair processes.

Key Publication:

Munir A, et al (2019). Efficacy of copolymer scaffolds delivering human demineralised dentine matrix for bone regeneration. J Tiss Eng 10: 1-16.

Full list at: www.cardiff.ac.uk/people/view/39516-waddington-rachel

Dr Ryan Moseley

MoseleyR@cardiff.ac.uk
+44 (0)29 2251 0649

BSc (Hons) Biochemistry, Swansea University, 1991; PhD Oral Biochemistry, University of Wales College of Medicine, 1996. Since 2017, Reader in Tissue Repair, Cardiff University.

His research interests are mechanisms underlying preferential (e.g. oral mucosa), normal (e.g. skin, bone) and impaired/ abnormal tissue repair (e.g. chronic wound, diabetic bone) responses and fibrosis (keloid scars); development of cellular, biomaterial and pharmaceutical strategies for enhanced oral-dermal wound healing and reduced scarring; characterization and development of dental pulp stem cells (DPSCs) for clinical applications.

Key Publication:

Alraies A, et al (2019). Discrimination of dental pulp stem cell regenerative heterogeneity by single cell raman spectroscopy. Tissue Eng Part C-Meth 25(8): 489-499.

Full list at: www.cardiff.ac.uk/people/view/39455-moseley-ryan

Dr Wayne Nishio Ayre

AyreWN@cardiff.ac.uk

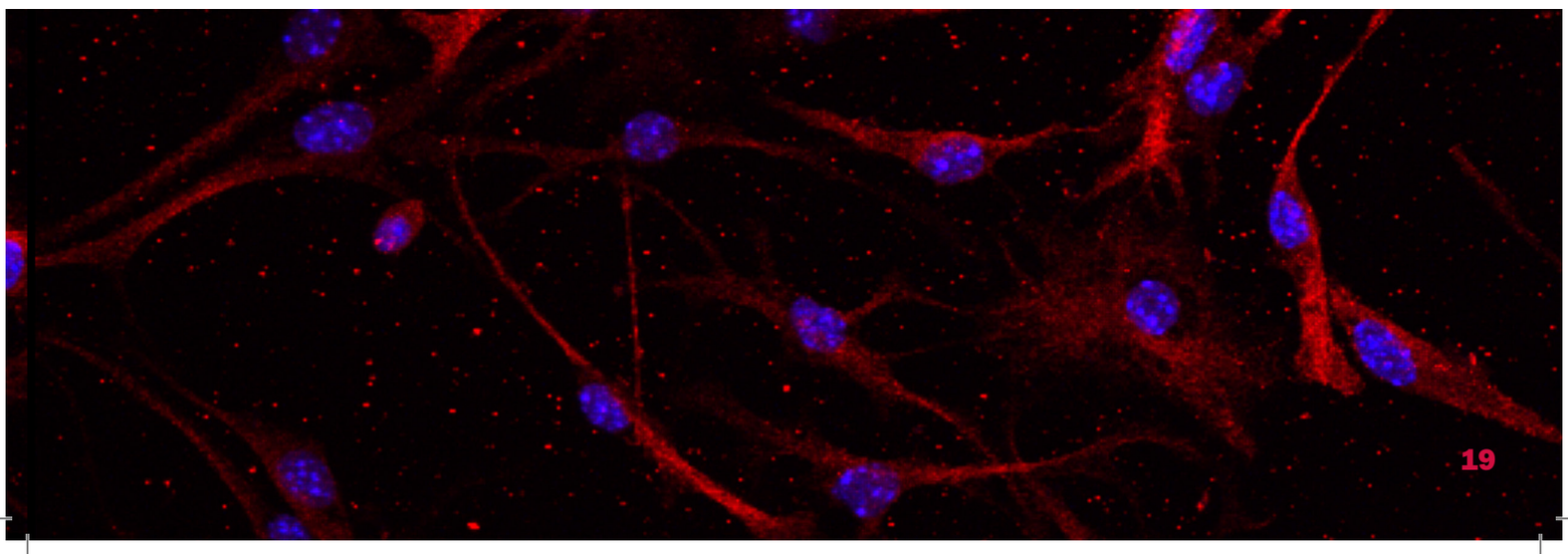
PhD, Mechanical Engineering, Cardiff University/Arthritis Research UK Biomechanics and Bioengineering Centre (2013); BEng Medical Engineering, Cardiff University (2009). Welsh Crucible - Future Research Leaders of Wales Programme (2017); British Orthopaedic Research Society – International Travelling Fellowship (2016); Cardiff Institute of Tissue Engineering and Repair Young Investigator Award (2015); IADR-PER GSK-Mineralised tissue group prize (2014); The Worshipful Company of Engineers Mercia Award in Medical Engineering (2014). Currently Lecturer in Biomaterials, School of Dentistry.

Dr Ayre's research interests are focusing around the design, development and testing of medical devices and biomaterials. His particular areas of interest revolve around using lipid coatings and drug delivery systems to enhance osseointegration and prevent infections of orthopaedic implants and dental materials.

Key Publication:

Melling G, et al (2018). Liposomal delivery of demineralised dentine matrix for dental tissue regeneration. Tissue Eng Pt A 24(13-14): 1057-1065.

Full list at: www.cardiff.ac.uk/people/view/142785-nishio-ayre-wayne



Dental Public Health

Our research focuses on oral health improvement. Our portfolio of research ranges from clinical trials of preventive dental technologies to studies designed to further understanding of and address oral health inequalities and projects to improve the delivery of dental care.

www.cardiff.ac.uk/research/explore/research-units/dental-public-health-unit

Our goals are:

To undertake research from a population perspective which will:

- inform dental health and care need in Wales and beyond
- contribute to the evidence base for effective preventive dental care
- change how dental care is delivered to maximise benefit for patients and public.

Whilst oral health has improved dramatically over the past three decades, dental caries (tooth decay) remains a significant public health problem. In common with most chronic health conditions, oral disease correlates closely with social and economic circumstances and the differences that exist between the most and least deprived in our society result in inequalities in oral health.

We are involved in a range of research projects which aim to enhance the evidence base for improving oral health and delivering dental care. While our work is based in Wales and we have a particular interest in oral health in the Principality, our collaborations and the outcome of our work is of relevance, locally, nationally and internationally.

We work closely with colleagues in Cardiff and Vale Local Health Board, Public Health Wales and the office of the Chief Dental Officer at Welsh Government. We contribute the oral health workpackage of the Health Care Research Wales-funded Primary and Emergency Care Research (PRIME) Centre Wales. We also host the Wales Oral Health Information Unit on behalf of Welsh Government and Public Health Wales.

Highlights of 2019:

- September 2019 saw the 10th Anniversary of the establishment of the “Designed to Smile”, national oral health improvement programme. Over the past decade, we have played a key role in supporting and evaluating the programme’s impact. Since implementation the number of 5-year olds affected by tooth decay has fallen by 12% - making a substantial difference to the well-being of children across Wales.
- We were awarded a substantial grant from Health and Care Research Wales under their Research for Patient and Public Benefit Programme. Named, OPTIMISE, this study, conducted in collaboration with the Data Innovation Research Institute in the School of Mathematics, is designed to develop a model of skill-mix use in NHS General Dental Services to optimise the delivery of value-based, preventive-led care.
- Our work on a large randomised controlled trial, funded by the NIHR (£1.9M) and being conducted in collaboration with colleagues in the Universities of Dundee, Leeds, Sheffield and York continues, following the completion of a successful pilot stage. The study is looking at the use of SMS technology to improve oral health promoting behaviours in young people.
- The International impact of our work has been recognised by the award of the William J. Gies Award for Clinical Research by the International Association for Dental Research (IADR). This prize is awarded to the best clinical research article published in the Journal of Dental Research. The prize was collected by Professor Chestnutt on behalf of the trial team at the IADR meeting in Vancouver, Canada (above).

Key Project Summary:

Patients' reasons for consulting a GP when experiencing a dental problem: a qualitative study

Cope AL et al, 2019. Brit J Gen Pract 68(677): e877-e883.

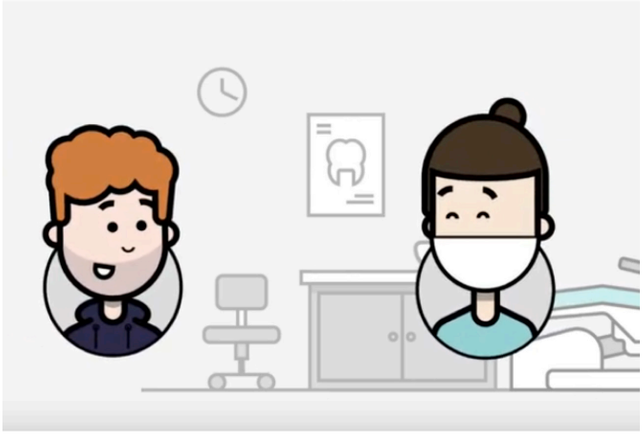
Background: There are approximately 380, 000 consultations for dental problems in UK general practice every year.

Aim: To explore the reasons why patients may consult a GP rather than a dentist when experiencing problems with their teeth or gums.

Method: A qualitative semi-structured interview study was designed, targetting adults who had consulted a UK GP with a dental problem in the previous 12 months. Participants were recruited via print and social media; internet adverts; HealthWise Wales, the Welsh national population research cohort; and word of mouth. In total, 39 telephone interviews were conducted, and transcripts thematically analysed.

Results: Participants' consultation behaviour was influenced by their interpretation of their symptoms; their perceptions of the scope of practice of primary care practitioners; the comparative ease of navigating medical and dental care systems; previous experiences of dental care, including dental anxiety and dissatisfaction with prior treatment; and willingness and ability to pay for dental care.

Conclusion: There are several reasons why patients may consult a GP with a dental problem. Effective interventions will need to break down the barriers preventing access to dental care. Accessible public-facing information on where to seek care for dental problems is required, and general practice teams should be able to signpost patients who present with dental problems, if appropriate. Dental providers should also be encouraged to maintain timely access to urgent care for their patients.



Watch the YouTube video created to disseminate the results of the study and to encourage the public to visit their dentist rather than their GP if they have a dental problem.

www.youtube.com/watch?v=e3z8f5MZ5eA

Linked Research Centres:

Professor Ivor Chestnutt leads the Oral Health and Primary Dental Care work package in the Health and Care Research Wales-funded Primary and Emergency Care Research (PRIME) Centre Wales. This multidisciplinary Centre aims to improve the health and wellbeing of people in Wales and internationally through: conducting high quality research on topics of national policy priority which contributes to the evidence base in primary and emergency care; ensuring that research findings are translated into policy and practice.

www.primecentre.wales

Within the Dental Public Health Unit, we host the Wales Oral Health Information Unit (WOHIU), led by Maria Morgan. The unit provides independent professional advice, quality assurance, data cleaning, data verification, data analysis and a reporting service on behalf of the Welsh Government commissioned via Public Health Wales. The WOHIU and the Wales Dental Epidemiology Co-ordinator work with the Community Dental Services and the Welsh Government (through the Office of the Chief Dental Officer and the Health Statistics and Analysis Unit in the Statistics Directorate) to deliver national oral health surveys.

www.cardiff.ac.uk/research/explore/research-units/welsh-oral-health

Professor Ivor G Chestnutt

ChestnuttIG@cardiff.ac.uk
+44 (0)29 2074 6680

Ivor Chestnutt is Professor in Dental Public Health at School of Dentistry, Honorary Consultant to Cardiff and Vale University Health Board and is registered as a Specialist in Dental Public Health. He is a graduate of the University of Edinburgh (BDS 1985) and received both his MPH (1995) and PhD (1992) degrees from the University of Glasgow. He holds Fellowships in dental surgery and dental public health from the Royal College of Surgeons of Edinburgh (1990 and 1998), the Royal College of Physicians and Surgeons of Glasgow (2003) and the Royal College of Surgeons, England (2002). Ivor is a Fellow of the Faculty of Public Health (2003) and a Fellow of the Higher Education Academy (2006). He is also the Clinical Director of the University Dental Hospital in Cardiff and is Director of Postgraduate studies in the School of Dentistry.

Professor Chestnutt's research interests include dental health services research, clinical trials of preventive dental products and dental epidemiology.

Key Publication:

Nor NAM, et al (2019). The prevalence of enamel and dentine caries lesions and their determinant factors among children living in fluoridated and non-fluoridated areas. Community Dent Health 36(3): 229-236.

Full list at: www.cardiff.ac.uk/people/view/39480-chestnutt-ivor

Maria Morgan

MorganMZ@cardiff.ac.uk
029 2074 4612

Maria Morgan is a public health professional with academic and health service experience. She leads the work of the Welsh Oral Health Information Unit funded by Welsh Government, which involves evaluating "Designed to Smile", the national child oral health promotion programme. She also contributes to public health research and education and works part-time as public health specialist for Public Health Wales.

Three main themes make up her research interests: public health nutrition, which continues early MPhil research; public health, both generic and dental, and dental epidemiology.

Key Publication:

Jones R, et al (2019). Family and friends: supporting oral care in care homes. Gerodontology 36(3): 258-266.

Full list at: www.cardiff.ac.uk/people/view/39445-morgan-maria

Dr Anwen Cope

CopeA1@cardiff.ac.uk
+44 (0)29 2074 6553

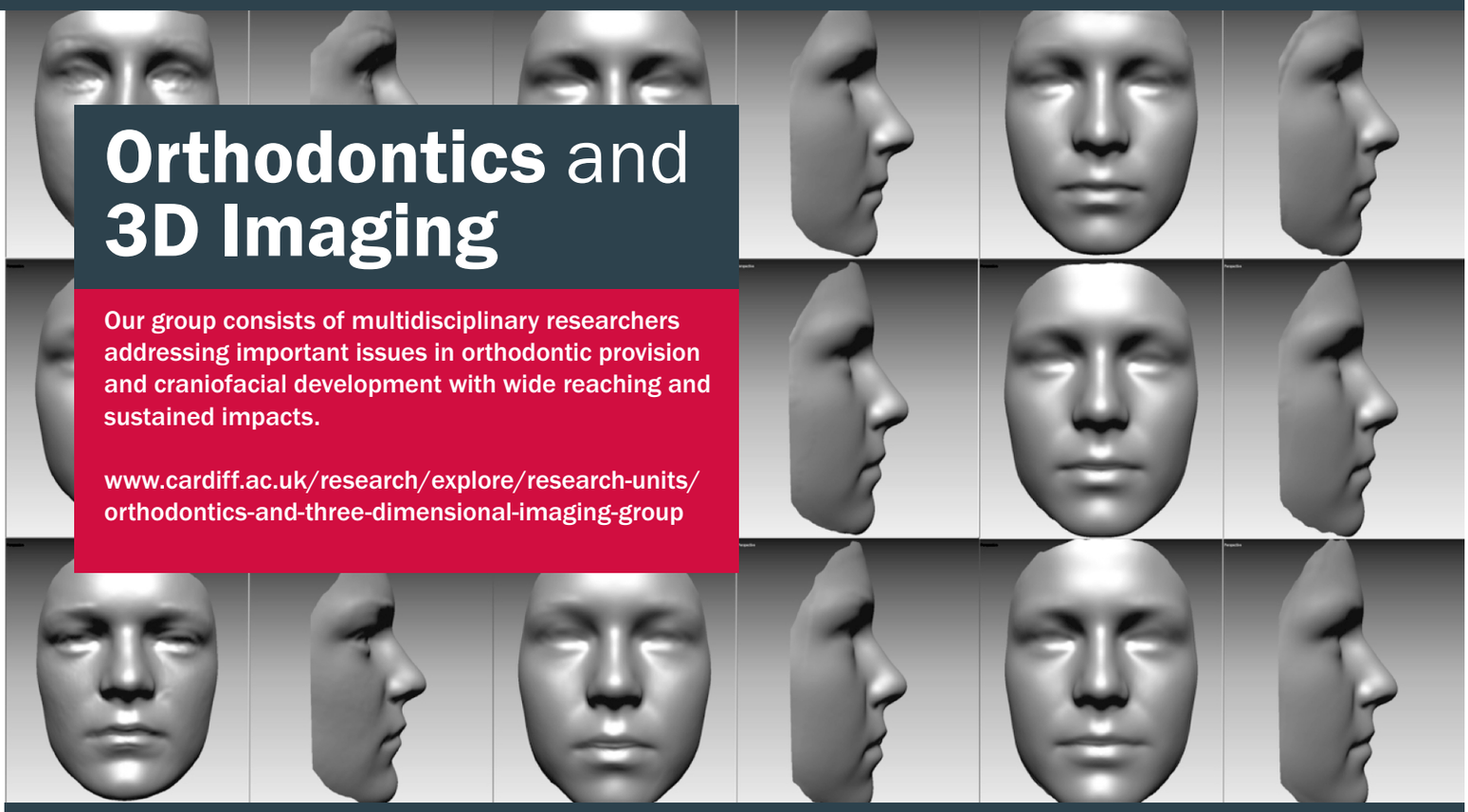
BDS, 2009, Cardiff University. MFDS, 2013, Royal College of Physicians and Surgeons of Glasgow. PhD (Medicine), 2015, Cardiff University. MPH, 2018, Cardiff University. Currently holds a Clinical Research Time Award from Health and Care Research Wales. Since 2015, an Honorary Clinical Lecturer in Dental Public Health in Applied Clinical Research and Public Health, School of Dentistry, Cardiff University and Specialty Trainee in Dental Public Health, Cardiff and Vale University Health Board.

Dr Cope is a dental health services researcher interested in the use of antibiotics in the management of dental problems in primary care; dental consultations in general medical practice; shared decision making in dentistry, and the use of skill-mix in the dental team.

Key Publication:

Cope A, et al (2019). Exploring the feasibility of using routinely collected data to produce antibiotic prescribing profiles for general dental practitioners in Wales. Community Dent Health 36(3): 177-180.

Full list at: www.cardiff.ac.uk/people/view/337589-cope-anwen



Orthodontics and 3D Imaging

Our group consists of multidisciplinary researchers addressing important issues in orthodontic provision and craniofacial development with wide reaching and sustained impacts.

www.cardiff.ac.uk/research/explore/research-units/orthodontics-and-three-dimensional-imaging-group

Our goals are:

- **Orthodontics**
  Understanding and appreciating different growth patterns and different face shapes in distinct population groups.

  Improving orthodontic services in terms of cost-efficiencies and cost-effectiveness.

- **3D imaging**
  Exploring the relative parental biological and environmental contributions to heritable traits.

  Highlighting what is known about shared facial traits, medical conditions and underpinning genetics and build on this to advance the field.

Highlights of 2019:

- Caryl Wilson Nagrani won the European Orthodontic Society Research Prize in Nice 2019. This prize acknowledges her work on “Cleft susceptibility loci contributions towards variations in normal lip phenotypes”
- Published article in European Journal of Orthodontics that is exploring the midline soft tissue surface changes from 12 to 15 years of age in three distinct country population cohorts (Richmond S, et al, Eur J Orthodont 2019, in press). By investigating homogeneous population groups (Welsh, Latvian and Finnish) we established that clearly distinct patterns of growth can be identified, with distinctly different magnitudes at different ages for the different country groups, sexes, and specific facial parameters.

There are several important reasons for exploring the genetics of normal-range variation in facial morphology:

- Disentangling the environmental factors and relative parental biological contributions to heritable traits can help to answer the age-old question “why we look the way that we do?”.
- Understanding the aetiology of craniofacial anomalies; e.g., unaffected family members of individuals with non-syndromic cleft lip/palate (nsCL/P) differ in terms of normal-range facial variation to the general population suggesting an etiological link between facial morphology and nsCL/P.
- Many factors such as ancestry, sex, eye and hair color as well as distinctive facial features (such as shape of the chin, cheeks, eyes, forehead, lips, and nose) can be identified or estimated using an individual’s genetic data, with potential applications in healthcare and forensics.
- Improved understanding of historical selection and adaptation relating to facial phenotypes, for example, skin pigmentation and geographical latitude.
- Highlighting what is known about shared facial traits, medical conditions and genes.

Linked Research Centres:

Prof Richmond is part of a multi-centre effort to link facial imaging data with genetics, including:

- University of Leuven, Belgium
- VisiGEN Consortium (Multi-centre consortium on visible genetics)
- University of Ljubliana, Slovenia
- The Latvian Academy of Medicine, Riga
- University of Bristol
- University of Pittsburgh, USA
- University of Rijeka, Croatia

Key project summary:

Investigating growth patterns in homogeneous white European populations.

Richmond S et al, (2019). Eur J Orthod, in press (cjz080). doi: 10.1093/ejo/cjz080.

Background: Genetics have a major influence on normal facial variation, and environmental factors are likely to have minor influences on face shape directly or through epigenetic mechanisms. Several studies have highlighted variations in the facial features in different White European population groups. To investigate this more systematically and provide a basis for these observations, we designed a longitudinal cohort study.

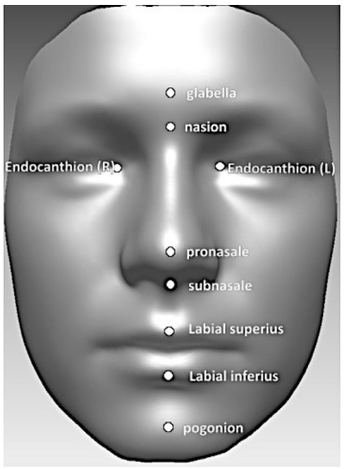
Objective: To determine the rate of change in simple midline facial landmarks in three distinct homogenous population groups (Finnish, Latvian, and Welsh) from 12.8 to 15.3 years of age. This age range covers the pubertal growth period for the majority of boys and girls.

Methods: Children aged 12 were monitored for facial growth in three countries [Finland (n = 60), Latvia (n = 107), and Wales (n = 96)]. Three-dimensional facial surface images were acquired (using either laser or photogrammetric methods) at regular intervals (6–12 months) for 4 years. Nine midline landmarks were identified (Fig 1) and the relative spatial positions of these surface landmarks were measured relative to the mid-endocanthion over a 4-year period in each of the country cohorts.

Results: This study reported the children who attended 95 per cent of all scanning sessions (Finland 48 out of 60; Latvia 104 out of 107; Wales 50 out of 96). Considerable facial variation was seen for all countries and sexes. There were clear patterns of growth that show different magnitudes at different ages for the different country groups, sexes, and facial parameters. The greatest single yearly growth rate (5.4 mm) was seen for Welsh males for men–pogonion distance at 13.6 years of age. Males exhibit greater rates of growth compared to females. Assessing centroid size (Fig 2) the growth of Welsh males is significantly different to the Finnish and Latvian cohorts. These variations in magnitude and timings of growth are likely to be strongly influenced by genetic ancestry as a result of population migration.

Conclusion: The midline points are a simple and valid method to assess the relative spatial positions of facial surface landmarks. This study confirms previous reports on the subtle differences in facial shapes and sizes of male and female children in different populations and also highlights the differences in magnitude and timings of growth for various midline landmark distances. The timing of growth of the face is important in respect to planning oro-facial interventive treatments. The different rates and patterns of facial growth must be taken into consideration.

Fig 1: Facial landmarks chosen and associated definitions



Landmark	Definition
glabella	The most prominent midline point between the eyebrows, identical to bony glabella on the frontal bone.
nasion	The point in the midline of both nasal root and fronto-nasal suture, always above the line that connects the two inner canthi, identical to bony nasion.
endocanthion (left and right)	Left and right inner eye commissures. The mid-endocanthion point was constructed (men) and used as the origin for comparisons.
pronasale	The most protruded point of the apex nasi, identified in lateral view of the rest position of the head.
subnasale	The midpoint of the angle at the columella base where the lower border of the nasal septum and the surface of the upper lip meet, not identical to bony nasospinale or anterior nasal spine. Identified in the base view of the nose, or from lateral view of the rest position of the head.
labiale superius	The midpoint of the upper vermilion line.
labiale inferius	The midpoint of the lower vermilion line.
pogonion	The most anterior midpoint of the chin, identical to bony pogonion of the mandible.

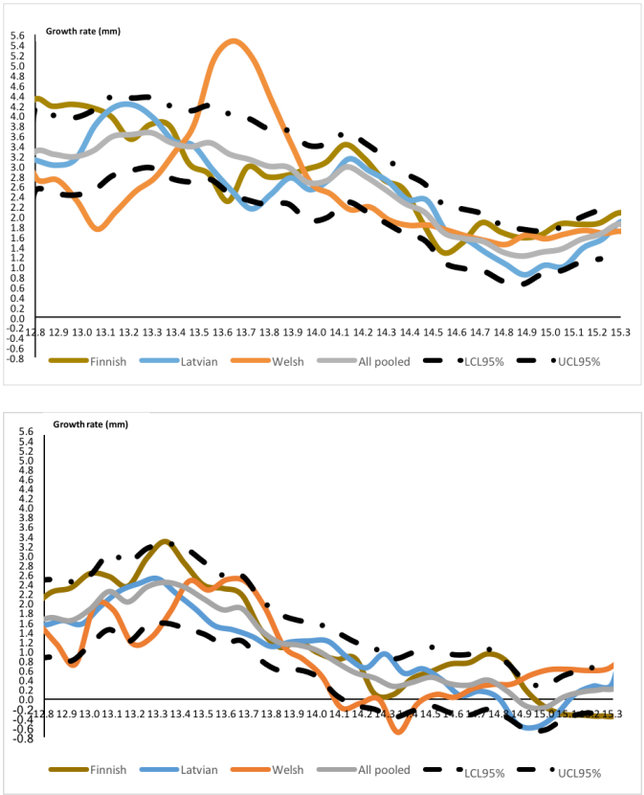


Fig 2: Centroid size for males (top) and females (bottom) for the 3 cohorts (Finnish, Latvian and Welsh children) individually and when pooled, with upper (UCL) and lower (LCL) confidence intervals

Reproduced from the article Richmond S et al, (2019). Exploring the midline soft tissue surface changes from 12 to 15 years of age in three distinct country population cohorts. European Journal of Orthodontics, cjz080.

Professor Stephen Richmond

RichmondS@cardiff.ac.uk
+44 (0)29 2074 2451

BDS (1979), DOrth, RCS (1984), MScD (1984), FDS, RCS (Ed) (1985), CHT, RCS (1989), PhD (1990), FDS.

Research interests: Wide variety of research involving orthodontic provision, orthodontic treatment need and outcomes as well as the interface with many disciplines using 3D facial imaging.

Key Publication:

Xiong Z, et al (2019). Novel genetic loci affecting facial shape variation in humans. eLife 8: e49898.

Full list at: www.cardiff.ac.uk/people/view/39436-richmond-stephen

Dr Alexei Zhurov

ZhurovAI@cardiff.ac.uk
+44 (0)29 2074 2447

BSc Applied Maths, MIPT (1988), MSc Applied Maths, MIPT (1990) Dolgoprudny, Russia. PhD Applied Maths, IPM RAS, Moscow, Russia (1995). Since 2001 Research Officer, Biomechanics and 3D Imaging Applied Research and Public Health.

Research interests: Three-dimensional analysis of the human face, contact biomechanics, biomechanics of soft tissues and FEM simulation. Theory of heat and mass transfer and chemical hydrodynamics. Nonlinear differential equations and exact solutions. Dynamic systems and computer algebra.

Key Publication:

Abbas HH, et al (2019). An automatic approach for classification and categorisation of lip morphological traits. PLos ONE 14(10): e0221197.

Full list at: www.cardiff.ac.uk/people/view/39394-zhurov-alexei

Dr Damian Farnell

FarnellD@cardiff.ac.uk
+44 (0)29 2251 0618

BSc (Mathematical Physics) Departments of Mathematics and Physics, UMIST, (1991). PhD ("Integrable and Non-Integrable Quantum Arrays") Department of Mathematics, UMIST, (1994). Post-Doctoral Research Associate, Universities of Manchester, Leeds, Munich, and Cologne, 1996-2003, 2007-2011. Lecturer of Ophthalmic Imaging, St. Paul's Eye Unit, Royal Liverpool University Hospital Trust, University of Liverpool, 2003-2006. Senior Lecturer of Mathematics, Division of Mathematics and Statistics, University of South Wales, 2011-2014. Since 2014, Senior Lecturer of Applied Mathematics in Dentistry, School of Dentistry.

Research interests: Biostatistics, medical imaging and image processing, pedagogy research, especially relating to mathematics and statistics teaching, numerical biosimulation, quantum magnetism and quantum many-body theory.

Key Publication:

Farnell DJJ, et al (2019). Multilevel Principal Components Analysis (mPCA) of age-related changes in facial shape in adolescents. Comput Meth Prog Bio 2019, in press (188:105272).

Full list at: www.cardiff.ac.uk/people/view/39526-farnell-damian

Alcohol and Violence

Through practical research on alcohol-related harms and violence, our leading academics, working in collaboration with external partners and organisations, have helped to understand, monitor and alleviate the causes of alcohol-related harms and violent behaviour.

www.cardiff.ac.uk/violence-research-group

Our goals are:

- to understand the causes and effects of alcohol misuse and violence and to produce real-world applications to prevent it
- to evaluate alcohol-related harms and violence prevention initiatives, working with service providers - health agencies, social services, criminal justice agencies, local governments and third sector organisations
- to evaluate the effectiveness of interventions designed to reduce the psychological, social and economic impacts of alcohol misuse and violence
- to translate effective innovations into local, national and international policy and practice.

The Violence Research Group draws on expertise from across Cardiff University. The strength and reputation of the group comes from its interdisciplinary research across the fields of psychiatry, public health, dentistry, criminal justice, police, psychology, materials science, computer science, social science and economics; and its extensive record of innovation and contributions to policy and alcohol-related harms and violence prevention.

Highlights of 2019:

- Recent work confirms that those from lower socio-economic status households are more likely to experience alcohol-related hospital admissions, a feature that is exacerbated by the same people being more likely to smoke tobacco and have a greater Body Mass Index. Furthermore, about a fifth of parents who drink excessively also consume illicit drugs, suggesting that for a significant minority of families, support should focus on both alcohol and drug use, not just one or the other.
- The EDARA project reported on the feasibility of “Drunk Tanks” to better manage drunkenness in UK city centres. Findings from this project suggest that such facilities are acceptable to those who use them and, in some cases, are preferred to A&E as the very drunk are typically unable to consent to treatment, it is important that diversion away from A&E is acceptable to this group.
- The National Violence Surveillance Network is now in its thirteenth year. This network collects assault-related injury data from A&Es across England and Wales. A newly developed collaboration with the Office for National Statistics now means these data contribute to key national projects looking at understanding the numbers of those who are victims of violence. Most recently, this programme of work has reported that there were 21,489 child attendances at A&Es for violence-related injury.

Linked Research Centres:

Professor Simon Moore is the Co-director of the **Crime and Security Research Institute**, which draws expertise from the Universities’ Police Science Institute, the Alcohol and Violence Research Group, and the Data and Knowledge Engineering Group.

www.cardiff.ac.uk/crime-security-research-institute

The Alcohol and Violence Research Group also works closely with **DECIPHer, the Centre for the Development and Evaluation of Complex Interventions for Public Health Improvement**. DECIPHer has a particular focus on developing and evaluating multi-level interventions that will have an impact on the health and well-being of children and young people.

decipher.uk.net/

Key project summary:

The acceptability of alcohol intoxication management services to users.

Irving A et al, 2019. Drug Alcohol Rev, in press.
doi: 10.1111/dar.13002

Background: Alcohol Intoxication Management Services (AIMS, sometimes known as "drunk tanks") are services that sit between drinkers and Accident and Emergency (A&E). They provide drinkers with a safe place, providing basic medical care for acute alcohol intoxication and minor injuries. Their intention is to reduce admissions to A&E and reduce ambulance journeys to A&E and consequently reduce the burden of drinkers on the NHS. In general, people suffering from acute alcohol intoxication do not require complex medical care, just a safe space to sober up. The important question posed by this study is: "Are they acceptable to users?" This is of importance as the very drunk can't usually consent and may prefer to go to A&E.

Discovery: The study conducted semi-structured interviews with people using a range of AIMS across England and Wales and carried out a survey of AIMS users. The results showed that most AIMS users followed a passive route to the centres, often having no recollection of taking the decision to go there. The theme continues through the interviews with participants unclear on who had treated them or what their roles were. However, the consensus was that the treatment they had received was compassionate and caring and the AIMS provided a safe space for the users to stay while they returned to sobriety. The survey indicated that the main reason for attending the AIMS was drinking, followed by minor injuries or feeling unwell. For the majority, the care required was low level with over 50% reporting they were provided with general support (e.g. having somewhere to sit, being given a sick bowl) or given water. This supports the view that transferring these patients to A&E is not necessary. In the main, respondents were positive about their experience of using AIMS and only a small minority would have preferred to be transferred to A&E.

Importance: The acceptability of a new healthcare service to patients is an important implementation outcome. This study is important given that the decision to attend an AIMS is often taken by someone other than the patient themselves so determining their opinions of the care they received there is key to demonstrating the suitability of the new service. The fact that only a small number would have preferred a different care pathway reflects the suitability of the centres. One important feature from the interviews was the feeling that the AIMS were a safe space, even when the respondents had a limited recall of the events of their attendance there. AIMS were also seen as a suitable intermediate response to going to A&E where users felt they may be a low priority due to the nature of their reason for attending. This study provides the first evidence to demonstrate that the AIMS pathway is not only acceptable to users, but also very popular.

Professor Simon C Moore

MooreSC2@cardiff.ac.uk
+44 (0)29 2074 4246

Professor of Public Health Research, Director of Alcohol & Violence Research Group, Co-director of the Crime and Security Research Institute, publicly appointed by the Welsh Minister for Health as an advisor to the Welsh Government on matters relating to alcohol misuse and substance abuse.

The aim of my research is to translate basic-level, fundamental science and apply it to the real world in order to improve community safety and the health of our communities. My work is multi-disciplinary, crossing psychology, neuroscience, economics, medicine, public health and other disciplines and typically involves practitioners and policy makers. All projects have a clear impact pathway, whether that is to inform policy and practice directly or to seed further work such as an implementation trial. Methods include "big data" data linkage projects, randomised controlled trials, computer modelling and simulation and various other approaches.

Key Publication:

Li C, et al (2019). The costs of negative affect attributable to alcohol consumption in later life: a within-between random longitudinal econometric model using UK biobank. PLos ONE 14(2): e0211357.

Full list at:

www.cardiff.ac.uk/people/view/39454-moore-simon-c

Dr Vaseekaran Sivarajasingam

Sivarajasingam@cardiff.ac.uk
+44 (0)29 2074 2441

Reader in Oral and Maxillofacial Surgery. Director of National Violence Surveillance Network of Emergency Departments in England and Wales. Core member of the Welsh Government, Emergency Care Data Set Implementation Group.

My research includes evaluations of public space CCTV and the measurement of injury from violence using Emergency Department (ED) records. This work demonstrates the reliability and validity of hospital data for this purpose. Stemming from this, I have studied violence using panel data relating to socioeconomic, injury and alcohol variables. I am the Director of the National Violence Surveillance Network (NVSN) of 117 EDs in England and Wales which has provided annual reports on trends in violence-related harm since 2000.

Key Publication:

Sivarajasingam V, et al (2018). Injury resulting from targeted violence: An emergency department perspective. Crim Behav Ment Heal 28(3): 295-308.

Full list at:

www.cardiff.ac.uk/people/view/39421-sivarajasingam-vaseekaran

Professor Jonathan Shepherd

ShepherdJP@cardiff.ac.uk

Emeritus Professor of Oral and Maxillofacial Surgery and Emeritus Professor at the Cardiff University Crime and Security Research Institute. Honorary professor at Deakin University, Australia. Publicly appointed by the Home Secretary as the Academy of Medical Sciences member of the Home Office Science Council. Independent member of the UK Cabinet Office What Works Council. NHS representative on the Welsh Government's ministerial Violence against Women Advisory Board. Founder trustee of the Chartered College of Teaching.

My research on clinical decisions, community violence and the evidence ecosystem has made many contributions to clinical and public policy and to legislation. Prompted by my discoveries I led the development of a prototype community safety partnership which I continue to chair and which was used as a model in the 1998 Crime and Disorder Act which mandated the creation of such partnerships across Great Britain.

Key Publication:

Mercer Kollar LM, et al (2019). Building capacity for injury prevention: a process evaluation of a replication of the Cardiff Violence Prevention Programme in the Southeastern USA. Inj Prev 2019, in press.

Full list at:

www.cardiff.ac.uk/people/view/39410-shepherd-jonathan

Guest Seminars

Owen R, INSIGNEO Institute for In Silico Medicine, University of Sheffield, Sheffield, UK.

"PolyHIPEs in bone tissue engineering."

Fiedler L, OxStem Cardio, University of Oxford, Oxford, UK.

"Translational approaches for driving repair in the cardiovascular system."

Newland B, School of Pharmacy, University of Cardiff, Cardiff, UK.

"Nanoscale and microscale biomaterials for applications in focal drug delivery."

Mackenzie I, Blizard Institute, Barts and The London, Queen Mary University, London, UK.

"***New mechanisms of metastasis of head and neck cancers."***

Caley M, Blizard Institute, Barts and The London, Queen Mary University, London, UK.

"The skin basement membrane, roles beyond cell attachment."

Astašov-Frauenhoffer M, University Center for Dental Medicine, University of Basel, Basel, Switzerland.

"***Oral biofilms and exopolysaccharides."***

Seib P, Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, UK.

"***Silk: Discovery thread for healthcare applications."***

Mahoney P, School of Anthropology and Conservation, University of Kent, Canterbury, UK.

"***Biorhythms and teeth in biological anthropology."***

Chen J, School of Engineering, University of Exeter, Exeter, UK.

"Multiscale tissue biomechanics in bioengineering."

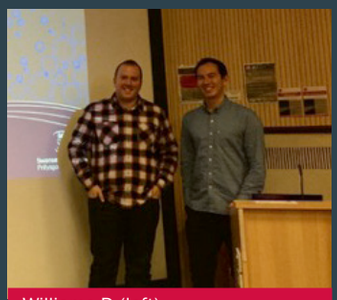
Dawson J, School of Medicine, University of Southampton, Southampton, UK.

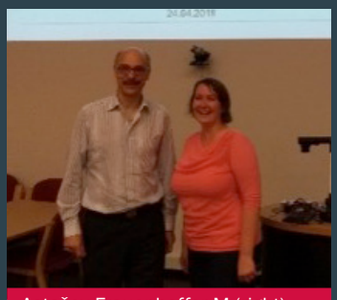
"Harnessing clay for regenerative medicine."

Williams D, School of Chemistry, Swansea University, Swansea, UK.

"Structure by design: engineering functional 'mesomaterials' utilising biodegradable copolymers."

Dawson J


Williams D (left)


Astašov-Frauenhoffer M (right)


Seib P

Research Day

KEYNOTE SPEAKER: Price D, School of Medicine, Cardiff University, Cardiff, UK:

"IELs, celiac disease and TCRs."

PhD successes

Zahraa Amer Hashim

Thesis Title:
Investigating the potential of biosurfactants in the control of tooth infections.

Supervisors:
Professor Rachel Waddington, Dr Melanie Wilson, Professor Jean-Yves Maillard (PHRMY).

Summary:

A shift from the "doomed organ" concept of an exposed pulp to the concept of "hope and retrieval" has been recently adopted with the introduction of vital pulp therapy. microbial contamination of the capped pulp remains a major cause of therapy failure and is the fundamental challenge of contemporary restorative endodontics. Treating endodontic infections costs the NHS in England and Wales around £12M every year. Current endodontic treatment strategies aim to eradicate bacteria from the root canal system by mechanical and chemical means. Besides their cost and time required to deliver treatment, the outcome of these strategies varies considerably, with the success rate ranging from 30- >90%. Biosurfactants are tension-active microbe-derived molecules with a potential anti-microbial/anti-adhesive activity. This project aimed to investigate the role of biosurfactants, especially probiotic bacteria-derived ones (Lp-BS) and a commercially-sourced rhamnolipid as novel endodontic therapies. Lp-BS, extracted from *Lactobacillus plantarum*, and rhamnolipid were tested for their anti-microbial/anti-adhesive activity against four endodontic pathogens. Lp-BS did not show anti-microbial activity, while rhamnolipid inhibited the growth of the four endodontic bacteria effectively. Moreover, two biosurfactants showed the potential to reduce the attachment of the tested pathogen strains onto surfaces coated with these surfactants. Rhamnolipid, when applied to an *ex vivo* rodent tooth model, demonstrated the ability to reduce bacterial attachment and growth in pulpal tissue without eliciting a significant inflammatory response. Lp-BS, on the other hand, exhibited significant toxicity on pulpal cells.

This work has provided the foundation for further investigation of the anti-adhesive, anti-microbial and immune-modulatory roles of Lp-BS and rhamnolipid. It opens future prospects for application of these novel biosurfactants in vital pulp therapies.

Joana Stokniene

Thesis Title:
Design and assembly of tailored oligosaccharides as polymer therapeutics for improved treatment of chronic respiratory disease.

Supervisors:
Dr Elaine Ferguson, Professor David Thomas and Dr Katja Hill.

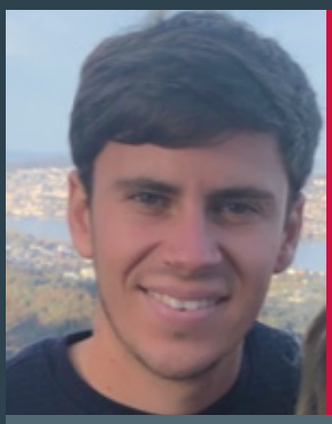
Summary:

Excessive use/misuse of antibiotics, especially in animal husbandry, has contributed to a dramatic increase in antimicrobial resistance. This occurred alongside a decrease in the development of new antibiotic therapies. At present, antibiotic resistance causes >700,000 deaths annually, identifying an area of clear need for alternative strategies to combat such infections. This project aimed to develop a targeted antimicrobial delivery system as an alternative approach to enhance drug efficacy and thereby to address this crisis.

The alginate-oligosaccharide, OligoG CF-5/20, jointly developed with the Norwegian biopharmaceutical company AlgiPharma AS as an inhalation therapy for cystic fibrosis, has previously been shown to inhibit bacterial growth, adherence and biofilm development, and to enhance the efficacy of conventional antibiotics against Gram-negative, multi-drug resistant bacteria. OligoG was further shown to alter mucin hydrogel networks in sputum, supporting its use in the treatment of pathologen-driven respiratory diseases. We hypothesised that conjugation of OligoG to an antibiotic, such as colistin or polymyxin B, could create a bi-functional polymer therapeutic combining the antimicrobial properties of both, polymer and drug, while at the same time reducing systemic toxicity of the polymyxins. Two different conjugation chemistries (ester and amide) were explored.

Antimicrobial activity of the OligoG-conjugates was similar to that of the parent antibiotic, but with more sustained bacterial growth inhibition. Both amide- and ester-linked colistin conjugates significantly disrupted the formation of Pseudomonas aeruginosa biofilms and induced bacterial death. OligoG conjugation also significantly decreased cytotoxicity and inflammatory cytokine production of colistin and polymyxin B when tested on human model cell line. An *in vitro* 'time-to-kill' model using *Acinetobacter baumannii* indicated that OligoG-ester-colistin conjugates reduced viable bacterial counts after 4 h, but no activity was observed in this set-up with OligoG-amide-colistin conjugates.

Amide-bound drug conjugates, which rely on enzyme degradation of the polymer backbone for release, may have reduced antimicrobial activity due to sugar residues remaining attached to the antibiotic. In contrast, drug conjugation via ester linkage appeared to allow complete separation of the parent molecules by esterase enzymes/ hydrolysis and thereby to reinstate the full antibacterial activity of the individual components.



Rob Knight

Thesis Title:

Small extracellular vesicles as anti-scarring agents

Supervisors: Professor Phil Stephens, Professor Aled Clayton (MEDIC), Dr Julie Albon (OPTOM), Dr Randolph Corteling (ReNeuron, Pencoed, Wales, UK)

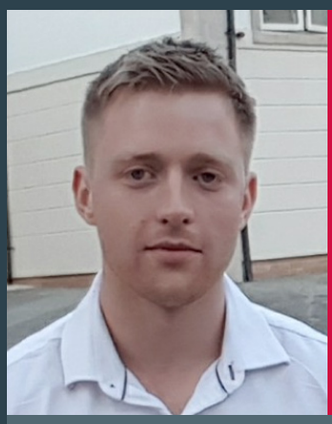
Summary:

Scar tissue formation during wound repair can be devastating for affected individuals and can lead to reduced tissue function or whole organ failure. Our group has previously isolated and characterised a novel, progenitor cell population from the buccal mucosa. These Oral Mucosa Lamina Propria-Progenitor Cells (OMLP-PCs) are multipotent, immuno-suppressive and anti-bacterial. Extracellular vesicles released by cells can constitute important biological signals. The smallest of the extracellular vesicles, termed small extracellular vesicles (sEVs), are of endosomal origin, typically range in size from 30-130nm and have demonstrated an important role in stem cell mediated repair. This project aimed to determine any potential preferential wound healing capabilities as well as anti-scarring capabilities of sEVs in a series of *in vitro* and *ex vivo* models.

Immortalised OMLP-PC lines (OMLP-PCL) demonstrated a normal fibroblast like morphology, expressed the expected progenitor cell markers but demonstrated some differences in respect to their multipotency and immunosuppressive properties. One OMLP-PCL completely mirrored the activities of the related cell strain and hence was utilised to produce sEVs. Vesicles isolated from this OMLP-PCL, were demonstrated to be sEVs as assessed by nanosight, cryo-EM and flow cytometry. OMLP-PCL and mesenchymal stromal cell (MSC) derived sEVs significantly increased both skin fibroblast proliferation and wound repopulation/migration *in vitro*. OMLP-PCL and MSC sEVs were also demonstrated to significantly inhibit myofibroblast formation *in vitro*, with OMLP-PCL sEVs demonstrating a more potent effect. Fluorescently labelled sEVs were taken up by epithelial cells in an *ex vivo* cornea culture model but demonstrated no significant effect on corneal re-epithelisation. Finally, sEVs produced using a scalable GMP compliant manufacturing process were demonstrated to retain these biological activities.

These findings demonstrated the anti-scarring capability of OMLP-PCL derived sEVs and are now undergoing future development and testing prior to *in vivo* analysis.

Publication: Yang Y, Knight R, Stephens P, Zhang Y (2019). Three-dimensional culture of oral progenitor cells: Effects on small extracellular vesicles production and proliferative function. J Oral Pathol Med in press. doi: 10.1111/jop.12981



Joshua Twigg

Thesis Title:

Oral ecosystem modulation and bacterial pneumonia

Supervisors: Professor David Williams, Dr Melanie Wilson, Dr Jonathan Lees (ENGIN)

Summary:

Bacterial pneumonia affects a disproportionate number of the elderly in the UK, with substantial morbidity and mortality. Mounting evidence implicates removable dentures as a potential nidus for respiratory pathogens to form a pathogenic reservoir which could seed colonisation and infection of respiratory tissues in susceptible individuals. However, research evaluating the denture-associated microbiome in patients with an active diagnosis of pneumonia is lacking. This research had two primary aims. Firstly, unrestricted characterisation of denture-associated bacterial communities in pneumonia patients and long-term care home residents, through 16S rRNA gene metataxonomic sequencing. Secondly, development of a model denture acrylic-associated biofilm incorporating clinically relevant respiratory pathogens, to allow exploration of inter-microbial and host-microbial interactions in infection and testing of novel anti-biofilm strategies.

We found significant shifts observed in species composition, diversity and richness in the denture-associated microbiome of pneumonia patients. Importantly, the relative abundance of putative respiratory pathogens in the denture-associated microbiota of pneumonia patients was significantly increased compared with respiratorily healthy care home residents. The magnitude of this increase was approximately tripled in denture-associated bacterial communities compared with other oral sites examined. An *in vitro* model of denture acrylic biofilms incorporating respiratory pathogens was developed and used to test a number of antimicrobial compounds. Additionally, the use of microwave energy delivered using a cavity resonator was tested against these biofilm models. This highly controlled application of microwave energy delivery showed considerable promise as a denture sterilisation modality.

The findings show the importance of the oral microbiota, particularly in denture-associated biofilms as a potential source of pathogens in bacterial pneumonia, paving the way for intervention studies. Furthermore, a promising novel antibiofilm strategy was found to be effective at sterilising acrylic biofilms. Further work is needed to develop microwave applicators to optimise antibiofilm activity without incurring detriment to denture materials.

Publication: Sands KM, Marchesi JR, Lewis MAO, Twigg J, Williams DW, Wilson M, Smith A, Wise MP (2016). Microbial profiling of dental plaque from mechanically ventilated patients. J Med Microbiol 65(2): 147-159.

Clotilde Haury

Thesis Title:

Attachment of peri-implant pathogens to laser melted abutments and the development of a novel antimicrobial coating

Supervisors:

Professor Alastair Sloan, Dr Wayne Nishio Ayre, Professor Rachel Waddington, Mr Quentin Jones, Mr Bryan Austin (Renishaw PLC, Wotton-under-Edge, UK), Mr Andrew Westcott (Renishaw PLC), Mr David Beeby (Renishaw PLC)

Summary:

Dental implant placement is undertaken increasingly frequently to restore the function and aesthetics of missing teeth. The abutment forms the interface between the implant and overlying crown, bridge or denture prosthesis. Despite reasonable long term survival of dental implants overall, inflammation of peri-implant tissues may develop in response to chronic insult from microbial biofilms formed on implant surfaces, leading to implant failure. Despite efforts in developing novel treatments, progression and recurrence of peri-implantitis is a major clinical problem. Therefore, a new focus on prevention rather than treatment of peri-implant conditions is crucial.

I found that the peri-implant pathogens *Fusobacterium nucleatum* (FN) and *Porphyromonas gingivalis* (PG) attached readily to laser melted titanium alloy, Ti6Al4V in the absence of aid from early colonisers and, in the presence and absence of artificial saliva. Interestingly, artificial saliva reduced FN attachment and encouraged the attachment of the more pathogenic PG to laser melted surfaces. A novel antimicrobial abutment coating was developed to reduce bacterial attachment and improve implant survival employing triclosan as the active agent. In the absence of artificial saliva, the triclosan-loaded liposomal coating showed high antimicrobial efficacy against both FN and PG. However, preconditioning of coated surfaces with artificial saliva reduced liposomal antimicrobial activity.

This work identified that the steps leading to bacterial colonisation of oral metallic implants may differ from the currently accepted sequence of events described in the literature. The developed novel liposomal coating demonstrated potential in preventing attachment and proliferation of clinically relevant implant pathogens and may help to reduce peri-implantitis risk in the future.

Shannon Turberville

Thesis Title:

Unravelling the mechanisms by which mutations in transglutaminase 6 cause ataxia.

Supervisors:

Professor Daniel Aeschlimann and Dr Konrad Beck.

Summary:

Transglutaminase 6 (TG6) is an enzyme that is predominantly expressed in a subset of neurons in the central nervous system and involved in the transamidation and deamidation of target polypeptides. Acquired autoimmunity or inherited deficiency resulting in lack of functional protein is associated with progressive neurological dysfunction, most commonly ataxia. Spinocerebellar ataxias (SCA) are a group of neurological diseases characterised by progressive imbalance, motor coordination deficits, and cognitive impairment. Mutations in TG6 have been linked to a specific form of SCA, now referred to as SCA35, using genetic linkage analysis.

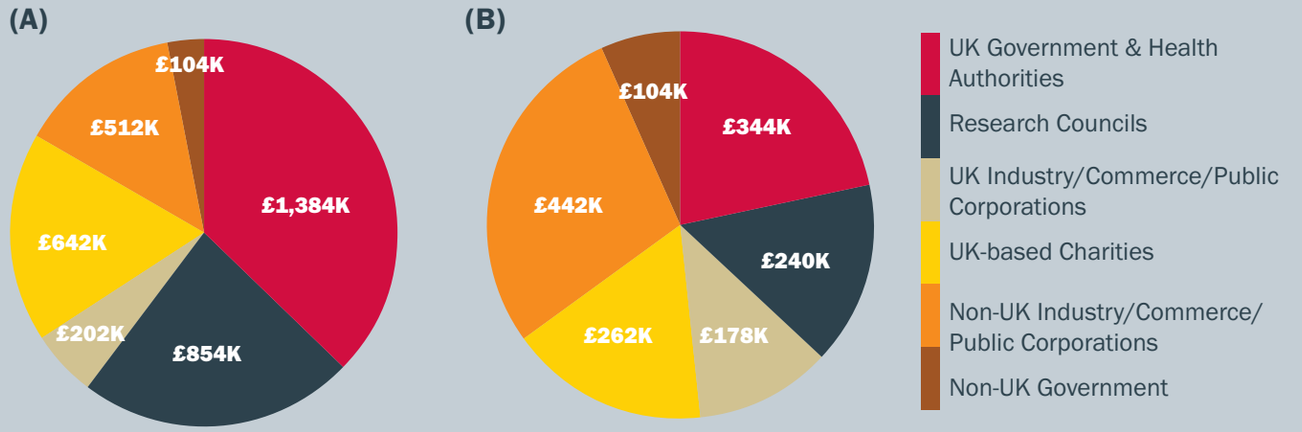
In order to enable future intervention in the underlying disease process, it is important to establish the mechanism by which the pathogenic TG6 mutants cause neurodegeneration. As part of an international consortium, our group has investigated the impact of these TG6 mutants in a cellular context, and has identified that some mutations initiate the unfolded protein response and mutants are targeted for proteolytic degradation by the proteasome, whilst others are not and the reason for their pathogenicity remains elusive (Tripathy *et al.* 2017). Therefore, the main aim of my project was to investigate the structure-function relationship of the pathogenic TG6 mutants. Molecular modelling approaches and bioinformatic analysis were used to assess the impact of TG6 mutations *in silico*, including the impact of mutations on different structural states of the enzyme as relevant to catalysis and on functionally important interactions. This revealed a new class of mutations that impaired function rather than impacting on overall structure. To test the accuracy of these predictions wildtype TG6 and TG6 mutant proteins were produced in an insect cell system at scale, followed by detailed biochemical characterization of proteins with regards to structure, stability and enzymatic functions. Conformational changes caused by the investigated mutations not only affected protein stability, but also compromised enzymatic activity in assays assessing specific functionalities, although to a varying degree. Taken together, these data substantiate the genetic-association findings by revealing functional deficits in the mutant enzymes and revealing that mutants can trigger neuronal cell death through multiple distinct pathways.

Publication: Tripathy D, Vignoli B, Ramesh N, Polanco MJ, Coutelier M, Stephen CD, Canossa M, Monin ML, Aeschlimann P, Turberville S, Aeschlimann D, Schmahmann JD, Hadjivassiliou M, Durr A, Pandey UB, and Basso M (2017). Mutations in TGM6 induce the unfolded protein response in SCA35. Hum Mol Genet 26(19): 3749-3762.

Research Funding

Overview of active grants

Our research groups were part of collaborative research awards with other institutions totalling £3,699K (A) for the financial year 2018-19, with £1,570K (B) being allocated to the School of Dentistry. Research funding for the financial year broken down per sector is given below.



Current major grants

List of substantial grants (≥500K) awarded since 2014 that involve our staff:

- Moore S (co-I) et al, Medical Research Council: "DECIPHer: Centre for the development and evaluation of complex interventions for public health improvement." £2,936K, 2014-19
- Moore S (PI) et al, Economic and Social Research Council: "Alcohol misuse: Electronic, longitudinal alcohol study in communities (ELAStiC)." £987K, 2015-18
- Thomas DW (co-I), Hill KE (co-I) et al, Norwegian Research Council/ AlgiPharma AS: "Treatment of chronic infective disease with alginate oligomer-based formulations." NOK 48,000K ≈ £4,300K (£394K, Cardiff award), 2015-18
- Moore S (PI), Sivarajasingam V et al, The Secretary of State for Health: "An evaluation of alcohol treatment centres: Implications for service delivery, patient benefit and harm reduction." £740K, 2016-18
- Aeschlimann D (co-I) et al, Versus Arthritis: "Arthritis Research UK Biomechanics and Bioengineering Centre Versus Arthritis." £2,000K, 2016-20
- Moseley R (co-I) et al, Qbiotics Ltd: "Elucidation of the underlying mechanisms of action by which novel epoxy-tigliane pharmaceuticals promote preferential wound healing responses." £545K, 2016-20
- Chestnutt I (co-I) et al, Health and Care Research Wales: "PRIME Centre." £1,780K, 2018-20
- Knauper V (co-I) et al, Biotechnology and Biological Sciences Research Council: "The regulation of protective immunity to viruses by L-selectin." £558K, 2019-22

New grants

New grants awarded to our staff in 2018/19 financial year (grants ≥ £40K per annum):

- Aeschlimann D (Principal sponsor), Dewitt S et al, Wellcome Trust ISSF Consolidator Award to Shologu N: "Synovial joint *in vitro* model that is scalable for medium throughput screening appplications." £51K, 2018-19
- Aeschlimann D, Dewitt S (co-I) et al, Versus Arthritis/Cardiff University PhD. "Validation of a stem derived cartilage model for osteoarthritis research and drug screening." £86K, 2018-22
- Ayre WN (PI), Ferguson E (Co-I), Engineering and Physical Sciences Research Council: "Contact angle goniometer and quartz crystal microbalance." £48K, 2018-20
- Ayre WN (Co-I) et al, Versus Arthritis PhD Studentship: "A novel antibacterial titanium implant technology for total joint arthroplasty." £111K, 2019-21
- Chestnutt I (co-I) et al, Health and Care Research Wales: "Developing a decision aid to support shared decision making regarding risk-based recall intervals in general dental practice." £185K, 2018-20
- Ferguson E (co-I) et al, Wellcome Trust ISSF: "Development of a nanomedicine approach to achieve simultaneous targeting of cancer and bacterial infections." £48K, 2018-20
- Knauper V (PI), Cardiff University Vice-Chancellor's International Scholarship for Research Excellence: "Novel cancer drugs EBC-46 and IngM regulate disintegrin and metalloproteinase (ADAM) activity - Impact on tyrosine kinase signalling in head and neck cancer." £130K, 2018-21
- Knauper V (co-I) et al, Biotechnology and Biological Sciences Research Council: "The regulation of protective immunity to viruses by L-selectin." £558K, 2019-22
- Milward P (PI), Farnell D (co-I), Williams D (co-I), Undisclosed industrial sponsor: "Evaluation of the cleaning performance of denture cleansers utilising an *in vitro* stain model with a diverse range of regionally relevant stains." £41K, 2018-19
- Moseley R (PI) et al, QBiotics Ltd: "Evaluation of novel epoxy-tigliane pharmaceuticals as modulators of impaired wound healing responses in chronic wound fibroblasts." £128K, 2018-19
- Sloan A (co-I) et al, Cancer Research Wales: "Mechano-transduction modelling of the bone niche driving prostate metastatic cancer." £147K, 2019-21
- Thomas D (co-I), Ferguson E (co-I), Hill K (co-I), Norwegian Research Council: "Novel alginate oligomer products for enhanced pharmaceutical delivery across mucosal barrier (Mucos-ALG)." £297K, 2018-22
- Thomas D (co-I), Hill K (co-I), Qbiotics Ltd: "Characterisation of novel epoxy-tigliane therapeutics in treatment of multi-drug resistant (MDR) wound and implant infections." £152K, 2019-22
- Waddington R (co-I), Dewitt S (co-I), Sloan A (co-I) et al, The Dunhill Medical Trust: "Identifying a utility for dentally derived extracellular vesicles to restore impaired bone healing associated with age-related systemic conditions." £127K, 2019-21
- Williams D (PI) Milward P (co-I), Undisclosed industrial sponsor: "Effect of brushing with abrasive toothpaste and brush heads on biofilm development and removal." £48K, 2018-20
- Williams D (co-I), Wellcome Trust ISSF: "Novel antibiotic for the treatment of multidrug-resistant Gram-positive bacteria." £50K, 2019-20
- Williams D (PI), Innovate UK: "Evaluation of novel XF drugs as bacterial resistance breakers." £224K, 2019-21

Public Engagement:

Our public engagement covers a wide range of activities, from educational placements to fun games events both in the South Wales area and with international outreach. The public are usually only exposed to the "headline" end results of research programmes that have taken many years to complete, so our engagement activities aim to raise the understanding of our research in progress and highlight to the public the importance and impact of the work on their every day lives.

Science in Health Live!

Science in Health Live! is an annual two-day Cardiff University event which has been running for 25 years. It is the UK's biggest science event for A-level students, designed to give students an insight into the science behind medicine and dentistry, showing them the range of career options open to them in healthcare, but also biomedical and other allied scientific fields. Drs Sarah Bamford, Sarah Youde (pictured), Maria Stack and Mrs Wendy Rowe hosted around 60 A-level students from across Wales and the South West giving presentations and practical demonstrations on microbiology, cell and molecular biology and imaging.

Nuffield Research Placements

Drs Elaine Ferguson and Siân Rizzo (left) provided a Nuffield Research Placement to an A-Level student from Lliswerry School, Newport, Gwent. The purpose of these placements are to offer students from a low socio-economic background the opportunity to spend 4-6 weeks in a STEM laboratory at a local University. The student, Bassmala Morkaz (right) was able gain experience in laboratory research in a leading research laboratory and ultimately produced a poster on the work she did which was presented at the celebration evening for all the local Nuffield Placement students held at Techniquest, Cardiff. Guest speakers at the event were Nobel Laureate Professor Sir Martin Evans and Chief Scientific Officer for Wales, Peter Halligan.

Science Pirates

Funded through a Wellcome Trust ISSF3 Public Engagement Proof of Concept Award, Science Pirates aimed to help the public to contemplate the following question: "Muscles respond to exercise by getting bigger and stronger, but how do bones respond?" A contemporary escape room concept was developed to provide a mental and physical adventure-based game to help participants answer this question. The pirate-theme escape room made it fun and provided the link to bones via the skull and crossbones image. Using a treasure map and decoding sheet, players navigated the escape room to identify answers needed to unlock a treasure box and escape. The decoding sheet encompassed questions related to bone biology, and the answers were found as QR codes which players scanned using a tablet to play information video clips to make it contemporary. The image shows an advertisement for the activity in the main shopping street of Cardiff. This was a runaway success attracting over 200 participants.

Child Health in Namibia

Senior clinical lecturer Dr Ilona Johnson and 4 final year dental students spent two weeks in Namibia as part of the University's Phoenix Project, a highly successful partnership between Cardiff University and the University of Namibia focusing on education and research in areas such as IT, mathematics, health and communication. The team used fun games and other interactive educational tools to help educate the children about the importance of oral health.

"It has been a massive success. We hope that this project is going to make a big difference in Namibia because we collected really good data."

Dr Nguundja Uamburu, Head of Dentistry at Katutura State Hospital

Research Awards:

IADR William J Gies prize

Professor Ivor Chestnutt

This award is given to the lead author of the best paper published in the Journal of Dental Research in the period of 1 July to 30 June in the period preceding the IADR General Session.

Chestnutt I et al, Fissure Seal or Fluoride Varnish? A Randomised Trial of Their Relative Effectiveness. J Dent Res 96(7): 754-761, 2017

Professor Chestnutt (third left) receiving the award from Professors D'Souza, (President of the IADR), Giannobile, (Editor of the Journal of Dental Research), and Ryan, (President of the American Association for Dental Research).

European Orthodontic Society Professor WJB Houston Research Award

Dr Caryl Wilson-Nagrani

This award is given in memory of Professor WJB Houston, Past President of the European Orthodontic Society to the best original, unpublished research in a field of orthodontic interest presented at the European Orthodontic Society Congress.

Publications 2019

Abbas HH, Hicks Y, Zhurov A, Marshall D, Claes P, Wilson-Nagrani C, Richmond S (2019). An automatic approach for classification and categorisation of lip morphological traits PLoS ONE 14(10): e0221197. doi: 10.1371/journal.pone.0221197

Ahmad P, Dummer P, Chaudhry A, Rashid U, Saif S, Asif JA (2019). A bibliometric study of the top 100 most-cited randomized controlled trials, systematic reviews and meta-analyses published in endodontic journals. Int Endod J 52(9): 1297-1316. doi: 10.1111/iej.13131

Al-Qarakhli A, Makki A, Yusop N,O'Brien-Waddington R, Moseley R (2019). Effects of high glucose conditions on the expansion and differentiation capabilities of mesenchymal stromal cells derived from rat endosteal niche. BMC Mol and Cell Biol 20: 51. doi: 10.1186/s12860-019-0235-y

Alraies A, Canetta E, O'Brien-Waddington R, Moseley R, Sloan A (2019). Discrimination of dental pulp stem cell regenerative heterogeneity by single cell raman spectroscopy. Tissue Eng Pt C Meth 25(8): 489-499. doi: 10.1089/ten.TEC.2019.0129

Alraies A, Cole D, Rees J, Glasse C, Young N, Waddington R, Sloan A (2019). Real-time binding kinetic analyses of the interaction of the dietary stain Orange II with dentin matrix. J Dent 80: 80-88. doi: 10.1016/j.jdent.2018.06.001

Alraisi H., Dummer P, Vianna M (2019). How is endodontics taught? A survey to evaluate undergraduate endodontic teaching in dental schools within the United Kingdom. Int Endod J 52(7): 1077-1085. doi: 10.1111/iej.13089

Aresi G, Moore S, Berridge D, Marta E (2019). A longitudinal study of European students' alcohol use and related behaviours as they travel abroad to study. Subst Use Misuse 54(7): 1167-1177. doi: 10.1080/10826084.2019.1567787

Atkin PA (2019). Human disease/clinical medical sciences for dentistry in early-years dental graduates: Transition from undergraduate study to clinical practice. Eur J Dent Educ 23(2): 199-203. doi: 10.1111/eje.12420

Atkin P, Cunningham A, Andrews L (2019). Specialty trainee views on the medical and oral disease: Elements of a special care dentistry curriculum. Eur J Dent Educ, in press. doi: 10.1111/eje.12465

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Nagoya University
Nagoya, Japan

Qatar University,
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Doha, Qatar

Isfahan University
Iran

Faculty of Dentistry,
University of Malaya,
Kuala Lumpur, Malaysia

Faculty of Dentistry,
Chiang Mai University,
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University Dental Hospital
Heath Park
Cardiff
CF14 4XY
dentalhos@cardiff.ac.uk
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