FRONTIERS 2016

The Art, Science and Future of Otorhinolaryngology

7 – 9 September 2016

Conference Booklet

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Celebrating 25 years in the pursuit of excellence in Otorhinolaryngology

Welcome

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Professor William B Coman

Dr Michael Jay

The tenth biennial scientific meeting sponsored by the Garnett Passe and Rodney Williams Memorial Foundation that presents the art, science and future of Otorhinolaryngology will be held from 7th to the 9th of September at the Sheraton Grand Mirage Resort on the Gold Coast.

It will be a particularly important event in the history of the Foundation. 2016 marks the 30th anniversary of the signing of the Trust Deed and the 25th year since the death of Barbara Williams whose desire, vision and persistence resulted in what has been a remarkable journey for so many talented people in the specialty.

This unique gathering of scientists and clinicians will showcase the very latest in research by leaders in their various fields of endeavour, interesting aspects within academic institutions and clinical practice in addition to views on scientific research into the next decade and the impact of information technology on medicine in the future.

Three international speakers will be joined by some of Australia's leading scientists and researchers that will include Foundation awardees presenting the results of their most recent work.

It promises to be an exciting, informative and educational experience across all the disciplines of Otorhinolaryngology.

The Trustees and Board members of the Foundation look forward to seeing you there.

Professor William B Coman

Trustee and Foundation Chairman

Dr Michael Jay

Trustee and Conference Convenor

The Garnett Passe and Rodney Williams Memorial Foundation.

International Keynote Speakers

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Professor Wytske Fokkens

Department of Otorhinolaryngology, Academisch Medisch Centrum, Amsterdam, The Netherlands

Wytske J. Fokkens is Professor at the Department of Otorhinolaryngology at the Academic Medical Center in Amsterdam. Her main field of interest is sinus surgery and mucosal pathology of the upper and lower airways. She is the secretary general of the ERS. She is the Chairman of the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS). Dr. Fokkens is a member of the executive committee of ARIA, and workpackage and center leader of GA2LEN, the EU network of excellence.

She is the author of more than 300 papers on allergy and rhinology that have been published in peer-reviewed journals. She has written a textbook on Rhinology: Rhinology and Skull Base Surgery, From the Lab to the Operating Room – An Evidence Based Approach, (Thieme) together with Georgalas. Since 15 years she organizes an advanced sinus surgery course. She serves as Editor in chief of *Rhinology* and Associate Editor of *Allergy* and *Clinical Respiratory Journal*. Recently she received the EAACI Paul Ehrlich award for improving experimental research, She is honorary member of EAACI and the Roumanian Rhinologic Society. She is married and has three children.

Professor Lawrence Lustig

Department of Otolaryngology, Columbia University College of Physicians and Surgeons, New York, United States

Lawrence R. Lustig, MD is an Otolaryngologist who specializes in Otology, Neurotology and Skull Base Surgery. Dr Lustig grew up in Northern California, and completed his undergraduate studies at the University of California at Berkeley. He graduated from the University of California at San Francisco (UCSF) School of Medicine, where he also completed his Otolaryngology residency. After residency, Dr Lustig completed his Neurotology and Skull Base Surgery Fellowship at Johns Hopkins University and remained on staff at Johns Hopkins through 2004. In 2004 he was recruited back to UCSF to lead the Division of Otology and Neurotology in the Otolaryngology Department. Most recently in 2014, he was recruited to Columbia University and New York Presbyterian Hospital where he practices today as the Howard W. Smith Professor and Chair of the Department of Otolaryngology.

Dr. Lustig's interdisciplinary research has helped pioneer cochlear gene therapy for genetic forms of hearing loss. He is also one of the lead investigators for the multicenter Novartis auditory hair cell regeneration trial. Additionally his lab has studied cochlear bone development and how the material properties of bone enclosing the inner ear contribute to hearing. Additional collaboration has included work with a pharmacologist at UCSF, where Dr. Lustig studied the mechanism of hearing loss caused by platinum-based chemotherapies. Dr. Lustig has published more than 125 articles in peer-reviewed journals, as well as book chapters. He co-edited a textbook, "Clinical Neurotology: Diagnosing and Managing Disorders of Hearing, Balance and the Facial Nerve."

He lives in New York City metropolitan region with his wife Heather and children Lila and Lauren.

International Keynote Speakers

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Dr Peter Rhys-Evans

Consultant ENT, Head and Neck Surgeon, The Royal Marsden, London, United Kingdom

After qualifying from St Bartholomew's Hospital in 1971, Mr Rhys-Evans trained in ENT/head and neck, and reconstructive surgery before spending a year doing a postgraduate degree as Resident in Head and Neck Cancer Surgery at the Gustave Roussy Institute at the University of Paris. In 1981 he was appointed Consultant ENT Surgeon at the Birmingham University Queen Elizabeth Hospital, and in 1986 was invited to take on the post of Chief of ENT/Head and Neck Surgery at The Royal Marsden Hospital in London.

His special interests are in voice and swallowing disorders, thyroid and salivary gland disease, benign and malignant tumours of the mouth, tongue, throat and larynx (voice box) and tumours of the neck. As a UK pioneer since the early 1980s in new techniques of endoscopic laser and conservation surgery for throat tumours, voice reconstruction following laryngectomy, and head and neck reconstruction, Mr Rhys-Evans and his team have developed many innovative techniques over the years.

With over 250 scientific publications, including four books, he has been an active contributor to the specialty. His award-winning textbook *Principles and Practice of Head and Neck Surgery and Oncology*, published in 2003 with a second edition in 2009, won a prestigious prize from the University of London for the 'best international publication in Otolaryngology' during the preceding five years. His valued reputation in his specialty is reflected in his membership of national and international societies and committees, and in presenting over 320 major lectures in 26 different countries.

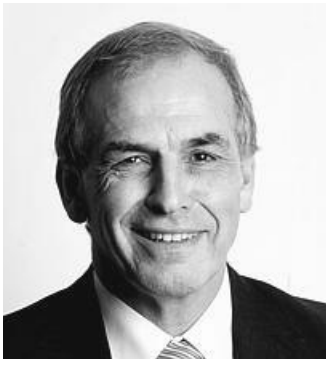
For the past ten years Mr Rhys Evans has been Executive Chairman of the Oracle Cancer Trust, based at The Royal Marsden and The Institute of Cancer Research. Since 2001 he has been responsible for raising over £5 million for head and neck cancer research and, with his colleagues, for establishing a very active research programme.

One of Peter's research interests since the 1980s has been in early human evolution and in May 2013 he was Organising Chairman of a 2 day International Conference "Human Evolution - Past, Present and Future" in London with guest speakers including Sir David Attenborough, Stephen Oppenheimer, Donald Johanson and Stephen Cunnane.

Invited Keynote Speakers

Professor Alan Finkel AO

The newly appointed Australian Chief Scientist



Professor Hugh Bradlow

Chief Scientist at Telstra

Professor Frank Gannon

Director and CEO of QIMR Berghofer Medical Research Institute

Professor Ian Frazer AC

The University of Queensland, Translational Research Institute Chair, TRI Foundation board

Invited Speakers

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Prof. Alan Mackay-Sim
Professor Emeritus, Eskitis Institute for Drug Discovery
Griffith University

Dr. Alkis Psaltis
Head of Department of Otolaryngology Head and Neck Surgery Senior Lecturer
The Queen Elizabeth Hospital, Adelaide and Division of Surgery, University of Adelaide

Dr. Bryony Nayagam
Research Fellow, Senior Research Fellow and Senior Lecturer
Garnett Passe and Rodney Williams Memorial Foundation and Bionics Institute and University of Melbourne

Associate Prof. David Cherry
Consultant
MLCOA

Prof. Ian Curthoys
Emeritus Professor of Vestibular Function
Vestibular Research Laboratory, University of Sydney

Dr. Jacob Thomas
Research Fellow
Centre for NanoScale Biophotonics at the University of Adelaide

Dr. James Earnshaw
Royal Brisbane Hospital

Dr. Rebecca Lim
Senior Lecturer
School of Biomedical Sciences and Pharmacy, Faculty of Health and Medicine, The University of Newcastle

Prof. Michael Halmagyi
Neurology Department
Royal Prince Alfred Hospital, Sydney

Dr. Andrew Zacest
Neurosurgeon
Royal Adelaide Hospital

Prof. Robert Shepherd
Director
The Bionics Institute (nee The Bionic Ear Institute)

Dr. Jeremy Pinyon
Postdoctoral Research Fellow
UNSW Australia

Dr. Allen Wang
ENT SET 1 trainee
Ear Sciences Centre, School of Surgery, The University of Western Australia and
Department of Otolaryngology, Head and Neck, Skull Base Surgery, Sir Charles Gairdner Hospital

Dr. Mark Smyth
Senior Scientist & Immunology Coordinator
QIMR Berghofer Medical Research Institute

Dr. Payal Mukherjee
Senior Clinical Lecturer
University of Sydney, RPA Institute of Academic Surgery

Prof. Peter John Wormald
Chairman and Professor of Otolaryngology Head and Neck Surgery
Professor of Skull Base Surgery, University of Adelaide

Prof. Peter Smith
Allergist and Molecular Immunology Director
Clinical Medicine Griffith University, Qld Allergy Services Southport, Allergy Medical Brisbane and Sydney

Associate Prof. Peter Santa Maria
The University of Western Australia

Associate Prof. Suren Krishnan
Chairman
Royal Adelaide Hospital

Prof. Michael McCullough
Professor of Oral Medicine
University of Melbourne

Emeritus Prof. Roland Sussex
The University of Queensland

Scientific Program

Thursday 8th September 2016

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THURSDAY 8TH SEPTEMBER		
SESSION 1: Chair - Prof. William B Coman		
8.30 - 8.40	Official welcome	Prof. William B Coman
8.40 - 9.10	Science, research and innovation for Australia into the next decade	Prof. Alan Finkel
9.10 - 9.50	Innate immunity in chronic rhinosinusitis	Prof. Wytske Fokkens
9.50 - 10.30	The Genetics of hearing loss	Prof. Lawrence Lustig
10.30 - 11.00	MORNING TEA	
SESSION 2: Chair - Prof. John Harris		
11.00 - 11.40	Surfers ear provides hard evidence of an acquatic phase in Man's early evolution.	Dr. Peter Rhys Evans
11.40 - 12.00	The International Sinonasal Microbiome Collaboration: Comparing geographic and microbiological differences in health and disease	Dr. Alkis Psaltis
12.00 - 12.15	Development of cochlear implant—driven gene therapy to enhance the bionic ear	Dr. Jeremy Pinyon
12.15 - 12.30	Insights from next generation sequencing of head and neck cancer	Prof. Michael McCullough
12.30 - 12.45	Creating animal models of chronic tympanic membrane perforation	Dr. Allen Wang
12.45 - 1.00	More spray and less blood - Avastin in Hereditary Heamorrhagic Telangiectasia	Dr. James Earnshaw
1.00 - 2.00	LUNCH	
SESSION 3: Chair - Prof. John Funder		
2.00 - 2.15	New Frontiers in cancer immunotherapy	Dr. Mark Smyth
2.15 - 2.30	Inside the developing human labyrinth	Dr. Rebecca Lim
2.30 - 2.45	3D printing, Augmented and Virtual reality. Its applications in Otolayrngology	Dr. Payal Mukherjee
2.45 - 3.05	The foundations for innovation and commercialization of medical devices	Dr. Peter Santa Maria
3.05 - 3.20	Using advanced magnetic imaging to map the human auditory brain stem.	Dr. Bryony Nayagam
3.20 - 4.00	Outcomes and impact of the Foundation in Otorhinolaryngology over 25 years	Prof. Rob Shepherd Prof. P J Wormald Prof. Alan Mackay-Sim Prof. Ian Curthoys Prof. Michael Halmagyi

Scientific Program

Friday 9th September 2016

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FRIDAY 9TH SEPTEMBER		
SESSION 4: Chair - Prof. John Furness		
8.30 - 9.10	Pathophysiology and treatment options in non allergic rhinitis	Prof. Wytske Fokkens
9.10 - 9.50	Cochlear gene therapy: Is it time?	Prof. Lawrence Lustig
9.50 - 10.30	Functional analysis of speech and swallowing in head and neck cancer patients	Dr. Peter Rhys Evans
10.30 - 11.00	MORNING TEA	
SESSION 5 – PAIN IN THE HEAD AND NECK : Chair - Dr. Andrew Zacrest		
11.00 - 11.15	The pathophysiology of pain	Associate Prof. David Cherry
11.15 - 11.35	The pain in rhinitis	Prof. Peter Smith
11.35 - 11.50	Facial pain – the case for sinus disease	Dr. Alkis Psaltis
11.50 - 12.10	Neuro immune mechanisms of pain and implications for analgesia.	Dr. Jacob Thomas
12.10 - 12.25	When to call for the neurosurgeon	Dr. Andrew Zacest
12.25 - 12.40	Pain, culture and communication	Emeritus Prof. Roland Sussex
12.40 - 1.00	Panel Discussion	
1.00 - 2.00	LUNCH	
SESSION 6: Chair - Dr. Michael Jay		
2.00 - 2.15	Integrating teams to focus on head and neck surgery	Prof. Frank Gannon
2.15 - 2.35	Presbycusis and noise induced hearing loss – Old problems and new paradigms	Prof. Lawrence Lustig
2.35 - 3.00	Ethics and surgical equipoise with changing paradigms in the treatment of	Assoc. Professor Suren Krish-
3.00 - 3.30	Exponential technologies and implications for the healthcare industry	Prof. Hugh Bradlow
3.30 - 4.00	The scourge of HPV and what lies ahead.	Prof. Ian Frazer

Social Program

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WELCOME DINNER

Wednesday 7th September

Location: Poolside Lawns, Sheraton Mirage Gold Coast
Timings: 1830 - 2130
Dress Code: Smart Casual

POSTER PRESENTATIONS

Thursday 8th September

Location: Ballroom and Ballroom Foyer, Sheraton Mirage Gold Coast
Timings: 1800 - 2330.
Dress Code: Smart Casual

CONFERENCE DINNER

Friday 9th September

Location: McLaren's Landing
Timings: 1800 - 2330. Please meet Event Travel Management Staff in the foyer of the hotel at 1800 sharp. The dinner is located outside of the hotel.
Dress Code: Please wear the shirt provided in your conference pack.

Conference Dinner Speaker

Professor Roland Sussex OAM

An emeritus professor of Applied Language Studies at the School of Languages and Comparative Cultural Studies of the University of Queensland, Brisbane, Australia. Sussex hosts a talkback program on language and linguistics on ABC radio in Queensland, Tasmania, South Australia and the Northern Territory and writes a weekly column, “Wordlimit”, for the newspaper The Courier-Mail.

General Information

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Venue

The only 5-star beachfront resort in Gold Coast, with beautiful rooms and exciting activities.

Set amongst 6 hectares of sparkling lagoons and tropical gardens, the newly refurbished resort features 295 rooms and suites and exquisite dining. Enjoy their amazing pool, fitness centre, spa facilities and surrounding beach to stay refreshed throughout your stay.

Breakfast

If you have booked accommodation through Event Travel Management, breakfast will be included in your room rate. Single rooms will include 1 x breakfast and Double rooms will include 2 x breakfasts.

Car parking

Parking is available for all attendees free of charge if you self-park below the resort. Access to parking is located in the hotel's driveway

Insurance

Delegates should make their own arrangements with respect to personal insurance.

Internet Access

There will be free WIFI in public areas. Complimentary Wi-Fi in accommodation rooms will be available if you sign for the SPG Pro Membership (Membership is complimentary).

Check-out

Check out time is 12:00. Late check outs are subject to availability and an additional fee may apply. Please liaise directly with the hotel for any late checkouts.

Name Badges

Name badges must be worn at all times during the conference. If you have lost or misplaced your name badge, please go to the registration desk for a replacement.

No Smoking Policy

The resort has a no smoking policy in their rooms and conference spaces. Please refer to hotel staff for allocated smoking areas. Please be aware that breach of the policy will result in a cleaning fee of $300, payable by the guest, to return the room to its original condition.

Registration Desk

Day/Date	Time	Location
Wednesday, 7th September	1400 - 1800	Sheraton Mirage Ballroom
Thursday, 8th September	0730 - 1630	Conference Level
Friday, 9th September	0730 - 1630	Conference Level

Transfer Information

Gold Coast Airport

30 minutes to the city by car, 50-60 minutes to the city by public transport.

TransLink's public transport network can get you to and from the Gold Coast Airport, and around the coast during your stay. TransLink's integrated network on the Gold Coast includes the G:link trams, Surfside bus lines and Queensland Rail. Visit translink.com.au or call 13 12 30 for information or to plan your journey.

The taxi rank is conveniently located outside of the terminal for travellers requiring transport.

For more information, please contact: Phone: 131 008 www.gccabs.com.au

Brisbane Airport

Catch the train - Brisbane Airport to Gold Coast

Airtrain services travel between Brisbane Airport to the Gold Coast every 15 minutes during the peak (and 30 minutes during the off-peak), making Airtrain the frequent and easy airport transfer.

Airtrain has ticket options to suit your travel needs. If you require an airport transfer direct to your Gold Coast accommodation or address consider Airtrain's Train & Transfer (AirtrainConnect) – our door to door service

Timetable for the Gold Coast line here for assistance with your train and bus journey planning visit www.translink.com.au

Session 1 : 8.40 to 9.10

SCIENCE, RESEARCH AND INNOVATIION FOR AUSTRALIA INTO THE NEXT DECADE

Professor Alan Finkel AO

The newly appointed Australian Chief Scientist

Dr Finkel commenced as Australia's Chief Scientist on 25 January 2016. He is Australia's eighth Chief Scientist.

Dr Finkel has an extensive science background as an entrepreneur, engineer, neuroscientist and educator.

Prior to becoming Chief Scientist, he was the Chancellor of Monash University and President of the Australian Academy of Technology and Engineering (ATSE).

Dr Finkel was awarded his PhD in electrical engineering from Monash University and worked as a postdoctoral research fellow in neuroscience at the Australian National University.

In 1983 he founded Axon Instruments, a California-based, ASX-listed company that made precision scientific instruments used at pharmaceutical companies and universities for the discovery of new medicines. After Axon was sold in 2004, Dr Finkel became a director of the acquiring company, NASDAQ-listed Molecular Devices.

In 2006, he focused his career in Australia and undertook a wide range of activities. He led the amalgamation that formed the Florey Neuroscience Institutes; he became Chair of the Australian Centre of Excellence for All-Sky Astrophysics (CAASTRO) and was a director of the ASX-listed diagnostics company Cogstate Limited. He was Executive Chair of the educational software company Stile Education, Chair of Manhattan Investment Group, Chief Technology Officer of Better Place Australia and Chair of Speedpanel Australia.

Committed to science education, Dr Finkel co-founded Cosmos Magazine, which in addition to magazine publishing operates a secondary schools science education program. At ATSE, he led the development and implementation of the STELR program for secondary school science, which has been adopted in nearly 500 Australian schools. Dr Finkel also established the Australian Course in Advanced Neuroscience to train early career neuroscientists and is patron of the Australian Science Media Centre.

Session 1 : 9.10 to 9.50

INNATE IMMUNITY IN CHRONIC RHINOSINUSITIS

Professor Wytske Fokkens

Department of Otorhinolaryngology, Academisch Medisch Centrum, Amsterdam, The Netherlands

Chronic rhinosinusitis (CRS) is a complex and heterogeneous disease that is characterized by airway inflammation. CRS can be divided in CRS with nasal polyps (CRSwNP), and CRS without nasal polyps (CRSsNP). Although in most patients with CRSwNP the inflammation is characterized by type 2 cells allergy does not seem to play an important role. The exact cause of the Th2 inflammation has been a source of a lot of speculation in which virus, staphylocus aureus and fungi has been mentioned as potential factors. In the past decade it has become clear that epithelial cells play a critical role in innate immune responses, and they can help to shape the nature of ensuing adaptive responses. Not only have epithelial cells from CRSwNP patients been shown to have defects in their ability to form tight junctions but maybe more important the epithelial cells themselves are active innate immune cells.

A very exciting recent development was the discovery of innate lymphoid cells (ILCs) as potential key players in the pathogenesis of CRSwNP and asthma. ILCs do not express antigen receptors but react promptly to "danger signals" and produce an array of cytokines that direct the ensuing immune response. ILCs are a family of effector cells that are important for protection against infiltrating pathogens and restoration of tissue integrity. Three major subsets have been defined on the basis of their phenotype and functional similarities to helper T cells. Group 2 ILCs (ILC2s) are known to produce type 2 cytokines, especially IL-5 and IL-13, and are activated by cytokines from epithelial cells such as IL-25, IL-33, and thymic stromal lymphopoietin (TSLP), which are also associated with type 2 inflammatory responses. We have demonstrated that ILC2s are highly elevated in nasal polyp tissues contrary to ILC1s and ILC3s that are diminished. Together these data suggested that an inflammatory environment alteres ILC composition. Although the precise roles of ILCs in CRS is still under investigation, it is clear that inhibition of ILC function represents a potential target that could provide novel treatments for CRS.

Session 1 : 9.50 to 10.30

THE GENETICS OF HEARING LOSS

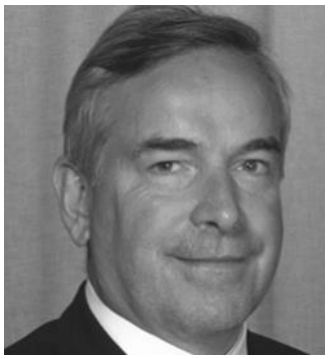
Professor Lawrence Lustig

Howard W. Smith Professor and Chair

Department of Otolaryngology-Head & Neck Surgery, Columbia University Medical Center & New York Presbyterian Hospital

It has been understood as early as the 1600's that many types of hearing loss have an inherited component. With advances in medical genetics over the past century, our understanding of the genetics of hearing loss has led to similar remarkable advances in our understanding of the anatomy and physiology of hearing. To date over 100 single genes have been identified that can contribute to hearing loss when mutated, however it is predicted that there are over 280. As we evolve into the era of 'NextGen' sequencing, it is anticipated that more subtle mutations across multiple genes may be identified that contribute to the most common forms of hearing loss that exist, include age-related hearing loss and susceptibility to noise-induced hearing loss.

This talk will outline the history of our understanding of the genetics of hearing loss and delve into several prominent examples of how the elucidation of the genetics in turn led to fundamental scientific breakthroughs in how we hear. We will also outline the shift from more classic Sanger sequencing technologies to NextGen Sequencing and how this will impact our understanding of the genetics of hearing loss in the future.



Session 2 : 11.00 to 11.40

SURFERS EAR PROVIDES HARD EVIDENCE OF AN AQUATIC PHASE IN MAN'S EARLY EVOLUTION

Dr Peter Rhys-Evans
Consultant ENT/Head and Neck Surgeon
Lister Hospital, London SW1

Otolaryngologists have long recognised the condition of aural exostoses, but their significance and the mechanism of formation has remained obscure. Their association with frequent swimming is well known and the fact that the condition is usually bilateral is predictable since both ears are immersed in water. However, why do they only grow in swimmers? Why do exostoses grow in the deep bony meatus at 2 or 3 constant sites? And , from an evolutionary point of view, what is or was the purpose of these rather incongruous protrusions?

The traditional "Savannah" theory of evolution suggests that our ancestral ape came down from the trees and stood upright to see further over the savannah and started to walk and run, hunting for game. However, if it was so advantageous for one branch of the family, why didn't other primates and mammals do the same?

Sir Alister Hardy, a marine biologist, noted that many of man's characteristics- loss of body hair, subcutaneous fat, our bipedal streamlined body, sweat glands and thermoregulatory system, were totally unique amongst terrestrial mammals and primates, but were commonly seen in aquatic and semi-aquatic mammals1.

This "Waterside Ape" theory suggests that as a result of the late Miocene drought when the deciduous forest habitat of the arboreal apes was decimated and replaced largely by savannah, our primate ancestor started foraging for new sources of food abundantly available in the estuaries, rivers, seashore and along the newly formed Great Rift Valley in East Africa where most of the early hominid fossils have been found. Initially wading in shallows, they extending their territory into deeper water, learning to swim and dive in search of food. The buoyancy of the water gradually allowed rotation of the pelvis, support of the spine and strengthening of the lower limbs. Back on dry land they were able to walk upright, freeing their arms developing increasing manual dexterity. Recent evidence has also shown that there are two lipoproteins essential for big brain development and that these are mainly found in seafood. Eventual migration out of Africa followed coastal routes.

In 1992 the senior author suggested that there were many ENT features that supported the theory of a significant aquatic influence during hominid evolution, including expansion of the sinuses in Man which would aid buoyancy in an aquatic habitat and that aural exostoses were evolved in early hominid Man for protection of the delicate tympanic membrane during swimming and diving by narrowing the ear canal in a similar fashion to other semi-aquatic species2. He proposed that if these exostoses were found in early hominid fossils, it would provide unique fossil evidence that early hominid Man spent considerable time immersed in water for the purpose of hunting for his survival and would provide a logical explanation for the puzzling Darwinian "Missing Link". We now provide evidence for this theory and propose a mechanism for the formation of exostoses.

Session 2 : 11.40 to 12.00

THE INTERNATIONAL SINONASAL MICROBIOME COLLABORATION: COMPARING GEOGRAPHIC AND MICROBIOLOGICAL DIFFERENCES IN HEALTH AND DISEASE

Dr Alkis Psaltis

Head of Department of Otolaryngology Head and Neck Surgery, The Queen Elizabeth Hospital, Adelaide

Senior Lecturer, Division of Surgery, University of Adelaide

Microbiomics in chronic diseases, including Chronic Rhinosinusitis (CRS), have undergone rapid advances in recent times. The introduction of Next Genomic Sequencing (NGS) technology has produced significant clinical insights regarding the bacteriology of these conditions. This presentation reviews the current studies that have used 16S rRNA sequencing to specifically investigate the microbiota profiles of patients with CRS, in a variety of contexts. In addition preliminary data on the international microbiome collaboration involving 12 centers world wide will be presented.

Session 2 : 12.00 to 12.15

DEVELOPMENT OF COCHLEAR IMPLANT—DRIVEN GENE THERAPY TO ENHANCE THE BIONIC EAR

Dr Jeremy Pinyon

Postdoctoral Research Fellow, UNSW Australia

Background: The cochlear implant (CI) electrode array has changed little over time, despite considerable advances in the speech processor capabilities. An aspiration is to improve the selective recruitment of spiral ganglion neurons (SGNs) along the length of the cochlea in a manner that more closely engages the intrinsic tonotopic mapping of the hearing organ. Hence, the biological aspect of the neural interface needs to be addressed. Central to this is closing the 'neural gap' between the electrodes and the surviving SGNs. The current spread that occurs at the stimulus levels required to recruit the atrophied SGN cell bodies within Rosenthal's canal is such that current position-based mapping is coarse, limiting perception. A range of neurotrophin delivery strategies stimulate peripheral neurite extension and promote survival of SGNs in cochleae of animal models of SNHL, but the challenge is to achieve this safely and direct and constrain the neurite extension so that a stable intimate relationship with the bionic array electrodes is achieved.

Objective: Our approach to this challenge has been to develop a way of using the CI electrode array for electric field focusing which drives local electrotransfer of naked plasmid DNA encoding brain-derived neurotrophic factor (BDNF) into the mesenchymal cells of the perilymphatic compartment of the cochlea close to the electrodes.

Method: Voltage pulses are delivered through the CI array to electroporate targeted mesenchymal cells close to the array. Using ex vivo and in vivo experiments with guinea-pig cochleae, supported by studies with HEK293 cell monolayers.

Results: We identified that the wiring configuration of the CI array was a key factor in the efficiency of gene delivery. Mapping of the electric field around the array in different configurations showed that field-focusing produced compression of field strength, enabling gene electrotransfer with voltages lower than those necessary for conventional electroporation. 'Dial-up' control of the shape and area of the region of transfected cells is possible by controlling the field focusing and voltage pulse parameters. Transfected mesenchymal cells express BDNF and within 7 days SGN neurite extension occurs beyond the osseous spiral lamina and into scala tympani.

Conclusion: Functional assessment using bipolar stimulation via the CI in a deafened guinea pig model indicated that this gene therapy treatment had the desired effects of lowering threshold current levels for SGN recruitment and increasing the dynamic range of the input–output function, indicative of progressive recruitment into the local SGN population as the current levels increased. These promising developments around local naked DNA–based gene electrotransfer in the cochlea support utilisation of this process for targeted neurotrophin gene therapy during CI surgery to enhance SGN survival and optimize the neural interface.

Funding:
Australian Research Council DP150104754 & LP0992098 with support from Cochlear Ltd. National Health and Medical Research Council, Garnett Pass and Rodney Williams Memorial Foundation.

Declaration:
Patents associated with this development are assigned to the New South Innovations, the commercialization arm of UNSW Australia. These findings have been published as: Pinyon et al. Sci. Transl. Med., 2014; and Browne et al., Gene Ther., 2016.

Session 2 : 12.15 to 12.30

INSIGHTS FROM NEXT GENERATION SEQUENCING OF HEAD AND NECK CANCER

Professor Michael McCullough
Professor of Oral Medicine
University of Melbourne

Introduction: Oral cavity squamous cell carcinomas (OSCCs) are the most prevalent head and neck malignancy and are a significant cause of mortality and morbidity, especially in the developing world. A better understanding of the molecular pathogenesis of OSCCs is essential for improved management of this disease. Clinical subgroups have been delineated and are of significant interest, particularly the non-smoking non-drinking (NSND) group and human papilloma virus (HPV) related tumours. Genomic characterisation of these clinical subgroups utilising next-generation sequencing techniques will help in understanding the genetic progression of oral carcinogenesis and guide us towards novel rational approaches for the treatment of this disease.

Methods: A custom 69 gene panel was designed based on an analysis of the Cancer Genome Atlas (TCGA) and targeted next-generation sequencing carried out on fresh frozen and formalin fixed paraffin embedded (FFPE) tissue from prospectively and retrospectively recruited OSCC patients presenting to the Royal Melbourne Hospital (n = 94). Detailed clinical annotation was collected for all patients. For the FFPE samples, computational pipelines were developed to reduce paraffin related artefact and identify somatic mutations.

Results: In our patient cohort, a high frequency of mutations were identified in known tumour suppressor genes TP53 (57%) and CDKN2A (22%). Sixteen patients (17%) were NOTCH1 mutant.

Conclusions: We have sequenced a large number of tumours from patients presenting to our centre. An effective technique has been developed to reduce paraffin-induced sequence artefact and identify somatic mutations, with similar mutation rates seen across both patient cohorts. This can be applied to other projects in the future.

Session 2 : 12.30 to 12.45

CREATING ANIMAL MODELS OF CHRONIC TYMPANIC MEMBRANE PERFORATION

Dr Allen Wang

ENT SET 1 Trainee

Ear Sciences Centre, School of Surgery, The University of Western Australia

Department of Otolaryngology, Head and Neck, Skull Base Surgery,

Sir Charles Gairdner Hospital

Tympanic membrane perforation (TMP) is a common clinical presentation worldwide, caused mainly by trauma, infections (e.g. otitis media) or ventilation tube removal/extrusion. Although the majority of acute TMPs heal spontaneously without intervention, those which fail to heal within three months are defined as chronic TMP. Chronic TMPs often stay permanently patent and are unlikely to close spontaneously. In these cases, surgical grafting is an option for treatment.

The development of novel graft materials for TM repair is required to undergo extensive in vitro and in vivo (i.e. animal models) evaluations prior to clinical trials. In order to fully examine the efficacy of a novel graft, a chronic TMP animal model that mimics the clinical condition of chronic TMPs in patients is paramount. In the current literature, various animal models have been reported, including rat, mouse, chinchilla, guinea pig and dog. However, these models are mostly of acute TMPs and not useful for assessment of materials for myringoplasty or tympanoplasty on chronic TMPs. Up to 94% of acute TMPs heal spontaneously without intervention, thus accelerating the healing of acute TMPs is of less practical value. In contrast, a chronic TMP animal model has more clinical relevance but an 'ideal' animal model has not yet been found.

Our research group has recently developed a novel method of creating chronic TMP in rats by using ventilation tube (VT) treatment combined with topical mitomycin/dexamethasone application. This method produced chronic TMPs staying patent up to ten weeks with a reasonable success rate of 70%. The procedure is simple, reproducible and reliable. Most importantly, we now have a successful chronic TMP animal model for evaluating various graft materials for myringoplasty. This animal model may assist evidence-based evaluation of new therapeutic interventions for repair of chronic TMPs in patients.

Session 2 : 12.45 to 13.00

MORE SPRAY LESS BLOOD—AVASTIN IN HEREDITARY HEAMORRHAGIC TELANGIECTASIA

Dr James Earnshaw
VMO
Royal Brisbane Hospital

HHT affects 1/5000 patients and management can be a dilemma. The Royal Brisbane Hospital has been using Bevacizumab for a cohort of these patients. Treatment with Bevacizumab seems to improve bleeding symptoms. We will look at this research and other research around the use of Bevacizumab in HHT patients.

Session 3 : 14.00 to 14.15

NEW FRONTIERS IN CANCER IMMUNOTHERAPY

Dr Mark Smyth
Senior Scientist & Immunology Coordinator
QIMR Berghofer Medical Research Institute

Head and Neck Cancer (HNSCC) is the fifth most common cancer worldwide, with approximately 1000 people dying each year in Australia from the disease. Novel immune-therapies, for example antibodies against cytotoxic T lymphocyte associated protein 4 (CTLA-4) and programmed death 1 (PD-1) are changing the landscape of cancer therapy, as best evidenced in advanced melanoma, NSCLC and more recently HNSCC with sustained tumour responses in a significant number of patients. We are researching three new immunotherapy approaches to combine with PD-1 blockade and the intention is to do this in the context of HNSCC with our clinical colleagues here in Brisbane.

Session 3 : 14.15 to 14.30

INSIDE THE DEVELOPING HUMAN LABYRINTH

Dr Rebecca Lim

Senior Lecturer

School of Biomedical Sciences and Pharmacy, Faculty of Health and Medicine

The University of Newcastle

Development of the human inner ear begins at approximately 4 weeks gestation (WG) with invagination of the otic placode. Our primary understanding of the development of the human inner ear arises from gross morphological studies that describe the growth and elongation of the semicircular canals and cochlea into the exquisite and complex labyrinth structure with which we are familiar. The intricate details of inner ear development from cell fate specification to functional neural innervation however have primarily been derived from animal models, mostly rodents.

In our studies we use a human foetal preparation of the peripheral vestibular system to establish the developmental timeline of hair cell differentiation, the expression of important hair cell functional proteins, and the innervation of hair cells by nerve fibres. Ultimately we hope to recapitulate this developmental chronology in regeneration studies.

To investigate hair cell differentiation we used the hair cell specific marker, myosin VIIa, and hair bundle markers including phalloidin and alpha-acetylated tubulin. As early as 10 WG some hair cells have already differentiated and express myosin VIIa, which is present in almost all vestibular hair cells by 12 WG. At the same stage of development, phalloidin and alpha-acetylated tubulin are expressed in stereocilia and kinocilium respectively suggesting hair bundle orientation and therefore cell polarity is already established by this time. Another important indicator of cellular maturity is the presence of the ribbon synapse marker C-terminal binding protein-2 (CtBP2). These results indicate that by 12 WG vestibular hair cells have the synaptic machinery necessary for cellular communication. To determine whether synapses were functional we measured neurotransmitter release in developing hair cells using patch clamp recordings. Our data show that between the ages of 11 – 14 WG there are two distinct populations of responsive hair cells; those with 'high sensitivity', that release more neurotransmitter and those with 'low sensitivity' releasing less neurotransmitter. We conjectured that these differences reflect the two types of hair cell found in the mature vestibular epithelium. In mature epithelia, type I and type II hair cells have distinct morphological and physiological characteristics. At 12 WG, however, we could not distinguish between the two types, morphologically. To determine if hair cells had physiologically differentiated into type I and type II hair cells we recorded their electrophysiological activity. Our recordings at this time point showed currents characteristic of type II hair cells only. We did not see evidence of currents that were commensurate with type I hair cells until 14 WG. At 14 WG, we also observed the first evidence of activity in the unique cup-like or calyx afferent terminals that only contact type I hair cells and transmit their balance signals to the central nervous system. It remains to be seen if high and low sensitivity is a marker of future hair cell function.

In summary, these results provide us with the first clear understanding of the developmental pattern of maturation in the human inner ear. This will help to improve current regenerative technologies and enhance prosthetic devices for hearing and balance.

Session 3 : 14.30 to 14.45

3D PRINTING, AUGMENTED AND VIRTUAL REALITY. ITS APPLICATIONS IN OTOLARYNGOLOGY

Dr Payal Mukherjee

Senior Clinical Lecturer

University of Sydney, RPA Institute of Academic Surgery

Introduction: Otolaryngology is plagued with complex three dimensional (3D) anatomical challenges. 3D printing, Augmented Reality and Virtual Reality offers new and innovative solutions in solving clinical challenges and overcoming educational boundaries.

Background: Clinical practice in Otolaryngology is faced with diverse anatomical challenges from reconstructing microtia and complex skull based defects to large head and neck reconstruction. The challenges increase operative time and the risk of potential complications (e.g. leaks, wound breakdown etc). 3D printing is a new and innovative tool that has a great potential to help address some of these challenges.

Methods: CT scans of patients with a diverse range of ENT disorders ranging from skull base cholesteatoma to exostosis were applied to 3D printing. When necessary for preoperative planning, printed bones were also drilled. The CT content was also developed into patient specific Augmented Reality content. MicroCT data of human temporal bones were used to develop virtual reality content. A range of uses were explored.

Results: These new methods are invaluable for 3 reasons: education, explanation of disease and surgical procedures to patients and for preoperative planning. The resolution of modern imaging is adequate and the accessibility to current 3D printers and smart devices makes this technology feasible, inexpensive and available with rapid turnover for use in routine clinical practice.

Conclusion: 3D printing, Augmented Reality and Virtual Reality opens new dimensions in the future of patient care in Otolaryngology with care and repair customized to patient specific anatomy and patient specific pathology.

Session 3 : 14.45 to 15.05

THE FOUNDATIONS FOR INNOVATION AND COMMERCIALISATION OF MEDICAL DEVICES

Dr Peter Santa Maria

Associate Professor

The University of Western Australia

Background: Too many inventors spend time inventing and building amazing medical devices but struggle when they come to commercializing them because of a failure to properly address an unmet medical need.

Aim: The medical device development and commercialization process will be explained using examples of the process developed by Stanford University's SPARK program that has been launched in Western Australia. The foundation for innovating medical comes from an understanding of the clinical problem and focusing it into a clinical need. As most device failures in commercialization can be focussed into a poor understanding of the problem which it is addressing, this is a critical stage in the invention process. The stakeholders in health care delivery need to be engaged from the beginning as in today's health economy the payers have final say on what medical devices make it to market. After moving into the ideation phase and developing a concept the potential device can be developed through understanding the intellectual property, clinical, technical, regulatory, reimbursement and business factors involved. Inventors should have a basic understanding of intellectual property not only to protect their idea but to make sure they can provide value for the next stage of development to be invested in. Along the way, clinicians benefit from collaboration especially with engineers and those with business experience. Industry engagement and mentorship, as the invention progresses, is also critical in crossing the "valley of death" of medical translation. Technical challenges can be overcome through early stage prototyping that can help develop the concept further without the need for large investment.

Conclusion: Medical device translation requires a multidisciplinary approach with industry engagement and mentorship. It benefits from a clear articulation of the unmet medical need at the beginning of the process.

Session 3 : 15.05 to 15.20

USING ADVANCED MAGNETIC IMAGING TO MAP HUMAN AUDITORY BRAIN

Dr Bryony Nayagam

Associate Professor

The University of Western Australia

Collectively, our current knowledge of the structural and functional connections in the auditory brainstem has been acquired from post-mortem dissections and mammalian models. Advances in structural magnetic resonance imaging (MRI; ie. fibre tractography) are now facilitating high-resolution fibre tracking studies of the human brain in situ. These non-invasive techniques will likely yield a better understanding of structural and functional connections in the living brain, and this may facilitate future development of MRI for neurodiagnostic and treatment management purposes.

Auditory processing at the level of the brainstem plays an essential role in the organisation, integration, and ultimately the perception of auditory information in the cortex. A number of neurodegenerative conditions report with abnormal auditory processing, and whilst a battery of clinical tests can readily identify abnormal neural activity in these individuals, the underlying VIIIth nerve and brainstem pathology remains elusive. The identification and quantification of white matter fibre projections in the human auditory brainstem may provide a more definitive indication of the location of any structural abnormalities in affected individuals, thus informing our understanding of the underlying pathology in these complex neurodegenerative diseases and ultimately therapeutic intervention.

Using advanced MRI fibre tractography, we are attempting to visualise the structural organisation and integrity of the human auditory brainstem in situ. Clear visualisation of the human auditory brainstem is considered a key first step required in order to develop structural MRI into a more refined neurodiagnostic tool in the future. This presentation will describe preliminary results obtained using fibre tractography of the normal hearing human auditory brainstem. These data include mapping key regions of interest (ie. the cochlear nucleus and inferior colliculi) and white matter fibre projections between these nuclei. By analysing extensive MRI data sets from both normal hearing and affected individuals, we can statistically compare the density of white matter fibre pathways in the brain. Deviations in the density and integrity of brainstem fibres in the abnormal compared to normal hearing individual may enable more accurate identification of central pathology. Additionally, this may facilitate the provision of the more appropriate treatment and/ or management of patients by neurologists and other health professionals in future.

Session 3 : 15.20 to 16.00

OUTCOMES AND IMPACT OF THE FOUNDATION IN OTORHINOLARYNGOLOGY OVER 25 YEARS

Prof. Rob Shepherd
Director
The Bionics Institute (nee The Bionic Ear Institute)

The Garnett Passe & Rodney Williams Memorial Foundation (GPRWMF) has had a major impact on Australian and New Zealand Otorhinolaryngology and its allied fields for over 25 years. This impact can be measured in research outcomes and the translation of this research to the clinic, training the next generation of clinicians and scientists, and improving clinical practice. Here I summarise the impact of the foundation through the Bionics Institute (BI; née the Bionic Ear Institute) and its long-term association with the Department of Otolaryngology, University of Melbourne.

Three BI researchers have been recipients of a GPRWMF Senior/Principle Research Fellowship including Prof R. Shepherd (1996), Prof C. McKay (1998) and Prof H. McDermott (2001). All three have made important contributions to cochlear implant/hearing aid technology and continue to play leadership roles in the field. Their research often includes Otology collaborators – notably Dr R. Briggs, Prof S. O'Leary, Dr M. Dahm and Dr M. Tykocinski.

A number of Institute based researchers have received GPRWMF project funding to undertake a variety of studies that have contributed to an improved understanding of the auditory system or have resulted in new or improved clinical outcomes. This work has included cochlear implant safety & efficacy (Drs J. Fallon & J. Marozeau), hair cell rescue (Dr R. Richardson), drug delivery technology (Drs L. Pettingill & A. Wise), efficacy of inner ear drug delivery (Dr E. King), response of the auditory system to deafness (Dr N. Rickards), fundamental studies of auditory system neuroanatomy (Dr A. Paolini), and the application of stem cells to treat a variety of inner ear pathologies (Dr B. Nayagam). This funding has kick-started careers and has resulted in the generation of further research through NHMRC and other peer-reviewed funding bodies as well as industry including Cochlear Ltd and Pfizer Inc.

In addition, the GPRWMF has funded the next generation of research leaders at the BI through PhD Scholarships. Notable awardees include Dr B. Wei (PhD 2007; Victorian Premier's Award for Health & Medical Research 2008); Dr P. Atkinson (PhD 2010; current position: Department of Otolaryngology, Stanford University); Dr N. Gunewardene (PhD 2014: Department of Otolaryngology, Harvard Medical School); and Dr S. George (PhD 2016: Department of Otolaryngology, Stanford University).

Finally, GPRWMF funding has provided less quantitative outcomes including the ability for BI staff to host and train dozens of visiting clinicians and researchers, and allowed Institute researchers to apply their knowledge of cochlear implants in order to develop new bionic devices including the bionic eye for the blind, neurobionics devices to treat Parkinson's disease and detect the onset of seizures; and potentially devices to treat autoimmune diseases such as Crohn's disease.

Session 3 : 15.20 to 16.00

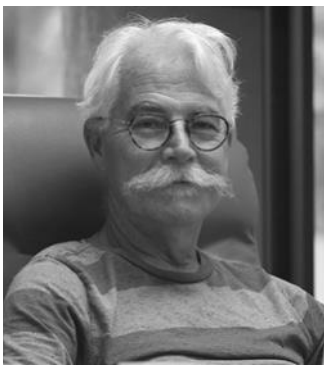
OUTCOMES AND IMPACT OF THE FOUNDATION IN OTORHINOLARYNGOLOGY OVER 25 YEARS

Prof. Peter John Wormald

Chairman and Professor of Otolaryngology Head and Neck Surgery

Professor of Skull Base Surgery, University of Adelaide

This presentation details the impact of the Garnett Passe and Rodney Williams Foundation on the development of Rhinology in Australasia. Rhinology as a subspecialty really started with the advent of endoscopic sinus surgery in the late 1980s by Stammberger and Kennedy. As the interest in the specialty grew in the 1990s so did the interest in the aetiopathogenesis of chronic rhinosinusitis and the academics that took up the sub-specilaty became fascinated with complex interactions that make up the various hypothesis surrounding this question. In Adelaide we took up this challenge to try to understand this fascinating disease. The academic department in Adelaide was formed in 1998 with one full time scientist and no track record of research. This presentation will outline the involvement of the Foundation in the development of the research in our department over the last 20 years. The other academic centres interested in Rhinology have been Richard Douglas in Auckland and Anders Cervin in Brisbane. I will also present the support that the Foundation has given these academic institutions.



Session 3 : 15.20 to 16.00

OUTCOMES AND IMPACT OF THE FOUNDATION IN OTORHINOLARYNGOLOGY OVER 25 YEARS

Prof. Alan Mackay-Sim

Professor Emeritus, Eskitis Institute for Drug Discovery

Griffith University

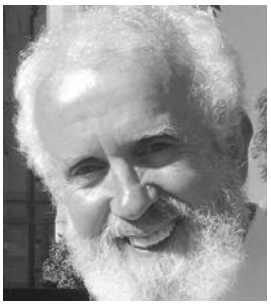
I was awarded a Senior Principal Resrach Fellowship in 1995, starting in 2006. My aim was to investigate neurogenesis in the human olfactory epithelium. Neurogenesis is the formation of new neurons, a process that is continual in the olfactory epithelium that replaces the olfactory sensory neurons that get damaged by disease or injury.

With this as a starting point I was interested in the stem cells that give rise to the new neurons and in the olfactory ensheathing cells that support their growth. We showed the stem cells were remarkably "potent", able to give rise to many cell types other than olfactory (muscle, blood, kidney, heart). From there we developed a stem cell bank with olfactory stem cells from patients with brain diseases and healthy controls, now containing about 300 cell lines. These are used to investigate schizophrenia, Parkinson's disease, Hereditary Spastic Paraplegia and several other conditions. By understanding the biological mechanisms of disease we use the cells to identify novel drug candidates as well as approved drugs that can be repurposed for rapid translation to clinical trials.

Olfactory ensheathing cells are therapeutic in animal spinal cord injuries, assisting growth of motor nerves through the site of injury. Our team carried out the first Phase I clinical trial of autologous olfactory ensheathing cell transplantation in paraplegia. Recently a team in Poland did the same in a patient and after 3 years of intense rehabilitation the patient can ride a bike.

Another interest of my lab has been clinical research. We developed Australian norms for the scratch'n'sniff Smell Identification Test and International norms for the Sniffin' Sticks test. We showed that olfactory loss with age is not inevitable but is associated with other illness or treatment, including Parkinson's disease, and loss of smell is predictive of loss of cognitive function, a risk for Alzheimer's disease. Through a Phase II clinical trial we showed that macrolides, like clarithromycin, at low dose are effective in treating chronic rhinosinusitis.

In this research I am indebted to many colleagues and students who are responsible for allowing me to take this path of discovery. I have worked with Chris Perry since the beginning and he still takes biopsies, 20 years later. Francois Feron, now a professor at the University of Marseilles, developed the cell culture protocols in the lab and drove a lot of the early biological work. John McGrath, a psychiatrist, got me interested in schizophrenia triggering the first patient studies. I am very grateful to Bill Coman for his mentorship. He has been a guide to the ENT world and his interest led to sabbaticals in the lab by Anders Cervin and Lennart Greiff. Bill encouraged me to take on ENT trainees to teach them about research, leading to PhD awards to Ben Wallwork (2006) and Brent McMonagle (2016). I am very proud of their success and expect that they will contribute greatly to the profession.



Session 3 : 15.20 to 16.00

OUTCOMES AND IMPACT OF THE FOUNDATION IN OTORHINOLARYNGOLOGY OVER 25 YEARS

Prof. Ian Curthoys
Emeritus Professor of Vestibular Function
Vestibular Research Laboratory, University of Sydney

Prof. Michael Halmagyi
Neurology Department
Royal Prince Alfred Hospital, Sydney

25 years ago it was a challenge to find out what was wrong with a dizzy patient. The caloric test was the standard test of just the horizontal canals and you all know the issues with calorics.

Outcomes

Research supported by GPRWMF has simply transformed the area of clinical vestibular testing

and also the basic knowledge of vestibular function which is the foundation of that testing. Now thanks to GPRWMF support there are simple, fast, non-invasive, cheap tests of every part of the peripheral vestibular system. The semicircular canals being tested by the video head impulse test – just measuring the eye movement during a brief head turn! And otolith function by measuring myogenic potentials to sound or vibration - the vestibular evoked myogenic potential test. Using sounds rather than sleds of centrifuges.

Complementing these stunning clinical successes, GPRWMF supported basic research has shown that vestibular receptor hair cells are very like cochlear receptor hair cells and that some vestibular neurons respond to very high frequencies (>3000Hz) just like cochlear hair cells. Forget the idea that the vestibular system is the “slow cousin” to the cochlea.

Impact

What has been the impact? The June 2016 meeting of the Barany Society showed that clinicians around the world have taken up these new tests at an astonishing rate, because these tests have been what clinicians have been waiting for the last century. More than half the papers used these new tests. Now in many vestibular clinics around the world, the vHIT is the first test given to dizzy patients – at last the caloric is being phased out much to the delight of patients! And otolaryngologists are discovering that some patients have conditions they had not dreamt of – bilateral vertical canal loss! And these tests are being used as functional indicators of stroke in ER.

Having been so successful in identifying vestibular loss, the tests are now being applied to longstanding problems – quantifying just how vestibular function changes in Meniere’s disease and vestibular migraine. Possible at last because these tests are so innocuous they can be given at short intervals – like 10 or 15 minutes apart.

This dramatic progress has come about because of the truly fantastic support of GPRWMF,

(for which we are very grateful) but also to the GPRWMF ideal of clinicians and scientists working together on clinically related research projects, as Michael Halmagyi and Ian Curthoys have for the last 40 years!

Session 4 : 8.30 to 9.10

PATHOPHYSIOLOGY AND TREATMENT OPTIONS IN NON ALLERGIC RHINITIS

Professor Wytske Fokkens

Department of Otorhinolaryngology, Academisch Medisch Centrum, Amsterdam, The Netherlands

Rhinitis is a multifactorial disease characterized by symptoms of sneezing, rhinorrhea, postnasal drip, and nasal congestion. Non-allergic rhinitis is characterized by rhinitis symptoms without systemic sensitization of infectious etiology. Based on endotypes, we can categorize non-allergic rhinitis into an inflammatory endotype with usually eosinophilic inflammation encompassing at least NARES and LAR and part of the drug induced rhinitis (e.g., aspirin intolerance) and a neurogenic endotype encompassing idiopathic rhinitis, gustatory rhinitis, and rhinitis of the elderly.

Treatment of NAR includes trigger avoidance, topical and systemic medications and surgery. When rhinitis is caused by a known etiologic factor, such as smoking or chemical exposure, the mainstay of treatment is trigger avoidance.

Several medications are widely utilized in the treatment of NAR, including oral and topical nasal antihistamines, intranasal and rarely systemic corticosteroids, anticholinergics (ipratropium bromide), capsaicin and intranasal injection of botulinum toxin Type A. Disease treatment should target the pathophysiology as much as possible. One can imagine that local corticosteroids and antihistamines (especially azelastine) are more effective in the inflammatory subgroups and neurogenic pathway modulators in the neurogenic endotypes. A cochrane review demonstrated that Capsaicin is an effective treatment for NAR. Nasal application of Botulinum toxin A seems to be safe and the effect of the treatment lasts 2-3 months. Ipratropium bromide controls well rhinorrhea in rhinitis of the elderly. Frequent application is usually recommended to achieve the optimal effect.

Surgical reduction can be considered to treat inferior turbinate hypertrophy, when it contributes to nasal obstruction and mucosal hypersecretion in chronic rhinitis. Vidian neurectomy, causing denervation of the autonomic supply of the nasal mucosa, can reduce the symptoms of rhinorrhea and nasal obstruction.

Session 4 : 9.10 to 9.50

COCHLEAR GENE THERAPY: IS IT TIME?

Professor Lawrence Lustig

Howard W. Smith Professor and Chair

Department of Otolaryngology-Head & Neck Surgery, Columbia University Medical Center & New York Presbyterian Hospital

For the past quarter century, treatment for hearing loss has largely been confined to hearing aids for mild-to-moderate losses, and cochlear implants for severe to profound losses. While these technologies are in and of themselves remarkable, there is no question that the ultimate goal of treatment should be restoration of normal auditory function. Advances in our understanding of the molecular biology and physiology of hearing has given us new potential tools to achieve this goal.

Gene therapy offers the promise of restoration of normal auditory function either through manipulation of molecular targets to regrow auditory hair cells, or to replace absent or non-functional proteins that lead to hearing loss. This talk will outline the current state of cochlear gene therapy, and in particular review efforts at hair cell and spiral ganglion neuronal regeneration, as well as discuss recent research towards treatment of genetic forms of hearing loss. Lastly, we will review the Atoh1 hair cell regeneration gene therapy trial in humans currently underway in the US.

Session 4 : 9.50 to 10.30

FUNCTIONAL ANALYSIS OF SPEECH AND SWALLOWING IN HEAD AND NECK CANCER PATIENTS

Dr Peter Rhys-Evans

Consultant ENT/Head and Neck Surgeon

Lister Hospital, London SW1

Head and neck cancer affects 500,000 new patients annually and curative treatment involves surgery or radiotherapy, with additional chemotherapy in advanced cases. Cure rates have improved considerably in the last few decades, especially in early stages, but since these cancers affect structures in the upper aero-digestive tract, they will have an impact on normal physiological functions of swallowing, voice and speech, as well as cosmetic appearance. This applies not only to the destructive effects of the initial tumour, but also to the effects of treatment to eradicate the cancer, which have both immediate and long-term side complications.

Functional assessment of these changes, before, during and following treatment, is very important to register the objective impact of the disease and treatment, so that analysis of these dynamic changes can allow pro-active therapy to be started as part of the management programme. The importance of pre-treatment assessment and early therapy is highlighted.

Recent developments in IMRT treatment has allowed more accurate and localised treatment of pharyngeal and laryngeal tumours to minimize the post-radiation damage to the pharyngeal constrictor muscles and salivary glands to try and improve functional outcome for swallowing and speech. Hopefully this will reduce the long-term problems that we see in follow-up, which are more related to treatment-related issues rather than tumour recurrence.

Session 5 : 11.00 to 11.15

THE PATHOPHYSIOLOGY OF PAIN

Associate Prof. David Cherry
Consultant
MLCOA

Pain

Significant advances in the understanding of pain mechanisms and subsequent treatment have been made in the last 30 years during the time in which I was the Director of the Pain Management Unit at Flinders Medical Centre, a small proportion of them directly related to the clinical research performed at our Unit. As a consequence the management of pain symptoms is no longer an art but is scientifically based.

The three fundamental causes of pain will be discussed together with the advances in how these are assessed – tests that are reasonably performed in any modern pain management facility. I regret to say that these tests are usually bypassed for a variety of reasons, resulting in poor diagnoses and hence even more catastrophically – poor treatment where the treatment becomes part of the problem.

The introduction of Palliative Care in Australia during this 30 year period has also had an influence on the manner in which those suffering from pain related to cancer or it's treatment are managed. Some of the invasive techniques for such sufferers practised by well intentioned NeuroSurgeons have been overtaken by more conservative measures but there seems to be an increase again in opiophobia – the fear of prescribing opioid drugs. The "rationale" for this will be discussed.

Scare campaigns by polititians, and equally poorly informed campaigners for patient rights, have put such terms as dependence, withdrawal and addiction before the appropriate use of opioid drugs such that many patients suffer unnecessarily.

I think pain is relatively easy to assess and therefore appropriately treat. Hopefully attendees will have the same opinion at the conclusion of this address.

Session 5 : 11.15 to 11.35

THE PAIN IN RHINITIS

Prof. Peter Smith

Allergist and Molecular Immunology Director

Clinical Medicine Griffith University, Qld Allergy Services Southport, Allergy Medical Brisbane and Sydney

Pain in the Upper Airways

Pain should be a protective aversion protective mechanism, however aberrant mechanisms and disease processes can cause pain and chronic morbidity . The trigeminal system detects and conveys a wide range of sensory information from the face, ear, sinuses, nose, throat and even the meninges and neck. The nasal airways, which have roles to warm, filter and humidity the 10-12 thousand litres of air that we breathe a day, also has the capacity to detect and respond to threats. Several of these sensory detection systems can interplay and even engage inflammatory responses. Some innate and adaptive immune mediators such histamine, proteases, prostanoids and kinins have part of their action via the transient receptor potential vanilloid receptor (TRPV1) - the capsaicin receptor - and Transient receptor potential ankyrin 1 receptor (TRPA1) – the wasabi receptor - to cause pain and evoke potentially protective mechanisms. TRPV1 is an ancient ion channel that detects and responds to multiple threats, resulting in the release of neuropeptides to cause sensory symptoms, mucous production and vasodilation within the area of the trigeminal nerve. The pivotal role of TRPV1 in non-allergic rhinitis is further reinforced by the efficacy of capsaicin desensitisation (capsaicin has several ligand points on this receptor) Mechanistically there appears to be a discord, as many known triggers of NAR do not agonise the TRVP1 receptor. Recognised NAR triggers such as the smells of nicotine, moulds (lactones) and pollens (thiols) are capable of agonising the T2R taste receptors in the nose to cause release of acetylcholine from specialised chemosensory cells, which lower the threshold of TRPV1 sensory nerve activation to exogenous and endogenous stimuli. Many NAR triggers are known agonise TRPA1. This channel is frequently co-expressed with TRPV1 in trigeminal sensory nerves and actually forms functional heterodimers with TRPV1. TRPA1 activation appears to be regulated by a dimer called Tmem100 expressed in the trigeminal system which can be modified by a peptide in pain models. Capsaicin also reduces TRPA1 ion channel activity and strong stimuli to TRPA1 can reduce TRPV1 ion channel function. Paracetamol works via TRPA1 and the analgesic tramadol works via TRPV1. SNPs of TRPA1 are starting to appear to be involved in hyper-algesia syndromes. Opioids enhance TRPV1 expression and function and this appears to be involved in post-opioid hyper-algesia although there is TRPV1 and mu-opioid interaction in the anti-nociceptive actions of opioids.

Session 5 : 11.35 to 11.50

FACIAL PAIN—THE CASE FOR SINUS DISEASE

Dr. Alkis Psaltis

Head of Department of Otolaryngology Head and Neck Surgery Senior Lecturer

The Queen Elizabeth Hospital, Adelaide and Division of Surgery, University of Adelaide

"Sinus Headaches" are one of the most common reasons patients seek referral to an otolaryngologist. Pain due to inflammation of the sinuses however, is actually an uncommon cause of headaches. This presentation will review the current literature and discuss the mechanisms and cause of non-sinogenic facial pain as well as less common sinogenic causes. Facial pain and sinonasal symptoms due to migraine will be discussed as well as pain in the setting of sinusitis, contact points and barotrauma.

Session 5 : 11.50 to 12.10

NEURO IMMUNE MECHANISMS OF PAIN AND IMPLICATIONS FOR ANALGESIA

Dr. Jacob Thomas

Research Fellow

Centre for NanoScale Biophotonics at the University of Adelaide

Opioids are considered the gold standard for the treatment of moderate to severe pain. However, heterogeneity in analgesic efficacy, poor potency and side effects are associated with opioid use, resulting in dose limitations and suboptimal pain management. Traditionally thought to exhibit their analgesic actions via the activation of the neuronal G-protein-coupled opioid receptors, it is now widely accepted that neuronal activity of opioids cannot fully explain the initiation and maintenance of opioid tolerance, hyperalgesia and allodynia. This talk will highlight the evidence supporting the role of non-neuronal mechanisms in opioid signalling, paying particular attention to the relationship of opioids and immune signalling.

Session 5 : 12.10 to 12.25

WHEN TO CALL FOR THE NEUROSURGEON

Dr. Andrew Zacest

Neurosurgeon

Royal Adelaide Hospital

Pain in the head and neck has a multitude of aetiologies and the pathophysiology can be complex due to the neuroanatomical overlap of multiple systems. The neurosurgeon is well positioned to assess patients with complex craniofacial pain conditions because of their neuroanatomical training and expertise in the surgical treatment of neurological disorders. This lecture will focus on neurosurgical causes of craniofacial pain and conditions for which neurosurgical interventions may be helpful including trigeminal neuralgia, intractable facial pain and some headache syndromes which may be treated by surgery, neuromodulation or radiosurgery. The comprehensive assessment of the pain patient, the use of a multidisciplinary approach and non surgical approaches will also be discussed.

Session 5 : 12.25 to 12.40

PAIN, CULTURE AND COMMUNICATION

Emeritus Prof. Roland Sussex

The University of Queensland

The difficulty of determining the presence and nature of pain has recently once again been confirmed in a series of communications in the flagship journal "Pain", in spite of many attempts to give them a firm somatic and experimental basis. Effective communicating about pain therefore has a particularly important role for health care professionals, patients, and others involved medically, socially and personally in the lived experience of the person in pain.

Body language is one common means of expressing pain. But body language is indeterminate and variable, so special weight is thrown on the capacity of language to capture the pain experience. But the language tools available, including the McGill Pain Questionnaire and its derivatives, are subject to factors of interpretation which render them less precise than has been hoped. In addition, issues of culture and cultural values have been shown to affect not only how we express pain, but how we feel it. Different cultures assign different values to pain and its expression. A necessary first step in understanding pain communication is consequently an appreciation of cultural factors which influence whether and how pain is expressed by people in pain with different cultural backgrounds.

This paper presents key cultural values in the communication of pain. It then proposes for discussion the question of "clinically relevant description of pain" and presents some parameters for tackling this issue.

Session 6 : 14.00 to 14.15

INTEGRATING TEAMS TO FOCUS ON HEAD AND NECK SURGERY

Professor Frank Gannon

Director and CEO of QIMR Berghofer Medical Research Institute

The need to translate research results into clinical practice is accepted by all, but is not always the reality. Researchers can be heavily engaged in the pursuit of answering questions that arise from their understanding of biology and clinicians may never benefit from this. Equally, clinicians can be insulated from the latest progress in research because their skills have been shown to be adequate to their tasks over the years and their focus may be on service delivery. By having a challenge to do better in the area of head and neck cancer, researchers at QIMR Berghofer and colleagues elsewhere have brought new options to address the ongoing questions in this area. Our approaches have included the skills of epidemiologists, immunologists, and molecular and cell biologists. Integrating these into targeted approach to improving the outcome of those with head and neck cancers has been an interesting experience and one that can be applied to other diseases.

Session 6 : 14.15 to 14.35

PRESBYCUSIS AND NOISE INDUCED HEARING LOSS— OLD PROBLEMS AND NEW PARADIGMS

Professor Lawrence Lustig

Department of Otolaryngology, Columbia University College of Physicians and Surgeons, New York, United States

Hearing loss is the most common sensory disorder world-wide, affecting over 250 million people. In the United States alone, the number of Americans with hearing loss has nearly doubled over the past 30 years, a majority of these being in the elderly, while over 30 million people in the US are exposed to hazardous levels of sound on a regular basis. Presbycusis and noise induced hearing loss are thus the 2 most common causes of the most common disorder seen, yet surprisingly little has changed in the way we treat these disorders over the past half century. However over the past several years, our understanding of these disorders has improved tremendously. This talk will outline the physiology of presbycusis and noise induced hearing loss, and how the combination of both genetics and the environment plays a major role in both these disorders. We will also review how such older concepts of 'temporary threshold shifts' are rapidly becoming outmoded since it is now known that sound loud enough to cause temporary hearing loss may actually result in a selective cochlear neuropathy, which in turn can accelerate age-related hearing loss. Thus, both noise-induced hearing loss and age-related hearing loss are inextricably intertwined. These concepts will not only impact future treatments, but should also be incorporated into public health policy.

Session 6 : 14.35 to 15.00

ETHICS AND SURGICAL EQUIPOISE WITH CHANGING PARADIGMS IN THE TREATMENT OF HEAD AND NECK CANCER

Associate Prof. Suren Krishnan OAM, FRACS

Chairman

Royal Adelaide Hospital

The challenges in surgery are numerous but foremost are the issues of ethics and integrity and the discipline of separating conflicts of interest when introducing new technologies.

The current emerging epidemic within head and neck oncology has been Human Papilloma Virus mediated squamous cell carcinomas of the oropharynx. The traditional surgical approaches to the oropharynx were fraught with significant morbidities. Literature demonstrating the efficacy of concomitant chemo-radiation protocols in the management of advanced laryngeal cancer made the case for non- surgical treatments to be considered as first line treatment modality by many multi disciplinary head and neck clinics. Furthermore this initial data was extrapolated to all head and neck subsites, including the oropharynx.

The introduction of robotic systems has provided a less morbid trans oral approach to the oropharynx. In addition, the unique biological behaviour of Human Papilloma Virus mediated Squamous Cell carcinoma has created clinical equipoise in decision making in the treatment of patients with these cancers.

The ethics and costs of introducing robotics in this changing paradigm of cancer management is a challenge for all clinicians wishing the best oncologic outcome with the least treatment associated dysfunction for their patients.

Session 6 : 15.00 to 15.30

EXPONENTIAL TECHNOLOGIES AND IMPLICATIONS FOR THE HEALTHCARE INDUSTRY

Professor Hugh Bradlow

Chief Scientist at Telstra

The next wave of digital transformation will be based on emerging technologies which are advancing at an exponential rate. These technologies have the potential to change the relationship between people mediated by technology, change our interactions with the physical world and change the way we interact with the technology itself. Their impact will be far reaching and will affect every aspect of the economy as well as the nature of work itself. No occupation and no profession will be immune to these changes, including medicine. This presentation provides an overview of these 'exponential technologies' and then looks at the impacts that they are likely to have on medicine in terms of avoiding injury, aiding diagnosis and changing treatment.

Session 6 : 15.30 to 16.00

THE SCOURGE OF HPV AND WHAT LIES AHEAD

Professor Ian Frazer AC

he University of Queensland, Translational Research Institute Chair, TRI Foundation board

Immunotherapy for HPV associated Head and Neck Cancer

Human papillomavirus (HPV) contributes to the burden of oropharyngeal cancer, and HPV associated tumours express HPV early proteins (E6 and E7) as tumour specific antigens. Immunotherapy for HPV associated cancers has to date proven relatively ineffective. We have used mouse models in which HPV early proteins are expressed in skin as transgenes, and skin is grafted to immunocompetent recipients, to determine the factors inhibiting HPV specific immunotherapy. In this model, local cytotoxic T cell functions are inhibited by local regulatory immune responses invoked by hyperproliferative epithelium. The inhibitory mechanisms prevent effective tumour elimination by T cells generated by immunotherapeutic vaccines. Some strategies for overcoming this inhibition will be discussed.

Thank You

gprwmf

Three million children say 'Thank you' to GPRWMF for supporting newborn hearing screening.

AUTHOR

H Coates
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BACKGROUND

In 1999 The Garnett Passe and Rodney Williams Memorial Foundation (GPRWMF) supported a study on universal newborn hearing screening incorporated within a $208,000 grant on Speech and Language outcomes for children with early detection of Sensori-Neural Hearing Loss (SNHL) at two Perth birthing hospitals. 1700 babies were screened and 4 were detected with profound SNHL. This prompted the WA Minister of Health to fund the first major State Newborn Hearing Screening Program (UNHSP) in Australia. In the following years, other States introduced UNHSPs and in 2009, all States and Territories were funded to offer hearing screening to all newborns. Since 2000, over 3 million babies have had their hearing screened at birth in Australia.

OBJECTIVE

To estimate the age of detection of Permanent Congenital Hearing Impairment (PCHI) prior and after UNHSPs. Review changes in Hearing Aid Fitting (HAF) to infants. Evaluate long term outcomes of early or late detection of hearing impairment on language and speech development. Estimate cost savings to Australia of early detection and habilitation of babies with PCHI via UNHSPs.

METHODS

Literature review, birth rates and estimated numbers of babies with SNHL were correlated with literature on the change in detection ages and HAF from Australian Hearing data.

RESULTS

The average age for detection of SNHL in 1997 was 25 months, while in 2015 the average age at diagnosis was 3 months. The rate of HAF to infants increased from 27% to 73% in the period of 2003-2009.

The National Acoustic Laboratory's LOCHI study showed that children with early detection and habilitation of SNHL with hearing aids before 6 months had improved language and speech skills at age 5 years.

It is estimated that 3700 babies have been detected with SNHL since the introduction of UNHSPs, with an estimated saving to the Australian Government in cost-benefit terms over lifetime of $3.7 billion.

CONCLUSION

The impact of funding by the GPRWMF, with aid from Australia's cochlear implant leadership and Australian Hearing, of studies into the benefit of UNHSP in Australia has been immense, with a flow-on effect leading to nationwide take-up of UNHSP by 2010 and significant improvement in the detection and habilitation of babies with PCHI, resulting in significant cost savings to Australia.

The next step is the establishment of a regional standardised database which will allow outcomes data to be performed on a National scale and monitor those children who may yet develop SNHL.

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ONE

Title:

Safer Australian Surgical Teams:

Raising awareness of non-technical skills in intraoperative teams

Author/s:
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Royal Australasian College of Surgeons

Background
The Royal Australasian College of Surgeons (RACS), Australian and New Zealand College of Anaesthetists (ANZCA), Australian College of Nursing (ACN) and the Australian College of Operating Room Nurses (ACORN) have developed a workshop on non-technical skills for intraoperative teams working in rural and regional Australia. The workshop entitled 'Safer Australian Surgical Teams' aims to enhance performance and teamwork in the operating theatre in order to improve patient safety by exploring ways to assess these skills utilising the three frameworks of: Non-Technical Skills for Surgeons (NOTSS), Anaesthetists' Non-Technical Skills (ANTS) and Scrub Practitioners' List of Intra-operative Non-Technical Skills (SPLINTS). These frameworks were derived from the aviation industry and use structured observation to rate behaviour which then forms the basis of feedback. The programme looks at the relationship between human factors and safer surgical practice, discusses the non-technical skills identified in each craft group's framework and explores team dynamics. Participants practise assessing non-technical skills utilising their craft framework while watching videos and simulated role plays. The faculty and participants in the workshops are anaesthetists, surgeons and operating room nurses.

Objective
To enhance performance and teamwork in the operating theatre in order to improve patient safety by exploring ways to assess these skills utilising the three frameworks of: Non-Technical Skills for Surgeons (NOTSS), Anaesthetists' Non-Technical Skills (ANTS) and Scrub Practitioners' List of Intra-operative Non-Technical Skills (SPLINTS).

Method
From 2014 to 2015, 9 workshops were delivered to 247 participants, funded by the Rural Health Continuing Education initiative.

Results
A chi-squared test of independence was conducted comparing evaluation results pre and post workshop. After participating in the workshop, participants significantly improved their attitude, confidence, knowledge, skills and intention to change behaviour.

Conclusion
A better understanding of how human factors effect performance Development of a language (taxonomy) for discussing non-technical skills Use of an assessment tool for non-technical behaviours Reflection on your own non-technical skills

TWO

Title
Handling a cochlear implant: measuring patient skills using a new survey

Authors
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Dona MP Jayakody, Ear Science Institute Australia, Subiaco, Australia
Robert H Eikelboom, Ear Science Institute Australia, Subiaco, Australia
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Background
As part of the cochlear implant rehabilitation program clinicians provide information, training and user manuals on the daily care and maintenance of the external components of the hearing implant system. However, little is known regarding the effectiveness of these techniques and the prevalence of CI device handling difficulties in populations of hearing implant users.

Objective
To investigate the ability of cochlear implant recipients to physically handle and care for their hearing implant device(s) and to identify factors that may influence skills. In order to assess device management skills a clinical survey was developed and validated on a clinical cohort of cochlear implant recipients.

Method
Development of the Cochlear Implant Management Skills (CIMS) and Self-administered CIMS (CIMS-self) surveys. Validation of the surveys was in a prospective random control design study of forty-nine postlingually deafened, experienced (more than 12 months), adult Cochlear CI recipients.

Results
The CIMS survey demonstrated high test-retest reliability (intraclass correlation coefficient = 0.878), inter-observer reliability (intraclass correlation coefficient = 0.972) and responsiveness to intervention (skills training). The CIMS-self survey demonstrated high test-retest reliability (intraclass correlation coefficient = 0.884), responsiveness to intervention, criterion validity (ICC = 0.765) and sensitivity (0.89). Association was found between cochlear implant device management skills and self-reported overall satisfaction with cochlear implant device.

Conclusions
This is the first study to demonstrate a range in device handling skills in cochlear implant recipients. The CIMS surveys offer clinicians and researchers a validated tool to systematically and objectively identify shortcomings in cochlear implant recipients' device handling skills and to measure change in skill following training.

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THREE

Title
EVIDENCE FOR IMMUNE CELL INFILTRATION, ACTIVATION, AND INFLAMMATION WITHIN THE AGEING MOUSE INNER EAR VESTIBULAR (BALANCE) SYSTEM

Author
MJ Bigland, AM Brichta, DW Smith

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Background
Our ability to maintain balance declines as we age, often leading to falls requiring hospitalisation. With an ageing population this is becoming an increasing health burden. A contributing factor to vestibular decline is thought to be impaired vestibular function, however, it is unclear whether age-related vestibular dysfunction is due to peripheral and/or central components of the vestibular system. Inner ear vestibular hair cells detect head motion and deterioration of hair cell function, including its ability to transduce mechanical energy into electrical signals, would be detrimental to overall vestibular system function

Objectives
Our study sought to determine whether peripheral vestibular organ function is compromised with ageing by characterising molecular changes that might contribute to age-related balance disorders.

Method
We performed microarrays on RNA samples dissected from young (3.5 months), middle (14 months), and old age (>28 months) mouse peripheral vestibular organs. We analysed the normalised array data to determine differential gene expression with age, using Transcriptome Analysis Console on Affymetrix GeneArrays using: ANOVA $P < 0.01$, False Discovery Rate < 0.25, Fold Change > 1.5. Differentially expressed gene lists were subjected to DAVID for identification of enriched biological pathways.

Results
Ageing caused a significant increase in the expression of genes associated with immune response pathways: e.g. Asthma, Primary immunodeficiency, Immune network for IgA production, Autoimmune thyroid disease, B cell receptor signalling, Systemic lupus erythematosus, Natural Killer cell mediated cytotoxicity, as well as Calcium signalling. Downregulated genes were associated with: sensory transduction, ion homeostasis, and inner ear development.

Conclusion
These data suggest that immune cell infiltration, activation, and inflammation, is instrumental in age-related peripheral balance disorders. Further evidence suggests these changes may be triggered by the breakdown of the blood labyrinth barrier as seen in other tissues with ageing. Further research in this area is required.

FOUR

Title
Use of a Nanoengineered Drug Delivery Carrier for Intracochlear Delivery of Otoprotective Substances in a Cochlear Implant Animal Model

Authors

R Telang[1], P Bird[2], S Vlajkovic[1], A Wise[3], F Caruso[4], PR Thorne[1]

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Background
Preservation of residual cochlear function after cochlear implantation (CI) is desirable for improved performance and preservation of the cochlea for future technology improvements. Whilst improved electrodes and surgical technique are important, the delivery of otoprotective substances is likely to be necessary to achieve this goal. In order to protect residual function, a substance must reach the cochlea in therapeutic concentrations to protect hair cells, supporting cells, and spiral ganglion neurons. Intracochlear delivery via nanoengineered drug delivery carriers offers drug release properties which should achieve this goal.

Objectives
To investigate the use of a nanoengineered drug delivery carrier to deliver an Adenosine A1 receptor agonists that will protect against the development of cochlear injury during implantation in a guinea-pig model.

Method
To evaluate their release kinetics, the drug delivery carriers were loaded with 100mM ADAC (adenosine amine congener), regadenoson and adenosine and left within 100 mL artificial perilymph solution (APS) for up to 12 weeks. Samples were taken at weekly intervals and concentration measured using LCMS/MS protocols. To assess the impact of release of these compounds on cochlear injury we have developed an animal model of CI surgery. Guinea-pigs are exposed to noise (16kHz, 120dBSPL, 30min) to produce a lesion in the basal cochlear turn and permanent high frequency (>8kHz) threshold shift of 90-100dB assessed using Auditory Brainstem Responses. A dummy CI electrode was inserted via a cochleostomy to induce low frequency sensorineural hearing loss.

Results
ADAC elution kinetics were consistently higher than the other compounds, followed by regadenoson. The guinea-pig CI model has successfully achieved high frequency hearing loss from noise and low frequency loss from surgical trauma.

Conclusion
In-vitro studies have confirmed excellent release of Adenosine A1 receptor agonists from the nanoengineered drug delivery carrier system. A reliable guinea-pig model has been developed for later use in both in-vivo pharmacokinetic studies and to investigate the otoprotective effects of Adenosine A1 receptor agonists.

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FIVE

Title

Automated audiometry: Translation into clinical practice

Authors:

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M. Atlas. Ear Science Institute Australia, Subiaco, Australia

Background

There is limited evidence to support the use of automated audiometry in a tertiary otolaryngology setting and how this technology could be used to increase efficiency and access to audiology and otolaryngology services.

Objective

To examine the accuracy of automated audiometry and its translation to clinical practice.

Methodology

A series of three studies examining the threshold accuracy, diagnostic accuracy and accuracy of asynchronous remote interpretations of automated audiometry in 42 clinically heterogeneous patients at an otolaryngology department in Western Australia.

Results

Threshold accuracy between manual and automated audiometry ranged from 5.12 – 9.68 dB. Accuracy for identifying disabling, conductive and unilateral hearing loss ranged from 86% to 100%. The use of automated audiometry did not significantly influence the diagnostic or management decisions of audiologists (n = 5) when interpreted remotely (α = 0.54 [95% CI 0.47, 0.60]; q = 0.97).

Conclusion

Automated audiometry is accurate and is a useful addition to clinical practice which has the potential to improve audiology efficiency and enable remote hearing assessments.

This series of experiments addresses three key issues of automated audiometry that have not previously been examined or reported. Firstly, we have shown that automated audiometry has sufficient accuracy to be used with a clinically diverse, tertiary otolaryngology population. Secondly, the application of novel, pre-defined diagnostic criteria is an accurate method of identifying common hearing impairments to increase efficiency in tertiary services or provide better access where audiological services are limited. Thirdly, whilst there are statistically significant differences in thresholds between automated and manual audiometry, these are of limited clinical significance and do not affect decisions regarding patient management when interpreted remotely in an asynchronous telehealth model.

SIX

Title

Endolymph movement visualized with light sheet fluorescence microscopy in an acute hydrops model

Authors

D Brown, C Southwell, C Pastras, I Curthoys. The University of Sydney, Sydney, Australia.*

Background

A clear understanding of where endolymph is absorbed is vital to our understanding of Meniere's disease. Techniques for investigating endolymph dynamics include micropipette recordings of fluid tracers in vivo, or imaging tracer diffusion in histological sections or MRI scans.

Objective

To visualize endolymph movement throughout the inner ear using Light Sheet Fluorescence Microscopy (LSFM).

Method

Via a glass micropipette, fluorescein isothiocyanate (FITC)-dextran dissolved in artificial endolymph was injected into scala media in anaesthetized guinea pigs. Functional measures were continuously performed throughout the injection. Temporal bones were harvested and processed for imaging on our custom-built LSFM.

Results

A substantial amount of the FITC-dextran appears to be transported into the endolymphatic sac, utricle and semicircular canals once endolymph volume had more than doubled, a volume associated with a sudden reduction in endolymphatic pressure. No FITC-dextran is observed in the perilymphatic compartments, suggesting that the membranous labyrinth remains intact.

Conclusion

Whilst this technique can only provide a post-mortem 'snap-shot' of fluid dynamics, it provides high-resolution 3D images of biomarker distribution. The presence of FITC-dextran in the utricle following sudden hydrops pressure relief supports theories that the utriculo-saccular duct opens suddenly in the presence of severe endolymphatic hydrops. The remarkable uptake of FITC-dextran into the periductal channels of the endolymphatic duct suggests that the duct is the primary region endolymph is absorbed.

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SEVEN

Title

A pilot study of breath volatile organic compounds (VOCs) in Head and Neck Squamous Cell Carcinoma detection

Authors

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Background

A key challenge for the early detection of head and neck squamous cell carcinoma (HNSCC) is the absence of low cost, non-invasive detection tools. Human exhaled breath includes volatile organic compounds (VOCs), H2 and 13CO2.

Objective

Our main aim was to develop a unique, non-invasive, ancillary breath test that could be used for the early detection of HNSCC.

Method

Participants were recruited from the Department of Otorhinolaryngology, Flinders Medical Centre, South Australia. Exhaled, alveolar breath samples were collected into FlexFoil® PLUS bags from newly diagnosed, histologically confirmed, untreated HNSCC patients and matched healthy controls. Patients were fasted for at least six hours prior to breath collection. Breath samples were immediately analysed by Selected Ion Flow Tube-Mass Spectrometry (SIFT-MS) to quantify VOCs previously associated with HNSCC (ethanol, undecane, acetonitrile, 2,2-dimethyl propanoic acid, camphene and isoprene). Breath 13CO2 was quantified using isotope ratio mass spectrometry, and breath H2 and CH4 was quantified by a QuinTron BreathTracker®. Data is expressed as mean±SEM

Results

To date, we have collected and analysed breath samples from n=7 in the HNSCC group and healthy controls. The mean patient age was 62y (range, 44-88). Sites of HNSCC were tongue (N=3), larynx (N=2), tonsil (N=1) and hypopharynx (N=1). Breath CH4 was higher in the cancer group (16.1 ± 4.7) compared to the controls (9.3±5.9). However, breath hydrogen was lower in the cancer group compared to
healthy controls (6.29±2.0 vs 10.4±4.3). No significant difference between groups was seen for other VOCs tested.

Conclusion

These preliminary results highlight the diagnostic potential of breath VOCs. The results of this study could lead to the development of a rapid, minimally invasive tool for detection and potentially screening of HNSCC.

EIGHT

Title

BENEFITS OF MESENCHYMAL STEM CELLS FOR WOUND HEALING IN THE TYMPANIC MEMBRANE

Authors

H Ong[1,2], S Redmond[2,3], R Marano[2,3], M von Unge[4], P Aabel[4], M Atlas[2,3], R Dilley[2,3]
[1]Murdoch University, [2]Ear Science Institute Australia, [3] Ear Sciences Centre, University of Western Australia, Perth Western Australia and [4]University of Oslo, Norway

Background

Despite a high regenerative capacity in tympanic membrane, some patients present with chronic perforations requiring surgical treatment. Stem cell treatments are just beginning to be explored as alternatives/ adjuncts in experimental studies. We have been developing knowledge about the repair of tympanic membrane with *in vitro* models. In the present study, we investigated the paracrine effects of human adipose-derived mesenchymal stem cells (ADSC) in normal and hypoxic (<0.1% O_2) conditions on wound healing mechanisms with human tympanic membrane (hTM) keratinocytes.

Objective

We hypothesized that ADSCs secrete paracrine factors effective in improving proliferation and migration responses of hTM keratinocytes. We tested the hypothesis with ADSC in both normoxic and hypoxic environments *in vitro*

Method

Conditioned media (CM) were collected to assess paracrine activity on hTM keratinocytes proliferation by MTS assay and their migration effects by scratch assays. ADSCs post-conditioning were then assessed for cytokine gene expression in a wound healing PCR array. ADSC in hypoxic conditions generated contrasting effects on gene expression and CM were further evaluated for effects on wound healing.

Results

TM keratinocytes grown in CM showed an acute increase in cell number (1.2 fold) compared against serum-free medium. A further significant increase was shown in hypoxic CM to 1.5 fold in proliferation and 1.3 fold in migration tests. The ADSC expressed a range of wound healing cytokines and under stringent conditions of hypoxia they further up-regulated several important candidates (e.g. VEGFA, MMP9, IL1B, F3) and down-regulated others (e.g. CXCL1, CXCL2, CCL7). Other important growth factors (EGF, HB-EGF, FGF2) were not expressed or not regulated.

Conclusion

Paracrine activities produced by ADSC under hypoxic conditions enhance wound healing properties of the human eardrum keratinocytes *in vitro*. Potential paracrine mediators from ADSC were identified by PCR and proposed as major wound healing effectors.

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NINE

Title
TYMPANIC MEMBRANE ORGAN CULTURE USING UMBO TISSUE EXPLANTS

Authors
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Background
Tissue engineering treatments to repair chronic perforations of the tympanic membrane (TM) are being developed with growth factors and materials, but there are surprisingly few relevant tissue culture models available to test these new solutions.

Objective
In this study we aimed to develop a simple three-dimensional culture model system based on rat tympanic membrane umbo grafted into a culture well insert membrane.

Methods
Rat TM was dissected free from the temporal bone and micro-dissected to make umbo and annulus tissue grafts. PET culture membrane was engrafted with TM tissues through a slit in the membrane and immersed in keratinocyte growth medium for long-term culture. Once established, cell populations were enzymatically harvested from the PET collecting membrane and sub-cultured, leaving the umbo graft in place to continue producing cells for further rounds of growth and harvest. Sub-cultured epithelia and fibroblasts were used for tissue engineering on porous silk scaffolds.

Results
We found that cell outgrowth from the graft produced sufficient cells to populate the membrane of similar surface area to the human tympanic membrane within two weeks. Tissue grafts from the annulus region also showed cell outgrowth but were not as productive. The umbo organoid supported substantial cell proliferation and migration under the influence of keratinocyte growth medium. Cells from umbo grafts were enzymatically harvested from the PET membrane and further expanded in routine culture. Cells were harvested consecutively from the same graft over multiple cycles. Harvested cells were characterized and used to test cell growth by proliferation and migration as well as grafting to a porous silk scaffold material as proof-of-principle for tissue engineering.

Conclusion
Umbo explants are robust tissues suitable for ongoing production of TM cell populations to generate tympanic membrane organoids and for testing novel tissue engineering scaffold materials. The model is simple enough to be widely adopted for tympanic membrane regeneration studies and has further promise as a tissue equivalent model to reduce animal testing during development and translation of novel tissue engineering approaches.

TEN

Title
A comparison of the AzBio and CUNY sentence recognition tests: A study on English speaking cochlear implant recipients in Australia

Authors
A Ebrahimi-Madiseh, R Eikelboom, D Jayakody, M Atlas
Ear Science Institute Australia, Perth, Australia; Ear Sciences Centre, School of Surgery, The University of Western Australia, Perth, Australia.

Background
The benefit of a cochlear implant device is measured by utilizing a number of speech tests. The commonly used CUNY (City University of New York) speech perception sentence test suffers from ceiling effects as early as three months after implantation, making longitudinal studies on the performance of the cochlear implant (CI) recipients challenging. The AzBio (Arizona Biomedical Institute) sentence test has been shown to be more suitable to this task; however, it has not been tested in an Australian population.

Objective
To compare the AzBio and CUNY sentence tests in postlingually deafened adult CI recipients, assessing ceiling scores and testing times.

Method
Phase 1: 25 adult participants, 18-40 years (M=30.9; SD=6.2), who speak Australian English as their first language. All participants had normal hearing sensitivity. Phase 2: 16 post-lingually deafened adult cochlear implant recipients, 18-65 years (M=48.8; SD=14.7). Speech perception of the participants was tested at three and six months post implantation with CUNY and AzBio sentence tests. Two random selections from the 15 AzBio words lists were used for the participants. Scores between 95-100% were considered to be ceiling scores.

Results
Phase 1: The intelligibility scores for AzBio sentence test across the 15 lists for the normal hearing participants ranged from 97-100% (Mean=99.5; SD=0.3). Mean testing time was 2.3 minutes (SD=0.17).

Phase 2: Intelligibility at 3 months post implantation across the 15 lists for AzBio ranged from 30 to 94% (M=73; SD=16.4) and for the CUNY test ranged from 72 to 100% (M=93; SD=9.7). At 6 months post implantation intelligibility AzBio scores ranged from 29 to 87% (M=63.3; SD=18.1), and CUNY scores from 71 to 100% (M=93.5; SD=9). 50.8% and 57.8% of participants reached ceiling CUNY scores at 3 and 6 months post-implantation respectively. However, no ceiling effects were found for the AzBio test at any time point. Mean testing times for the AzBio were 2.96 (SD: 0.8, range 2.24 to 5.29) and 2.73 (SD: 0.5, range 2.23 to 4.8) minutes for the tests conducted 3 and 6 months post-implantation respectively.

Conclusion
The AzBio test is a reliable test for post-lingually deafened cochlear implant recipients, with no ceiling scores recorded. The test times are reasonable for incorporation into a clinical test battery. Further work is required to develop a normative data set for different age groups in Australian English speaking population.

gprwmf

ELEVEN

Title

Management options for mixed and conductive hearing losses: A comparison of BAHA Attract and BAHA Connect.

Authors

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Ear Science Institute Australia, Perth, Australia; Ear Sciences Centre, School of Surgery, The University of Western Australia, Perth, Australia.

Background

Percutaneous bone conduction implants e.g. BAHA Connect, have been used to manage conductive and mixed hearing losses since early 1980s. They provide direct sound transmission to the cochlea by an extruding abutment. The BAHA Attract is a passive transcutaneous device delivering the sounds through the skin via a magnetic coupling. It has been suggested that transcutaneous transmission reduces output of the device by 5 to 20 dB. The impact of output reduction on patients' subjective and objective outcomes has not been investigated. The aim of this study was to compare BAHA Attract and BAHA Connect to determine whether new recommendations are warranted.

Method

10 BAHA Attract users with conductive or mixed hearing loss, mean age 60.8 (SD=10.8) years, 30 BAHA Connect users with similar types and degree of hearing loss implanted in the same time frame; mean age 50.8 (SD=18.2) years. Outcomes were measured using direct bone conduction, on a test band preoperatively and loaded on implant post-operatively. CNC words scores and APHAB were assessed at 3, 6 and 12 months post implantation.

Results

There was a significant improvement in post-operative CNC scores compared to pre-operative scores ($P<0.01$). There was a statistically significant relationship between the type of processors and CNC scores ($P<0.01$). The results for the remaining outcome measures are still being analysed and will be reported.

Conclusion

Passive transcutaneous implants can be considered in rehabilitation of conductive and mixed hearing losses. However, candidacy and device selection should be carefully examined.

TWELVE

Title:

DIFFERENT MICRORNA EXPRESSION IN HUMAN PAPILLOMAVIRUS ASSOCIATED OROPHARYNGEAL SQUAMOUS CELL CARCINOMAS

Authors

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Introduction

Squamous cell carcinoma (SCC) of mucosal head and neck sites (HNSCC) is the sixth most common cancer world-wide, and continues to have a high morbidity and mortality rate. Human papillomavirus (HPV) is responsible for approximately half of oropharyngeal SCCs, and a smaller proportion of SCCs occurring at other mucosal head and neck sites. While the clinical differences between HPV-associated and smoking or alcohol associated HNSCC is well established, the biological mechanisms underlying each disease remain poorly understood. MicroRNAs (miRs) are small, non-coding, single strands of RNA which regulate gene expression at a post-transcriptional level, playing a demonstrated role in a wide variety of cellular functions from growth and differentiation through to apoptosis. Several have been identified to have oncogenic or tumour suppressive functions in a number of human cancers. While a number of studies have investigated miRNA expression in HNSCCs, discrepancies in methodology, anatomical site and sample size have caused a wide variation in results. Further, only four studies to date have included HPV status as an independent factor.

Methods

Total RNA was extracted from fifty-two formalin-fixed paraffin-embedded (FFPE) tonsillar SCC specimens. Clinical, lifestyle and pathological data was obtained retrospectively. A microarray was performed at LC Sciences, using v.21 of miRBase. The results were analysed using Genespring.

Results

HPV status was associated with forty-nine differentially regulated miRNAs with a fold change (FC) of >2.0 ($p<0.01$). MiR-16-2, miR-150, miR-155, miR-146a, miR-342 and miR-3607 were also significantly associated with HPV status (FC >2.0, $p<0.0001$). Forty-five miRNAs were differentially expressed in association with p16 status (FC >2.0, $p<0.01$). Analysis of combined HPV and p16 status resulted in differential expression of three miRs: miR-146a, miR-150 and miR-155 (FC >2.0, $p<0.001$). Different miRNA expression profiles were also seen with smoking status and tumour recurrence.

Conclusions

Human papillomavirus is associated with significant differences in microRNA expression in oropharyngeal SCCs, possibly consistent with a different mechanism of carcinogenesis in these tumours.

gprwmf

THIRTEEN

Title

EFFECTS OF COCHLEAR IMPLANT USE ON BINAURAL PROCESSING

Authors

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Background

Bilateral cochlear implantation is increasingly common, particularly for young children, and results in an improvement in performance for both sound localization and speech discrimination in noise compared to unilateral implantation. However, the improvements are small and performance remains inferior to that of normal listeners. Animal and psychophysical studies have shown that long-term deafness from a young age degrades processing of interaural time differences (ITDs) but not interaural level differences (ILDs).

Objective

The effects of chronic bilateral cochlear implant use on binaural processing are less clear. We therefore examined the effects of chronic bilateral cochlear implant use on ITD and ILD sensitivity in long-term neonatally deafened animals.

Methods

Three groups of cats were used: two normal hearing controls (NHC), two neonatally profoundly deafened unstimulated cats (NDUS) and four neonatally profoundly deafened cats that received approximately 6 months of bilateral intra-cochlear electrical stimulation from clinical cochlear implants and speech processors (NDS). Single-unit responses (n = 110, 60, 86 for the NHC, NDUS, and NDS groups, respectively) to electric binaural stimulation with a range of ITDs and ILDs were recorded from the central nucleusi of the inferior colliculus bilaterally, using 32-channel silicon arrays (NeuroNexus).

Results

ITD sensitivity was significantly poorer in both the neonatally deafened groups compared to the normal hearing animals (Kruskal-Wallis test, $p < 0.05$), and there was no difference between the stimulated and unstimulated groups ($p > 0.05$). ILD sensitivity was not different between the groups ($p > 0.05$).

Conclusions

The use of bilateral clinical cochlear implants does not prevent/reverse the degradation in ITD processing that occurs following long-term deafness from a young age. Whether experience with appropriate ITD cues would improve ITD processing still needs to be examined. ILD processing is largely unaffected by either long-term deafness or chronic stimulation.

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FOURTEEN

Title

Identification of therapeutic strategies in Head and Neck Squamous Cell Carcinoma

Authors

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Background

Head and neck squamous cell carcinoma (HNSCC) is the sixth most prevalent cancer world-wide, with 600,000 new cases reported annually. In Australia, around 3000 new cases are diagnosed each year, and more than 750 patients die of the disease. The current five year survival rate of HNSCC is only 40 – 50%. HNSCC is a highly heterogeneous disease caused by alcohol and tobacco use, HPV infection and radiation. The current conventional treatment regimens (surgery, radiation, and chemotherapy) are non-selective, and are administered regardless of the etiology or molecular drivers.

Our laboratory has recently made a major contribution towards understanding the molecular drivers of HNSCC with the identification of a novel GRHL3/GSK3B/c-MYC proto-oncogenic network that is activated in these cancers. This pivotal finding was enabled through the use of a unique mouse model, which will now allow us to test targeted therapies in HNSCC.

Objective

The objective of the study is to determine the efficacy of targeting Grhl3-dependent pathways driving HNSCC using an orthotopic mouse model.

Method

HNSCC cell lines representative of the different subtypes of HNSCC will be transfected with a luciferase reporter construct, and positive cells selected on fluorescence orthotopically implanted in the tongue of NSG mice to study the tumor growth, metastatic potential and the signalling signature. Once the tumors are established, the mice will be grouped into two cohorts, one being treated with either iBET 151 and the other group serving as a control. The tumor progression and the response to therapy will be monitored by weekly *in vivo* imaging with our Bioluminescence detector.

Results

HNSCC cell lines representing different subtypes of HNSCC (SCC-25, SCC-1, Detroit and SCC-47) were successfully grown in nude mice orthotopically with nodal and lung metastasis. Treatment with IBET-151, inhibited the growth of SCC-25 in nude mice and significantly improved the overall survival. However SCC-1 and Detroit showed only partial response to IBET-151, however the mice showed reduced nodal metastasis. Several *in vitro* studies including cell cycle analysis, apoptosis assay and colony formation assay were performed to support the therapeutic efficiency of c-Myc inhibitor I-BET 151 in HNSCC cell lines. *In vitro* studies indicate that the proliferation of cell lines that solely express GRHL3/GSK3B/c-MYC proto-oncogenic axis (SCC-25) was completely inhibited by Myc inhibition. However the cell lines that co-express PI3 kinase pathway and/or MAP Kinase pathway (SCC-47, Detroit and SCC-1) showed partial response in proliferation to Myc inhibition.

Conclusions

Inhibition of GRHL3/GSK3B/c-MYC pathway with Myc inhibitor IBET 151 has shown beneficial effect in treating HNSCC. However in HNSCCs with multiple signalling pathways were activated needs to be treated with combination therapy.

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FIFTEEN

Title

Microbiota dysbiosis and chronic inflammatory disease: insights from the microbial ecology of chronic rhinosinusitis

Authors

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Background

Despite considerable research, the aetiology of chronic rhinosinusitis (CRS) remains poorly understood. Recent work has begun to investigate associations between patterns in resident microbial communities and distinct immunological profiles of CRS, exploring potential aetiological roles in driving different clinical phenotypes of this complex chronic inflammatory condition.

Objective

The aim of this study was to assess resident bacterial communities and underlying mucosal inflammatory profiles, investigating associations which may contribute to the phenotypic heterogeneity seen in CRS.

Methods

Bacterial communities and local inflammatory response were assessed in 105 patients with extensive bilateral CRS undergoing endoscopic sinus surgery (ESS) and 29 controls undergoing ESS for indications other than CRS. Patient groups were delineated on the basis of phenotypic variants (with/without polyps) as per EPOS guidelines for CRS, and clinical parameters including asthma and cystic fibrosis. Bacterial communities were characterised via 16S rRNA gene amplicon sequencing, and quantified by qPCR. Mucosal inflammatory profiles were analysed using the BD™ Cytometric Bead Array and immunohistochemistry.

Results

Controls and idiopathic CRS subjects tended to be dominated by members of the genera Corynebacterium and Staphylococcus, together with lower abundances of several other genera, including Streptococcus, Moraxella and Haemophilus. Microbial community dysbiosis (imbalance), involving changes in bacterial community structure and reduced diversity, together with increased inter- and intra -patient variability, was more apparent than any specific community associations with CRS. Dysbiotic communities were variably dominated by the genera Staphylococcus, Streptococcus, Haemophilus, Pseudomonas, Moraxella, or Fusobacterium, and were more common in subjects with asthma or cystic fibrosis. Furthermore, a relationship between aberrant community types and the inflammatory process emerged, irrespective of the phenotypic variants of CRS: elevated inflammatory signalling (interleukin-6) and cells (T cells, B cells, macrophages and neutrophils) were associated with depletion of normal community members, including Corynebacterium spp., Propionibacterium spp., Peptoniphilus spp., and Anaerococcus spp., reduced community diversity, and increased bacterial load.

Conclusions

Microbial community dysbiosis may play a role in the pathogenesis and severity of CRS, particularly in some variants. Improved understanding of interactions between resident microbes and the host tissues and immune system in this spectrum of inflammatory disease will have significant implications for improving treatment of this morbid condition.

SIXTEEN

Title

Changes in the bacterial microbiome of patients with chronic rhinosinusitis after endoscopic sinus surgery.

Authors

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Background

Endoscopic sinus surgery improves symptoms for many chronic rhinosinusitis (CRS) patients by enlarging the size of sinus ostia, improving mucociliary clearance and facilitating access for topical therapies. However, the effect of surgery on the sinonasal microbiota remains poorly understood.

Objective

To examine the changes in bacterial communities in CRS patients before and after surgery.

Method

Swab samples were taken from the middle meatus of 23 patients undergoing endoscopic sinus surgery. Follow up swabs were taken in clinic (mean 120 days post-surgery). Symptom scores and antibiotic use were recorded. Bacterial communities were characterized using 16s rRNA gene-targeted amplicon sequencing and bacterial abundance was measured using quantitative PCR. Co-existing asthma, aspirin sensitivity, antibiotic use and presence of polyps were controlled for.

Results

Unpredictable shifts in bacterial community composition were seen postoperatively. ESS was associated with increased bacterial richness. Many taxa had changes in average relative abundance and prevalence. *Staphylococcus* was the only dominant taxa to increase significantly in relative abundance (P=0.002). Individually, 18 out of 23 (78%) patients had increases in *Staphylococcus* following surgery despite postoperative anti-*Staphylococcus* directed antibiotic therapy. Changes in bacterial communities were driven more by inter-subject variability (P=0.007) than other study factors. *Finegoldia*, a minority taxon, was associated with a reduction in abundance following endoscopic sinus surgery, increases in patients with higher symptoms scores and reductions in patients with reduced total bacterial burden.

Conclusion

This study has documented changes in bacterial composition and abundance in the middle meatus following endoscopic sinus surgery. The complexity of these changes reflects the variability between patients. The data do not support the notion that outcomes following ESS may be due to obvious changes in the microbiome. Modern molecular techniques highlight the currently limited knowledge of the impact of therapies on the microbiology of CRS.

gprwmf

SEVENTEEN

Title

The impact of endoscopic sinus surgery on paranasal physiology in simulated sinus cavities.

Authors

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Background

Surgery has been shown to improve quality of life for patients with chronic rhinosinusitis (CRS) and improve long-term outcomes, however the mechanism by which this is achieved is not well understood. In particular, postoperative physiological changes in the sinus cavities remain poorly characterized. The direct measurement of changes in airflow, pressure, temperature, humidity and intranasal spray distribution following surgery is technically challenging. Fortunately, recent applications of computational fluid dynamics have allowed for the modeling of human airway physiology, and may have a role in estimating postoperative changes.

Objective

To examine the effects of surgery on the paranasal sinus environment by applying computational fluid dynamic techniques to three-dimensional anatomic models representing a spectrum of operative procedures. Specifically, this study seeks to characterize changes in airflow, temperature, pressure, humidity and drug distribution to describe likely environmental changes with ESS.

Method

Computed tomography images from a normal control, a patient with CRS pre and postoperatively, and a patient following an endoscopic Lothrop procedure (ELP) were used to create four three-dimensional models of the sinus cavities. Changes in physiologic parameters and topical drug distribution were modeled (inhaled air at 16°C and 10% humidity) at the maxillary ostium, frontal recess and sphenoid ostium.

Results

Large differences were seen between models. Following surgery, the maxillary ostia were found on average to be cooler (by 2.4°C), with an increased airflow (0.26 m/s (from 0 m/s)), and a 9% reduction in absolute humidity. Sphenoid ostial parameters followed a similar trend. Significant changes in frontal recess physiology were seen following ELP in which the recess was 4.2°C cooler, had increased airflow (0.76 m/s) and a 17% reduction in absolute humidity. Topical drug distribution increased with surgery, particularly after ELP.

Conclusion

Surgery changes the geometry and physiology of the paranasal sinuses. These changes are likely to have an impact on wound healing, mucociliary function and microbial ecology in postoperative cavities. Application of this model to further understand the effects of surgery may help to optimize surgical techniques and improve topical drug delivery.

EIGHTEN

Title

A Novel study on the impact of hearing loss on cognitive functions: Baseline non-verbal cognitive assessment results

Authors

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Background

Age-related hearing loss has been linked to cognitive decline and dementia in the elderly (Lin et al., 2011). However, the link between hearing loss and cognitive decline have been mostly investigated using verbally loaded cognitive measures. Inability to access auditory/visual test materials due to sensory impairment (hearing loss) could hinder performance in cognitive assessments and may result in over/ under-estimation of the cognition in the elderly with hearing loss (Dupis et al., 2015).

Objective

This cross sectional study investigated the effects of hearing loss on a number of cognitive functions (e.g. episodic memory, executive function, working memory, attention and verbal recognition memory) using a battery of non-verbal test materials. Further, impact of hearing loss on psychological status (anxiety, depression and stress) of older adults was examined.

Methods

A total of 101 participants (40 males M = 65.96 $\pm$ 10.89 years; 51 females M = 60.51 $\pm$10.32 years) were recruited for the study. Based on bilateral four-frequency average (0.5, 1, 2, & 4 kHz) hearing thresholds, participants were divided into three categories: normal hearing (NH: n = 40, M = 57.88 $\pm$ 9.26 years of age), mild to moderate hearing loss (MMH: n = 48, M = 67.04 $\pm$ 9.73 years of age) and moderately -severe to profound hearing loss (MSPH: n = 13, M = 65.46 $\pm$ 13.48 years of age). All participants completed a hearing assessment, a computerised test battery of cognitive functions (Cambridge Cognition, Ltd) and the depression anxiety and stress scale (DASS-21).

Results

Linear regression analysis was conducted to investigate the effects of hearing loss on cognitive functions. We controlled for age, gender, premorbid IQ, depression scores in all regression analysis. Better ear four-frequency average thresholds (0.5, 1, 2, & 4 kHz: 4 PTA) was significantly associated with the performance on working memory ($p < .05$) and paired associative learning ($p = .02$) tasks. In addition, better ear 4 PTA hearing levels significantly predicted ($p <.05$) depression, anxiety and stress scores after controlling for the effect of age, gender & premorbid IQ.

Conclusion

Hearing loss was inversely associated with working memory and paired associative learning abilities. Moderately-severe to profound hearing loss had more impact on the cognitive functions compared to mild hearing loss. These results emphasize the importance of using non-verbal cognitive tests in assessing cognitive functions of older adults with a hearing loss.

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NINETEEN

Title

Automated audiometry: Translation into clinical practice

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Background

There is limited evidence to support the use of automated audiometry in a tertiary otolaryngology setting and how this technology could be used to increase efficiency and access to audiology and otolaryngology services.

Objective

To examine the accuracy of automated audiometry and its translation to clinical practice.

Methodology

A series of three studies examining the threshold accuracy, diagnostic accuracy and accuracy of asynchronous remote interpretations of automated audiometry in 42 clinically heterogeneous patients at an otolaryngology department in Western Australia.

Results

Threshold accuracy between manual and automated audiometry ranged from 5.12 – 9.68 dB. Accuracy for identifying disabling, conductive and unilateral hearing loss ranged from 86% to 100%. The use of automated audiometry did not significantly influence the diagnostic or management decisions of audiologists (n = 5) when interpreted remotely (α = 0.54 [95% CI 0.47, 0.60]; q = 0.97).

Conclusion

Automated audiometry is accurate and is a useful addition to clinical practice which has the potential to improve audiology efficiency and enable remote hearing assessments.

This series of experiments addresses three key issues of automated audiometry that have not previously been examined or reported. Firstly, we have shown that automated audiometry has sufficient accuracy to be used with a clinically diverse, tertiary otolaryngology population. Secondly, the application of novel, pre-defined diagnostic criteria is an accurate method of identifying common hearing impairments to increase efficiency in tertiary services or provide better access where audiological services are limited. Thirdly, whilst there are statistically significant differences in thresholds between automated and manual audiometry, these are of limited clinical significance and do not affect decisions regarding patient management when interpreted remotely in an asynchronous telehealth model.

TWENTY

Title

Performance of ultrafine intranasal QVAR spray, aqueous metered dose pumps and nebuliser as modelled by computational fluid dynamics

Authors

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Background

Endoscopic sinus surgery for the treatment of chronic rhinosinusitis (CRS) is not always successful at controlling mucosal inflammation and improving symptoms. Part of the cause of disease recalcitrance may be difficulties in distributing topical corticosteroids in the postoperative sinonasal cavity. It has been demonstrated that smaller particle sizes more easily penetrate the nasal valve and reach the sinuses. Many studies have simulated aqueous metered dose pumps and nebuliser particle deposition in the maxillary sinus post antrostomy. The deposition to more challenging areas such as the frontal and sphenoid sinuses has not been well described. QVAR is a pressurised metered dose corticosteroid inhaler which delivers extremely small particles. We hypothesised that this physical characteristic may improve intranasal drug deposition.

Objective

To evaluate and optimise the performance of QVAR against aqueous metered dose pumps and nebulisers in the postoperative sinuses using computational fluid dynamics.

Method

A three-dimensional postoperative model of the sinuses was constructed using the computed tomographic scan of a 20 year old Caucasian male with CRS. Using a validated computational fluid dynamics method, the deposition of a nebuliser, aqueous metered dose pump and QVAR were simulated. All modalities were simulated at their characteristic particle sizes and at three different flow rates (5, 10 and 15 litres per minute).

Results

In this simulated model, greater sinus deposition was seen with smaller particle sizes (QVAR and nebuliser), although these particles were associated with greater nasal cavity escape. The greatest deposition to the middle meatus, maxillary and sphenoid sinuses was seen with a nebulised 20 micron particle (up to 12.4%), however the frontal sinus was poorly penetrated by all devices. Large particles from aqueous pumps demonstrated less escape and the highest overall deposition, but was associated with less sinus deposition. Less escape was seen at higher flow rates for all devices. As flow rate increased from 5 to 15 litres per minute, an increase in particle deposition of 160% was observed for QVAR (1.1 micron particle). Meanwhile, inconsistent changes were seen with the nebuliser and very small changes were seen with the aqueous pump.

Conclusion

This computational fluid dynamics study shows that QVAR and nebulisers surpass aqueous pump performance in paranasal sinus particle deposition, especially at higher rates of inhalation flow. The clinical significance of this is yet to be determined. In practice, nebulisers may lose in convenience and compliance what they offer in deposition.

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TWENTY ONE

Title
A review of the safety and efficacy of local anti-infective agents in the clinical setting.

Authors
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Background
Antibiotic resistance is an issue of global concern and is very much a threat to modern healthcare. Evidence is emerging to support the use of local anti-infective agents in the treatment of a range of infectious pathology that would otherwise result in an antibiotic prescription. Whilst anti-infective agents have been around for a long time, the indications for use are gradually changing to incorporate a wider range of pathology. It is generally accepted that the use of anti-infective agents is an essential preventative control measure against the spread of nosocomial infections and multi-drug resistant bacteria within hospital and other healthcare and community settings.

Objective
This study reviews and compares the efficacy and safety of anti-infective agents, namely povidone-iodine (P-I), benzalkonium chloride, chlorhexidine, reactive oxygen species such as hypochlorous acid, alcohol, and silver sulphasalazine.

Method
A comprehensive review was undertaken of studies assessing the safety and efficacy of various local anti-infective agents in various clinical settings. We searched PubMed, MEDLINE, the Cochrane Trial Registry (through July 2016) and relevant article biographies.

Results
A 2010 Cochrane Review of topical silver sulphadiazine found there is insufficient evidence to establish whether silver-containing dressings or topical agents promote wound healing or prevent wound infection. A 2016 Cochrane Review found that povidone-iodine had no significant impact on the risk ratio of blood stream infection (BSI) or catheter colonisation.

Comparative trials of alcohol based chlorhexidine versus povidone-iodine found chlorhexidine to be superior with respect to the endpoints of BSI and all-cause mortality.

Randomised control trials of sodium hypochlorite solution versus active controls for the prevention of catheter-related BSI showed hypochlorous acid has 80-100 times the antimicrobial potency of sodium hypochlorite.

A 2016 Cochrane Review of surgical hand sanitisers and the impact on surgical site infections found no firm evidence that one type of hand sanitiser was superior to another amongst studies comparing soap and water, chlorhexidine, povidone-iodine or alcohol.

In regards to safety, twenty commercial wound and skin cleansers were evaluated for cytotoxic effects on mouse dermal fibroblasts. Electrolytically generated hypochlorous acid was the least cytotoxic followed by chlorhexidine, hydrogen peroxide, and povidone-iodine.

Conclusion
Reactive oxygen species such as hypochlorous acid appear to be the most efficacious and safe of the local anti-infective agents reviewed in this study. However further studies are required that directly compare anti-infective agents in various clinical settings.

TWENTY TWO

Title
A systematic review of the role of viruses in chronic tonsillitis.

Authors
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R Douglas, University of Auckland, Auckland, New Zealand.
M Mahadevan, Starship Children's Hospital, Auckland, New Zealand.

Background
Viral colonisation of human tissue contributes significantly to multiple disease states, but its role in the development of tonsil infection is unclear. Understanding the aetiology of chronic tonsillitis is important in clinical decision making of this commonly treated disease.

Objective
To assess the correlation between viral colonisation of tonsillar tissue in chronic tonsillitis and in noninfectious hyperplastic tonsils.

Method
Systematic review of studies assessing the correlation between viral colonisation in tonsillar tissues of patients undergoing tonsillectomy for either chronic tonsillitis or noninfectious causes. Included studies hypothesised that viruses played a role in the development of chronic tonsillitis. All included studies investigated the presence of viruses in tonsillar tissue removed for various indications. Included studies must have used polymerase chain reaction (PCR) testing for virus detection. We searched PubMed, MEDLINE, the Cochrane Trial Registry (through July 2016) and relevant article bibliographies. Studies were systematically reviewed by 2 independent reviewers for inclusion. Reported results of virus testing between tissues removed for infectious or noninfectious causes were systematically reviewed.

Results
Six studies met inclusion criteria and had suitable data for pooling (n=603). Of these, 4 studies measured viral colonisation of tonsillar tissue in paediatric populations. Two studies analysed tissue in both adult and paediatric populations. Non-infectious indications for tonsillectomy-included sleep related breathing disorder, obstruction, sleep apnoea, and tonsillar hypertrophy. Overall viral colonisation was found to be significantly present more often in tissue samples removed secondary to recurrent infection rather than noninfectious indications. This was true of Epstein-Barr virus, Bocavirus, polyomavirus WU, human parainfluenzaviruses, and human adenoviruses. The exception to this was A and B influenza viruses and human enterovirus, which were seen, more commonly in hypertrophic tonsils.

Conclusion
Viral colonisation was found to be more prevalent in tonsillar tissue with chronic or recurrent infections. The reviewed studies suggest that certain viruses may play a role in the development or pathogenesis of chronic tonsillitis and others may contribute to tonsillar hypertrophy.

gprwmf

TWENTY THREE

Title
An evaluation of the necessity of pharyngeal surgery at the time of ventilation tube insertion in patients with middle ear effusion.

Authors
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Background
Adenoidectomy and adenotonsillectomy are commonly performed operations at the time of myringotomy plus ventilation tube insertion (MVTI) in children with otitis media with effusion (OME). However the literature that supports the use of these techniques is controversial. A key limitation in our ability to move forward is our lack of understanding in regards to the role of the adenoids in OME. Theories include that of mechanical obstruction of the eustachian tube versus the pathogen reservoir hypothesis. It is important as clinicians to understand if there are significant benefits in adenoidectomy or adenotonsillectomy at the time of MVTI given that these procedures are not without risks.

Objective
The aim of this retrospective cohort study was to evaluate the incidence of children less than 10 years of age who underwent subsequent MVTI procedures following an initial MVTI with and without tonsillectomy or adenoidectomy.

Method
Data was obtained from Auckland District Health Board (ADHB) clinical records department following institutional approval through the ADHB research office. A de-identified extraction of all hospital morbidity records belonging to persons who underwent a MVTI procedure between January 1, 1996 and June 2016 was performed. Demographic, diagnostic, and procedural data was included in the extraction. International Classification of Disease (ICD) coding was used to distinguish between myringotomy alone and MVTI.

Results
There were 11,941 children less than 10 years of age who underwent at least one MVTI procedure from January 1996 to June 2016. Eighteen percent underwent pharyngeal surgery at the time of first MVTI procedure, and of these, 2% (309) had pharyngeal surgery in the absence of adenoid or tonsil disease. Adenoid surgery at time of MVTI was associated with reduced odds of subsequent MVTI procedures in children with or without adenoid/tonsil disease. There were no observed differences in the length of hospital stay between MVTI alone and with adenoidectomy. However procedures involving tonsillectomy required an additional bed day per procedure. Patients who had tonsillectomy were also more likely to have postoperative hemorrhage.

Conclusion
Patients who underwent adenoidectomy +/- tonsillectomy at the time of first or subsequent MVTI were less likely to require further MVTI surgery. This supports the theory that pharyngeal surgery should be performed at the time of initial MVTI in appropriate cases.

TWENTY FOUR

Title
Clinical experience with Microdacyn® wound care in recalcitrant wounds of the head and neck.

Authors
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Background
Recalcitrant wounds and the infections associated with them are responsible for a considerable increase in morbidity, mortality and cost of healthcare. The use of biocides is an essential measure in wound care management within hospital and other healthcare and community settings. Frequent use of several existing biocidal agents can cause dermatological or respiratory health problems in health workers, can cause damage or corrosion to equipment, and increasing resistance is rendering them ineffective against bacteria, viruses, fungi, spores, eukaryotes, and biofilms. From out of this need for more effective, safe, and non-cytotoxic topical antimicrobial agents, a class of pH neutral electrolytically activated water solutions (NEW) have been developed. Microdacyn® is the trade name of the NEW product that we will refer to in this study.

Objective
This retrospective cohort study evaluates the efficacy of Microdacyn® wound care in the treatment of recalcitrant wounds of the head and neck at a major tertiary hospital.

Method
Patient data was collected from November 2015 to June 2016 at the tertiary head and neck surgical unit at Auckland City Hospital in New Zealand. All patients had recalcitrant wounds treated with Microdacyn® wound care following head and neck surgery. All patients were treated in the same center and by the same clinician.

Results
Twenty-six patients were included in the study cohort; 19 were male and 7 female. Mean age was 69 years (range 29-90 years). Mean duration of treatment was 11.5 days (Range 3-25 days). Wound types included orocutaneous fistulae, peristomal defects, pinna necrosis, perichondritis, an intra-oral defect with exposed mandible, wounds following incision and drainage of abscesses, infected lacerations, a non-healing neck wound following radiotherapy, infected thigh donor site following split skin graft harvest, pharyngocutaneous fistulae, radiotherapy burns, infected cavity post debridement of partial free flap necrosis, infection/ dehiscence of wound closure sites, and a nasocutaneous fistula. Orocutaneous fistulae were the largest cohort (5/26 wounds). All patients were satisfied with Microdacyn® wound care products. No patients reported pain or discomfort. Clinical staff noted a significant improvement in wound healing at a faster than expected rate. Clinical staff also reported that Microdacyn® wound care products were easy to use and very well tolerated by patients.

Conclusion
Microdacyn® wound care products provide clinicians with a well-tolerated and effective biocidal agent that compliments standard wound care therapy in the treatment of recalcitrant head and neck wounds.

gprwmf

TWENTY FIVE

Title

Immunological and bacterial anatomy of the human palatine tonsil.

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Background

Commensal bacteria colonize the extensive folds and crypts of the palatine tonsils soon after the infant is born. These microbes subsequently affect the innate immune response of the mucosa, and may be a significant factor in protecting or predisposing the infant to mucosal infection depending upon the composition of the microbial community that is established. Understanding the complexities of the tonsillar-associated microbiota, and especially the manner in which they interact with the host innate immune response, is vital for the development of future treatment options.

Objective

In this study we aim to expand our knowledge of the immunological anatomy of the human palatine tonsil and map out where bacteria are located in relation to anatomical structures in tonsil tissue.

Method

A single palatine tonsil removed from a healthy 7-year-old female with recurrent tonsillitis was fixed in Carnoy's solution and then embedded in paraffin wax. The entire tonsil was cut in sections at 4 microns every 250 microns along a coronal section. CD3 cells were stained brown with a rabbit antibody to identify T-cells and CD20 cells were stained black with a Mouse antibody to identify B-cells. A gram stain with crystal violet followed by safranin was then used to identify bacteria and highlight supporting connective tissue. The MetaSystems Vslide Scanner then captured all twenty-three slides as high-resolution images.

Results

Images obtained give a clear representation of the immunological anatomy of the human palatine tonsil. B and T lymphocytes are clearly demonstrated by the employed staining techniques. The extensive crypt system of the tonsil is demonstrated. Bacteria are demonstrated in the crypts, surface, and within the tonsil tissue itself.

Conclusion

This study furthers our understanding of the immunological anatomy of an entire human palatine tonsil by offering a visual demonstration of the location and proportions of lymphocytes in the tissue. It also provides us with a better understanding of the location of bacteria in a three dimensional sense.

TWENTY SIX

Title

Slowing the progression of age-related hearing loss:
Rationale and study design of the ASPIRIN in HEARING, retinal vessels imaging and neurocognition in older generations (ASPREE-HEARING) trial

Authors

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Background

Age-related hearing loss (ARHL) is a leading cause of disability in older people. Low-grade inflammation and microvessel pathology may be responsible for initiating or exacerbating some of the hearing loss associated with ageing. A growing body of evidence demonstrates an association of hearing loss with cognitive decline. A shared aetiological pathway may include a role of inflammation, alongside vascular determinants.

Objective

The ASPREE-HEARING study aims to determine whether low-dose aspirin delays the onset or decreases the rate of progression of ARHL, and if so, whether this decrease in progression is also associated with retinal microvascular changes and/or greater preservation of cognitive function.

Methods

A three year double-blind, randomized controlled trial of oral 100 mg enteric-coated aspirin or matching placebo, enrolled Australians aged ≥70 years with normal cognitive function and no overt cardiovascular disease. The primary outcome is the change in mean pure tone average (PTA) hearing threshold (decibels) in the better ear, over a 3-year period. Secondary outcomes consist of changes in retinal microvascular indicators and changes in cognitive function. Participants are recruited from a larger trial, ASPirin in Reducing Events in the Elderly (ASPREE), which is designed to assess whether daily low dose aspirin will extend disability-free life.

Results

Of 1262 participants recruited in 2014, the mean (SD) PTA for the right ear at baseline was 27.5dB (14.5) for those aged 70-74 years; 33.4dB (15.3) in the 75-79 year age group; 37.5dB (16.6) in the 80-84 year age group; and 44dB (14.2) in those aged ≥85 years. Eighteen month measurements are currently underway, with the 3 year measures scheduled for 2017.

Conclusion

ASPREE-HEARING will determine whether aspirin slows development or progression of ARHL, and will interrogate the relationship between inflammatory and microvascular mechanisms that may underlie the effects of aspirin on ARHL. This study will improve understanding of the patterns of comorbidity with, and the relationships between, ageing and ARHL, alongside modeling the impacts of ARHL.

gprwmf

TWENTY SEVEN

Title
Short-term retention of the active and passive vestibulo-ocular reflex gain after incremental adaptation training.

Authors
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Background
Incremental vestibulo-ocular reflex (VOR) gain (eye-velocity/head-velocity) adaptation training increases the VOR response by a larger amount in a shorter period of time compared to conventional training that relies on a constant, large retinal image error signal to drive adaptation.

Object
We sought to determine the short-term (1 hour) time-course of VOR retention after incremental VOR adaptation training. We tested the effect of passive versus active adaptation training and varied the post-training test time interval.

Method
We tested 9 normal subjects over 5 separate 1 1/2 hour sessions. We compared active versus passive VOR adaptation training lasting 15 minutes with the VOR gain challenged to increment, starting at unity, by 0.1 every 90 seconds towards one side only (this adapting side was randomised to be either left or right). We measured the VOR gain in darkness at 10 minute versus 20 minute versus a 60 minute intervals for 1 hour post-training. The training was active or passive for the 10 and 20 minute interval sessions, but only active for the single 60 minute interval session (i.e., 2 x 2 + 1 = 5 conditions). In order to test the VOR gain a room -fixed visual target was generated directly in front of the subject, which disappeared when the head moved away 0.8 degrees from neutral.

Results
The active and passive VOR gains both increased by ~11% after active training. The VOR gain when tested once only (60 minute interval) 1 hour post-training was 10% higher than pre-training. When tested for 1 hour every 20 minutes post-training, the gains were all ~ 10% higher than pre-training. However, when the gain was tested for 1 hour every 10 minutes, there was a steady decrease in retention, so that at 10, 20, 30, 40, 50 and 60 minutes the gain increase compared to pre-training was 11%, 10%, 9%, 8%, 7% and 6%, respectively. Towards the non-adapting side the gain increase was fixed at ~3%.

Conclusion
The stationary visual fixation stimulus generated when testing the VOR provided visual feedback acting to drive the adapted side gain down to unity. Shorter test time intervals resulted in greater exposure to this visual stimulus. Hence, our data suggest that VOR adaptation is completely retained over 1 hour as long as there is no visual feedback signal driving de-adaptation.

TWENTY EIGHT

Title
The role of the mammalian efferent vestibular system in vestibulo-ocular reflex gain adaptation and compensation

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Background
The precise mechanisms underlying vestibular adaptation and compensation in mammals remain to be determined. The predominantly cholinergic Efferent Vestibular System (EVS), an extensive pathway from the brainstem to the inner ear that can modify peripheral vestibular organ output, could be involved in both forms of plasticity.

Objective
We investigated the vestibulo-ocular reflex (VOR) response before and after VOR adaptation training, and compensation after unilateral labyrinthectomy (UL), in control and α9-knockout mice, which have a compromised EVS.

Method
We measured the VOR gain (eye-velocity/head-velocity) in 26 α9-knockout mice and 27 CBA129 controls. Mice underwent: baseline testing, gain-increase adaptation (x1.5) or gain-decrease adaptation (x0.5) training that consisted of a 40 minute visual stimulus synchronized to horizontal whole-body rotations (0.5Hz, peak-velocity 20°/s).We also measured the VOR gain in 20 α9-knockout mice and controls 1, 5 and 28 days after UL.

Results
Adaptation (difference in VOR gain to gain-increase and gain-decrease adaptation as a percentage of gain-increase) was significantly reduced in untreated α9-knockout mice (17%) compared to untreated controls (53%), a reduction of ~70%. Chronically compensated (28 days after UL) α9 knockout mice had ~50% lower gain for both ipsilesional and contralesional rotations compared to chronically compensated control mice. Control mice regained ~75% of their baseline function for ipsilesional and ~90% for contralesional rotations. Whereas, α9 knockout mice only regained ~30% and ~50% function, respectively, leaving the VOR severely impaired for rotations in both directions.

Conclusion
Our results show that loss of alpha9-nAChRs severely affects VOR adaptation and compensation, suggesting that complimentary central and peripheral EVS-mediated adaptive mechanisms are needed to optimally drive vestibular plasticity.

gprwmf

TWENTY NINE

Title
The visual background affects vestibulo-ocular reflex incremental gain adaptation

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Background
Incremental vestibulo-ocular reflex (VOR) gain (eye-velocity/head-velocity) adaptation training increases the VOR response by a larger amount in a shorter period of time compared to conventional training that relies on a constant, large retinal image error signal to drive adaptation.

Objective
We sought to determine the effect of background light level and laser target intensity on VOR gain adaptation.

Method
We tested 12 normal subjects over 10 separate sessions. For sessions 1-8, the background light level during adaptation training was: dark, 0.1, 0.2, 0.3, 0.5, 0.7, 1 and 475 lux. For sessions 9-10 the laser target intensity was halved with background at dark and 0.1 lux. The adaptation training lasted 15 minutes and consisted of left/right active head impulses. The VOR gain was challenged to increment, starting at unity, by 0.1 every 90 seconds for rotations to one side (the adapting side) and fixed at unity towards the non-adapting side. We measured active and passive VOR gains before and after training.

Results
Active and passive VOR gains were similar under the different lighting conditions. There was no difference between head impulse type (active vs passive) VOR gains ($P = 0.967$) and brightness did not affect the VOR gain ($P = 0.392$). However, there was a close to significant interaction between light level and head impulse type ($P = 0.101$), suggesting that active VOR gains were affected most by the training light level, especially at the darker levels. There was a significant interaction between the training light level with side (adapting vs non-adapting; $P < 0.001$). In the dark, the post-training VOR gain towards the adapting side (1.05 ± 0.09) was 9.9 ± 5.9 % higher than pre-training (0.96 ± 0.08). At 0.1, 0.2, 0.3, 0.5, 0.7 and 1 lux the gain increase was 8.4 ± 3.4 %, 7.2 ± 3.8 %, 6.2 ± 3.3 %, 6.9 ± 3.6 %, 7.2 ± 3.2 % and 7.9 ± 3.4 %, respectively. At 475 lux, the VOR gain increase towards the adapting side (2.9 ± 2.7 %) was the same as the 3.4 ± 3.3 % increase towards the non-adapting side averaged across all light levels.

Conclusion
Our data suggest incremental adaptation training increases the VOR gain when performed at or below 1 lux. It's not clear whether background light level alone or target contrast (relationship between background light level and target brightness) is the main characteristic of the 'error signal' driving adaptation.

THIRTY

Title
Could precision medicine be tailor-made for metastatic Head and Neck Cancers?

Authors
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Background
Metastasis remains the major cause of deaths in head and neck cancers (HNC). Despite improvements in diagnosis and therapy, over 1020 HNC patients die and 4520 new cases are reported annually in Australia. Circulating tumour cells (CTCs) are shed from HNC tumour deposits and circulate in patients' peripheral blood, representing an important window into metastasis. Despite its clinical importance, little is known about the genetic makeup of these tumour cells. Minimally invasive techniques are required for the identification of patients who are at an increased risk of metastasis, or are not responding to therapy.

Objective
An approach utilised in other solid cancers is the identification and enumeration of circulating tumour cells (CTCs) in the peripheral blood of patients. Low numbers of CTCs has been a bottle-neck in the field to date.

Methods
As a proof of principle study, 25 advanced stage HNC patients (treatment naive, no clinical/radiographic evidence of metastasis) had bloods enriched for circulating tumour cells through negative selection and cultured in 2D and 3D culture environments under hypoxic conditions (2% O_2, 5% CO_2).

Results
CTCs were detected in 14/25 (56%) of patients (ranging from 1-15 CTCs/5 mL blood). Short term CTC cultures were successfully generated in 7/25 advanced stage HNC patients (5/7 of these cultures were from HPV+ patients). Blood samples from which CTC culture was successful had higher CTC counts ($p=0.0002$), and were predominantly from HPV+ patients ($p=0.007$).

Conclusions
This is the first study to culture HNC CTCs *ex-vivo*. Further studies are warranted to determine the use of short term expansion in HNC and the role of HPV in promoting culture success. We hypothesise that CTC culture responses to HNC therapies will parallel patients clinical responses, paving the way to a clinical trial in which personalised medicine will be adjusted based on CTC culture response to therapeutic agents.

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THIRTY ONE

Title

Burkholderia pseudomallei rapidly infects the brainstem and spinal cord via the olfactory and trigeminal nerves after intranasal inoculation.

Authors

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Background

Melioidosis is a potentially fatal disease that is endemic to tropical northern Australia and south-east Asia with a mortality rate of 14-50%. The bacterium Burkholderia pseudomallei is the causative agent which infects numerous parts of the human body, including the brain which results in the neurological manifestation of melioidosis. Neurological melioidosis is particularly prevalent in northern Australian patients and involves brainstem infection, which can progress to the spinal cord.

Objective

The olfactory and trigeminal nerves constitute direct conduits from the nasal cavity into the brain. The purpose of this study was to determine whether the bacteria can use the olfactory and trigeminal nerves to invade the central nervous system (CNS).

Method

We intranasally inoculated mice with B. pseudomallei and tracked the progression of bacteria from the nasal cavity into the CNS using immunohistochemistry.

Results

We found that the olfactory epithelium responded to intranasal B. pseudomallei infection by widespread crenellation followed by disintegration of the neuronal layer to expose the underlying basal layer which the bacteria then colonised. With the loss of the neuronal cell bodies, olfactory axons also degenerated and the bacteria then migrated through the now open conduit of the olfactory nerves. Using immunohistochemistry, we demonstrated that B. pseudomallei migrated through the cribriform plate via the olfactory nerves to enter the outer layer of the olfactory bulb in the brain within 24 hours. As the trigeminal nerve projects into the brainstem, we investigated whether the bacteria could continue along this nerve to penetrate the CNS. After intranasal inoculation of mice, B. pseudomallei caused low-level localised infection within the nasal cavity epithelium, prior to invasion of the trigeminal nerve in small numbers. B. pseudomallei rapidly invaded the trigeminal nerve and crossed the astrocytic barrier to enter the brainstem within 24 hours and then progressed over 2000 µm into the spinal cord. To rule out that the bacteria used a haematogenous route, we used a capsule-deficient mutant of B. pseudomallei, which does not survive in the blood, and found that it also entered the CNS via the trigeminal nerve.

Conclusion

These results demonstrate that B. pseudomallei invasion of the nerves of the nasal cavity leads to direct infection of the brain and bypasses the blood brain barrier. In particular, B. pseudomallei can infect the brain and spinal cord via branches of the trigeminal nerve that innervate the nasal cavity within 24 hours of intranasal inoculation.

THIRTY TWO

Title

Enhancing the use of olfactory glia for nerve repair – natural product drug discovery using three-dimensional cell cultures.

Authors

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Background

One of the promising strategies for neural repair therapies is the transplantation of olfactory ensheathing cells (OECs) which are the glial cells of the olfactory system. While results are encouraging, improvements need to be achieved for effective therapy development. Most medicines on the market are derived from natural products and screening of natural products is an effective strategy to identify potential new drugs. Traditional culturing methods in which cells are grown in two-dimensional plates do not necessarily provide the optimal cell-cell interactions. In contrast, three-dimensional (3D) in vitro cell growth allows cells to more closely mimic in vivo cell interactions. Combining high through-put drug screening with 3D cultures is a challenge but one which will likely improve the identification of new drugs for neural repair.

Objective

To develop new three-dimensional culturing methods for use in natural product drug screening, and to identify natural products that stimulate the activity of OECs.

Method

We have developed the floating liquid marble which is a liquid droplet coated with hydrophobic powder and placed on a liquid bath. Floating liquid marbles allow the OECs to freely associate and interact to produce OEC spheroids with uniform shapes and sizes. We have screened natural products and used in vitro proliferation, migration and phagocytosis assays to identify that compounds that can potently the stimulate the activity of OECs.

Results

Floating liquid marbles enable the culturing of OECs and other cells within volumes of 10 µL which minimises the reagents needed for high through-put assays. The constant movement of the liquid marbles allows the cells to freely associate. In co-culture assays, we found that OECs mixed with astrocytes, but did not mix so closely with Schwann cells. We have screened natural compounds using 2D and 3D assays. Low-dose curcumin (0.5 µM) applied to OECs strikingly modulated the dynamic morphology, increased the rate of migration by up to 4-fold, and promoted significant proliferation of the OECs. Most dramatically, low-dose curcumin stimulated a 10-fold increase in the phagocytic activity of OECs. Stimulation of the phagocytic activity is of particular interest for neural repair therapies as removing cell debris from an injury site will enhance the ability for axons to regenerate.

Conclusion

Three-dimensional culturing of cells in liquid marbles provides superior cell interactions and is suitable for drug screening. We have identified that curcumin stimulates activities of OECs that are favourable for neural repair.

gprwmf

THIRTY THREE

Title

Behavioural and preliminary electrophysiological analysis of the mouse vestibular system.

Authors

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Background

Our sense of balance is essential in carrying out everyday tasks. During aging there is an increased risk of experiencing loss of balance and subsequently falls, although the precise mechanisms that underlie this are unknown.

Objective

Here we aim to characterise vestibular-mediated changes in balance performance with age and the electrophysiological characteristics of vestibular hair cells and calyces in a slice preparation of the mouse crista ampullaris.

Methods

Experiments were approved by The University of Sydney Animal Ethics Committee and the University of Colorado IACUC. *Behaviour* – C57BL/6 mice of ages 1 (n = 3), 10 (n = 7), 13 (n = 6) and 27-28 (n = 8) months were trained to walk 30 cm unassisted to a darkened goal box before and after a vestibular stimulation (rotation from 0 to 3 Hz over 20s). Walking trajectories were measured and used to compare mice at each age point. *Electrophysiology* – Horizontal cristae were isolated from C57BL/6 mice, embedded in agarose and an 80 um-thick slice preparation made for whole-cell voltage-clamp experiments from type I (n = 6), and II (n = 7) hair cells at room temperature.

Results

Behaviour –Walking trajectory of mice prior to the vestibular stimulus changed with age ($p = 0.001$), such that trajectories deviated markedly in older animals. Importantly, the effect of the vestibular stimulus on walking trajectory was also age-dependent, although this change was non-linear ($p > 0.05$). Post hoc analysis revealed walking trajectories for 1-month-old mice (before: 6.90 ± 1.66 mm vs. after: 6.64 ± 1.85 mm) were significantly less affected by the vestibular stimulus than 10 ($p < 0.01$), 13 ($p < 0.01$), and 27-28 month-old mice ($p < 0.01$).

Electrophysiology – Preliminary recordings from the slice preparation during a series of depolarising steps were used to calculate maximum conductance for outward K^+ currents in type I and II hair cells. Mean maximum conductances for type I hair cells from 1-month-old mice were higher than those of type II vestibular hair cells (83.11 ± 40.13 nS vs 29.56 ± 16.32 nS, $p< 0.05$).

Conclusion

The impact of vestibular stimulation on older mice is reflected in reductions in motor performance. Type I hair cells recorded from a mouse slice preparation have higher maximum conductance for outward K^+ currents than type II hair cells.

THIRTY FOUR

Title

Unlocking the functional capacity of sinonasal microbiota using microbial DNA enrichment techniques

Authors

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Background

The role of the sinus microbiota, including bacteria, fungi and viruses, in health and disease has not been well characterised. This is due, in part, to the overwhelming proportion of contaminating host DNA compared with recovered microbial DNA.

Objective

A methods study examining different techniques for removing contaminating host DNA before metagenomic sequencing was conducted. We hypothesized that the enrichment techniques would improve recovery of microbial information from sinus swab samples.

Method

Twelve samples were taken from each of three adult patients recruited from Auckland City Hospital, New Zealand who were undergoing functional endoscopic sinus surgery for chronic rhinosinusitis (CRS). Pairs of swabs from each patient were subjected to three microbial DNA enrichment methods: 1. A series of centrifugation steps, followed by a standard DNA extraction, 2. A standard DNA extraction followed by enrichment of microbial DNA using NEBNext® Microbiome DNA Enrichment kit, and 3. Whole-genome amplification following the previous enrichment strategies. Additionally, a no-treatment control and a whole-genome amplified control from each patient were sequenced. Paired-end shotgun metagenome sequencing was conducted on the Illumina HiSeq platform. Each enrichment method and the no-treatment controls were assessed for effectiveness based on the proportion of recovered microbial sequence reads to human-assigned sequences. In addition to metagenomics sequencing, we also applied Bacteria--targeted 16S rRNA gene sequencing to assess bacterial community composition.

Results

After sequence quality filtering, the centrifugation method returned the highest proportion of microbial reads (1.1 ± 1.7%) compared to the no-treatment control (0.15 ± 0.07%), however, this result was not significantly different to the other methods (all *p*-values > 0.05). The effectiveness of the enrichment techniques was inconsistent, indicated by the large standard deviations from each mean.

Conclusion

Treating samples with various enrichment techniques alters microbial community structure in an unpredictable manner. The data suggest that the chosen enrichment techniques were not optimal. We recommend fewer samples per metagenomics sequencing run to increase depth of sequencing without altering in situ microbial community composition.

gprwmf

THIRTY FIVE

Title
Changes in neural activity in the inferior colliculus following acute electrical stimulation of the round window in an animal model of tinnitus

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Background
Tinnitus is the perception of sound in the absence of external acoustic stimuli. It often occurs as a result of damage to the cochlea, which causes a change in the afferent input, leading to maladaptive plastic changes in central auditory neurons. Cochlear implant use can suppress tinnitus in people with severe tinnitus. It is thought that re-establishment of neural activity reverses the plastic changes responsible for tinnitus. However, the extent of suppression remains variable and the mechanism(s) responsible are unknown. Consequently, there has been only limited clinical use of bionic devices to treat tinnitus. The current study examined the acute effects of electrical stimulation from a round window electrode on neural firing in the central nucleus of the inferior colliculus (ICC).

Methods
Adult guinea pigs were used (n=11). Auditory brainstem responses (ABRs) were measured before and following acoustic deafening. Eight animals were unilaterally deafened (10 kHz, 124 dB SPL, two hours). The acoustic startle reflex was used to obtain behavioural evidence of a tinnitus percept. Data was obtained before deafening, and in the two week period following deafening, after which an acute electrophysiological experiment was carried out. Animals were anaesthetised and a platinum ball electrode was placed on the round window membrane. A 32 channel probe was inserted along the tonotopic gradient of the ICC. Spontaneous neural activity and responses to acoustic input was measured before and immediately following a one hour period of electrical stimulation (bipolar pulses delivered in 100 ms bursts (100 pps), at 5 Hz). The cochleae were then collected for histology.

Results
A significant shift in hearing thresholds was observed following noise deafening and inner and outer hair cell lesions were observed in the basal turn. Behavioural evidence of tinnitus was observed in half the noise deafened animals via the startle reflex. There was evidence of hyperactivity in the spontaneous firing rates of ICC neurons with characteristic firing frequencies >10 kHz exhibiting significantly higher firing rates than neurons with characteristic frequencies of <10 kHz (ANOVA $p<0.001$). There was a significant reduction in spontaneous firing rates following the acute bout of electrical stimulation (ANOVA $p<0.001$).

Conclusions
Electrical stimulation from a bionic device can be used to alter neural firing properties associated with tinnitus and therefore help in determining the neural correlates of tinnitus. The potential use of a round window implant may provide a therapeutic option for people with intractable tinnitus.

This work was funded by the NHMRC and supported by the Victorian Government through its Operational Infrastructure Support Program.

THIRTY SIX

Title
Aetiology of oral cavity cancer in non-smokers: an exploration utilising Next-Generation Sequencing

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Background
Almost 20% of oral cavity cancers occur in a non-smoking population. Multiple studies have explored whether the human papilloma virus (HPV) could be responsible, other studies have suggested that chronic dental trauma may play a role.

Objective
We sought to explore whether HPV, or genetic and transcriptome changes could explain the development of oral cavity cancer in a non-smoking population. We also sought to explore whether oral cavity cancers differ in their genome and transcriptome based upon tumour location.

Method
Utilising DNA exome and RNA sequencing we performed a prospective observational study, by collecting fresh samples from participants attending head and neck clinics in Brisbane.

Results
HPV was present in 4.54% of samples, all being current smokers. There was no significant clustering of samples on a Principal Component Analysis of the RNA sequencing data when exploring participants smoking status. Results from RNA sequencing were consistent with known changes within other cancers. Transcriptome changes within participants who were current or ex-smokers were consistent with other cancers caused by tobacco exposure.

Conclusion
In the non-smoking population, HPV is unlikely to be a significant cause of oral cavity cancers, and there is unlikely to be single genetic or transcriptome changes which explain the development of these cancers.

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