Sir John Walsh Research Institute Research Symposium 2016

Thursday 1 and Friday 2 September
Dunedin Public Art Gallery

Programme and Abstracts

Sir John Walsh Research Institute

The Sir John Walsh Research Institute (SJWRI), a Research Centre of the University of Otago, advances research and increases knowledge for the improvement of oral health in New Zealand, and provides a national focus for dental research. The Institute's innovative, future-focused, interconnected research programmes cover the spectrum of oral health research, from the molecular, through biological systems to the health of populations.

The SJWRI is integral to New Zealand's only Faculty of Dentistry, ranked as one of the best dental schools in the world, and its members have well-established productive collaborations across the University and with other institutions in New Zealand and worldwide. Our mission is to undertake research that underpins our teaching and clinical practice, and that translates discoveries into measurable health improvements for all New Zealanders. The Institute is named after Sir John Walsh, Dean of Dentistry from 1946 to 1971, a strong advocate for research in dentistry and oral health.

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The 2016 SJWRI Research Symposium is made possible by the generous support of 3M Oral Care.

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Symposium programme

Thursday, 1 September 2016

8.30am *Registration* DPAG Auditorium, Level 1

9.00am *Welcome*

Professor John Broughton
ASSOCIATE DEAN (MĀORI), FACULTY OF DENTISTRY

Professor Paul Brunton
DEAN, FACULTY OF DENTISTRY

Professor Richard Cannon
DIRECTOR, SIR JOHN WALSH RESEARCH INSTITUTE

CLINICAL AND TRANSLATIONAL RESEARCH I (Auditorium)

CHAIR: PROFESSOR RICHARD CANNON

9.15am Professor Ian Tucker
ASSOCIATE DEAN (RESEARCH COMMERCIALISATION), DIVISION OF HEALTH SCIENCES

9.35am Professor Warwick Duncan

10.10am Del Carlini
BLIS TECHNOLOGIES

10.30am Morning tea in the ODT Gallery
3M ORAL CARE DISPLAY

CLINICAL AND TRANSLATIONAL RESEARCH II (Auditorium)

CHAIR: PROFESSOR WARWICK DUNCAN

11.00am Associate Professor Brian Monk
Contracted research

11.20am Dr Dawn Coates
Could geranylgeraniol be a treatment for Bisphosphonate-Related Osteonecrosis of the Jaw?

11.40am Dr Carolina Loch Santos da Silva
From the laboratory to clinical practice and back: ultrastructure and properties of carious deciduous teeth treated using the Hall Technique

12.00pm Mohammad Alansary, PhD candidate
Primary teeth pulp cells, not only MSCs, but a population with a unique "stem cell" signature

12.15pm Leonid Lander, DClinDent candidate
Alveolar ridge preservation in the sheep model

12.30pm Lunch in the ODT Gallery
3M ORAL CARE DISPLAY

DENTAL EPIDEMIOLOGY AND PUBLIC HEALTH I (Auditorium)

CHAIR: PROFESSOR MURRAY THOMSON

1.15pm Dr Dara Shearer
Periodontitis and early CVD markers

1.30pm A/Prof Lyndie Foster Page
Oral health-related quality of life in Northland young people

1.45pm Daniel Sim [H]
Exploring socioeconomic status differences in young children's oral health

2.00pm Deanna Beckett [M]
Concordance between the CPQ_{11-14} ISF:16 and the CHU9D among participants in a clinical trial

2.15pm Dr Susan Moffat
New Zealand's School Dental Service: Adapting in times of change

[B] BDS STUDENT
[H] BDS (HONOURS) STUDENT
[D] DOCTORATE OF CLINICAL DENTISTRY (DCLINDENT) CANDIDATE
[M] MASTER OF PUBLIC HEALTH CANDIDATE
[P] DOCTOR OF PHILOSOPHY (PHD) CANDIDATE

MOLECULAR MICROBIOLOGY I (Conference Room, Level 2)

CHAIR: ASSOCIATE PROFESSOR GEOFFREY TOMPKINS

1.15pm Golnoush Madani [P]
Role of cysteine residues in Candida albicans Cdr1p efflux pump expression and function

1.30pm Danyon Graham [B]
The molecular basis of triazole inhibition of an antifungal target

1.45pm Alia Sagatova [P]
Investigating triazole mediated resistance in yeast

2.00pm Dr Mikhail Keniya
Structure of the azole drug target from pathogenic fungi

2.15pm Syarida Safii [P]
Effect of medical-grade manuka honey on dental plaque-associated bacteria and hydroxyapatite beads in vitro

2.30pm Dr Peter Cathro
Proteomic analysis of Enterococcus faecalis cell membrane proteins under alkaline stress conditions

2.45pm Afternoon tea in the ODT Gallery
3M ORAL CARE DISPLAY

DENTAL EPIDEMIOLOGY AND PUBLIC HEALTH II (Auditorium)

CHAIR: PROFESSOR MURRAY THOMSON

3.15pm Dr Jonathan Broadbent
Oral-health-related beliefs, behaviours and outcomes: a life-course study

3.30pm Prof Murray Thomson
Steering clear of the fashionable in oral health research

MOLECULAR MICROBIOLOGY II (Conference Room)

CHAIR: ASSOCIATE PROFESSOR GEOFFREY TOMPKINS

3.15pm James Dawson [D]
Implant surface decontamination - an ex vivo study investigating the effects of diode laser irradiation on implant surface biofilm

3.30pm Dr Nick Heng
Streptococcus kieseri sp. nov. from the New Zealand brushtail possum

3.45pm Gemma Cotton [P]
Silver nanoparticle-based hydrogel for treatment of periodontal disease

4.00pm SJWRI Research Symposium Poster Session, ODT Gallery
Drinks and nibbles

Friday, 2 September 2016

8.30am *Registration* DPAG Auditorium, Level 1

9.00am **Keynote presentation** (Auditorium)
Professor Alison Rich
The microenvironment of Oral Squamous Cell Carcinoma

9.25am 3M Oral Care presentation, Janice Pitt
How good are your connections? It's in the Science, not magic!

CRANIOFACIAL BIOLOGY AND CLINICAL ORAL PHYSIOLOGY I (Auditorium)

CHAIR: DR LI (PETER) MEI

9.45am Associate Professor Julia Horsfield
DEPARTMENT OF PATHOLOGY, DUNEDIN SCHOOL OF MEDICINE
How zebrafish can help understand craniofacial biology

10.15am Catherine Carleton, DClinDent candidate
A novel model for exploring the causes and treatments of craniofacial birth defects

10.30am **Morning tea in the ODT Gallery**
3M ORAL CARE DISPLAY

CRANIOFACIAL BIOLOGY & CLINICAL ORAL PHYSIOLOGY II (Auditorium)

CHAIR: DR LI (PETER) MEI

11.00am A/Prof George Dias
DEPARTMENT OF ANATOMY
Resorbable keratin-based biopolymer as a bone substitute material

11.30am Yana Itskovitch [D]
Engineering 3-D constructs of human bone matrix in a mechanically-active environment

11.45am Gareth Benic [D]
Efficacy of oral probiotics in managing biofilm formation in patients wearing fixed orthodontic appliances

12.00pm Ghassan Idris [P]
Efficacy of twin-block for the treatment of paediatric sleep disordered breathing: a randomised clinical tria

12.15pm Carrol Jin [H]
Survival analysis of different orthodontic retainers

DENTAL EDUCATION
(Conference Room)

CHAIR: DR LEE ADAM

11.00am Dr Lee Adam
Evaluate to improve: Useful approaches to student evaluation

11.30am Hanna Olson
Perceived stressors of Bachelor of Oral Health students

11.50am Calum Fisher [H]
Development of a social accountability measure for the dental environment

12.10pm Dr Lee Smith
Undergraduate oral health student and teachers' understandings of professionalism

12.30pm **Lunch in the ODT Gallery**
3M ORAL CARE DISPLAY

ORAL MOLECULAR AND IMMUNOPATHOLOGY I (Auditorium)

CHAIR: PROFESSOR ALISON RICH

1.15pm Dr Benedict Seo
Profiling the effect of endoplasmic reticulum stress in oral cancer

1.45pm Muhammed Yakin [D]
Endoplasmic reticulum stress modulates the pathogenesis of oral cancer through STAT3-pathway-dependent immune responses

2.15pm Hina Narayan [P]
Cigarette smoke, DNA methylation and oral cancer

BIOMATERIALS AND ORAL IMPLANTOLOGY I (Conference Room)

CHAIR: ASSOCIATE PROFESSOR NEIL WADDELL

1.15pm Lisa Falland [P]
Development of a translucent brain simulant for ballistic testing

1.45pm Wendy Jansen van Vuuren
Effect of condensation on flexural strength of porcelain

2.15pm Abdullah Barazanchi [D]
Examination of novel 3D printed cobalt chromium alloy and its applications in dentistry

2.45pm **Afternoon tea in the ODT Gallery**
3M ORAL CARE DISPLAY

ORAL MOLECULAR AND IMMUNOPATHOLOGY II (Auditorium)

CHAIR: PROFESSOR ALISON RICH

3.15pm Kullasit Chutipongpisit [D]
Lymphangiogenic factors in oral cancer

3.45pm Dr Haizal Hussaini
Research in oral cancer - where to from now?

BIOMATERIALS AND ORAL IMPLANTOLOGY II (Conference Room)

CHAIR: ASSOCIATE PROFESSOR NEIL WADDELL

3.15pm Frances Ruddiman [D]
To be advised

3.35pm A/Prof Neil Waddell
Building stability of dental porcelains: particle size, shape, and distribution

4.00pm **Presentation of Institute and Symposium Awards, ODT Gallery**
Closing remarks from Professor Richard Cannon, SJWRI Director
Drinks and nibbles

Abstracts

Thursday sessions

Author affiliations are University of Otago unless otherwise noted.

WELCOME

Thursday 9.00am-9.15am, DPAG Auditorium (Level 1)

Professor John Broughton
ASSOCIATE DEAN (MĀORI), FACULTY OF DENTISTRY

Professor Paul Brunton
DEAN, FACULTY OF DENTISTRY

Professor Richard Cannon
DIRECTOR, SIR JOHN WALSH RESEARCH INSTITUTE

CLINICAL AND TRANSLATIONAL RESEARCH

Thursday 9.15am-12.30pm, DPAG Auditorium (Level 1)

Session chair: Professor Richard Cannon (Session I), Professor Warwick Duncan (Session II)

9.15-9.35am

Professor Ian Tucker

ASSOCIATE DEAN (RESEARCH COMMERCIALISATION)
DIVISION OF HEALTH SCIENCES

The Division of Health Sciences promotes research excellence by encouraging the development of products, services, and policies that provide health, social, and economic benefits.

Universities are the intellectual powerhouses of New Zealand. We are actively pursuing the translation of our research into products and services because that will benefit our society—health, wellbeing and the economy.

Professor Ian Tucker is Health Sciences Associate Dean for Research Commercialisation. He provides strategic overview for the Division in the translation of these discoveries into practical applications.

http://www.otago.ac.nz/healthsciences/research/innovation

9.35-10.10am

Professor Warwick Duncan

Preclinical model, Clinical question

SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY

How do preclinical animal models relate to Clinical and Translational Research? Translation from "bench to bedside" has been defined as "the process of applying discoveries generated during research in the laboratory, and in preclinical studies, to the development of trials and studies in humans" (Rubio et al. 2010), the desired endpoint being "the production of a promising new treatment that can be used clinically or commercialized ("brought to market")." (Woolf 2008). At Te Kaupeka Pūniho, our research team has developed various animal models for initial testing of dental devices and materials, prior to use in human patients. This presentation will discus the relationship between preclinical and clinical research, using examples from our research.

10.10-10.30am

Del Carlini

BLIS TECHNOLOGIES

Blis Technologies is a company that commercialises science, and specifically the science originally developed by Professor John Tagg of the Microbiology Department at Otago University. Blis has had an erratic commercial history since its inception, but over the past two years has settled into a more coherent business with revenues rising in excess of 100% for each of the past two years and the company has given the NZX guidance that it is on course for revenues of $8 million and to achieve profitability for the first time. Del Carlini will present the 10 key essentials critical for the commercialisation of science based on the lessons from the Blis Technologies experience.

For the past 25 years Del Carlini has developed a career in business strategy with a specialisation in marketing and communications. He has a science degree, a masters in economics and is near the end of a PhD in military strategy through the Otago University Department of Politics. He is a part time lecturer in that department teaching Foreign Policy and has also

been an advisor to the board and management of Blis Technologies since 2014.

11.00-11.20am

Associate Professor Brian Monk

Contracted research

SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY

Contracted research is a form of translational research that presents significant opportunity for the School of Dentistry to work with and be rewarded by clients wishing to utilize the clinical and research skills of faculty. I will use my experience over the last four decades to discuss how contracted research can be undertaken and used to help research flourish.

11.20-11.40am

Dr Dawn Coates

Could geranylgeraniol be a treatment for Bisphosphonate-Related Osteonecrosis of the Jaw?

DE Coates, S Zafar, MP Cullinan, TJ Milne, BK Drummond, GJ Seymour

SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY

Aim: To investigate whether geranylgeraniol (GGOH) can reverse the *in vitro* effects of zoledronic acid (ZA) on cells associated with Bisphosphonate-Related Osteonecrosis of the Jaw (BRONJ).

Methods: The effects of ZA and GGOH on human primary gingival fibroblasts, alveolar osteoblasts, and monocyte-derived osteoclasts were investigated. All primary cells were phenotyped and three patients used to generate each primary cell type. *In vitro* assays conducted included proliferation, apoptosis, gene expression and protein production. In addition osteoblast assays for bone nodule formation, mineralisation and migration where conducted. TEM was used to investigate the cellular morphology in response to ZA and GGOH treatment.

Results: In human gingival fibroblasts and alveolar osteoblasts GGOH reversed the effects of ZA on proliferation, apoptosis and migration. Significant fold regulation changes in angiogenic and osteogenic genes when treated with ZA were partially reversed with GGOH. Osteoclasts upregulated the anti-angiogenic gene CXCL10 in response to ZA. TEM revealed that ZA induced morphological changes consistent with apoptosis and that GGOH resulted in the appearance of intracellular vesicles associated with cell recovery.

Conclusion: Since 2010 when Pharmac started funding the intravenous ZA drug Aclasta®, there has been a dramatic rise in the number of patients receiving this therapy in NZ (317 in 2010 to 10,820 in 2015). A treatment regime for those patients that develop BRONJ is problematic and there is no currently accepted drug therapy. This research indicates the possible therapeutic potential of GGOH in reversing the adverse effects of ZA, which can result in BRONJ.

11.40am-12noon

Dr Carolina Loch Santos da Silva

From the laboratory to clinical practice and back: ultrastructure and properties of carious deciduous teeth treated using the Hall Technique

C Loch, L Jansen van Vuuren, W Duncan, D Boyd, L Foster Page

SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY

Aim: The Hall Technique (HT) is a non-invasive, durable and patient-friendly treatment alternative for the management of caries in primary teeth. Advantages include no need for anaesthetics, tooth preparation or caries removal. Ongoing clinical trials in NZ suggest a higher success compared to conventional restorations. Here we examined the ultrastructural, biomechanical and chemical properties of exfoliated HT-treated carious teeth compared to conventional stainless steel crowns (SSC).

Methods: 12 HT-treated and 5 control SSC deciduous molar teeth were embedded in methyl methacrylate, sectioned, radiographed, mounted and polished. Mechanical properties of carious and sound tissue were quantified using nanoindentation. Thick-sections were then carbon-coated and examined via scanning electron microscopy imaging (SEM) and energy-dispersive X-rays (EDX).

Results: Elastic modulus (E) and hardness (H) values for sound enamel averaged 97.4 and 4.51 GPa, while dentine averaged 26.38 and 0.92 GPa respectively. Mean E and H values for carious lesions averaged 15.03 and 0.51 GPa for HT-treated teeth, while control specimens averaged 25.32 and 1.18 GPa. SEM images showed evidence of extensive demineralisation and hard-tissue damage and loss in carious areas. Chemical mapping using EDS showed lower Ca/P ratios for in carious lesions in HT-treated teeth (1.97) compared to controls (2.07).

Conclusion: Lower mechanical properties values and lower Ca/P ratios in HT-treated teeth reflect the lack of caries tissue removal during clinical intervention. Future analyses with larger samples and an *in vitro* model will help us elucidate reasons for clinical effectiveness of the Hall Technique.

12.00-12.15pm

Mohammad Alansary

PhD candidate

Primary teeth pulp cells, not only MSCs, but a population with a unique "stem cell" signature

M Alansary, B Drummond, L Friedlander, GJ Seymour, MP Cullinan, DE Coates

SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY

Aim: The aim of this study was to characterise primary teeth pulp cells at the three defined stages of root

resorption through *in-vitro* immunocytochemistry and differentiation studies.

Methods: Primary teeth pulp cells were isolated and cultured by the explant culture technique from three stages of root resorption. Characterisation via immunocytochemistry and flow cytometry was performed followed by differentiation into the three germ layers, neuronal and cardiomyocytes progenitors.

Results: Primary teeth pulp cells from all groups of root resorption expressed the mesenchymal "stromal" cell markers CD90, CD105, and CD73 proteins, which was further confirmed quantitatively using flow cytometry fulfilling the requirements proposed by the International Society of Cellular Therapy. In addition, cells expressed the neural progenitor markers nestin and DLX2, and embryonic stem cell markers Oct4, NANOG and SOX2.

The differentiation of the primary teeth pulp cells into the embryonic germ layers was confirmed by the expression of Otx2 (Ectoderm), Brachyury (Mesoderm) and SOX17 (Endoderm). In addition; cells differentiated into cardiomyocyte progenitors expressing TNNT2 and KNX2.5. Neuronal induction was confirmed through the expression of the neural stem cell markers nestin, SOX1, SOX2 and PAX6.

Conclusion: Primary teeth pulp cells can be classified as a unique heterogeneous population of "ectomesenchymal" cells with a "pluripotent stem cell" signature.

There was no detected difference in stem cell marker expression or the differentiation potential among root resorption groups. This research revealed that primary pulp stem cells can produce neural, cardiomyocyte and germ layer lineages for clinical applications.

12.15-12.30pm

Leonid Lander
DClinDent candidate (Periodontology)

Alveolar ridge preservation in the sheep model

L Lander, J Leichter, PR Schmidlin, WJ Duncan

SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY

Post extraction remodelling of the alveolar ridge results in significant reduction in the width of the ridge, which may preclude the placement of dental implants. Alveolar ridge preservation (ARP) procedures have been shown to reduce these changes, and thus are desirable, especially when the buccal plate is partially missing. Bovine-derived xenografts with porcine collagen membrane (BX) are considered the "gold standard" against which novel ARP materials should be compared. Four equine collagen products developed for ARP were tested: membrane (CM), cone with/without biphasic phosphate particles (CC, CO), and cone with integrated membrane (CS).

Aim: To compare four novel products against BX in a novel sheep mandibular extraction socket model with standardised buccal defect.

Methods: In 11 animals, mandibular premolars were extracted and standardised 5x2 mm buccal dehiscence defects were created. The sockets were grafted (Latin-square allocation) with BX, CC, CS, CO, CO+CM or ungrafted control (CON). The animals were euthanised after 16 weeks. Socket healing, new bone formation and reduction in the alveolar ridge width were analysed in undemineralised sections.

Results: No distinctive pattern of healing was noted for any of the materials. BX particles were partially resorbed by osteoclast-like multinuclear cells. Remnants of equine collagen-based products were not observed. BX grafted sites, compared to CON, showed a threefold decrease in reduction of the alveolar ridge width ($p=0.002$). Width preservation achieved by equine collagen products compared to non-grafted controls was not statistically significant, however better results were observed in groups CS and CO+CM.

Conclusion: A challenging extraction socket model with buccal defects representative of a "real-life" clinical situation was created. The test materials did not preclude new bone formation and were completely resorbed during the healing period, whereas BX-grafted sites have shown only partial resorption of the graft. The test materials, unlike the "gold standard" BX, were unable to demonstrate significant width preservation, although the results suggested that barrier membranes play an important role in ARP procedures.

DENTAL EPIDEMIOLOGY AND PUBLIC HEALTH

Thursday 1.15-4.00pm, DPAG Auditorium (Level 1)

Session chair: Professor Murray Thomson

1.15-1.30pm

Dr Dara Shearer

Periodontitis and early CVD markers

DM Shearer[1], WM Thomson[1], CM Cameron[2], G Wilson[3]

1. DEPARTMENT OF ORAL SCIENCES AND SIR JOHN WALSH RESEARCH INSITUTE, FACULTY OF DENTISTRY
2. DEPARTMENT OF PREVENTIVE AND SOCIAL MEDICINE
3. DEPARTMENT OF OPHTHALMOLOGY

Aim: To examine associations between periodontitis at ages 32 and 38 and retinal vascular abnormalities at age 38.

Methods: Periodontal probing depth and bleeding on probing data collected during the age-32 and age-38 assessments in the Dunedin Multidisciplinary Health and Development Study were used to quantify inflamed periodontal tissue and intra-oral inflammatory load. Digital retinal vascular imaging data were collected during the age-38 assessment. Retinal vascular calibres were summarised as central retinal artery equivalent (CRAE) and central retinal vein equivalent (CRVE). Multiple regression models were used to examine associations between CRVE and (1) the inflammatory load at age 38 and (2) the change in inflammatory load between ages 32 and 38.

Results: Neither the inflammatory load of periodontitis at 38 nor the changes in inflammatory load 32-38 were found to be associated with changes in the retinal microvasculature. On average, men had a bigger CRVE than women, and smokers had a bigger CRVE than non-smokers.

Conclusion: Periodontitis was not found to be associated with changes in the retinal microvasculature at this relatively early stage in the life course. It is possible that that any influence of periodontitis on cardiovascular health develops later in life. However, it is also possible that periodontitis is not involved in the causal chain comprising systemic inflammation, retinal microcirculation and CVD risk.

1.30-1.45pm

Associate Professor Lyndie Foster Page

Oral health-related quality of life in Northland young people

E Clark[1], LA Foster Page[2], K Larkins[1], WM Thomson[2]

1. ORAL HEALTH UNIT, NORTHLAND DISTRICT HEALTH BOARD
2. DEPARTMENT OF ORAL SCIENCES AND SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY

Aim: To investigate whether a tooth brushing programme improves young people's oral health-related quality of life in a community with high caries experience.

Methods: A tooth brushing intervention trial was conducted in five Northland Schools. One large school was designated the intervention school with the others acting as the control. The intervention school had a supervised 2-minute brushing protocol implemented after lunch every school day. Baseline and follow-up data were collected in February and December 2015. This included the short-form 16-item impact CPQ11-14 OHRQoL measure. Clinical examinations were conducted in community clinics with posterior bite-wing radiographs taken. These were read later and used to adjust the caries diagnoses for the mesial, occlusal and distal surfaces of the primary and permanent posterior teeth. Mean CPQ11-14 and domain scores were compared at baseline and follow-up using paired t-tests. Effect sizes were calculated by dividing the mean of the change in scores by the standard deviation of the baseline score, in order to give a dimensionless measure of effect.

Results: 240 children were followed up (72%) at 9 months, with slightly fewer than half (46%) in the tooth brushing group. Children in the study (48% female) ranged in age from 10 to 13 years, with nearly two-thirds Māori. The overall mean dmft/DMFT was 6.5 (SD 3.3). The overall mean CPQ11-14 scores at baseline and at follow up were 12.2 (SD 7.6) and 10.0 (SD 7.1) respectively, showing an overall significant improvement in OHRQoL in Northland children. Children taking part in the tooth brushing intervention had a significant improvement in both domains (symptoms and wellbeing) and overall OHRQoL (paired t-tests, $P<0.001$). A moderate effect size (0.5) for OHRQoL improvement was seen in the tooth brushing group, with no real effect seen in the control group (0.1).

Conclusion: A tooth brushing programme in Northland had a significant positive effect on young people's OHRQoL.

1.45-2.00pm

Daniel Sim
BDS (Honours) student

Exploring socioeconomic status differences in young children's oral health

D Sim[1], L Foster Page[1], WM Thomson[1], CM Cameron[2]

1. DEPARTMENT OF ORAL SCIENCES AND SIR JOHN WALSH RESEARCH INSITUTE, FACULTY OF DENTISTRY
2. DEPARTMENT OF PREVENTIVE AND SOCIAL MEDICINE

Aim: This project aims to compare different measures of SES in describing caries experience and self-reported quality of life in young children. The validity of the Scale of Oral Health Outcomes for 5-year-old children (SOHO-5) will also be examined.

Methods: This cross-sectional study utilises the baseline data collected from an ongoing randomised controlled trial in Wanganui. All children who were aged 3 to 7 years and enrolled in Wanganui Community Oral Health Service were initially invited to participate in the trial. The baseline data included socio-demographic information (age, sex and ethnicity), and included four measures of SES (NZDep, NZiDep, school decile and parental education). Children completed the 11-item SOHO-5 questionnaire. Examinations were conducted in dental clinics. Bitewing radiographs were taken at the time of the clinical examination and used to adjust the caries diagnosis. The data was analysed using Stata 14 IC.

Results: 501 children were included in the study. Children (47.5% female) ranged in age from 3 to 8 years, with 32.5% Māori. Their mean dmfs was 5.8 (SD 6.5). The mean SOHO-5 score was 1.3 (SD 1.9, range 0-12). Māori children were found to have significantly higher caries experience (13.5% caries free, mean dmfs 8.1) than non-Māori children (31.8% caries free, mean dmfs 5.7). While the different SES measures showed varying levels of correlation with caries experience, children with lower socioeconomic status generally had greater caries experience regardless of the choice of

SES measure. The SOHO-5 demonstrated validity across quantitative and qualitative oral health indicators.

2.00-2.15pm

Deanna Beckett

Master of Public Health student

Concordance between the CPQ_{11-14}ISF:16 and the CHU9D among participants in a clinical trial

D Beckett[1], LA Foster Page[1], WM Thomson[1], CM Cameron[2], G Wilson[3]

1. DEPARTMENT OF ORAL SCIENCES AND SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY
2. DEPARTMENT OF PREVENTIVE AND SOCIAL MEDICINE

Aim: To investigate the feasibility of obtaining quality adjusted life years (QALY) information using a general health measure (CHU-9D) as a proxy for oral-health-related quality of life measures.

Methods: We used the CHU-9D to measure quality of life (QoL) in children, as well as the 16-item CPQ_{11-14} to measure oral-health-specific QoL, in a study in which children were followed for up to four years. Dental health and socio-demographic data were collected throughout. This presentation will describe the preliminary results from this work.

Results: The overall mean dmfs for participants was 6.4 (6.8 SD), with 18% recorded as having no caries. Caries experience in the permanent dentition was low, with no children presenting with a DMFS score above 1. The mean score for the CPQ_{11-14}ISF:16 was 11.7 (8.6 SD). The mean CHU9D score was 0.88 (0.09 SD). More results will be presented.

2.15-2.45pm

Dr Susan Moffat

New Zealand's School Dental Service: Adapting in times of change

SIR JOHN WALSH RESEARCH INSTITUTE, UNIVERSITY OF OTAGO

This historical research project used key sources, such as the New Zealand Dental and Oral Health Therapists' Association oral archives and the *New Zealand School Dental Service Gazettes*, to trace the development of New Zealand's School Dental Service (SDS). The SDS was established as a unique solution to an overwhelming health issue. Supported by New Zealand's welfare state policies, the Service went from strength-to-strength with its goal to extend care to all children, a resolve tested by economic depression, war, and the 'baby boom'. Despite these difficulties, the SDS developed innovative solutions to issues encountered, bringing more children under its care each year and, at the same time, offering aid to other countries wishing to establish similar services. Oral health surveys conducted during the 1970s, however, would reveal that New Zealand children had heavily-filled teeth and that adults were still losing their teeth at an early age. Nevertheless, the SDS proved adaptable and willing to change, implementing a new caries diagnosis and preventive programme which rapidly reduced the filling rate. Unfortunately, the SDS would face further problems over the next few decades, with cuts in funding in the 1970s and 1980s leading to the Service becoming somewhat outdated, and major social and economic reforms in the 1990s having a negative effect on children's oral health. In more recent years, the SDS has been reinvented once more, with the Government investing in its transition to a Community Oral Health Service with a focus on preventive care.

3.15-3.30pm

Dr Jonathan Broadbent

Oral-health-related beliefs, behaviours and outcomes: a life-course study

JM Broadbent[1], J Zeng[2], LA Foster Page[1], SR Baker[3], S Ramrakha[4], WM Thomson[1]

1. SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY
2. DEPARTMENT OF PREVENTIVE AND SOCIAL MEDICINE
3. UNIT OF DENTAL PUBLIC HEALTH, SCHOOL OF CLINICAL DENTISTRY, UNIVERSITY OF SHEFFIELD, SHEFFIELD, UK
4. DEPARTMENT OF PSYCHOLOGY

It is challenging to model and describe the pathways to poor adult oral health. Intergenerational effects, social factors, health beliefs, and health behaviours interact as they act over time to determine a person's oral health. Using data from the Dunedin Multidisciplinary Health and Development study (a longstanding birth cohort), a generalized structural equation modeling approach was used to investigate the relationship among oral health–related beliefs, behaviors in early adulthood, and dental health outcomes and quality of life in adulthood (age 38 y). Parental oral health–related beliefs and socio-economic status were associated with the study members' oral health–related beliefs, which in turn predicted toothbrushing and dental service use. Toothbrushing and dental service use were associated with the number of untreated carious and missing tooth surfaces in adulthood. The number of untreated carious and missing tooth surfaces were associated with oral health–related quality of life. Intergenerational factors and various aspects of people's beliefs, SES, dental attendance, and self-care operating since the childhood years can affect adult oral health.

3.30-4.00pm

Professor Murray Thomson

Steering clear of the fashionable in oral health research

SIR JOHN WALSH RESEARCH INSTITUTE, UNIVERSITY OF OTAGO

Fashions in dental research come and go. You can see how it happens. Someone reports a hitherto-undescribed association from a survey and "over-interprets" the findings. That finding gets replicated in other cross-sectional studies; the media gets involved; work gets underway to elucidate putative biological

mechanisms; funding bodies get interested; and research centres get set up as the new field burgeons. Eventually, the whole thing gradually loses steam for a number of reasons, chief among which are the failure to confirm a causal relationship, and the use of more appropriate study designs, measures and analyses to investigate the issue. One of the initial problems in such a phenomenon is the early and inappropriate use of the language of causality. This paper will consider the issues involved and make some recommendations for improving the accuracy of scientific writing.

MOLECULAR MICROBIOLOGY

Thursday 1.15-4.00pm, DPAG Conference Room (Level 2)

Session chair: Associate Professor Geoff Tompkins

1.15-1.30pm

Golnoush Madani
PhD candidate

Role of cysteine residues in Candida albicans Cdr1p efflux pump expression and function

G Madani, E Lamping, HJ Lee, RD Cannon

SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY

Aim: Oral candidiasis is a common fungal infection of the mucous membranes of the mouth, which is most frequently caused by the opportunistic pathogen *Candida albicans*. The increasing incidence of antifungal drug resistance is a serious clinical concern, particularly for immunocompromised individuals. Overexpression of the plasma membrane ATP-binding cassette (ABC) transporter Cdr1p is the main cause of multidrug resistance. To gain insights into the Cdr1p structure we intend to perform cysteine-crosslinking studies between parts of Cdr1p that are predicted to be in close proximity.

Methods: For cysteine-crosslinking, we require a Cdr1p molecule that has all 23 Cys replaced with Ser or Ala but retains its native pump function. Unfortunately, the Cys-less Cdr1p mutant we constructed was inactive. In order to determine which Cys were essential for Cdr1p expression and/or function, we created 22 different Cys-deficient Cdr1p mutant versions and tested their function in the model yeast *Saccharomyces cerevisiae*. We also measured their expression and cellular localization with the help of a C-terminally fused green fluorescent protein (GFP) tag.

Results: The most critical residues for Cdr1p function were four highly-conserved Cys in extracellular loop 6 and Cys1106 between nucleotide binding domain 2 and transmembrane domain 2. Replacing Cys1106 with Ile1106 in a Cdr1p mutant that had all but the six essential extracellular Cys replaced with Ser or Ala almost fully recovered Cdr1p function.

Conclusion: These Cdr1p studies provide insights that will help the design of novel efflux pump inhibitors to overcome drug resistance in oral *Candida* infections.

1.30-1.45pm

Danyon Graham
BDS student

The molecular basis of triazole inhibition of an antifungal target

DO Graham[1], RK Wilson[1], MV Keniya[1], A Sagatova[1], MA Woods[1], M Sabherwal[1], JDA Tyndall[2], BC Monk[1]

1. SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY
2. NATIONAL SCHOOL OF PHARMACY

The widely-used and well-tolerated azole antifungals prevent synthesis of the fungal-specific sterol ergosterol by inhibiting lanosterol 14α-demethylase (Erg11p). Triazole prophylaxis in immunocompromised patients has selected for the emergence of more difficult to treat Erg11p mutants of *Candida albicans* and *Aspergillus fumigatus*, limiting therapeutic options.

This study investigated the structural and functional effects of two common, clinically-relevant mutations (Y140H and I471T) in Erg11p using the model yeast *Saccharomyces cerevisiae* (ScErg11p). Mutants of the *ScERG11* open-reading-frame were constructed using PCR-based site-directed mutagenesis. Gel-purified recombinant transformation cassettes encoding ScErg11p Y140H, I471T, or Y140H+I471T were transformed into the hyper-expressed *PDR5* locus of a host *S. cerevisiae* strain. Genomic DNA from transformants was sequenced at the *PDR5* locus to confirm successful integration. Liquid minimum inhibitory concentrations for 80% growth inhibition (MIC_{80}) of control wild-type and mutant cells were measured for short-tailed (fluconazole and voriconazole), long-tailed (itraconazole and posaconazole) triazoles and the novel medium-tailed tetrazole VT-1161. Y140H enzyme in complex with fluconazole was purified and a high resolution X-ray crystal structure obtained.

The MIC_{80}s of Y140H cells for fluconazole and voriconazole were two-fold higher than wild-type cells ($P < 0.001$, ANOVA). The I471T second-site mutation further increased the MIC_{80}s for fluconazole and voriconazole three-fold ($P < 0.001$, ANOVA). Cells expressing the Y140H and I471T mutations individually and collectively retained wild-type susceptibility to VT-1161, itraconazole and posaconazole. X-ray

crystallography revealed that the Y140H mutation modifies a water-mediated hydrogen bonding network to the hydroxyl group of fluconazole.

VT-1161 contains the comparable hydroxyl group yet its binding to ScErg11p was unaffected by the mutations. More extensive hydrophobic interaction between ScErg11p and a medium or long tail may stabilise the drug within the binding cavity, limiting the desensitising effect of the single and double mutations. These findings will contribute to the development of next-generation azoles that will circumvent the resistance problem.

1.45-2.00pm

Alia Sagatova
PhD candidate

Investigating triazole mediated resistance in yeast

A Sagatova, RK Wilson, M Sabherwal, MV Keniya, JDA Tyndall*, BC Monk

SIR JOHN WALSH RESEARCH INSTITUTE
*NATIONAL SCHOOL OF PHARMACY

Aim: To investigate the effect of *Candida albicans* lanosterol 14α-demethylase (Erg11p, CYP51) mutations on enzyme structure and function, including different types of triazole drugs, by using *Saccharomyces cerevisiae* Erg11p as a model.

Methods: The *C. albicans* CYP51 mutations Y132F/H, G464S and the double mutation Y132F G464S have been reproduced in a hexahistidine-tagged version of *S. cerevisiae* Erg11p (ScErg11p6×His). Microdilution assays were used to determine triazole susceptibilities of these strains. Purified preparations of the enzyme were used to produce crystals for X-ray crystallographic analysis. Data collection was carried at the Australian Synchrotron (Melbourne, Australia).

Results: The microdilution assays revealed that strains overexpressing ScErg11p6×His Y140F/H or Y140F G464S (*S. cerevisiae* numbering) had reduced susceptibility to the short-tailed triazoles fluconazole and voriconazole but not the long-tailed triazole itraconazole. The ScErg11p6×His G464S mutant strain had triazole susceptibility patterns similar to the wild type strain.

The high-resolution (2.05 Å) structure of wild type ScErg11p6×His in complex with fluconazole revealed a water-mediated hydrogen bonding network between residue Y140 and the drug. The crystal structures of the ScErg11p6×His Y140F/H mutants showed that the mutations have disrupted this water-mediated hydrogen-bonding network.

Conclusion: The disruption of the water-mediated hydrogen bond in the Y140F/H and Y140F G464S mutants is proposed to weaken the interactions between the drug and the mutant enzyme and cause resistance. These observations explain the reduced susceptibility to fluconazole and voriconazole and the retention of susceptibility to itraconazole of this mutant, as the long-tailed drugs do not have the hydroxyl group, involved in the water-mediated hydrogen bonds.

2.00-2.15pm

Dr Mikhail Keniya

Structure of the azole drug target from pathogenic fungi

MV Keniya[1], RK Wilson[1], MA Woods[1], M Sabherwal[1], AA Sagatova[1], JDA Tyndall[2], BC Monk[1]

1. SIR JOHN WALSH RESEARCH INSTITUTE AND DEPARTMENT OF ORAL SCIENCES, FACULTY OF DENTISTRY
2. NATIONAL SCHOOL OF PHARMACY

Aim: Fungal pathogens *Candida albicans* and *Candida glabrata* possess substantial risk for general health and agriculture. Lanosterol 14α-demethylase (CYP51, Erg11p) is a cytochrome P450 mono-oxygenase required for sterol biosynthesis and is the target of azole antifungal drugs. The development of novel drugs require understanding of the intramolecular interactions in the drug -binding pocket.

Methods: Genes of 14α-lanosterol demethylase from *Candida albicans* and *Candida glabrata* with C-terminal hexa-His tag and selective marker were heterologously over-expressed in model yeast *S.cerevisiae*. The endogenous ScERG11 was subsequently removed. Resulting strains were characterized by *In vivo* azole resistance assays (MIC). The proteins were detergent extracted from cell membranes following with two-step purification and concentration. Erg11 preparations were loaded with itraconazole (ITC) and crystallised using hanging drop technique. The X-ray diffraction of the crystals was done at Australian synchrotron.

Results: Resulting strains confer resistance (MIC_{80} up to 3x) to various azole drugs. Strain expressing CaErg11p showed un-expected lower resistance to short and middle-tailed azoles comparing with long-tailed ones. Full-length structures of CaErg11px6His and CgErg11px6His in complex with itraconazole were obtained at resolution of 2.9Å and 2.4Å respectively.

Conclusion: The structures obtained resemble striking similarity with the Erg11p from *S.cerevisiae* previously obtained by our group in high resolution as APO form and with different ligands. This further validates usage of ScErg11 for virtual screens and rational drug design. *In vivo* difference in resistance of CaErg11 expression strain to long and short-tailed azoles found in this study is likely due to the role of cognate NADPH-CYP450 reductase, which need to be co-expressed.

2.15-2.30pm

Syarida Safii
PhD candidate

Effect of medical-grade manuka honey on dental plaque-associated bacteria and hydroxyapatite beads in vitro

S Safii[1], W Duncan[1] G Tompkins[1], N Medlicott[2]

1. DEPARTMENT OF ORAL SCIENCES AND SIR JOHN WALSH RESEARCH INSTITUTE
2. NATIONAL SCHOOL OF PHARMACY

Background and Aim: Topical application of manuka honey is effective in the treatment of burns and soft-tissue infections. The aims of this study were to assess antibacterial activity of medical-grade manuka honey against dental plaque-associated bacteria and to evaluate demineralisation caused by the honey *in vitro*.

Methods: Minimum bactericidal concentration (MBC) of manuka honey was compared to white clover honey against a variety of plaque-associated bacteria. pH of the honeys was adjusted to neutral and the MBCs were compared. Hydroxyapatite (HA) beads were incubated with manuka and clover honeys, in the absence and presence of *Streptococcus mutans*, and the resulting decalcification measured.

Results: Manuka honey (non-peroxide antibacterial activity level ≥20) was bactericidal against the majority of bacteria tested, with the exception of *S. mutans*. The bactericidal activity of manuka honey following adjustment to neutral pH, was largely maintained. Incubation of HA beads in diluted honey resulted in significant solubilisation of calcium and inclusion of *S. mutans* promoted further demineralisation by both types of honey. Calcium solubilisation was correlated with $[H^+]$.

Conclusion: Medical-grade manuka honey is antimicrobial toward representative oral bacteria generally and the gram-negative anaerobes associated with gingivitis are particularly sensitive. However, the relative resistance of cariogenic *S. mutans* in association with the high concentrations of fermentable carbohydrates, and the direct demineralisation of oral hard tissues caused by the naturally low pH of honey, mitigate against the application as a sustained release adjunct in the treatment of periodontal disease.

2.30-2.45pm

Dr Peter Cathro

Proteomic analysis of Enterococcus faecalis cell membrane proteins under alkaline stress conditions

P Cathro[1,4], P McCarthy[2], P Hoffmann P[3], P Zilm[1]

1. ORAL MICROBIOLOGY LABORATORY, THE UNIVERSITY OF ADELAIDE
2. NEUROVASCULAR RESEARCH LABORATORY, CENTRE FOR CANCER BIOLOGY, UNIVERSITY OF SOUTH AUSTRALIA
3. ADELAIDE PROTEOMICS CENTRE, THE UNIVERSITY OF ADELAIDE
4. SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY

Aims: To quantify cell membrane protein expression of *E. faecalis* V583 at an imposed growth rate using continuous culture at pH 11 compared to pH 8.

Methods: *E. faecalis* V583 was grown in a chemostat at pH 11 and 8 at one-tenth the organism's maximum growth rate. Following membrane shaving and membrane digest, heavy- or light-isotope-coding protein labels were added to the samples. The samples were combined, the relative proportion of membrane proteins identified using Liquid chromatography electrospray ionisation mass spectrometry and MaxQuant analysis and then $\log_2$ transformed. The proteins that deviated by more than one standard deviation from the mean were considered to be up- or down-regulated.

Results: Six proteins had a $\log_2$ H/L ratio (pH 11/pH 8) greater than one SD of the mean including: Polysaccharide biosynthesis family protein; Glycosyl hydrolase, family 20; Glycerol uptake facilitator protein; whilst five proteins had a $\log_2$ ratio one SD less of the mean: PTS system IIC component; PTS system IID component; C4-dicarboxylate transporter; PTS system mannose-specific IID component.

Conclusion: When cultured at an imposed slow growth rate, pH11 conditions resulted in an altered expression of several membrane proteins. Collectively these membrane proteins appear to be involved in the transition to biofilm formation seen at pH 11. It was hypothesised that the capsule observed at pH 11 protects the cell from destructive OH- ions whilst concentrating H+ ions and substrates required for the electrochemical gradient close to the cell membrane.

3.15-3.30pm

James Dawson
DClinDent candidate (Periodontology)

Implant surface decontamination - an ex vivo study investigating the effects of diode laser irradiation on implant surface biofilm

J Dawson, G Tompkins, J Leichter, A Tawse-Smith

DEPARTMENT OF ORAL SCIENCES AND SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY

Aim: To determine both the bactericidal and physical effect of diode laser irradiation on a natural biofilm formed *in vivo* on titanium discs. To establish clinical recommendations for the minimum laser energy required to effectively kill biofilm bacteria colonizing implant surfaces.

Methods: Ten periodontally healthy participants wore intraoral appliances containing six titanium discs (R_a=0.96 +/- 0.23 μm) for 96 hours. Discs were sequentially removed and irradiated using various laser protocols. Following irradiation the discs were immediately stained using bacterial viability stain (BacLight® LIVE/ DEAD™) and viewed under confocal laser scanning microscopy to assess bacterial viability and biofilm thickness.

Results: Diode laser irradiation resulted in a dose-dependent bactericidal effect. Maximum antimicrobial efficacy resulted at 75 J/cm^2 laser fluence and plateaued above this. No damage to the implant surface was evident by scanning electron microscopy following laser fluences up to 150 J/cm^2. The biofilm was not completely removed but the mass was significantly reduced with irradiation up to 100 J/cm^2.

Conclusion: Diode laser (810nm) kills intraoral biofilms formed on a roughened titanium surface at fluences

that do not damage the titanium surface. Non-viable biofilm remnants endure on the titanium surface following irradiation but the consequences of this upon healing remains to be determined.

3.30-3.45pm

Dr Nicholas C. K. Heng

Streptococcus kieseri sp. nov. from the New Zealand brushtail possum

NCK Heng[1], C Benn[1], JDF Hale[2], JG Ross[3], GR Tompkins[1], JA Kieser[1], J-AL Stanton[4]

1. SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY
2. BLIS TECHNOLOGIES LTD, DUNEDIN
3. FACULTY OF AGRICULTURE AND LIFE SCIENCES, LINCOLN UNIVERSITY
4. DEPARTMENT OF ANATOMY

Aim: Members of the gram-positive bacterial genus *Streptococcus* inhabit many sites in humans and animals. Whilst some are pathogenic, most streptococci are commensals. During a streptococcal survey of the New Zealand brushtail possum (*Trichosurus vulpecula*), one particular isolate (*Streptococcus* strain CB1) appeared to be a novel species by biochemical (API Strep) and genetic (16S rRNA gene) analyses. *Streptococcus* CB1 has been designated *Streptococcus kieseri* and the aim of this study was to sequence its genome.

Methods: The *S. kieseri* genome was sequenced using two next-generation DNA sequencing technologies. Data were assembled using MIRA v4.0, and homology searches of DNA or protein databases utilised appropriate BLAST algorithms.

Results: The DNA sequencing phase yielded between 33- and 240-fold coverage of the genome. The assembled data comprised 40 contiguous sequences (contigs) totalling 2.0 Mbp with a G+C content of 40%. The chromosome of *S. kieseri* CB1 contains five ribosomal RNA operons and approximately 2,300 open reading frames. Although the organisation of the CB1 genome resembles that of the *Streptococcus mutans* group, multilocus analysis of several essential genes (e.g. *groEL*, *gyrB* and *rpoB*) indicates otherwise. Other notable features of the genome include a 23-kbp bacteriophage, several classes of mobile genetic cassettes (IS elements), and genes involved in genetic competence (DNA uptake). *S. kieseri* CB1 does not exhibit any antimicrobial (bacteriocin) activity, a finding supported by the absence of known bacteriocin loci in the genome sequence.

Conclusion: *Streptococcus kieseri* strain CB1 is the first possum-borne species to be isolated and fully sequenced.

3.45-4.00pm

Gemma Cotton
PhD candidate

Silver nanoparticle-based hydrogel for treatment of periodontal disease

GC Cotton[1,2], DR Schwass[2], GR Tompkins[2], WJ Duncan[2], CJ Meledandri[1,3]

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2. DEPARTMENT OF ORAL SCIENCES AND SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY
3. THE MACDIARMID INSTITUTE FOR ADVANCED MATERIALS AND NANOTECHNOLOGY

Aim: We have synthesised a silver-nanoparticle (AgNP) antimicrobial and biocompatible hydrogel towards the goal of creating a new and effective treatment strategy for the management of periodontal disease and peri-implantitis. This talk will highlight the novel synthesis and demonstrate the antibacterial action of the hydrogel *in vitro*.

Methods: Synthesis of size-controlled, specifically-functionalised AgNPs through a microemulsion technique, were subsequently used for hydrogel preparation. Dynamic light scattering and transmission electron microscopy (TEM) were used for nanoparticle characterisation. Characterization of the AgNP-hydrogel was achieved by cryo-TEM, micro-CT imaging and oscillatory shear tests. Antimicrobial activities were evaluated using a real-time fluorometric viability assay using a range of bacteria: *Escherichia coli, Staphylococcus aureus (oxford), Pseudomonas aeruginosa, Streptococcus mutans, Strep. mitis, Enterococcus faecalis* and *Strep. gordonii*.

Results: AgNP suspensions contained stable, spherical, 2 – 7 nm particles. Specific surface enhancement of the AgNPs enabled cross-linking upon polymerisation of the hydrogel, chemically binding the AgNPs within the matrix. The AgNP-hydrogel possessed higher mechanical strength when compared to a non-AgNP-containing hydrogel. The AgNP-hydrogel caused a viability reduction in all microorganisms within 5 min, ranging from 70% to 40%, with MBC = 9.8 µg Ag for all tested species.

Conclusion: Our novel gel supports AgNPs in a stable form preventing aggregation and deactivation of the AgNPs. It is envisaged that our nanosilver gel formulation has the potential to manage periodontitis and peri-implantitis more efficiently than currently applied methods. It utilises biodegradable polymers, offers an effective antimicrobial action, has low potential for bacterial resistance and is biocompatible and mucoadhesive.

POSTER SESSION

Thursday 4.00-5.00pm, DPAG ODT Gallery (Level 2)

Titles and authors of posters in the competition will be published on the day.
Awards will be presented on Friday afternoon.

Friday sessions

9.00-9.25am

Professor Alison Rich

Keynote presentation: *The microenvironment of Oral Squamous Cell Carcinoma*

SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY

Oral squamous cell carcinoma (OSCC) continues to be associated with significant morbidity and mortality. Research into OSCC has moved beyond potentially malignant and malignant keratinocytes to the broader tumour microenvironment (TME).

We have shown increased numbers of regulatory T cells in the stroma of OSCC compared with control tissues and suggested they may exert their effects through association with FAS death receptors and/or toll-like receptors. Analysis of gene expression has shown significant variation in regulation of immune tolerance genes in cervical lymph nodes with metastases from primary OSCC by comparison with the primary tumour. Significantly more cells expressing the pro-inflammatory cytokine interleukin (IL)-17 were present in the TME associated with OSCC than in non-specifically inflamed tissues. Cell culture studies showed IL-17 enhanced the invasive potential of OSCC cell lines with up-regulation of matrix metalloproteinase expression.

OSCC cells have been shown to be relatively resistant to apoptosis when subjected to endoplasmic reticulum (ER) stress and ER stress was associated with differential regulation of tumour-promoting cytokines in the TME. We have found alterations in angiogenic protein and gene expression in OSCC. Lymphangiogenesis, with its potential to increase the capacity for metastatic spread, is crucial within the primary TME and we have found clear evidence of increased lymphangiogenesis in OSCC by comparison with inflamed controls. The next step is the synthesis of these findings to develop tools to assess prognosis and to develop interventions to promote the immune system to work against cancer cells and/or to intervene in specific molecular processes.

9.25-9.45am

Janice Pitt

How good are your connections? It's in the Science, not magic!

SCIENTIFIC AFFAIRS MANAGER, 3M ORAL CARE ANZ

Connections – bonding keeps it all together more than you think. From aerospace to Dentistry, a look at "connection" and how it works for you in clinical practice and beyond. Every day we apply our science to make your life better.

Connecting- past, present and future.

- 3M Science Applied to life – what 3M Oral Care brings to your clinical practice.
- How it all works, bonding and curing, making it all stick.
- 3M^{SM} Health Care Academy – our commitment to education and clinical excellence.

Janice is currently Scientific Affairs Manager for 3M Oral Care ANZ with primary responsibility for the Direct Restorative category. Janice has a degree in Microbiology, initially enjoying R&D in the exciting Biotechnology industry before joining 3M Health Care in Regulatory affairs. In 2001 Janice moved into the 3M Dental business and was hooked on dentistry! Janice has a broad experience across R&D for the full 3M Oral Care product Portfolio and has held several important roles in Technical and Business development across ANZ and Asia. Janice has been part of the evolution in 3M Oral Care and has seen many advances in dental technology and science and is as ever excited by the bright future of this industry and Profession.

CRANIOFACIAL BIOLOGY AND CLINICAL ORAL PHYSIOLOGY

Friday 9.45am-12.30pm, DPAG Auditorium (Level 1)

Session chair: Dr Li (Peter) Mei

9.45-10.15am

Associate Professor Julia Horsfield

How zebrafish can help understand craniofacial biology

T Newman[1], B Leeke[1], C Carleton[2], M Leask[1], M Hampton[3], J Horsfield[1]

1. DEPARTMENT OF PATHOLOGY, DUNEDIN SCHOOL OF MEDICINE
2. DEPARTMENT OF ORAL SCIENCES AND SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY
3. CENTRE FOR FREE RADICAL RESEARCH, UNIVERSITY OF OTAGO CHRISTCHURCH

When babies are born with a developmental disorder, it is often very difficult to know what went wrong *in utero*. To demystify the process of embryo development, we

can look to other models. The zebrafish is an animal in which development happens externally. Zebrafish lay transparent eggs, which allow us to observe development from one cell to a complete animal over just a few days. Because zebrafish share most of their developmental genes with humans, what we learn about development in zebrafish can be widely applicable to vertebrates, including humans. In this talk, I will highlight how zebrafish can help us understand normal and abnormal development. I will use examples from our group's research to show how zebrafish can help understand human developmental (including craniofacial) disorders and how they might ultimately help us find cures or preventative strategies.

10.15-10.30am

Catherine Carleton
DClinDent candidate (Orthodontics)

A novel model for exploring the causes and treatments of craniofacial birth defects

C Carleton[1], B Leeke[2], M Leask[2], M Farella[1], J Antoun[1], J Horsfield[2]

1. DEPARTMENT OF ORAL SCIENCES AND SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY
2. DEPARTMENT OF PATHOLOGY, DUNEDIN SCHOOL OF MEDICINE

Aim: Previous research showed that the oxidative stress-inducing compound auranofin (AFN) might cause craniofacial cartilage defects in zebrafish embryos. The aim of this study was to determine how environmental causes of craniofacial birth defects affect the growth and survival of cells contributing to the craniofacial skeleton during embryonic development. A second objective was to determine whether factors that enhance cell survival, such as antioxidant molecules, could rescue craniofacial defects.

Methods: AFN was applied to zebrafish embryos and the resulting phenotype was characterised at 5 days post-fertilisation (dpf). TUNEL staining was used to determine whether craniofacial defects were due to cell death. An antioxidant, Riboceine (RBC), was added in conjunction with AFN to investigate whether the defect caused by AFN could be rescued via promoting cell survival. The structure of the craniofacial cartilages were analysed using an alcian blue stain. Quantitative reverse-transcriptase polymerase chain reaction (qRT-PCR) was used to analyse expression of antioxidant genes.

Results: AFN caused defects in craniofacial cartilage of 5 dpf zebrafish embryos and led to greater numbers of TUNEL-positive, apoptotic cells. RBC consistently 'rescued' the jaw defect caused by oxidative stress and led to a decreased number of TUNEL-positive cells compared to embryos treated with AFN only. Embryos treated with AFN had abnormal cranial cartilage, giving a 'gap-jaw' appearance with the alcian blue stain. AFN also caused the upregulation of antioxidant genes at 24 hpf and 48 hpf time points

Conclusion: Oxidative stress in zebrafish results in craniofacial cartilage defects that can be rescued by an antioxidant. These findings may have translational significance, as treatment with antioxidants may help to prevent craniofacial defects in children, especially in families where there is an identified genetic or environmental risk.

11.00-11.30am

Associate Professor George Dias

Resorbable keratin-based biopolymer as a bone substitute material

DEPARTMENT OF ANATOMY
OTAGO SCHOOL OF MEDICAL SCIENCES

Biodegradable materials that degrade after fulfilling their function are significant in orthopaedics field. Keratin, a structural protein abundant in wool & hair, is ideally suited for the development of such materials through a combination of tough physical properties and rich chemical biological functionality. The author's group have shown that keratin is a versatile biocompatible biopolymer and can be used to produce matrices with a wide range of forms and potential functions.

Porous keratin hydroxyapatite constructs where prepared with pore structure compatible to bone and a 3mm defect in sheep tibia was used as an in vivo model. Histological examination revealed that the constructs were highly biocompatible. The nature of the cellular response to the implants was similar to the mechanism by which autologous bone is osseointegrated. This suggests that keratin have the potential to perform in applications where autologous bone is currently used.

11.30-11.45am

Yana Itskovitch
DClinDent candidate (Orthodontics)

Engineering 3-D constructs of human bone matrix in a mechanically-active environment

Y Itskovitch, M Meikle, T Milne, M Farella, R Cannon

SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY

Aim: 1) To develop a 3-D hydrogel cell-culture model for engineering artificial mineralized bone matrix *in vitro;* 2) Validate assays for the measurement of osteoblast proliferation and hydroxyapatite deposition; 3) Examine suitability of the model for the study of mRNA expression under mechanical strain.

Methods: Human foetal calvarial osteoblasts (HCO) and femoral osteoblasts (HFO) were cultured in thiol-modified hyaluronan-gelatin-PEGDA cross-linked hydrogel. Two degrees of cross-linking were used and cell proliferation and hydroxyapatite deposition was quantified over a 21-day culture period. Confocal microscopy was also used to assess the penetration of the hydrogel by the assay dyes. An enhanced cross-linked hydrogel was used for mechanical strain

experiments. Quantitative polymerase chain reaction (qPCR) was used to measure mRNA expression of alkaline phosphatase (ALP), osteocalcin (OC) and bone morphogenetic protein 2 (BMP2) genes.

Results: Cell proliferation and hydroxyapatite deposition increased for each cell line over 21 days. The highly cross-linked hydrogel was found to be a better scaffold for osteoblast attachment. Confocal microscopy showed assay stains had limited hydrogel penetration. A cyclic compressive mechanical load did not affect ALP expression in both the HCO and HFO ($p \geq 0.132$) but it caused a 53.9-fold increase in BMP2 in the HFO group ($p = 0.0043$). No OC mRNA was detected in either group.

Conclusion: Thiol-modified hyaluronan-gelatin-PEGDA cross-linked hydrogel is a suitable scaffold for the study of osteoblast proliferation and hydroxyapatite deposition *in vitro.* Further experiments are required to assess the differences in the responses of calvarial and femoral osteoblasts to mechanical strain.

11.45am-12noon

Gareth Benic
DClinDent candidate (Orthodontics)

Efficacy of oral probiotics in managing biofilm formation in patients wearing fixed orthodontic appliances: A triple-blind randomized placebo-controlled trial

G Benic, M Farella, P Biggs, N Heng, R Cannon, L Mei

SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY

Aim: To investigate the efficacy of the oral probiotic Streptococcus salivarius M18 on managing biofilm formation in patients wearing fixed orthodontic appliances.

Methods: The study was designed as a prospective, randomized, triple-blind, two-arm parallel-group, placebo-controlled trial. Sixty-four patients undergoing fixed treatment consumed 2 lozenges daily of probiotic (n=32) or placebo (n=32). The outcome measures were plaque index (PI), gingival index (GI) and halitosis-causing volatile sulphur compound (VSC) levels. Oral microflora was analysed utilising next-generation sequencing of the bacterial 16S rRNA gene.

Results: No significant differences in PI and GI scores were found between probiotic group and placebo-control group ($p > 0.05$). The level of VSCs significantly decreased in both probiotic group (VSC reduction = -8.5%, $p = 0.015$) and placebo group (VSC reduction = -6.5%, $p = 0.039$) after 1-month. However, after the 3-month follow-up, VSC levels of the placebo-control group returned to baseline levels whereas those of the probiotic group decreased further compared to baseline readings (-10.8%, $p=0.005$). The next-generation sequencing showed that the oral ecology of both groups was similar and that there was a significant increase in the abundance of streptococci in both the probiotic and placebo group over time.

Conclusion: Oral probiotic S. salivarius M18 reduced the VSC levels in patients with fixed appliances but did not decrease their plaque or gingival indices. The influence of probiotic S. salivarius M18 on oral microflora seems to be minimal. A longer intervention and follow-up period are needed.

12.00-12.15pm

Ghassan Idris
PhD candidate

Efficacy of twin-block for the treatment of paediatric sleep disordered breathing: a randomised clinical trial

G Idris[1], B Galland[2], CJ Robertson[1], M Farella[1]

SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY
DEPARTMENT OF WOMEN'S AND CHILDREN'S HEALTH

Aim: the objective of this study was to test the efficacy of mandibular advancement appliances (MAS) for the management of Sleep-Disordered Breathing (SDB) and associated symptoms in children.

Methods: The study was carried out as a single-blind crossover randomised controlled trial (RCT) with administration of both an Active and a Sham MAS. Eighteen children were recruited in the trial and randomly assigned to a treatment sequence, starting with either the Active or the Sham MAS. Participants wore the appliances for three weeks, separated by a two-week washout period. For each participant, home-based polysomnographic data were collected four times before and after each treatment period. The apnoea hypopnea index (AHI) and snoring frequency (snoring time and number of snoring episodes) were assessed as the main outcome variables.

Results: Compared to a Sham MAS, wearing an Active MAS resulted in a significant reduced AHI ($p=0.002$). The separate assessment of AHI in supine and non-supine sleeping positions revealed that only the former was significantly influenced by treatment, with a reduction of 4.1 events per hour (95% CI=1.8-6.4; $p<0.001$). Snoring time was 46.3 minutes shorter with the Twin-Block than with the Sham appliance (95% CI=14.5-78.1; $p=0.004$). Compared to a Sham MAS, the Active MAS also reduced SDB symptoms, as represented by PSQ-SRBD, OSA-18, and BASC-2 scores ($P \leq 0.028$). IGF-1 levels and EES scores, however, did not differ between the two treatment periods ($P=0.172$ and $P=0.431$, respectively).

Conclusion: Within the limitations of this study, it can be concluded that wearing a mandibular advancement splint over a short period can be beneficial for children affected by SDB.

12.15-12.30pm

Carrol Jin
BDS (Honours) student

Survival analysis of different orthodontic retainers

C Jin[1], L Mei[1], F Bennani[2], A Gray[3], M Farella[1]

1. DEPARTMENT OF ORAL SCIENCES AND SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY
2. DEPARTMENT OF ORAL REHABILITATION AND SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY
3. DEPARTMENT OF PREVENTIVE AND SOCIAL MEDICINE

Aims: To investigate the survival time of different orthodontic retainers and to identify the predictors of retainers' failures.

Methods: A total of 591 retainers, including Hawley retainer, vaccum formed retainer, lingual fixed retianter and combination retainers, were included in the study. Patients' gender, age, dates of retainer insertion and failure were recroded. Survival for each type of retainers was graphed using Kaplan-Meier plots. Cox's proportion hazards regression was used to model failure along with demographic characteristics. For categorical variables with more than two levels, Wald tests were used to assess overall significance with pairwise comparisons between levels if this is significance.

Results: The survival time was the longest for lingual fixed retainers (median = 1604 days and Hawley retainers (1529 days), followed by the combination retainers (258 days), and then vacuum formed retainers (105 days) ($p<0.05$). For lingual fixed retainers, no significant difference was found between maxillary (1497 days) and mandibular (1604 days) ($p = 0.341$). No difference was found among different types of combination retainers ($p = 0.078$). The main reasons of retainers' failures varied for each individual type: Hawley retainers were most likely to be lost (52%), fixed retainers were most likely to debond (63.46%), and fracture was the most common cause for vacuum formed retainer (43.48%) and combination retainers (41.86%).

Conclusions: Lingual fixed retainers and Hawley retainers have longer survival time than vaccum formed retainers and combination retainers. The main reasons of retainers' failures are lost and breakage.

DENTAL EDUCATION

Friday 11.00am-12.30pm, DPAG Conference Room (Level 2)

Session chair: Dr Lee Adam

11.00-11.30am

Dr Lee Adam

Evaluate to improve: Useful approaches to student evaluation

L Adam[1], C Goulding[2]

1. SIR JOHN WALSH RESEARCH INSTITUTE AND OFFICE OF THE DEAN, FACULTY OF DENTISTRY
2. HIGHER EDUCATION DEVELOPMENT CENTRE

Aim: Many university teachers evaluate their teaching, however, only some use student evaluations to improve their teaching. An individual teacher's approach to evaluations may be a deciding factor in whether or not they use their evaluations to improve their teaching. In this presentation, we identify some useful approaches to using student evaluation data for improving teaching.

Methods: We conducted focus groups with award-winning University Of Otago teachers who use student evaluations to improve their teaching. We used a general inductive approach to analyse the research data and identify how these teachers approach their evaluation data.

Results: The award-winning teachers we spoke with took a reflective approach to student evaluations. They aimed for constant improvement in their teaching, and regarded evaluation data as formative feedback that they could then apply to improve learning outcomes for their students. In this presentation we describe this 'improvement approach' to evaluation data and offer it for other teachers to emulate.

Conclusion: We argue that if teachers take this reflective, formative, student-centred approach, they can also use student evaluations to improve their teaching.

11.30-11.50am

Hanna Olson

Perceived stressors of Bachelor of Oral Health students

H Olson, L Adam, S Moffat, A Tawse-Smith

SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY

Despite a recent trend to investigate students' stressors in dentistry learning environments, there is little research on students' stressors in the oral health learning environments. The findings from this study aimed to identify perceived stressors of Bachelor of Oral Health students at the University of Otago Faculty of Dentistry.

All Bachelor of Oral Health students (n=135) were invited to complete an online modified version of the Dental Environmental Stress Survey. The survey consisted of 39 questions: 7 collecting demographic information, 1 free comment box, and 31 items related to various potential sources of stress which students were asked to rate on a 5-point Likert-type scale ranging from 'not at all stressful' to 'extremely stressful'.

Data were analysed using SPSS software. The response rate was 36.3%, with 52.0% of respondents being first-year students (BOH1) and participants from second (BOH2) and third (BOH3) year equally distributed (21.2% and 23.1% respectively). Of all the items, students perceived 'fear ofbeing unable to catch up if behind' and 'examinations and assessments' as their

greatest stressors. Overall, academic requirements were the cause of most stress for the students. Stressors related to the clinical environment were highest for second-year students; this is when students start seeing patients.

Several potential stressors netted an equal distribution of responses across the 5-point scale, and we discuss possible reasons for this. We conclude the presentation by outlining how we might respond to these findings in order to better support students in their learning, and discuss directions for future research.

11.50-12.10pm

Calum Fisher
BDS (Honours) candidate

Development of a social accountability measure for the dental environment

C Fisher[1], L Foster Page[1], J Zeng[2], J McMillan[3], K Lyons[4], V Chen[5], B Gibson[6]

1. DEPARTMENT OF ORAL SCIENCES AND SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY
2. DEPARTMENT OF PREVENTIVE AND SOCIAL MEDICINE
3. BIOETHICS CENTRE, DIVISION OF HEALTH SCIENCES
4. DEPARTMENT OF ORAL REHABILITATION AND SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY
5. WELLINGTON HOSPITAL
6. SCHOOL OF CLINICAL DENTISTRY, UNIVERSITY OF SHEFFIELD (UK)

Aim: To develop a social accountability measure for the dental environment

Methods: A standard approach for questionnaire design. This involved a secondary data analysis of the modified Medical Students' Attitudes Towards Underserved (MSATU) questionnaire using exploratory factor analysis (EFA) on three hypothesised factors. Following data analysis, an expert panel of eight academics assessed content validity of the measure to guide modification. Face validity was conducted with 6 students. A pilot study was carried out with BDS students (N = 32). Further testing involved a larger sample of BDS students (N = 209). EFA was used to explore the structure behind social accountability and assess construct validity.

Results: Secondary data analysis of the modified MSATU did not support the three hypothesised factors. Following the expert panel, items were modified for the New Zealand context and domain headings were dropped. Of the 22 items carried forward to face validity, 13 were revised, and 1 was removed. The pilot identified issues regarding anonymity; participants may knowingly alter their answers to reflect a higher degree of social accountability. To overcome this, socio-demographic fields were dropped. EFA of the final data revealed a 3-factor model with 15 items for measuring social accountability. Eigenvalues for the three factors were 4.832, 2.102, and 1.128. Before rotation, they explained 32.2%, 14.0%, and 7.5% of the total variation in the data respectively.

Conclusion: The 15-item social accountability measure appears to measure the concept of social accountability in New Zealand dental students. Further testing is required to ensure its robustness.

12.10-12.30pm

Dr Lee Smith

Undergraduate oral health student and teachers' understandings of professionalism

R Ahmadi, L Smith, L Adam

DEPARTMENT OF ORAL SCIENCES, FACULTY OF DENTISTRY

Numerous studies focusing on students' developing understandings of professionalism in dentistry exist. However, there is a paucity of studies focusing on dental therapy and hygiene students' understandings of professionalism and how they develop professionalism through their undergraduate course. In this presentation we report findings from research carried out in one New Zealand dental school, which aimed to document a group of Bachelor of Oral Health students' conceptualisations of professionalism, and the skills, values and behaviours they associate with the term.

Electronic surveys were emailed to all oral health students currently enrolled in (first year), or who had recently completed a paper with a professionalism module (past students). Ten first year students and 13 past students completed the survey.

Surveys were also sent to educators who taught in the same dental school, to report on how they could identify when oral health students were exhibiting professionalism. In total, 11 dental educators completed the surveys and two focus groups were also conducted with dental educators (three participants per focus group).

Ten of the 11 dental educators maintained that students placed little importance on learning about professionalism, but this was something that increased as they progressed through their course. By contrast, all the student participants reported that learning about professionalism was vitally important. Participants from all three groups linked the same values and skills with professionalism, which included demonstrating empathy and respect with patients, possessing highly developed communication, teamwork and clinical skills, and maintaining a professional appearance. There were slight variations in responses between the three groups however, with some past students stating that studying hard was an aspect of professionalism, while the other two groups did not. Further, some staff listed developing time management skills as an aspect of professionalism that students need to develop over their course of study, but none of the student participants mentioned this aspect. We conclude the presentation with a discussion of the importance of educating oral health students about professionalism in their formal coursework.

ORAL MOLECULAR AND IMMUNOPATHOLOGY

Friday 1.15-4.00pm, DPAG Auditorium (Level 1)

Session chair: ProfessorAlison Rich

1.15-1.45pm

Dr Benedict Seo

Profiling the effect of endoplasmic reticulum stress in oral cancer

B Seo, D Coates, G Seymour, A Rich

SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY

Aim: Endoplasmic reticulum stress (ERS) leads to the activation of the unfolded protein response (UPR), which has been implicated in both the promotion and impediment of cancer. The role of the UPR in oral squamous cell carcinoma (OSCC) remains elusive. In this study the effect of ERS in OSCC in relation to cancer cell biology and UPR gene and protein expression was examined.

Methods: OSCC and normal oral keratinocyte (NOK) cell lines were subjected to ER stress using tunicamycin (test) and control conditions without tunicamycin. Viability and apoptosis assays were performed to examine the cellular response to ER stress. qRT^2-PCR and ELISA were performed to investigate the expression of UPR genes and proteins with and without ERS.

Results: ERS induction with tunicamycin resulted in distinct responses in NOK and OSCC. NOK showed decreased cell viability and increased apoptosis whereas OSCC demonstrated marked resistance to apoptosis when compared to control cells. ERS caused a trend towards up-regulation of UPR genes. DDIT3, HTRA4 and HSPA1L were significantly up-regulated in OSCC compared with NOK. Without ER stress, SREBP1 was significantly up-regulated in OSCC compared with NOK. After tunicamycin treatment CREB3L3 was significantly up-regulated in OSCC. The expression of SREBP1 protein decreased in NOK upon ER stress, whereas it increased in OSCC. CREB3L3 protein expression showed significant variation between cell lines.

1.45-2.15pm

Muhammed Yakin

DClinDent candidate (Oral Pathology)

Endoplasmic reticulum stress modulates the pathogenesis of oral cancer through STAT3-pathway-dependent immune responses

M Yakin, B Seo, A Rich

SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY

Aim: Signal transducer and activator of transcription (STAT)-3 lies at the convergence point of key pathways involved in many malignancies including oral squamous cell carcinoma (OSCC). Endoplasmic reticulum stress (ERS) and the unfolded protein response (UPR) promote either survival or apoptosis in different cancers. The aim of the study was to investigate the expression of STAT3 pathway-related genes and proteins under ERS in OSCC.

Methods: Three normal oral keratinocyte (NOK) and three OSCC cell lines were subjected to tunicamycin (an agent known to induce ERS) for 24 hours or to the vehicle medium as control. A focussed STAT3 Pathway Array was used to analyse the modulation of the STAT3 pathway gene expression under ERS using qPCR. The expression of key regulated proteins was investigated in the cell lines using immunocytochemistry (ICC) and in OSCC and normal oral mucosa (NOM) tissue using immunohistochemistry (IHC) using tissue microarray (TMA) technology.

Results: ERS resulted in up-regulation of IL6 receptor 1 (IL6R1) gene in NOK cell lines ($p=0.001$) and IL5 ($p=0.005$) and IL22 ($p=0.024$) in OSCC cell lines. Leukaemia inhibitory factor receptor (LIFR) gene was up-regulated in OSCC cell lines ($p=0.04$). ICC showed greater extent of STAT3 ($p=0.019$) and LIFR ($p=0.042$) protein expression in treated NOK than untreated NOK cell lines. IHC showed more STAT3 ($p=0.046$) and IL6R ($p=0.027$) protein expression in OSCC than in NOM tissue.

Conclusion: The gene and protein regulation patterns show that ERS plays a role in immune-modulation in the tumour microenvironment in OSCC by up-regulating tumour-promoting cytokines.

2.15-2.45pm

Hina Narayan

PhD candidate

Cigarette smoke, DNA methylation and oral cancer

H Narayan, T Milne, H Hussaini, G Seymour, A Rich

DEPARTMENT OF ORAL DIAGNOSTIC AND SURGICAL SCIENCES, FACULTY OF DENTISTRY

Aim: To investigate the effect of cigarette smoke condensate (CSC) on the DNA methylation status of genes involved in TGF-β signaling in oral epithelial cells (OEC) and human gingival fibroblasts (HGF).

Methods: Cell proliferation was evaluated in OEC (OKF-4, OKF-6 and OKP-7) and three primary HGF cell lines treated with 0-600µg/mL CSC for 24, 48 or 72 hours using CellTiter-Blue assay (Promega). Relative levels of CYP1B1 mRNA (known to be upregulated in smokers) were assessed in RNA purified from CSC-treated and control cells to validate the cigarette smoke treatment model. DNA promoter methylation was evaluated using the TGF-β signaling Methyl-Profiler PCR Array (SABioscience, Qiagen), and the differentially

methylated genes were assessed using a duplex Taqman assay.

Results: CSC concentrations ≥200 and 50µg/mL were toxic in HGF and OEC respectively. CYP1B1 gene expression was found variably upregulated with CSC treatment in HGFs, OKF-4 and OKF-6; but downregulated in OKP-7. In HGF, only LTBP2 of the 22 genes in the array was 2% hypermethylated in HGF-1. In OEC, SMAD3 and BMP4 were hypermethylated by 4% and 7% in OKF-4 and OKF-6 respectively; while in OKP-7, SMAD3, BMP4 and LTBP2 were hypomethylated by 8%, 35% and 12% respectively. SMAD3 gene expression was 3.6 and 2.2-fold upregulated in OKF-4 and OKF-6 respectively, while 1.5-fold downregulated in OKP-7.

Conclusion: The in vitro cigarette smoke treatment is valid. In OEC, affected methylation changes led to altered gene expression in SMAD3, which is known to have a role in cellular proliferation and differentiation, and is also implicated in carcinogenesis.

3.15-3.45pm

Kullasit Chutipongpisit
DClinDent candidate (Oral Pathology)

Lymphangiogenic factors in oral cancer

K Chutipongpisit, VP Parachuru, HM Hussaini, LT Friedlander, AM Rich

SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY

Aim: To investigate the differences, if any, in the expression profile of lymphatic markers and lymph vessel density (LVD) in oral squamous cell carcinoma (OSCC) in relation to non-specifically inflamed connective tissue (ICT) and normal oral mucosa (NOM) using immunohistochemistry (IHC). Selected antibody markers' specificity to lymphatic endothelial cells (LECs) was also investigated with double-labeling immunofluorescence (DLIF).

Methods: Archival formalin-fixed paraffin-embedded specimens (28 OSCC, 10 ICT and 6 NOM cases) were processed using IHC with antibodies against the lymphatic markers D2-40, LYVE-1, VEGFR3 and Prox-1. Within each specimen six hotspots were chosen at 200x magnification. The positively stained cells and vessels were identified and counted to determine the vessel density per 1.56mm2. One-way ANOVA with 5% level of significance was used to analyse the differences between the three groups. DLIF was used to qualitatively investigate the specificity of D2-40 and LYVE-1 to LECs.

Results: There was a higher expression of D2-40 (p=0.001) and Prox-1 (p=0.001) in the OSCC group when compared with both control groups. No statistically significant differences were observed between the OSCC group and the NOM group for LYVE-1 expression and between all groups for VEGFR3 expression. DLIF showed that D2-40 marker is the most specific for LECs.

Conclusions: These results establish that the OSCC tumour microenvironment possesses significantly more lymphatic vessels expressing D2-40 and Prox-1 than the control groups. This increase in LVD may play a role in facilitating lymphatic invasion and later metastases. These molecular entities may serve as potential anti-oral cancer therapeutic targets. D2-40 is the most specific LEC antibody marker when applied on OSCC tissues.

3.45-4.00pm

Dr Haizal Hussaini

Research in oral cancer - where to from now?

SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY

Oral cancer, particularly oral squamous cell carcinoma, is the sixth most common cancer worldwide. Key research into oral cancer is happening in many research institutions and universities around the world. This research will provide more information on the cause, clinical management and ways of preventing this debilitating disease from occurring. Currently, work is concentrated on analysing DNA changes and methylation via new methods such as RNAseq which investigates the transcriptomic profile of oral cancer. Another area which is receiving a lot of interest is exploration of new chemotherapy drugs that can enhance the immune system to fight oral cancer cells. This arose from increased understanding of cancer immunology, particularly how cancer cells escape from the immune system. Our group and others have investigated escape mechanisms in primary oral cancer as well as in metastatic cervical lymph nodes, usually the first site of oral cancer spread. It is anticipated that research in cancer immunology will lead to interventions promoting our own immune system rather than debilitating surgery, radiotherapy or non-targeted chemotherapy.

BIOMATERIALS AND ORAL IMPLANTOLOGY

Friday 1.15-4.00pm, DPAG Conference Room (Level 2)

Session chair: Associate Professor Neil Waddell

1.15-1.45pm

Lisa Falland
PhD candidate

Development of a translucent brain simulant for ballistic testing

L Falland[1], JN Waddell[1], MS Lazarajan[2], MC Jermy[2], T Winter[1], D Tong[1], PA Brunton[1]

1. SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY
2. DEPARTMENT OF MECHANICAL ENGINEERING, UNIVERSITY OF CANTERBURY

Aim: Investigation of two mixtures, agar/glycerol/water (A) and glycerol/water (B), as suitable brain simulants.

Methods and Materials: For both mixtures, test specimens (n=15) (50x27x37mm) were fabricated and conditioned to 12°C, 22°C, and 26°C prior to testing. Fresh deer brain specimens (n=20) were sourced, prepared to the same dimensions and conditioned to 12°C and 37°C. The density of the mixtures was measured and compared to values of human brain reported in the literature. High velocity impact tests were carried out using a 0.22 caliber air riffle pellet and recorded with a high speed camera as it passed through the specimens, allowing for vertical displacement and energy loss calculation.

Results: Mixture A at 22°C was translucent enough to visualize the formation of the permanent and temporary cavity and had similar vertical expansion and contraction rates to the deer brain at 37°C. Mixture A at 26°C had a slightly higher energy loss compared to the deer brain at 37°C. Mixture A at 22°C displayed a very close similarity to post damage patterns of deer brain and had a density similar to human brain.

Conclusion: Of the mixtures tested, the agar/glycerol/water mixture (A), conditioned to 22°C was the most suitable brain simulant for ballistic testing.

1.45-2.15pm

Wendy Jansen van Vuuren

Effect of condensation on flexural strength of porcelain

W-A Jansen van Vuuren, CST Khoo, BSK Ng, JN Waddell, B Al-Amleh

DEPARTMENT OF ORAL REHABILITATION AND SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY

Statement of problem: Limited research is available on the effects of condensing veneering porcelain has on the physical, mechanical and aesthetics properties of bi-layered prosthetic fixed restorations.

Purpose: To evaluate and compare the effect of ultrasonic condensing on the biaxial flexural strength, translucency and density of a nano-leucite porcelain.

Materials and methods: ISO standard 6872:2008(E) was followed to fabricate 70 discs with Reflex veneering porcelain (Wieland Dental, Germany). Specimens were divided into two groups; ultrasonically condensed (n=30) and bulk packed (non-condensed) (n=30). Biaxial flexural strengths tests were performed and Weibull modulus calculated for each group. The remaining 10 discs were divided into two groups (n=5) as above. A spectrophotometer (VITA, Germany) was used to calculate the transparency parameter for each group. The same 10 specimens were used to calculate their density, using Archimedes' principle. Independent-samples t-test was conducted using SPSS (IBM, USA) to compare the results between ultrasonically condensed and bulk packed groups.

Results: No significant difference was recorded between the groups in any of the performed tests ($P<0.001$). However, ultrasonic condensing resulted showed a higher Weibull modulus in the fractured discs.

Conclusion: Ultrasonic condensing veneering porcelains powder before firing may not be necessary to improve mechanical properties, porosity reduction, or translucency parameter compared to bulk packed techniques. Nevertheless, caution is advised when interpreting these results, due to the shape factor in making disc forms when compared to porcelain layering on clinical crown forms.

Clinical Implications: The notion that condensing increases the strength of porcelain is duly dismissed in the case of nano-leucite Reflex.

2.15-2.45pm

Abdullah Barazanchi
DClinDent candidate (Prosthodontics)

Examination of novel 3D printed cobalt chromium alloy and its applications in dentistry

SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY

Additive manufacturing or 3D printing is becoming an alternative to subtractive manufacturing or milling in the area of computer-aided manufacturing. Research on material for use in additive manufacturing is ongoing and there are a wide variety of materials currently being used or are being developed for use in dentistry. Some materials however, such as cobalt chromium, still lack sufficient research to allow definite conclusions about the suitability of their use in clinical dental practice. The presentation will examine current production method of cobalt chromium and introduce

the results from physical testing of specimens produced using three common production methods including additive manufacturing. It will also discuss possible applications for such technology in restorative dentistry

3.15-3.35pm

Frances Ruddiman
DClinDent candidate (Periodontology)

Abstract not available at time of publication

3.35-4.00pm

Associate Professor Neil Waddell

Building stability of dental porcelains: particle size, shape, and distribution

JH Lee, K Kano, JN Waddell

SIR JOHN WALSH RESEARCH INSTITUTE, FACULTY OF DENTISTRY

Objectives. This study aimed to analyse whether physical properties of dental veneering porcelain such as particle size and size distribution affected their stability under dry and wet conditions, and whether observations correlated with existing research on powder systems from different industries.

Methods. Four dental veneering porcelains by Vita, Noritake, Shofu and Wieland manufactured for porcelain-fused-to-metal crowns were tested in their green state by a tilting box technique to find their angle of repose. The same porcelains were tested for stability in wet environments by determining the greatest water it can hold before saturation. These factors were then compared to scanning electron microscopy analyses of the porcelain granules' particle size and size distribution.

Results. The angle of repose was Vita, 34.55°; Wieland, 29.71°; Noritake, 23.93°; Shofu, 22.85° and greatest ml/g of water held before saturation was Wieland, 3.90m; Noritake, 2.94; Vita 2.88 and Shofu 1.81.

Significance. The ability for a quantifiable measure of porcelain powder stability can contribute greatly to the assessment and improvement of their conduciveness to veneering in all-ceramic and PFM restorations.

PRESENTATION OF AWARDS

Friday 4.00-4.30pm, DPAG ODT Gallery (Level 2)

Presented by Professor Richard Cannon, Director SJWRI

INSTITUTE AWARDS

Sir John Walsh Award for Research Excellence

Strategic Research Prize

Research Publication Awards

Postgraduate Research Publication Award

Research Supervisor Award

SYMPOSIUM AWARDS

Best oral presentation in each session (selected by Session Chairs)

Best poster presentation (undergraduate, postgraduate and staff awards)