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The Queen Elizabeth Hospital

25th Anniversary

Research Day 2016

Programme & Abstracts

Friday 21 October

Basil Hetzel Institute

37a Woodville Road, Woodville South

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TQEH Research Day 2016

25th Anniversary

CONTENTS

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Welcome to The Queen Elizabeth Hospital Research Day 2016. This is a special event this year as we are celebrating our 25th Research Day here at The Queen Elizabeth Hospital and the Basil Hetzel Institute! Everyone who has played a role in the event, as presenters, organisers and sponsors over the years should feel proud of this accomplishment. I would particularly like to acknowledge the Committee of Graduate Studies (Medical Staff Society, The Queen Elizabeth Hospital) for their foresight and enthusiasm in initiating the first Research Day back in 1992 and for their ongoing involvement over the years. Research Day has now become a major event in the research calendar and is acknowledged as playing an important role in the professional development of the next generation of researchers.

This year, the Committee was pleased to receive 34 Abstracts. Twenty students will give oral presentations on Research Day and the other 14 will take part in the Poster Competition. The preliminary Poster Competition will be held on Tuesday 18 October from 9.30 to 11.30 am and the Poster Finals will be held from 1.20 to 2.00 pm on Research Day. Please support the presenters at all these sessions!

Many people have contributed to the success of this Day and we would like to thank all those involved. In particular, we thank:

- Our Major Sponsor, The Hospital Research Foundation
- Other University, Hospital and Corporate Sponsors who have sponsored prizes and the catering
- Our Plenary Speaker, Professor Anne Kelso AO
- <u>Chairs of the sessions</u>
  Joanne Young
  Andrea Yool
  Eric Gowans
  Guy Maddern
  Dan Wijesundara
  John Beltrame
  Tim Price

- Abstract judges and judges for Oral and Poster presentations

Robert Adams	John Licari
Kristin Carson	Lorraine Mackenzie
Yuliy Chirkov	Doan Ngo
Clare Cooksley	Bill Panagopoulos
Pallave Dasari	Mahnaz Ramezanpour
Joe Dawson	Isuru Ranasinghe
Paul Drew	Betty Sallustio
Andreas Evdokiou	Brian Smith
Rob Fitridge	Eric Smith
James Gray	Aaron Sverdlov
Branka Grubor-Bauk	Rosanna Tavella
Jenny Hardingham	Amanda Townsend
Ehud Hauben	Sarah Vreugde
Catherine Hill	Jim Wang
Amy Holmes	Sam Whittle
Wendy Ingman	Joanne Young
Chandra Kirana	Solomon Yu
Sue Lester	Peter Zalewski

- Members of the Research Day Organising Committee for the work they have put in throughout the year in planning Research Day

Rebecca Anderson	Jenny Hardingham
Sarah Appleton	Shelley Hay
Yuliy Chirkov	Sue Lester
Abbey Flanagan	Fiona Smithson
Gwenda Graves	Dan Wijesundara

- Kathryn Hudson for her great efforts in obtaining sponsorship

We hope that you enjoy Research Day 2016! If you have any comments on this year's programme, or any ideas for the future, please do not hesitate to speak to one of the members of the Organising Committee. The next Committee would be happy to take any feedback into account when planning for next year's event, which will commence in the near future.

Prue Cowled
Chair, Organising Committee
Research Day 2016
Principal Medical Scientist
Discipline of Surgery, TQEH

2016 TQEH Research Day Plenary Lecture

Professor Anne Kelso AO

CEO NHMRC

"Medical research: why we mustn't stop now"

Following her PhD at the University of Melbourne, Professor Kelso undertook research in the field of immunology, first in Switzerland and then at the Walter and Eliza Hall Institute of Medical Research in Melbourne and the Queensland Institute of Medical Research in Brisbane. From 2000 until 2006, she was also Director/CEO of the Cooperative Research Centre for Vaccine Technology. She then returned to Melbourne as Director of the WHO Collaborating Centre for Reference and Research on Influenza from 2007 until she took up her role with NHMRC in April 2015.

Professor Kelso has served on many boards and advisory committees for research institutions, the Australian Government and WHO, and is currently a member of the Government's Australian Medical Research Advisory Board (advising the Minister for Health on the strategy and priorities for the Medical Research Future Fund), the National Research Infrastructure Roadmap Expert Working Group and the Engagement and Impact Steering Committee. She was appointed Officer in the Order of Australia in June 2007 for service to science.

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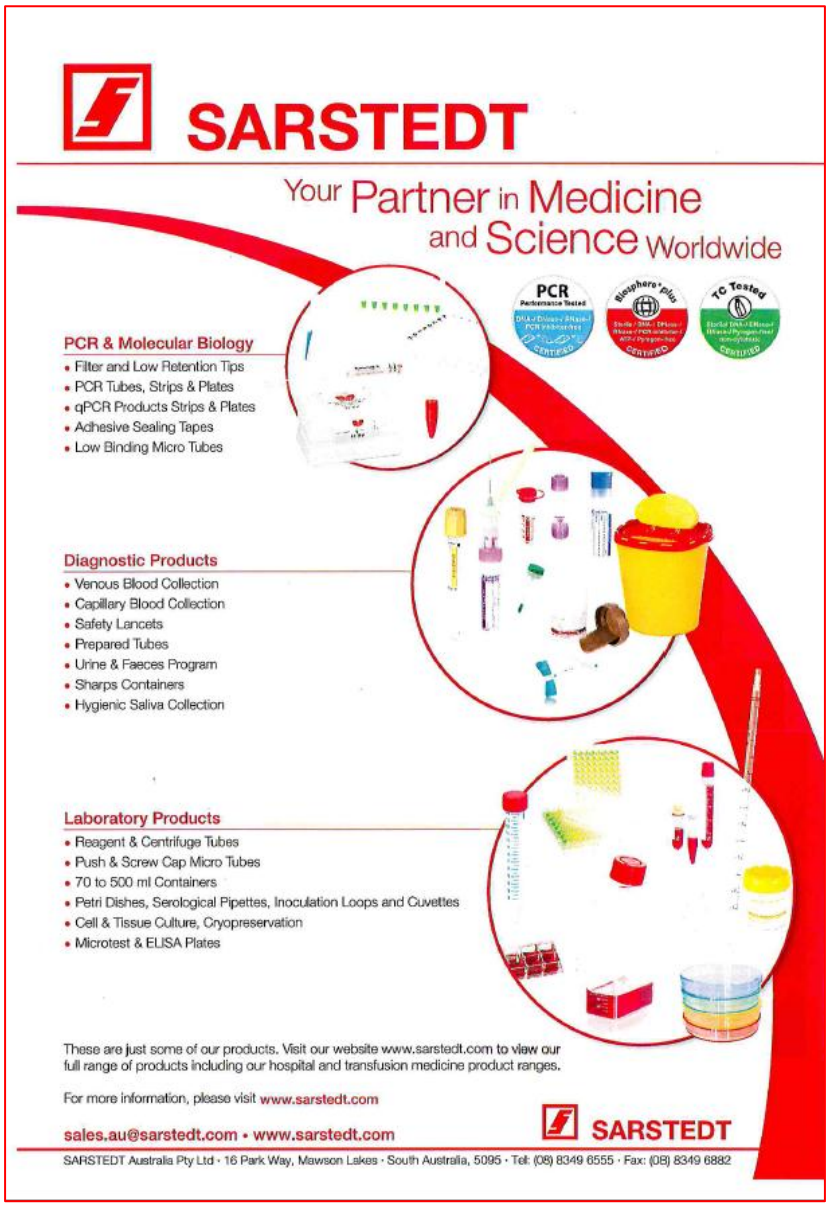
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Mini-Oral Session for the Poster Competition

Tuesday 18 October: 9.30 – 11.00am

Chair: Dr Prue Cowled

Abstract 1

9.30: Maddison Archer, Pallave Dasari, Andreas Evdokiou, Wendy Ingman

Immune Regulation of Fibroblast Activity and Mammographic Density in Women

Abstract 4

9.35: Sarah Bernhardt, Wendy Ingman, Timothy J Price, Amanda R Townsend

Co-treatment with estrogen and progesterone change gene expression in breast cancer cells

Abstract 8

9.40: Zenab Dudhwala, Gordon Howarth, Paul Drew, David Moore, Adrian Cummins

Crypt fission and expression of β-catenin in the small intestine of humans

Abstract 13

9.45: Harshani Jayasinghe, Carson KV, Peters M, Clifton, V, Smith BJ

Interventions for tobacco use prevention in Indigenous youth: A Cochrane systematic review and meta-analysis

Abstract 17

9.50: Victor Lamin, Amenah Jaghoori, Rachel Jacobczak, Irene Stafford, Tamila Heresztyn, Michael Worthington, James Edwards, Fabiano Viana, Robert Stuklis, David P Wilson and John F Beltrame

Mechanisms Responsible for Serotonin Vascular Reactivity Sex-differences in the Internal Mammary Artery

Abstract 19

9.55: Vasilios Liapis, Aneta Zysk, Mark DeNichilo, Irene Zinonos, Shelley Hay, Vasilios Panagopoulos, Alexandra Shoubridge, Christopher Defelice, Vladimir Ponomarev, Wendy Ingman, Gerald J Atkins, David M Findlay, Andrew CW Zannettino and Andreas Evdokiou

Anticancer efficacy of the hypoxia activated prodrug evofosfamide is enhanced in combination with the proapoptotic receptor agonist drozitumab against osteosarcoma

Morning Tea 10.00 - 10.30am

Mini-Oral Session for the Poster Competition *(continued)*

Abstract 20
10.30: Ana Macedo, Amy Holmes, Michael Roberts
Getting under the skin – is receptor solution important?

Abstract 21
10.35: Makutiro Masavuli, Danushka Wijesundara, Branka Grubor-Bauk, Eric Gowans
A novel DNA-based virus-like particle vaccine against hepatitis C virus

Abstract 11
10.40: Hasan Imam, Yuliy Chirkov, John Horowitz
Cardio-protective agent Perhexiline ameliorates impaired adenylate cyclase signalling in patients with cardio-vascular diseases

Abstract 24
10.45: Mian Ooi, Drilling A, Richter K, Vreugde S, Psaltis A, Wormald PJ
Novel topical anti- Staphylococcus aureus biofilm agent Deferiprone and Gallium Protoporphyrin: Safety and Efficacy in an in vivo sheep sinusitis model

Abstract 31
10.50: Alex Shoubridge, M.O. DeNichilo, P.J. Anderson, I. Zinonos, J. Field, S. Hay, V. Panagopoulos, A. Evdokiou
Peroxidases and their role in promoting bone repair and regeneration

Abstract 32
10:55: SY Surikow, TH Nguyen, B Raman, M Chapman, G Licari, K Singh, I Stafford, JD Horowitz
Role of Peroxynitrite-Stimulated PARP-1 Activation in the Pathogenesis of Takotsubo Cardiomyopathy

TQEH Research Day 2010

Professor Basil Hetzel donated his painting by Avril Thomas
to the Basil Hetzel Institute

Left to right: Professor John Beltrame, Professor Basil Hetzel, Avril Thomas and Professor Richard Ruffin

Friday 21 October

8.15 - 9.15am: Honours and Summer Vacation Students
Chair: A/Prof Joanne Young

Abstract 2
8.15: B.Assadi-Khansari, Liu S, Ajero C, Chua SJ, Horowitz JD, Sverdlov AL, Ngo DT
Follistatin-like 3 is elevated in acute heart failure patients

Abstract 5
8.30: Dongqing Chen, Nathan Procter, Vincent Goh, Saifei Liu, SuJen Chua, Bahador Assadi-Khansari, John D. Horowitz, Aaron L. Sverdlov, Doan T.M. Ngo
New onset atrial fibrillation is associated with elevated galectin-3 and follistatin-like 3 level

Abstract 6
8.45: Su Jen Chua, Chukwudiebube Ajaero, Bahador Assadi-Khansari, Andrew Mcgavigan, John Horowitz, Aaron Sverdlov, Doan Ngo
Galectin-3 is markedly elevated in severe heart failure and predicts improvement in left ventricular volumes post-cardiac resynchronisation therapy

Abstract 14
9.00: Arvind Jothin, Amanda Drilling, Mianli Ooi, Alkis Psaltis, Sarah Vreugde, Peter-John Wormald
Comparative, randomised controlled trial assessing the safety and efficacy of manuka honey augmented with methylglyoxal targeting bacterial infections and biofilms in patients with Chronic Rhinosinusitis in a clinical setting

9.15 - 10.15am: Junior PhD Students (Laboratory)
Chair: Professor Andrea Yool

Abstract 3
9.15: Vahid Atashgaran, Simon Barry, Pallave Dasari, Wendy Ingman
Progesterone regulation of transcription factor Elf5 in human mammary epithelial cell lines and its effects on downstream cytokine expression

Abstract 10
9.30: S Fong, A Drilling, S Vreugde, A Psaltis, P-J Wormald
Bacteriophage therapy for treating Pseudomonas aeruginosa infections in chronic rhinosinusitis

Abstract 18
9.45: Aden H Lau, Susan Lester, Judy Ou, Sophia Moraitis, Shaun McColl, Maureen Rischmueller, Peter-John Wormald, Sarah Vreugde
Tertiary Lymphoid Organs in Recalcitrant Chronic Rhinosinusitis

Abstract 7
10.00: Christopher DiFelice, Irene Zinonos, Vasilios Panagopoulos, Mark DeNichilo, Andreas Evdokiou
The Inflammation-Fibrosis Link? A Jekyll and Hyde Role for Peroxidase Enzymes

10.15 - 10.45am: Morning Tea, Trade and Poster displays

10.45 - 11.45am: Senior PhD students (Laboratory)
Chair: Professor Eric Gowans

Abstract 22
10.45: D Miljkovic, C Kirana, J Ou, S Moraitis, A Psaltis, PJ Wormald S Vreugde,
Discordant frequencies of tissue-resident and circulating CD180-negative B cells in chronic rhinosinusitis

Abstract 25
11.00: Judy Ou, Amanda Drilling, Clare Cooksley, Stephen Kidd, Alkis J Psaltis, Peter-John Wormald, Sarah Vreugde
Innate Immune Response of NuLi-1 Cells to Staphylococcus aureus Small Colony Variant Infections

Abstract 26
11.15: Helen M Palethorpe, Eric Smith, Paul Drew
The effect of fibroblasts on androgen signalling in oesophageal adenocarcinoma cell lines *in vitro*

Abstract 29
11.30: Katharina Richter, Nicky Thomas, Peter-John Wormald, Sarah Vreugde
Silver nanoparticles to tackle clinically relevant biofilms

12.00 - 1.00pm: Plenary Lecture

Professor Anne Kelso AO
CEO, NHMRC
"Medical research: why we mustn't stop now"

Chair: Professor Guy Maddern, Director of Research TQEH

1.00 - 2.00pm: Lunch and Trade Displays

1.20 - 2pm: Poster Competition Finals
Chair: Dr Dan Wijesundara

2.00 - 3.00pm: Clinical Research Group 1 (Clinical Trainees)
Chair: Professor John Beltrame

Abstract 27
2.00: D.V. Patel, D.L. Chan, L. Moody, E. Segelov, S. Singh
Optimal follow-up strategy for resected neuroendocrine tumours: A systematic review

Abstract 28
2.15: T Perera, V Broadbridge, W Patterson, T Price, A Townsend, K Pittman, M Moldovan, R Roberts-Thomson
Efficacy, safety and cost of ipilimumab for patients with metastatic melanoma in a real-world setting

Abstract 33
2.30: Ben Thurston, Guilherme Pena, Prue Cowled, Rob Fitridge
Measurement of psoas muscle cross-sectional area at the level of the L3 vertebra is reproducible between observers and is associated with poor outcomes following EVAR

Abstract 34
2.45: Tsung Woo, Solomon Yu, Renuka Visvanathan, Robert Adams
The Association Between Sarcopenia and Quality of Life is Different in Community Dwelling Older Australian Men and Women

3.00 - 4.00pm: Clinical Research Group 2 (Clinical Higher Degrees)
Chair: Professor Tim Price

Abstract 9
3.00: Scott Ellis, Martin Varley, Stuart Howell, Markus Trochsler, Guy Maddern, Peter Hewett, Tina Runge, Soeren Torge Mees
Skill Retention in Single-Incision Laparoscopic Surgery versus Traditional Laparoscopic Surgery

Abstract 15
3.15: Zoe Kopsaftis, Richard Wood-Baker, Christopher Cates, Phillippa Poole
Influenza vaccine for patients with chronic obstructive pulmonary disease: Cochrane review and meta analysis

Abstract 12
3.30: Agathe Daria Jadczak , Joanne Dollard , Neha Mahajan, Renuka Visvanathan
Older peoples' perspectives on being advised about exercise - What role do general practitioners play? A qualitative study

Abstract 16
3.45: Clementine Labrosciano, John Beltrame, Rosanna Tavella, Isuru Ranasinghe.
Readmissions following Cardiovascular Hospitalisations: A Systematic Review of the Contemporary Australian Literature

4.00pm: Drinks, nibbles and prize presentations

ABSTRACT 1

IMMUNE REGULATION OF FIBROBLAST ACTIVITY AND MAMMOGRAPHIC DENSITY IN WOMEN

Maddison Archer, Pallave Dasari, Andreas Evdokiou, Wendy Ingman
Breast Biology and Cancer Unit, Department of Surgery, University of Adelaide

Mammographic density is a strong risk factor for breast cancer - women with dense breasts can have a 4-6 times increased risk. Mammographic density is the proportion of the breast occupied by white areas on a mammogram. The biological mechanisms that underpin mammographic density and cancer risk is poorly understood. High density tissue is characterised by an increased abundance of collagen, epithelium and stroma, and less fat. There is some evidence that inflammatory mediators may be driving increased breast density. The objective of this study are to investigate the effect of immunoregulatory proteins on fibroblast activity by primary mammary fibroblasts from healthy breast tissue.
Fibroblasts from 3 high and 4 low density patient breast tissue samples were treated with transforming growth factor beta (TGFB), eosinophil peroxidase (EPO), chemokine ligand 2 (CCL2) and tumour necrosis factor alpha (TNFA) for 72hrs. Soluble collagen I deposition was measured by ELISA, and mRNA expression of genes involved in extracellular matrix and collagen metabolism were analysed using RT-PCR. Significance was inferred at $p<0.05$ using paired sample t-test.
Treatment of fibroblasts (n=7) with eosinophil peroxidase significantly increased soluble collagen I deposition, while TGFB, CCL2 and TNFA all reduced soluble collagen I compared to untreated controls. There was high variability in gene expression between treatment groups. There appeared to be no inherent differences in activity between fibroblasts isolated from high and low density tissue, though this may be due to low sample size.
TGFB, CCL2 and TNFA may not contribute to high mammographic density by soluble collagen I deposition. Future experiments will increase sample size, and investigate how these cytokines effect collagen crosslinking and production of insoluble collagen by mammary fibroblasts. This will provide insight into the underlying mechanisms of mammographic density and the associated cancer risk.

LAY DESCRIPTION

Mammographic density is the areas of a woman's breast that appear white on mammograms. Women with very white breasts have an increased breast cancer risk. Currently, it is unknown what causes this increased risk. This study is investigating how the immune system may be causing mammographic density. This is done using cells of the breast called fibroblasts. These cells produce collagen, which is abundant in high density breasts. These cells were treated with immune system proteins and how the cells activity changes was examined. This will help us understand what causes some breasts to have increased density and cancer risk.

ABSTRACT 2

FOLLISTATIN-LIKE 3 IS ELEVATED IN ACUTE HEART FAILURE PATIENTS

B.Assadi-Khansari, Liu S, Ajero C, Chua SJ, Horowitz JD, Sverdlov AL, Ngo DT
BHI-Cardiometabolic group, TQEH-Cardiology unit

Background: Follistatin-like 3 is an extracellular regulator of the TGF-β superfamily member activin A. FSTL-3 transcripts have been found to be unregulated in myocardium from patients with severe heart failure (HF), and are associated with severity of the disease. Furthermore, FSTL-3 has been identified as a possible modulator of stress-induced cardiac hypertrophy following pressure overload in mice.
Aims and Hypothesis: In this study, we sought to examine whether:
1) FSTL-3 is elevated in patients with HF vs. age-matched controls, and
2) FSTL-3 is elev elevated in patients with acute decompensated HF vs. those with chronic HF
3) FSTL-3 levels change 5 weeks after an acute HF episode.
Methods and Results: We measured plasma levels of FSLT-3 in: 1) healthy ageing volunteers (n=67, age 68±6 yrs), 2) patients with acute HF (n=45, 71±13), and 3) patients with chronic HF (n=28, 71±10). Plasma FSTL-3 levels were significantly higher patients with acute HF (mean 16,220 ± 8645 pg/mL) vs, chronic HF (10,205 ± 5636 pg/mL, $p<0.01$) patients vs. healthy ageing volunteers (5601 ± 955.4 pg/ml, $p<0.001$).
N=27 patients who were admitted to hospital due to acute decompensated HF, blood samples were taken to assess for FSTL3 levels at baseline and 5 weeks after treatment. While there was no difference in NT-proBNP levels in patients with acute HF upon admission (median, 3997 pg/mL vs. 5 weeks of follow-up, 2678 pg/mL) ($p=0.4$); FSTL-3 levels were significantly reduced (mean ±SD, 14,117 ± 7374 pg/mL vs. 12,744 ± 5573 pg/mL, $p<0.05$).
Conclusion: We observed that plasma levels of FSTL-3 are increased in HF patients, more so in acute vs chronic HF, independent of NT-proBNP differences. These results suggest that FSTL-3 is a potential sensitive biomarker to detect changes in HF, prior to changes in NT-proBNP.

LAY DESCRIPTION

Heart failure (HF) is when the heart can't meet the body's oxygen needs. Follistatin-like 3 (FSTL3) is a protein that is secreted by heart cells, more so in HF but secreted FSTL3 levels have yet to be studied. In mice it was shown to regulate heart changes during stress.
We looked at FSTL3 levels in people with acute and chronic HF and found they had higher levels than healthy people, and people with acute HF had higher levels than chronic HF. We also found that FSTL3 levels dropped 5 weeks after treatment of acute HF.
Our data supports the link between FSTL3 and HF and suggests that FSTL3 could be used in monitoring HF and its recovery.

ABSTRACT 3

PROGESTERONE REGULATION OF TRANSCRIPTION FACTOR Elf5 IN HUMAN MAMMARY EPITHELIAL CELL LINES AND ITS EFFECTS ON DOWNSTREAM CYTOKINE EXPRESSION

Vahid Atashgaran, Associate Professor Simon Barry*, Dr Pallave Dasari, Associate Professor Wendy Ingman
Breast Biology and Cancer Unit, Department of Surgery *Paediatrics, Women's & Children's Hospital

Progesterone (P4) is a key hormone that controls mammary epithelial cell proliferation, regulates immune system cells in the mammary gland, and promotes mammary carcinogenesis. The molecular regulation of P4-driven immune cell control is not well understood but is likely to involve transcription factors and cytokines as mediators. Transcription factor E74-like factor 5 (ELF5) is expressed by mammary epithelial cells, and is suggested to play a role in mammary epithelial cell-immune cell crosstalk. Our objective is to investigate the transcriptional regulation of P4 action on immune signalling cytokines using a human breast cancer cell line.

To investigate the role of P4 in regulation of cytokine expression in vitro, human mammary epithelial cell line T47D was treated with ethanol control or P4 (100nM) for 72 hours in triplicate. Messenger RNA encoding transforming growth factor 1 (TGFB1), CXC motif chemokine 12 (CXCL12), S100A8, S100A9, and ELF5 were analysed by real-time PCR. To further investigate the role of ELF5 in mediating cytokine expression, T47D cells were transiently silenced by siRNA oligos prior to hormone treatments and the mRNA expression of cytokines was assessed. The cultures were repeated 5 times and analysed by Mann Whitney U test with significance inferred at $p<0.05$.

There was an increase in ELF5 mRNA expression, and this was associated with significant elevated expression of pro-inflammatory cytokines S100A8 and S100A9 and suppression of TGFB1, and CXCL12. With the knockdown of ELF5, mRNA expression of TGFB1 and S100A8 was induced by 60%, compared to the cells transfected with non-targeting siRNA.

These findings suggest that P4-regulated cytokine secretion by mammary epithelial cells may be mediated by ELF5. P4-regulated epithelial cell cytokine secretion may produce an immune microenvironment in the breast which promotes tumorigenesis in this tissue. Studies using other cell lines as well as animal models will further explore these findings.

LAY DESCRIPTION

Breast cancer is the most common cancer in women. Progesterone is a hormone that travels around the body during specific stages of the menstrual cycle, affecting the structure of the breast and promoting breast cancer. We show that progesterone affects the abundance of certain proteins which are related to the immune system in the breast. As a result, the ability of immune cells to protect from cancer may be weakened, thus increasing breast cancer risk. Finding out how progesterone affects breast cancer risk can help us identify new methods to treat and prevent breast cancer.

ABSTRACT 4

CO-TREATMENT WITH ESTROGEN AND PROGESTERONE CHANGE GENE EXPRESSION IN BREAST CANCER CELLS

Sarah Bernhardt*+, Wendy Ingman*+, Timothy J Price#+, Amanda R Townsend#
*School of Medicine, Discipline of Surgery, Breast Biology and Cancer Unit, The Queen Elizabeth Hospital + University of Adelaide, Adelaide SA #Department Medical Oncology, The Queen Elizabeth Hospital

Introduction: Diagnostic tests which use gene expression profiling to diagnose breast cancer are being adopted in the clinic. However, despite their availability to premenopausal women, these tests were developed and validated predominantly in postmenopausal women. Thus, the accuracy of these tests was never validated in the context of hormonal fluctuations in estrogen and progesterone that occur during the menstrual cycle. In general, there is a lack of research on how hormonal fluctuations associated with the menstrual cycle can affect the expression of genes involved in diagnostic tests. The aim of this project is to identify how estrogen (E2) and progesterone (P4) co-treatment affects the expression of genes involved in breast cancer diagnosis. We hypothesise that co-treatment of breast cancer cells with E2 and P4, in comparison to E2 treatment alone, will result in significant changes in gene expression.
Method: Breast cancer cell lines ZR-75-1 and T47D were pre-treated with 10nM E2 for 72hrs, prior to treatment with either 10nM P4 or vehicle control (VC) for 16hrs. In parallel, cells were treated with VC only as a control. Expression of key genes involved in currently used diagnostic tests were quantified through RT-PCR. Gene expression in cells co-treated with E2 and P4 was compared to cells treated with E2 alone.
Results: In T47D cells, E2 and P4 co-treatment resulted in decreased ER and PR gene expression, and an increase in EGFR expression, in comparison to E2 treatment alone. Consistent with the loss of ER expression, there was a decrease in expression of genes associated with ER function (Bcl-2 and FoxA1). In addition, co-treatment of cells resulted in an increased expression Cyclin D. Consistent with these results, co-treatment of ZR-75-1 cells with E2 and P4 resulted in decreased ER and PR, and increased EGFR, gene expression.
Conclusion: Co-treatment of breast cancer cells with E2 and P4 alters the expression of genes involved in breast cancer diagnosis

LAY DESCRIPTION

Tests which use gene expression profiling to diagnose breast cancer were developed in older women who do not menstruate. In young women, hormones estrogen and progesterone fluctuate dramatically during the menstrual cycle. Currently, it is unknown how menstrual cycling affects gene expression, and the impact this has on breast cancer diagnosis. This project used breast cancer cells to identify how hormones associated with the menstrual cycle can affect gene expression. We found that gene expression changed with exposure to menstrual hormones, which suggests that menstrual cycling may impact breast cancer diagnosis in young women.

ABSTRACT 5

NEW ONSET ATRIAL FIBRILLATION IS ASSOCIATED WITH ELEVATED GALECTIN-3 AND FOLLISTATIN-LIKE 3 LEVELS

Dongqing Chen, Nathan Procter, Vincent Goh, Saifei Liu, SuJen Chua, Bahador Assadi-Khansari, John D. Horowitz, Aaron L. Sverdlov, Doan T.M. Ngo
Cardiology Unit, The Queen Elizabeth Hospital

Background: Atrial fibrillation (AF) is a common cardiac arrhythmia, associated with increased risk of stroke and cardiac mortality. Atrial remodeling and atrial fibrosis have been suggested to participate in the pathogenesis of AF. Follistatin-like 3 (FSTL3) and Galectin-3 (Gal-3) are secreted proteins that has regulatory roles in fibrosis, inflammation and tissue repair. Both have been reported to be associated with cardiac remodeling in heart failure. Furthermore, Gal-3 levels have been shown to predict atrial remodeling and incidence of AF. Thus, in this study, we sought to examine whether differential FSTL3 and Gal-3 levels predict chronicity of AF.
Methods and Results: 134 patients hospitalized with AF were evaluated (mean age 69±12 yrs). Of those, 34 patients (26%) were diagnosed with new onset AF. Plasma Gal-3 and FSTL3 levels were measured by commercially available ELISA assay. On univariate analyses, patients with new onset AF had i) NT-proBNP significantly higher Gal-3 levels vs those with chronic AF (mean 9.4ng/mL±3.3 vs. 8.0±3.5, $p<0.05$) and ii) tended to have higher FSTL3 levels ($p<0.1$). High Gal-3 levels were also significantly correlated with NT-proBNP levels ($R=0.3$, $p<0.01$), CRP levels ($R=0.3$, $p<0.01$), and CHA2DS2VASc scores ($R=0.2$, $p<0.05$). On multivariate analysis, adjusting for age, gender, and creatinine, both high Gal-3 and FSTL3 levels remain independent correlates of presence of new onset AF ($p<0.05$ and $p=0.006$, respectively). Additionally, the combination of highest quartile of FSTL3 and Gal-3 was further predictive of new onset AF ($p<0.05$) on multivariate analysis.
Conclusions: Recent onset of AF is associated with elevated Gal-3 and FSTL3 levels. This suggests that these could be used as new blood biomarkers of recent onset AF with the potential to predict atrial fibrosis and remodeling. The combination of Gal-3 and FSTL3 may further enhance their diagnostic utility and form part of the multimarker strategy for assessment of AF.

LAY DESCRIPTION

People with Atrial fibrillation (AF) have irregular heart beats, and they have significantly increased risk of stroke and death. Cardiac enlargement is thought to be the major cause of AF as well as thickening and scarring of the heart, as seen in newly diagnosed AF.
There are 2 proteins galectin-3 (Gal-3) and follistatin-like 3 (FSTL3) that regulate thickening, scarring and tissue repair. In this study, we found that new onset AF is significantly associated with elevated Gal-3 and FSTL3, which predict the onset of new AF independently. Together, these biomarkers could be used as part of the multimaker strategy for the assessment of AF.

ABSTRACT 6

GALECTIN-3 IS MARKEDLY ELEVATED IN SEVERE HEART FAILURE AND PREDICTS IMPROVEMENT IN LEFT VENTRICULAR VOLUMES POST-CARDIAC RESYNCHRONISATION THERAPY

Su Jen Chua*#, Chukwudiebube Ajaero*#, Bahador Assadi-Khansari*#, Andrew Mcgavigan*^, John Horowitz*#, Aaron Sverdlov*#, Doan Ngo*#

* Basil Hetzel Institute of Translational Research, The Queen Elizabeth Hospital # Department of Cardiology, University of Adelaide ^ Department of Cardiology, Flinders University

Introduction: Cardiac Resynchronisation Therapy (CRT) is commonly used in the management of patients with heart failure (HF). Although CRT improves symptoms and survival in most patients, about one-third of CRT recipients do not obtain clinical benefit from CRT. It has been suggested that cardiac fibrosis may play a role in determining the response to CRT.

Galectin-3 (Gal-3) is a circulating protein that has regulatory roles in fibrosis, inflammation and tissue repair. Several recent clinical studies have reported an association between Gal-3 levels and cardiac remodeling as well as adverse clinical outcomes in patients with HF. However, the association between baseline Gal-3 levels and response to CRT in severe HF has not been established.

Aims: To investigate the relationship between i) Gal-3 levels and presence of HF compared to an age-matched healthy cohort; ii) Baseline plasma Gal-3 levels and reverse remodeling in patients undergoing CRT implantation.

Methods: Plasma Gal-3 levels were compared in 28 patients (aged 71.2±9.7) with predominantly severe HF (70% NYHA class III or IV) undergoing CRT and 67 age-matched healthy controls. Transthoracic echocardiogram and blood collection for routine biochemistry, NT pro-BNP and Gal-3 levels were performed in the healthy cohort and in the severe HF cohort prior to and 6 months post-CRT implantation. There was a significant increase in Gal-3 levels in patients with HF compared to those with healthy ageing. Baseline Gal-3 levels correlated significantly with post-CRT improvements in left ventricular volumes as measured by echocardiography ($p<0.05$). On multivariate analyses, Gal-3 remained the only independent predictor of these echocardiographic measures of response after adjustment for age, gender, NT pro-BNP and NYHA class ($p<0.05$).

Discussion / Conclusion: Plasma Galectin-3 is a promising biomarker of response to CRT. It has discriminatory potential between patients with severe HF and patients with healthy ageing.

LAY DESCRIPTION

Heart failure (HF), impaired heart pumping, is a common debilitating disease. Patients with severe HF receive a potentially lifesaving but expensive treatment device, cardiac resynchronisation therapy (CRT). Unfortunately, one-third of CRT recipients do not respond. Heart scar tissue formation is a suggested cause. Galectin-3 is a novel protein that is known to mediate this process and may predict response to CRT. In this study, we found that high Galectin-3 levels identified poor responders to CRT among severe HF patients. This suggested that Galectin-3 is an inexpensive tool that may pinpoint those most likely to benefit from CRT.

ABSTRACT 7

THE INFLAMMATION-FIBROSIS LINK? A JEKYLL AND HYDE ROLE FOR PEROXIDASE ENZYMES

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Background: Fibrosis, or scarring, is the exaggerated response to a traumatic event and is typically characterised by the excessive accumulation of extracellular matrix components, predominantly type–I collagen. Current treatments for fibrotic disorders, such as idiopathic pulmonary fibrosis and atrial fibrillation, target the inflammatory cascade, but they have been widely unsuccessful, largely because the identification of key molecules and processes remain unclear. Peroxidases, proteins released by immune cells, are often found within fibrotic tissue within various organs. However, the molecular mechanisms by which they mediate the microenvironmental milieu within these fibrosing tissues are largely unknown. Methods: MRC5 human fetal lung fibroblasts were grown to confluency and then exposed to different concentrations of peroxidases for 72 hours. The production of soluble type-I collagen by fibroblasts was examined using enzyme–linked immunosorbent assays and Western blotting assays. Fibroblast migration was evaluated using transwell–migration assays. Results: Peroxidases (6.25–0.049 µg/mL) dose-dependently increased the production of soluble type–1 collagen in lung fibroblasts. Mechanistically, peroxidases were able to induce type–1 collagen release without regulating collagen α1 mRNA levels. Pre–treatment with 4–ABAH (250 µmol/L, $P<0.05$), a potent catalytic domain inhibitor of peroxidases, markedly reduced peroxidase–induced collagen production in lung fibroblasts. Furthermore, peroxidases (5 µg/mL, $P<0.05$) significantly increased lung fibroblast migration compared to control cells. Conclusion: In summary, our findings provide evidence to suggest that peroxidases may play a fundamental role in promoting fibrosis by regulating fibroblast recruitment and collagen extracellular matrix biosynthesis. Our data also highlight that therapeutic inhibition of peroxidase activity may provide a novel effective treatment option for patients with fibrotic disease.

LAY DESCRIPTION

While the underlying cause of fibrosis (scarring) is typically inflammation, the identification of key molecules and processes have remained unclear. New findings implicate peroxidases, molecules released by inflammatory cells, in inducing cells called fibroblasts to produce high levels of collagen. However, no one has yet investigated the effects of peroxidase-mediated collagen production to the development of fibrosis. The aim of this study is to investigate the contribution peroxidases have to the development of fibrosis and whether blockage of peroxidase activity represents a viable therapeutic approach for patients with fibrotic disease.

ABSTRACT 8

CRYPT FISSION AND EXPRESSION OF β-CATENIN IN THE SMALL INTESTINE OF HUMANS

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Introduction: The small intestine is immature in pre-term infants. Intestinal pit like structures, crypts, divide longitudinally from the base during growth and development of the intestine, a process called 'crypt fission'. This study compared the expression of β-catenin in healthy human duodenal tissues in infants, children and adults as previous study indicates higher expression of β-catenin promotes division of stem cells in mice during infancy compared to adulthood.
Objective: To compare the expression of β-catenin in the human duodenum at different ages, and its correlation with crypt fission.
Methods: Duodenal archival tissues were stained for β-catenin expression using an indirect immunoperoxidase polymer technique. The samples were divided into infant (<2 y, n=7), children (2 to 18 y, n=7), or adult tissue (n=7), and analysed using image with cumulative signal analysis using a Matlab program to assess intensity of staining.
Results: β-catenin was expressed in all infants, children and adults, especially at the base of crypts where the stem cells reside. There was higher intensity of staining at the base of the crypts in all tissue samples compared to the rest of the crypt region. Mean crypt fission was 4.5%, 0.8%, and 2% in infants, children and adults, respectively.
Conclusion: β-catenin was expressed in all tissue samples. Further study needs to be undertaken to run statistical analysis and to ascertain any difference in the groups for both β-catenin expression and crypt fission.

LAY DESCRIPTION

The small intestine stays immature in pre-term infants resulting in conditions such as necrotizing enterocolitis, volvulus and intestinal atresia. The treatment is surgery and removal of the intestine leading to Short Bowel Syndrome (SBS). Intestinal glands, known as crypts, divide during growth of the intestine, a process called crypt fission (peaks at 11-14 days in rats). This study seeks to understand how intestinal stem cells promote crypt fission by the Wnt β-Catenin signaling pathway. The significance and expected outcomes of the study is that it could be used to treat to SBS in humans.

ABSTRACT 9

SKILL RETENTION IN SINGLE-INCISION LAPAROSCOPIC SURGERY VERSUS TRADITIONAL LAPAROSCOPIC SURGERY

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Background: Training in laparoscopic surgery is important not only to acquire and improve skills but also avoid the loss of acquired abilities. Previously published data suggests a longer learning curve for single-incision laparoscopic surgery (SILS) than for traditional laparoscopic surgery (LS). Any difference in the retention of skills, however, has not been investigated. The aim of this single-centre, prospective randomized study was to assess skill acquisition of different laparoscopic techniques and identify the point in time when acquired skills deteriorate to baseline.
Methods: Sixty surgical novices underwent LS and SILS baseline training (BT), performing two validated simulation tasks (peg transfer and precision cutting). Participants were randomised into three groups for skills retention testing (RT) at 8, 10 or 12 weeks. Performance was measured in seconds to task completion with time penalties incurred for inaccuracies. Participant baseline demographics were collected via questionnaire.
Results: 92 % of the participants completed BT, achieving the tasks within the required time frame for proficiency. Univariate and multivariate analyses revealed that SILS ($P < 0.0001$) and precision cutting ($P < 0.0001$) were significantly more difficult. Males performed significantly better than females ($P < 0.005$). For LS, a deterioration of skills (comparison of BT vs RT) was not identified; however, for SILS a significant deterioration of skills (comparison of BT and RT values) was demonstrated for all groups ($P < 0.05$).
Discussion & Conclusion: Our data confirm that complex laparoscopic tasks (cutting) and techniques (SILS) are more difficult to learn and acquired skills more difficult to maintain. Acquired LS skills were maintained for the whole observation period of 12 weeks but SILS skills had deteriorated at 8 weeks. These data show that acquisition and maintenance of LS and SILS skills is divergent and training curricula need to take these specifics into account.

LAY DESCRIPTION

Training in keyhole surgery is important to develop and maintain skills. Single incision laparoscopic surgery (SILS) uses only one keyhole, compared to three or more in traditional laparoscopic surgery (LS). It takes longer to develop SILS skills than LS skills. Retention of SILS skills had not been studied.
Skill retention in 60 training doctors was tested in a virtual operation. The results confirm that SILS skills are more difficult to learn and are not kept at 8 weeks. LS skills are kept for at least 12 weeks. This indicates that SILS training sessions need to occur more frequently than LS training sessions for optimal skill maintenance.

ABSTRACT 10

BACTERIOPHAGE THERAPY FOR TREATING PSEUDOMONAS AERUGINOSA INFECTIONS IN CHRONIC RHINOSINUSITIS

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Background: Pseudomonas aeruginosa (PA) infections are prevalent amongst chronic rhinosinusitis (CRS) sufferers, particularly in recalcitrant disease and cystic fibrosis (CF) patients. Many PA strains form biofilms that are resistant to antibiotics. Lytic bacteriophages (phages) are viruses that infect and replicate within bacteria, eventually causing bacterial death by lysis. This study aims to assess the efficacy of a phage cocktail in eradicating PA biofilms in vitro.
Methods: 35 PA isolates from CRS patients (19 CF and 16 non-CF patients) were typed using multi-locus sequence typing (MLST). Resistance to commonly used antibiotics was assessed using standard Minimal Inhibitory Concentration (MIC) assays. 48-hour biofilms were, treated with four different PA phages, as well as a cocktail of all four phages (CTPA) followed by assessment of the biofilm biomass using a crystal violet assay. Pre- and post-treatment phage titrations were performed to confirm replication of the phages. Differences between the treatment and control wells were assessed using the Friedman's test followed by post-hoc Wilcoxon signed-rank tests with Bonferroni correction.
Results: MLST showed all PA strains to be distinct. CTPA treatment significantly reduced biofilm biomass in 62% and 74% of strains compared to control wells at 24 and 48 hours post-treatment, regardless of antibiotic resistance ($p<0.05$). The decrease in biofilm biomass was accompanied by a rise in post-treatment phage titres for all except one strain.
Conclusion: A single dose of phages is able to significantly reduce biofilms formed in vitro by a range of PA isolates from CRS patients, both with and without CF. This represents an exciting potential targeted treatment option for PA biofilm infections and resistant bacteria.

LAY DESCRIPTION

Infections due to bacteria are a common problem in chronic sinusitis. Many of these infections are caused by a species of bacteria called Pseudomonas aeruginosa (PA). This study looks into whether bacteriophages, viruses that infect and kill bacteria, can be used to treat PA infections. Different strains (types) of PA were sampled from 35 people who suffer from chronic sinusitis. These bacteria were grown and treated in the laboratory with 4 different bacteriophages. The bacteriophages were able to lower the amount bacterial growth in the majority of strains, meaning that in the future they could be used to treat PA infections in patients.

ABSTRACT 11

CARDIO-PROTECTIVE AGENT PERHEXILINE AMELIORATES IMPAIRED ADENYLATE CYCLASE SIGNALLING IN PATIENTS WITH CARDIO-VASCULAR DISEASES.

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Cardiovascular homeostasis depends on normal physiology of circulating blood platelets. However, impairment in platelet response to anti-aggregatory autacoids such as nitric oxide (a cGMP stimulant) and prostacyclin (PGI2, a cAMP stimulant via IP receptor) occurs in cardiovascular diseases, including stable angina pectoris (SAP) and diabetes mellitus (DM). We have shown previously that NO resistance can be ameliorated by a prophylactic anti-ischemic agent perhexiline (Pex).The current study sought to evaluate: (1) the impact of SAP, DM or both on cAMP signaling, and (2) the effect of short-term Pex therapy on this.
Methods: We evaluated 14 normal subjects, 14 SAP patients undergoing cardiac catheterization, and 14 DM patients with SAP of whom 6 were to start Pex. We used prostaglandin E1 (PGE1) as a surrogate for PGI2, and Forskolin (Fsk), a direct activator of adenylate cyclise (AC), against ADP (2.5µM)-induced platelet aggregation in whole blood.
Results: Inhibition of aggregation by PGE1 (30nM) was diminished by 20% in patients with SAP ($p<0.03$) and DM/SAP ($p<0.05$), in comparison with healthy subjects. However, response to Fsk (5µM), was diminished (by 21%; $p<0.03$) only in patients with DM/SAP, suggesting that in SAP there is a defect in signal transduction from IP receptors to AC, while in DM/SAP there is an impairment in AC enzymatic function. Six DM/ SAP patients were treated with Pex for 2 weeks (200mg/day). Platelet responsiveness to both PGE1 and Fsk improved: there was a left-ward shift in the PGE1 concentration-response curve with a 2.2-fold ($p<0.03$) decrease in PGE1 IC50, and also a 54% increase ($p=0.04$) in Fsk anti-aggregatory effect.
Conclusion: Both SAP and DM/SAP are associated with impairment in platelet PGI2/AC signaling, but at different sites: in SAP, there is a defect in signal transduction from IP receptors to AC, while in SAP/DM there is impairment of AC enzymatic activity. Pex therapy has the potential to improve platelet AC/cAMP signaling

LAY DESCRIPTION

Platelets are special type of blood cells. They initiate blood clots by sticking together, following a highly tuned regulatory process. Platelet regulation is compromised in patients with stable angina and diabetes. To work out what is going wrong with platelet regulation and how it could be restored, we measured platelet aggregation and its suppression by biochemicals known to interfere with certain steps in regulation of platelet activity. We have identified two such spots of damage. When patients were treated with a cardio-protective drug perhexiline, the impaired platelet function was improved.

ABSTRACT 12

OLDER PEOPLES' PERSPECTIVES ON BEING ADVISED ABOUT EXERCISE - WHAT ROLE DO GENERAL PRACTITIONERS PLAY? A QUALITATIVE STUDY

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Background: Exercise has proven to be beneficial for numerous age-related diseases and is considered as the most effective strategy to prevent frailty, a prevalent geriatric syndrome observed in clinical practice. General practitioners (GPs) have the potential to increase older peoples' participation in exercise by providing advice on exercise or prescribing exercise. However, little is known about older peoples' perspectives on the advice they have received relating to exercise. This study aimed to explore older people's opinions in relation to being advised about exercise and their perceptions of the GP's role in promoting exercise for older people.

Methods: Semi-structured interviews were conducted with twelve community-dwelling older (mean 83.42 ± 5.99) participants screened frail or at risk of frailty using the FRAIL Screen. Their attitudes towards exercise, the advice received, their access to relevant information and their perceptions of the general practitioner's (GP's) role in promoting exercise were explored. Thematic analyses was used to analyse data.

Results: The participants had mostly a positive attitude to exercise and indicated a preference for being advised firstly by their GP and then other health care professionals. The majority of participants reported no or limited recollection of exercise advice received from their GPs. Participants also reported difficulties accessing advice and information on exercise, and indicated that community councils and GP practices should promote exercise for older people more actively.

Conclusion: This research has identified a gap in current practice demonstrating the importance of GPs in advising older people about exercise. This should be viewed as an opportunity where change might lead to increased participation in exercise by older people.

LAY DESCRIPTION

Little is known about older peoples' perspectives on being advised about exercise. Interviews were conducted with older participants to explore their attitudes towards exercise, the advice received, their access to relevant information and their perceptions of the general practitioner's (GP's) role in promoting exercise. The participants indicated a preference for being advised firstly by their GP, but the majority received no or only limited advice from their GPs. Participants also reported difficulties accessing advice on exercise and indicated that community councils and GP practices should promote exercise for older people more actively.

ABSTRACT 13

INTERVENTIONS FOR TOBACCO USE PREVENTION IN INDIGENOUS YOUTH: A COCHRANE SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Addiction to nicotine usually begins during early adolescence; Indigenous youth commence smoking at an earlier age and bear a disproportionate amount of substance-related morbidity and mortality as a result. Aim: To evaluate the effectiveness of tobacco prevention interventions for Indigenous youth (< 25 years) and to summarise these approaches for future prevention programs. Methods: The Cochrane Tobacco Addiction Group's register, electronic databases and bibliographies of identified studies were searched up until 2nd of December 2015. Randomised, non-randomised and controlled clinical trials having intervention durations of at least 3 months were included. Interventions could include school-based initiatives, community interventions and family programs. Stanard Cochrane recommnedations and techniques were used for data collection and analysis. The primary outcome sought was influence on smoking behaviour and the secondary outcomes looked at were attitudes, knowledge and self-efficacy. Results: Of 155 citations six studies met the inclusion criteria. They all involved some form of school based intervention and follow-up ranged between six months to five years. For the primary outcome of tobacco prevention, five studies showed no evidence of any effect and one favoured control arm at final follow-up. Smokeless tobacco use was reported in three studies with no evidence of any effect. Attitudes and self-efficacy were also reported in one trial showing no difference between groups whilst a statistically significant benefit was observed for knowledge in one trial.Conclusion: This review identifies a paucity of data for tobacco prevention initiatives tailored to Indigenous youth. The significant result in favour of the control group for the primary outcome of tobacco prevention in one study is disturbing and highlights that assumptions of 'any intervention is a good intervention' cannot be made.

LAY DESCRIPTION

The numbers of people who smoke have not fallen in Indigenous populations as drastically as it has done in the wider communities around them. Approximately twice as many Indigenous youth are smoking daily compared to their non-indigenous counterparts. This is alarming because addiction to nicotine begins during early childhood and the teenage years. Smoking causes many long-term health problems in these communities including high death and disease rates. My review found that programs being rolled out to target young Indigenous smokers were not having enough of an effect and that more tailored research was desperately needed in this area.

ABSTRACT 14

COMPARATIVE, RANDOMISED CONTROLLED TRIAL ASSESSING THE SAFETY AND EFFICACY OF MANUKA HONEY AUGMENTED WITH METHYLGLYOXAL TARGETING BACTERIAL INFECTIONS AND BIOFILMS IN PATIENTS WITH CHRONIC RHINOSINUSITIS IN A CLINICAL SETTING

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OBJECTIVES: Bacterial biofilms are known to play a role in the pathogenesis of recalcitrant chronic rhinosinusitis (R-CRS). Manuka Honey (MH) augmented with methylglyoxal (MGO) has demonstrated antibiofilm activity both in-vitro and in an ovine model of CRS. This study evaluates the safety and efficacy of this treatment in R-CRS patients.
METHODS: 30 patients with diagnosed R-CRS and active infection (indicated by a positive sinonasal swab) were randomised to either receive 14 days treatment of twice daily 16.5% MH + 1.3 mg/mL MGO sinus rinses and 10 days of placebo antibiotics (MH), or 14 days treatment of twice daily saline flushes and 10 days of culture directed antibiotic therapy (CON). Swabs were taken pre- and post-treatment to compare efficacy of both treatments. Patients were also assessed via symptom scores and endoscopic videos (SNOT-22), taken at time = 0, 2 weeks, 3 months & 6 months to evaluate short and long-term clinical outcomes. Comparisons between the MH group and CON will be performed using Fisher's exact test. Symptom scores and endoscopic sinus scores will be analysed with a student's T-test, or Mann-Whitney U test for the nonparametric equivalent. Significance will be designated as $p < 0.05$.
RESULTS: 18 patients have satisfactorily completed the treatment course so far. Of CON patients, 5/10 returned a negative sinonasal culture post-treatment, compared with 0/8 MH patients ($p = 0.0359$). SNOT-22 scores taken at t=0 and 2 weeks show no significant decrease in both MH (3.786 ± 3.839, n=8) & CON (7.625 ± 6.508, n=10) groups ($p = 0.6329$).
CONCLUSION: Preliminary results show that saline rinses and culture-directed antibiotic therapy were more effective at eradicating infection compared to MH + MGO. Symptom scores decreased between pre and post treatment in both groups, however there was no significant difference between the two groups.

LAY DESCRIPTION

Chronic Rhinosinusitis (CRS) is a debilitating condition which affects a small subset of the population. It refers to repeated infection of the sinuses, which are air-filled cavities in the nose. Generally, the treatment for sinusitis is medical therapy first, or if that fails, surgery, but some in some patients even surgery is not enough to treat this disease.
Manuka honey is a special type of honey that is found in New Zealand, and has special antibacterial properties. We propose to incorporate this antibacterial honey into a sinus rinse, with the goal of producing a low-cost, effective, safe treatment option for surgically resistant CRS.

ABSTRACT 15

INFLUENZA VACCINE FOR PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE: COCHRANE REVIEW AND META ANALYSIS

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Background: Influenza vaccinations are currently recommended in the care of people with COPD, but these recommendations are based largely on evidence from observational studies with very few randomised controlled trials (RCTs) reported. Influenza infection causes excess morbidity and mortality in people with COPD, however, there is also the potential for influenza vaccination to cause adverse events. Objectives: To evaluate the evidence from RCTs for the effectiveness of influenza vaccination in people with COPD. Outcomes of interest were exacerbation rates, hospitalisations, mortality, lung function and adverse events. Methods: The Cochrane Airways Group Specialised Register of trials, grey literature and reference lists of articles were searched up to January 2016. RCTs that compared live or inactivated virus vaccines with placebo, either alone or with another vaccine in persons with COPD or chronic bronchitis were included. Data extraction was carried out by two independent reviewers. Results: Eleven RCTs were included for analysis. Meta-analysis of two studies highlighted a significant reduction in total number of exacerbations with inactivated vaccine in COPD patients compared to placebo (weighted mean difference (WMD) -0.37, 95% confidence interval -0.64 to -0.11, P=0.006). There was no evidence of an effect on hospitalisations with use of vaccine compared to placebo (OR 0.33, 95% CI 0.09 to 1.24, P=0.52) or mortality (OR 0.87, 95% CI 0.28 to 2.70, P=0.81). Effects on lung volume could not be meta-analysed, however, narrative synthesis demonstrated no significant differences between vaccine and placebo for included studies. Also according to narrative synthesis, local adverse events were higher for the vaccinated group but were moderate and transient in nature. Conclusion: This review confirms findings of previous large observational studies; that inactivated vaccine reduces exacerbations in people with COPD, substantiating routine use in practice.

LAY DESCRIPTION

Influenza vaccine is almost universally recommended for best practice management of people with chronic obstructive pulmonary disease (COPD). This review of the existing literature aimed to collate and appraise the existing evidence to underpin this practice. Eleven studies were reviewed showing that the inactivated type of influenza vaccine, usually injected into the muscle, decreases “flare-ups” of COPD. Injection with inactivated influenza vaccine was linked to an increase in local side effects, e.g. pain at the site of injection, however, these were not serious and are considered to be outweighed by the long term benefit of vaccination.

ABSTRACT 16

READMISSIONS FOLLOWING CARDIOVASCULAR HOSPITALISATIONS: A SYSTEMATIC REVIEW OF THE CONTEMPORARY AUSTRALIAN LITERATURE

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Background: International studies suggest hospital readmissions after cardiovascular events are common, preventable and costly yet the burden of readmissions in Australia is uncertain. We performed a systematic review to summarise the understanding of readmissions in Australia.
Methods: Using a MEDLINE search of publications from 1990 to 2016, we included observational and interventional studies with a primary focus on readmissions following a cardiovascular hospitalisation in adult Australians. We excluded publications without original data and studies with composite endpoints that failed to report readmission data separately.
Results: 23 articles (13 observational, 10 interventional) met the inclusion/exclusion criteria. Observational studies (9 single-centre, 4 multi-centre) focused on readmissions for heart failure (n=4) and other conditions were uncommon (stroke n=3, myocardial infarction n=1, other n=4). Most (8/13) observational studies reported 1-month readmission rates that ranged from 6.3 to 27% with the variability explained by the condition, whether the study counted all-cause or disease-specific readmission and whether readmission to other hospitals were included. The highest rates of readmission were reported among the few multicentre studies (4/10) that counted all-cause readmissions and readmissions to other hospitals using linked data. Almost all (7/10) compared home-based nursing intervention to standard clinic follow-up for heart failure, 4 interventions showed a reduction in readmission. We could not identify any studies from Australia that evaluated the preventability of readmissions, associated healthcare costs or readmissions among indigenous patients.
Conclusions: There is a paucity of publications describing the burden of readmissions particularly for conditions other than heart failure. The reported readmission rates in current studies are highly variable in part due to the methodological limitations in how readmissions are counted.

LAY DESCRIPTION

In the United States approximately 1 in 5 patients are readmitted to hospital following heart related admissions, but in Australia the extent to which readmissions are affecting our community is uncertain. We searched for Australian articles reporting readmissions after heart related hospitalisations and found only 23 studies in the past 25 years. Most studies reported a readmission rate after 1-month ranging from 6.3% to 27% which could be explained by inconsistent methods. We believe more research is needed to understand why so many patients are readmitted to hospital to improve overall patient care.

ABSTRACT 17

MECHANISMS RESPONSIBLE FOR SEROTONIN VASCULAR REACTIVITY SEX-DIFFERENCES IN THE INTERNAL MAMMARY ARTERY

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Background: Females have increased in-hospital mortality and poor outcome following coronary artery bypass grafting (CABG). A potential contributing factor is female vascular hypersensitivity to endogenous vasoconstrictors thereby inducing myocardial ischemia. This study examined sex-differences in serotonin and thromboxane A2 (U46619)-induced vasoconstrictor responses in isolated internal mammary artery (IMA). The role of (1) the endothelium, (2) nitric oxide (NO), (3) prostaglandin (PG) and (4) receptor activity state, was evaluated in any observed sex-difference.

Methods: Male and female IMA were obtained from patients undergoing CABG and segments mounted in an organ bath. Cumulative concentration-response curves were established for serotonin and U46619, with the mechanisms responsible for sex-differences evaluated by: (1) endothelium denudation, (2) endothelial nitric oxide synthase (NOS) inhibition of vascular responses and NO quantification using electron paramagnetic resonance (EPR), (3) cyclooxygenase (COX) inhibition of vascular responses and PG metabolite quantification using mass spectrometry, and (4) quantification of receptor abundance and phosphorylation status.

Results: Compared with males, female IMA were hyper-reactive to serotonin but not U46619. The female hyper-reactivity to serotonin was (1) abolished by endothelial denudation, (2) unaffected by NOS inhibition, with no difference in EPR-assessed NO levels, (3) abolished by COX inhibition, with a trend in reduced 6-keto PGF1α but not PGF2α levels in females, and (4) unrelated to the abundance and phosphorylation of serotonin2A and serotonin2B receptors.

Conclusions: These data indicate that female IMA are hyper-reactive to serotonin but not U46619, with the former attributable to an endothelium-dependent COX pathway involving impaired 6-keto PGF1α production compared with males.

LAY DESCRIPTION

Females with heart surgery have increased post-operative death compared with males. The potential reasons for this is said to be multifactorial. We looked at the conduit vessel to see if these constrict and dilate differently in male and female and we found that female vessel constrict more than those of male to serotonin, which was further associated to decrease prostacyclin expression. This could potentially have profound effects on the overall outcome of female following open-heart surgery and sex specific treatment with prostacyclin will be beneficial in female to decrease post-operative death.

ABSTRACT 18

TERTIARY LYMPHOID ORGANS IN RECALCITRANT CHRONIC RHINOSINUSITIS

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Background: Chronic Rhinosinusitis (CRS) is a persistent inflammatory condition of the sinus epithelium. Tertiary lymphoid organs (TLOs) have been found in chronic inflammatory diseases and are often associated with severe inflammation. However, their presence in CRS has not been studied.

Aim: To investigate the prevalence and the potential role of TLOs in CRS.

Methods: Sinonasal tissue with matched clinical history was obtained from CRS patients with nasal polyps (CRSwNP), CRS without nasal polyps (CRSsNP) and non-CRS controls. mRNA was analyzed using a microfluidic qPCR array, generating an expression profile of 29 TLO-related genes. Relative expression was determined by normalizing to 2 housekeeping genes and to non-CRS controls. Haematoxylin & Eosin stained tissue sections from 158 patients were analyzed for the presence of TLO-like lymphoid aggregates. Representative samples from the 3 groups were analyzed by immunofluorescence for the presence of TLOs. Associations between TLO and clinical data were analysed by Monte Carlo simulated exact tests. All analyses within CRS patients were stratified by CRS subgroups.

Results: TLOs were observed in 28/75 CRSwNP (37%), 6/59 CRSsNP (10%), and in 0/24 control patients. TLOs were exclusive to CRS patients compared to non-CRS controls ($p=0.002$) and were 5.2-times more prevalent in CRSwNP than in CRSsNP patients ($p=0.003$). 17 TLO-related genes had increased relative expression in CRSwNP patients ($p<0.05$). TLOs were associated with disease recalcitrance ($p=0.01$), as defined by the number of previous operations, and with tissue eosinophilia ($p=0.003$).

Conclusion: Our data indicates that recalcitrant CRSwNP patients demonstrate massive inflammation with TLO formation in association with tissue eosinophilia. Analysis of matched gene expression and histopathology data suggests that CRS patients could be at different stages of TLO development. Our findings have potentially important prognostic and therapeutic implications.

LAY DESCRIPTION

Our research aims to understand inflammatory processes in chronic rhinosinusitis (CRS), a disease that causes breathing problems and pain. We are primarily interested in immune structures called tertiary lymphoid organs (TLOs), which can contribute to chronic inflammation. We have demonstrated that TLOs are present exclusively in CRS compared to controls and are more prevalent in patients who develop nasal polyps. Patients with TLOs are more likely to have relapsing CRS, requiring more intensive treatment, including surgery. Therefore, TLOs may have a role in predicting the disease course and may be targeted by novel treatments.

ABSTRACT 19

ANTICANCER EFFICACY OF THE HYPOXIA ACTIVATED PRODRUG EVOFOSFAMIDE IS ENHANCED IN COMBINATION WITH THE PROAPOPTOTIC RECEPTOR AGONIST DROZITUMAB AGAINST OSTEOSARCOMA.

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Tumour hypoxia is a major cause of treatment failure for a variety of malignancies. However, hypoxia offers treatment opportunities as exemplified by the development of compounds that target hypoxic regions within tumours. Evofosfamide is a prodrug engineered by linking the hypoxia seeking 2-nitroimidazole moiety to the cytotoxic bromo-isophosphoramide mustard (Br-IPM). When evofosfamide is delivered to hypoxic regions, the DNA cross linking toxin, Br-IPM, is released. This study assessed the anticancer efficacy of evofosfamide in combination with the Pro Apoptotic Receptor Agonist drozitumab against osteosarcoma using both in vitro and in vivo systems.

In vitro, evofosfamide cooperated with drozitumab, resulting in a dose-dependent increase in cytotoxicity to human osteosarcoma cells selectively under hypoxic conditions, whereas primary normal human osteoblasts under the same conditions were relatively resistant to treatment. In vivo, the anticancer efficacy of evofosfamide combined with drozitumab against osteosarcoma was evaluated and in an orthotopic mouse model of human osteosarcoma progression and metastasis. Bioluminescence was used to monitor tumor burden and cancer-induced bone destruction was measured using micro-CT.

Animals transplanted with osteosarcoma cells directly into their tibiae and left untreated developed mixed osteolytic/osteosclerotic bone lesions and subsequently developed lung metastases three weeks post cancer cell transplantation. Evofosfamide as a single agent reduced tumor burden in bone and cooperated with drozitumab to protect the bone from osteosarcoma-induced bone destruction while also reducing the growth of pulmonary metastases.

These results suggest that evofosfamide may be an attractive therapeutic agent, with strong anticancer efficacy alone and in combination with drozitumab against osteosarcoma.

LAY DESCRIPTION

The drug which is named evofosfamide, kills cancer cells by becoming active in low oxygen conditions, which is common for most cancers, including cancer in the bone. This study examined the effects of evofosfamide alone and in combination with the drug known as drozitumab. Cancer cells were injected into the bone of mice and the mice were then treated with these drugs. Evofosfamide alone and in combination with drozitumab reduced tumour growth in the bone of mice. These results suggest that evofosfamide and drozitumab maybe attractive drugs for the treatment of cancer in the bone.

ABSTRACT 20

GETTING UNDER THE SKIN – IS RECEPTOR SOLUTION IMPORTANT?

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Introduction In vitro percutaneous absorption studies are an alternative to using live animals when studying the dermal penetration of compounds, such as drugs, pesticides, and cosmetics. The Organization for Economic Co-operation and Development guidelines advise that for permeation studies several different receptor solutions can be used. However the lack of in vitro/in vivo correlation in permeation studies may be caused by lack of solubility in the chosen receptor solutions. Possibly leading to an underestimation of the permeation of molecules in vitro. This would've dire consequences potentially translating into toxic systemic concentrations after dermal exposure. This has not been assessed to date. This work aims to establish if the permeability coefficient (Kp) and permeation flux (Jflux) are affected by the solubility of a set of model compounds in different receptor solutions to ex vivo human epidermis.

Methods The permeation through ex vivo human epidermis of a series of carbon-14 radiolabeled alcohols (C2-C10) with activities from 2-55mCi/mmol, topically applied in aqueous solutions, was determined at room temperature in side-by-side Franz cells during 0-96 hours. The different receptor media described in the guidelines were compared. A student's t-test for paired samples was used to analyse the data.

Results In different receptor solutions the Kp and the Jflux increased from 1.0-65.5 cm.h-1 and 0.002-0.24 mol/cm2, as the molecular weight and lipophilicity increased. There was a significant difference ($p<0.05$) for the highest lipophilic compound.

Conclusion The guidelines for permeation studies should be re-examined and an appropriate receptor solution identified.

LAY DESCRIPTION

Permeation studies are used to assess how drugs, pesticides and cosmetics cross the skin and these are regulated by standardised world guidelines. We are concerned safety exposure limits may be inaccurately determined due to choice of receptor solution leading to a dangerous underestimation of the amount of test compound penetrated. We hypothesise this is due to a lack of solubility of the test compound in the chosen receptor fluid. We used a series of compounds and demonstrated that the choice of receptor fluid affects penetration through the skin for compounds that are poorly water soluble. We advocate a review of the current guidelines.

ABSTRACT 21

A NOVEL DNA-BASED VIRUS-LIKE PARTICLE VACCINE AGAINST HEPATITIS C VIRUS

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Hepatitis C virus (HCV) infection affects ~170 million people worldwide as a result of a lifelong persistent infection. No vaccines are available and therapeutic options are limited partly due to the high cost and associated side-effects. Recently novel DNA-based vaccine formulations, which include the use of virus-like particles (VLPs) have generated promising outcomes. Generally, VLP vaccines are produced in vitro by transfecting cells with a plasmid or virus encoding the gene of interest, followed by purification before delivery to patients. The current study aims to generate VLPs in vivo by vaccination with a recombinant DNA vaccine encoding the HCV structural proteins (core, envelope-(E1) and E2), which can self-assemble into VLPs. We have previously reported that a DNA vaccine encoding perforin (PRF) can induce cell death, resulting in release of natural adjuvants known as damage associated molecular pattern (DAMPs) as well the viral antigen, followed by enhanced cell mediated immunity. In this study we will use this mechanism to ensure the release of the VLPs in vivo and realise the adjuvant effect of the DAMPs, thus mimicking the effect of vaccination with live attenuated virus vaccines. We have successfully generated DNA vaccine constructs encoding core, E1 and E2 as well as PRF. We have also shown that there is an association between core and E2 detectable by immunoprecipition by antibodies against E2 but not against core. This suggests the formation of a particle in which the core is protected from direct interaction with anti-core antibodies, indicative of VLP formation. Mice vaccinated with constructs encoding CoreE1E2 and PRF developed higher cell mediated immune responses compared with animals vaccinated with other test vaccines. We are currently in the process of evaluating the humoral immune responses and protective potential of these vaccines in mice. We hope these studies will help in the development of more effective HCV vaccines in the future.

LAY DESCRIPTION

HCV is a major global public health problem. A vaccine against HCV is a cheaper alternative to antiviral therapies, especially in low-income countries. Using a DNA-based approach, we hope to design new and inexpensive vaccines which produce HCV proteins that can self-assemble into VLPs that closely resemble the native virus but are unable to cause infection. These VLPs are exposed and recognised by the immune system following their release by the vaccine. We will determine if administration of these vaccines provides protection against HCV infection with the potential to reduce HCV infections worldwide.

ABSTRACT 22

DISCORDANT FREQUENCIES OF TISSUE-RESIDENT AND CIRCULATING CD180-NEGATIVE B CELLS IN CHRONIC RHINOSINUSITIS

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Introduction: The unconventional Toll Like Receptor (TLR) CD180 is implicated in chronic inflammatory diseases, however, its role in chronic rhinosinusitis (CRS) has yet to be investigated.
Objective: To study the expression of CD180, its homologue TLR4 and associated proteins Myeloid Differentiation (MD) factors MD1 and MD2 on mucosal and systemic immune cell populations in relation to serum IgG levels. We hypothesized that CD180 would be increased in CRS patients compared to controls and that this would correlate with reduced IgG amounts in these patients.
Methods: Mucosal and peripheral blood samples were prospectively collected from CRS patients and non-CRS controls. The expression of TLR4, MD1, MD2 and CD180 was investigated using qRT-PCR, immunohistochemistry and flow cytometry. Serum IgG levels were determined using ELISA.
Results: A total of 70 patients were recruited to the study. CRS with nasal polyp (CRSwNP) patients had significantly increased mRNA expression of CD180, MD1 and MD2 compared to controls (5.54, 2.1, 2.38 fold respectively, Kruskal-Wallis $P<0.01$). Flow cytometry showed increased mucosal B-cell numbers in CRSwNP compared to controls (3.82 +/- 1.35 vs 0.58+/- 0.29, Kruskal-Wallis $P<0.01$). B-cells lacking CD180 were lower in CRSwNP tissue compared to CRSsNP and controls (21.07 +/- 6.41 vs 41.61 +/- 7.82 vs 40.06 +/- 8.06, Kruskal-Wallis $P<0.01$) but higher in blood (39.18 +/- 8.3 vs 17.95 +/- 7.82 and 12.49 +/- 4.92, Kruskal-Wallis $P\leq0.05$). There was a positive correlation between CD180 negative blood B-cell numbers and serum IgG levels ($r = 0.36$).
Conclusion: Changes in mucosal and peripheral CD180 expressing B-cells were identified in CRSwNP patients. A positive correlation between CD180 negative blood B-cell numbers and serum IgG levels suggests a role for these cells in the IgG-dependent immune response in these patients.

LAY DESCRIPTION

Chronic rhinosinusitis is a disease characterised by nose blockage and severe facial pain. Immune cells contribute to this pain and inflammation. Some patients with severe forms of the disease have grape like growths called polyps present. In this current study we identified immune cell differences in patients with polyps compared to those without; possibly leading to a therapeutic target in treating the ongoing inflammation of the disease.

ABSTRACT 23

RECOMBINANT HUMAN LUBRICIN FOR PREVENTION OF POSTOPERATIVE INTRA-ABDOMINAL ADHESIONS IN A RAT MODEL

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Background: Postoperative intra-abdominal adhesions are a major cause of morbidity and mortality and heavy burden to health care resources. At present, numerous introduced adhesion prevention products demonstrated some benefit but none is consistently effective. The aim of this study is to examine the effectiveness of recombinant human lubricin in preventing intra-abdominal adhesion formation.
Materials and Methods: A total of 62 male Wistar Albino rats were randomly assigned to the study. 6 rats were used to the initial pilot study and 56 rats were randomized into 4 groups: (i) control caecal abrasion; (ii) treatment caecal abrasion with 0.5mg/mL lubricin solution; (iii) control caecal enterotomy and primary closure; and (iv) treatment caecal enterotomy and primary closure with 0.5mg/mL lubricin solution. Rats were sacrificed 3 and 21 days post-operatively for pilot and main study respectively. Macroscopic and microscopic adhesion severity was graded by blinded investigators.
Results: For the pilot study, all 6 rats successfully reached the end point. In the caecal abrasion group, adhesions were significantly reduced for the treatment group macroscopically ($p = 0.001$) as well as microscopically (Fibrosis $p = 0.009$, Inflammation $p < 0.0001$). In the caecal enterotomy group, adhesions were less reduced for the treatment group from macroscopic ($p = 0.011$) and microscopic grading (Fibrosis $p = 0.500$, Inflammation $p = 0.206$).
Conclusions: Recombinant human lubricin significantly reduced intra-abdominal adhesions in caecal abrasion group and less in the caecal enterotomy group. Future study using higher concentration of lubricin solution is needed to investigate its toxicity and more profound anti-adhesion property in significant operations.

LAY DESCRIPTION

Abdominal surgeries cause undesirable tissue adhesions resulting in various short and long term complications, leading to a substantial burden on healthcare systems worldwide. Currently, there are number of introduced adhesion prevention products which are sub-optimal and unable to completely prevent adhesion formation and its complications. Therefore, developing a malleable, robust and easy to use product that is more effective and safe in preventing adhesions is essential. Lubricin solution has been proven to reduce adhesions in orthopaedic surgeries and is also believed to show promising results in abdominal surgeries.

ABSTRACT 24

NOVEL TOPICAL ANTI- STAPHYLOCOCCUS AUREUS BIOFILM AGENT DEFERIPRONE AND GALLIUM PROTOPORPHYRIN: SAFETY AND EFFICACY IN AN IN VIVO SHEEP SINUSITIS MODEL

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OBJECTIVES: Increasing antimicrobial resistance has presented new challenges to the treatment of recalcitrant chronic rhinosinusitis fuelling a continuous search for novel nonantibiotic antibiofilm agents. This study aims to assess the safety and efficacy of Chitodex gel, combined with novel antibiofilm agents Deferiprone and Gallium Protorporphyrin (CD-DG) as a topical treatment against S. aureus biofilms in vivo. Deferiprone and Gallium Protoporphyrin (DG) exert their antibiofilm effects by targeting the essential iron metabolism pathways of S. Aureus. Deferiprone has also been found to improve wound healing with its anti-proliferative effects on nasal fibroblasts.
METHODS: To assess efficacy we used a sheep sinusitis model. 15 sheep were divided into three groups of 7 day treatments, n= 5 sheep (10 sinuses) per treatment; (1) twice daily saline flush (NT), (2) Chitodex gel (CD) with twice daily saline flush, and (3) CD-DG gel with twice daily saline flush. Biofilm biomass across all groups was compared using LIVE/DEAD BacLight stain and confocal scanning laser microscopy. To assess safety, 8 sheep were divided into two groups of 7 day treatments, n= 4 sheep (8 sinuses) per treatment; (1) Chitodex gel (CD) with twice daily saline flush, and (2) CD-DG gel with twice daily saline flush. Tissue morphology was analysed using histology and scanning electron microscopy (SEM).
RESULTS: The safety study showed no cilia denudation on SEM and no change in sinus mucosa histopathology when comparing CD-DG to CD treated sheep. COMSTAT2 assessment of biofilm biomass showed a significant reduction in CD-DG treated sheep compared to NT controls ($p = 0.03$, One-way ANOVA, Kruskal-Wallis test).
CONCLUSION: The results indicate that CD-DG is safe and effective against S. aureus biofilm in a sheep sinusitis model and could represent a viable treatment option in the clinical setting.

LAY DESCRIPTION

Amidst rising antibiotic resistance we are in search of new ways to treat chronic rhinosinusitis (CRS), which is a persistent inflammation of the nose caused by bacteria. In this study we used a sheep model with induced CRS and tested a new nonantibiotic drug combined with a gel with wound healing properties. The gel is able to sit within the nose and slowly releases the nonantibiotic compound increasing the contact time with bacteria that are otherwise hard to reach. This drug then kills the bacteria by depriving their food source. We conclude that this treatment is safe and effective and could potentially help patients with recurrent CRS.

ABSTRACT 25

INNATE IMMUNE RESPONSE OF NULI-1 CELLS TO STAPHYLOCOCCUS AUREUS SMALL COLONY VARIANT INFECTIONS

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Background: Staphylococcus aureus (S. aureus) small colony variants (SCVs) can survive within the host intracellular milieu and are associated with chronic relapsing infections. However, it is unknown whether host invasion rates and immune responses differ between SCVs and their wild-type counterparts. This study used a stable S. aureus SCV (SK2SCV) developed from a clinical isolate (SK2WT) in inflammation-relevant conditions. Intracellular infection rates as well as host immune responses to SK2WT and SK2SCV infections were investigated.
Method: NuLi-1 cells were infected with either SK2WT or SK2SCV, and the intracellular infection rate was determined over time. mRNA expression of cells infected with each strain intra- and extracellularly was analyzed using a microfluidic qPCR array to generate an expression profile of 39 genes involved in the host immune response. Two tailed t test was used to compare between cells infected by the each of S. aureus strain and negative controls.
Results: No difference was found in the intracellular infection rate between SK2WT and SK2SCV. Whereas extracellular infection induced a robust pro-inflammatory response, intracellular infection elicited a modest response. Intracellular SK2WT infection induced mRNA expression of TLR2 (fold change 2.45, p= 0.002), pro-inflammatory cytokines (IL1B, fold change 2.62, p= 0.005 and IL6, fold change 4.27, p= 0.005) and tissue remodelling factors (MMP9, fold change 4.88, p= 0.05). In contrast, intracellular SK2SCV infection induced up regulation of only TLR2 (fold change 3.12, p=0.05) and IL6 (fold change 5.05, p= 0.05).
Conclusions: Whereas host intracellular infection rates of SK2SCV and SK2WT were similar, SK2SCV intracellular infection induced a less widespread up regulation of pro-inflammatory and tissue remodelling factors in comparison to intracellular SK2WT infection. These findings support the current view that SCVs are able to evade host immune detection to allow their own survival.

LAY DESCRIPTION

Staphylococcus aureus (SA) is a common pathogen that can cause serious infections in human. This cunning bacteria has many different survival strategies to enable them to adapt to difference environments. One of these is to reduce toxin production and grow very slowly to avoid being detected and eliminated by the host they infected. We demonstrated that when human cells were infected by the slow growing SA, there was less immune response in comparison to the normal growing SA. This finding allowed us to gain further understanding in how the slow growing SA is able to avoid being recognised by the host in order to prolong their own survival.

ABSTRACT 26

THE EFFECT OF FIBROBLASTS ON ANDROGEN SIGNALLING IN OESOPHAGEAL ADENOCARCINOMA CELL LINES IN VITRO

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Background and Aims: Nuclear localisation of androgen receptor (AR) and expression of androgen responsive gene FKBP5 in oesophageal adenocarcinoma (OAC) suggest AR is functional and are associated with decreased survival, yet AR expressing OAC cell lines failed to grow in monoculture with concentrations of androgen typically used in vitro. We therefore investigated whether fibroblasts could modify growth and androgen signalling in OAC.
Methodology: The AR-negative OAC cell line, OE33 was stably transduced with AR and green fluorescent protein (GFP) then grown, with or without 10 nM of AR ligand 5α-dihydrotestosterone (DHT), in monoculture or direct co-culture with different fibroblasts; neonatal foreskin (NFF), mammary (MF), nasal from chronic rhinosinusitis with nasal polyp (CRSwNP) and PShTert myofibroblasts from benign prostatic hyperplasia (PShTert). Cell growth was measured by cell counts, nuclear translocation by immunocytochemistry, and the expression of androgen-responsive genes by quantitative real-time reverse-transcription PCR.
Results: In monoculture, and direct co-culture with NFFs, MFs, or CRSwNP, DHT inhibited the growth of OE33-AR cells ($P < 0.0001$). AR translocated completely to the nucleus with downregulation of cyclin B1 (CCNB1) and upregulation of FKBP5. In contrast, PShTert myofibroblasts permitted growth. AR was localised to the cytoplasm and nucleus. FKBP5 was upregulated with no downregulation of CCNB1, suggesting either differential regulation of androgen signalling by PShTert or the ability of PShTert to override the typical effect of CCNB1 following its response to androgen.
Conclusion: This is the first study to investigate whether fibroblasts alter the response of an OAC cell line to androgen. The PShTert myofibroblast produced a differential response to androgen in OE33-AR cells with results consistent with clinical findings. This suggests certain fibroblasts can modify response to androgen in OAC.

LAY DESCRIPTION

We have shown that sex hormones, namely androgens, may be involved in the poor prognosis associated with a lethal cancer that is rising in incidence called oesophageal adenocarcinoma (OAC). Using OAC cell lines that express the androgen receptor that binds to androgens, we are investigating how androgens affect this cancer and how fibroblasts, a cell type that produces the structural framework of the tissue, may influence this response. This will improve our understanding of the role of androgens in OAC and may lead to treatments.

ABSTRACT 27

OPTIMAL FOLLOW-UP STRATEGY FOR RESECTED NEUROENDOCRINE TUMOURS: A SYSTEMATIC REVIEW

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Background: The incidence of neuroendocrine tumours (NETs) has doubled over the last 20 years with an increasing number of proven systemic treatment strategies (ref). The optimal follow-up protocol for this patient population remains undetermined. This abstract reports a systematic review of follow up strategies for NETs from 1996-2016.undertaken by COMMNETS in order to develop optimal follow-up strategy for patients with resected NETs.
Method: A systematic search strategy was carried out of the MEDLINE and Cochrane Library databases and abstracts of major meetings (ASCO, ESMO, NANETS, and ENETS). Inclusion criteria included Prospective studies or retrospective studies of more than 25 patients that described follow up strategy for surgically resected non-metastatic NETs Merkel cell cancer and small cell/large cell carcinomas of the lung were excluded.
Results: Twelve studies were included for full review which described follow-up strategies post-resection of NETs. Of these, 10 were retrospective and two were prospective studies, but no randomized studies were found. The studies reported no consistent follow-up strategies and were marked by limitations including insufficient data, methodological bias and between-study heterogeneity. No formal data synthesis was possible. One study examined "rigorous" follow-up (defined as clinical review and CT, MRI or somatostatin receptor scintigraphy at least yearly) versus non-rigorous follow-up, but showed no difference in relapse rates.
Conclusions: There is little reported evidence to definitively guide the optimal follow-up strategy in resected NETs. This systematic review has identified a gap and a need for vital research into different aspects of follow-up.

LAY DESCRIPTION

Neuroendocrine tumours (NETs) are rare tumours and surgical removal of the localize tumour is the key treatment. NETs tend to recur many years after initial surgery. However, the optimal follow-up strategy after surgery is undetermined. We search and review systematically to locate studies in the different database and through abstracts of the major conference to develop optimal follow strategy. Only twelve studies were eligible for this review. No formal guideline synthesis was possible due to lack of sufficient data. This systematic review has identified a gap and a need for vital research into different aspects of follow-up of NETs.

ABSTRACT 28

EFFICACY, SAFETY AND COST OF IPILIMUMAB FOR PATIENTS WITH METASTATIC MELANOMA IN A REAL-WORLD SETTING

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BACKGROUND: Ipilimumab, a CTLA-4 receptor antibody, has improved survival in metastatic melanoma patients. Toxicities of ipilimumab are immune-related, and can be thought of as a "clinical cost". The financial cost of ipilimumab is also significant, each cycle costing about $30,000.(1) This study aimed to do a retrospective case review of metastatic melanoma patients treated with ipilimumab. We hypothesised that while ipilimumab has a large financial cost, the survival benefit would be notable and toxicities manageable.
METHODS: Metastatic melanoma patients from The Queen Elizabeth Hospital were identified and case notes reviewed. Data collected included demographic, ipilimumab treatment and toxicity, and hospital admission details. The data was analysed using a Mantel-Haenszel chi squared test.
RESULTS: There were 23 patients identified (13 males), all with survival data. On average, 4 cycles of ipilimumab were given per patient (range 1 to 8 cycles), totalling 92 cycles. The median overall survival was 15.4 months, with a trend towards better survival in patients with no brain metastases at diagnosis (P = 0.002) or a normal LDH (P = 0.090). Treatment toxicity occurred in 14 patients (61%). There were 13 admissions for toxicity, with corticosteroids given during 11 admissions, and 3 patients requiring infliximab. The cost of ipilimumab was $2.76 million, excluding nurse and hospital chair costs. Each cycle of ipilimumab was associated with 8.3 additional days of hospitalisation (95% CI 2.3, 14.3; P = 0.009).
CONCLUSION: Treatment with ipilimumab was associated with a considerable median overall survival in melanoma patients. However, this treatment comes at a cost, related to both adverse effects and financial costs, which need to be considered when defining its role into the future.

REFERENCE

1. EviQ. Malignant melanoma metastatic ipilimumab [Online], 2015 [cited 2016 6 Feb]. Available from: https://www.eviq.org.au/Protocol/tabid/66/id/1307/Default.aspx.

LAY DESCRIPTION

Melanoma kills over 1500 people in Australia each year. In the past, no treatments have worked well for this cancer. Ipilimumab is a new treatment for melanoma that uses your body's defence cells to fight the cancer. However, it costs about $30,000 per treatment. We looked at all the people treated with ipilimumab at The Queen Elizabeth Hospital (23 patients). On average, patients lived for 15 months after having treatment. We noted about half the patients had side effects, although these were manageable. Overall, we showed that these patients had a good survival with ipilimumab compared to older treatments, offering hope for the future.

ABSTRACT 29

SILVER NANOPARTICLES TO TACKLE CLINICALLY RELEVANT BIOFILMS

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Background: Infectious diseases are linked to bacterial biofilms that frequently cause failure of medical therapies and recurrence of disease. The biofilm state enables bacteria to be protected from the immune system and to survive medical treatments, thereby contributing to the emergence of antibiotic-resistant bacteria. Alternative therapies are urgently needed. Whilst the antimicrobial activity of spherical silver nanoparticles (AgNP) is well described in planktonic bacteria, little is known about the antibiofilm effect and the influence of particle shape. We hypothesised that spherical and cubic AgNP exhibit different antibiofilm efficacy against clinically relevant biofilms, while being not toxic to airway epithelial cells.
Methods: Biofilms of Staphylococcus aureus (SA), methicillin-resistant SA (MRSA) and Pseudomonas aeruginosa (PA) were grown in microtiter dishes. After 48 hours growth at 37°C, biofilms were exposed for 1 hour to AgNP of different shape (spheres or cubes) or ciprofloxacin (CIP) as antibiotic control. The antibiofilm activity was assessed by the AlamarBlue viability assay. Toxicity studies were carried out using the lactate dehydrogenase assay in Nuli-1 airway epithelial cells. Experiments were conducted in triplicates; results were analysed using one-way ANOVA.
Results: Silver cubes achieved 100% biofilm killing (BK) in all biofilms, however, cell culture data revealed toxicity in Nuli-1 cells (25% viability). In contrast, silver spheres were not toxic (99% viable cells) and exhibited significant ($p<0.05$) antibiofilm activity against SA, MRSA and PA biofilms with 98%, 94% and 95% BK, respectively, compared to CIP with 90%, 74% and 93% BK.
Conclusion: This study showed significant antibiofilm efficacy of both spherical and cubic AgNP against SA, MRSA and PA biofilm compared to CIP. While toxicity limits the utilisation of silver cubes, silver spheres are a safe and promising non-antibiotic approach to tackle clinically relevant biofilms.

LAY DESCRIPTION

A major threat to human health is the rise of superbugs, i.e. microorganisms (bacteria) like Golden Staph become resistant to antibiotics. Resistance emerges as bacteria are covered in a protective slime called biofilm to survive the immune attack and antibiotics. Worldwide millions of people suffer from biofilm infections like recurring nose infections or non-healing wounds. To fight superbugs in biofilm, a new antibiotic-free therapy is proposed. Silver particles as small as 1/1000 the width of human hair were shown to move through biofilm and kill resistant Golden Staph. This therapy is a promising treatment joining the war on superbugs.

ABSTRACT 30

BRAIN METASTASIS IN ADVANCED COLORECTAL CANCER: RESULTS FROM THE SOUTH AUSTRALIAN METASTATIC COLORECTAL CANCER (SAmCRC) REGISTRY.

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Background: The SAmCRC registry has been enrolling patients since February 2006. Patterns of care have evolved leading to longer survival. Brain metastasis is considered rare in mCRC and surveillance imaging does not routinely include the brain. The reported rate ranges from 0.6% to 3.2%. We have analysed the SAmCRC registry to assess the frequency of brain metastasis in the South Australia population and the timing of presentation, which may guide the timing of appropriate surveillance assessments.
Methods: The SAmCRC registry was analysed to assess the number of patients presenting with brain metastasis during their lifetime. Patient characteristics are reported and overall survival was analysed using the Kaplan–Meier method.
Results: 4100 patients have been entered into the registry between between 2nd February 2006 and 31st March 2016. Only 59 patients on the registry at the time of analysis had developed brain metastasis (1.4%). The clinical characteristics of those with brain metastasis were as follows: median age 65.3 years and more likely female (51%). Where KRAS mutation status of the tumour was known, the majority had a detected KRAS mutation (55%); thirty one (53%) had craniotomy performed and 93% had whole brain radiotherapy. The median survival from diagnosis of brain metastasis was 4.2 months (95% CI 2.9-5.5). Patients undergoing craniotomy and radiotherapy had superior survival (8.5 months versus 2.2 months, respectively). Data from SAmCRC confirm that brain metastases are rare and the median time to development is about 2 years.
Conclusions: Patients with brain metastases are younger, more likely female and KRAS mutant which may allow patient selection for inclusion of CT Head imaging. Clinicians should be mindful of including imaging of brain in their surveillance protocol given the potential for surgical resection and stereotactic radiotherapy techniques.

LAY DESCRIPTION

Patterns of care for mCRC have evolved leading to longer survival with median now reaching 30 months. Brain metastasis is considered rare in mCRC and surveillance imaging does not routinely include the brain on neurologically asymptomatic cancer patients. The reported rate of brain metastasis ranges from 0.6% to 3.2%. We have analysed the SAmCRC population-based registry to assess the frequency of brain metastasis in the SA population and the timing of presentation and potential risks factors, which may guide the timing of appropriate surveillance assessments.

ABSTRACT 31

PEROXIDASES AND THEIR ROLE IN PROMOTING BONE REPAIR AND REGENERATION

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Bone repair is a highly coordinated process that involves numerous cell types, growth factors and extracellular matrix (ECM) components. Osteoblasts recruited to the fracture site from surrounding tissues have a central role in new bone formation. They are responsible for the synthesis and deposition of a collagen-rich ECM that is subsequently mineralised. The early recruitment of inflammatory cells is critical for normal bone healing. These cells release peroxidases, whose functional involvement in bone repair has mainly been studied in the context of providing oxidative defence against invading microorganisms. Our laboratory has recently made a new discovery showing the ability of peroxidases to directly stimulate collagen biosynthesis and generate a mineralised ECM in-vitro. Therefore, the objective of this study was to assess the potential of peroxidases to promote bone repair in-vivo using a calvarial critical size defect (CSD) mouse model. To assess the ability of peroxidases to promote bone regeneration, a 3mm defect was created on the right parietal bone of mice (n=14). The defect was filled with a biodegradable scaffold loaded with peroxidases or saline. Live microCT imaging was used to monitor bone regeneration over time. We showed that scaffolds pre-loaded with peroxidases significantly inhibited bone regeneration within the defect site, after 8 weeks. We concluded that the CSD model, which heals by intramembranous ossification, is not a suitable model for testing the bone regenerative potential of peroxidases. A pilot study was conducted on sheep using a drill-hole defect model, which showed increased bone regeneration by peroxidases. Despite also healing via intramembranous ossification, this model is expected to generate a greater inflammatory response, which may promote peroxidase function. Further studies will be conducted to validate the drill-hole defect model to confirm the therapeutic potential of peroxidases in bone repair.

LAY DESCRIPTION

When a bone breaks, many cells within the body coordinate with each other to repair the fracture. This complex process requires the recruitment of many different cell types. Recruitment of white blood cells during inflammation is one of the most critical stages for normal repair. This stage of healing is of particular interest as these cells are known to release a specific group of enzymes. These enzymes have a role in providing defence against bacteria, however we have evidence that they promote the activity of bone forming cells. We aim to confirm this discovery in animals to determine their therapeutic potential in bone repair.

ABSTRACT 32

ROLE OF PEROXYNITRITE-STIMULATED PARP-1 ACTIVATION IN THE PATHOGENESIS OF TAKOTSUBO CARDIOMYOPATHY

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Background: Takotsubo Cardiomyopathy (TTC) is an inflammatory disorder of the myocardium with associated energetic impairment, triggered by transient exposure to high concentrations of catecholamines, usually occurring in aging women. Previous rat models have shown that β2-adrenoceptor activation and a shift from Gs- to Gi-protein signalling may initiate the process, but the intracellular transduction pathway is not yet delineated. We have previously shown evidence of nitrosative stress, implying peroxynitrite release, in both a rat model and in myocardium of patients dying of TTC. Given that peroxynitrite activates poly(ADP-Ribose) polymerase (PARP-1), which induces energetic depletion, we sought to investigate the possible role of PARP-1 activation in our rat model of TTC.
Methods: TTC was induced in 10 female Sprague-Dawley rats via I.P injection of isoproterenol (ISO) and LV myocardium was evaluated after 24 hours; untreated rat hearts were used as controls (n=10). Myocardial content of the peroxynitrite marker 3-Nitrotyrosine (3-NT) and of the PARP-1 product poly(ADP-Ribose) (PAR) were evaluated by immunohistochemistry. The role of PARP-1 was assessed in a subsequent series of 10 rats, treated with PARP-1 inhibitor 3-aminobenzamide (3AB). Expression of the inflammatory activator thioredoxin interacting protein (TXNIP) was also measured.
Results: Isoproterenol induced impairment of LV apical radial strain ($p=0.0002$). In hearts of ISO rats there was a significant increase in content of 3NT ($p=0.0024$), PAR ($p<0.0001$) and TXNIP ($p<0.001$). Accumulation of 3NT and TXNIP was selectively periapical ($p=0.03$ and $p=0.002$ respectively). 3AB significantly ($p<0.001$) attenuated the contractile impairment following ISO.
Conclusion: These data support the concept that peroxynitrite induced activation of PARP-1 is important in mediating negative inotropic effects and energetic impairment seen in TTC. PARP-1 inhibitors represent a potential therapeutic modality in TTC patients.

LAY DESCRIPTION

Stress (Tako-Tsubo) cardiomyopathy is associated with intense myocardial inflammation and prolonged energetic impairment. We demonstrate that in a rat model, inflammation reflects substantially the presence of nitrosative stress, which impairs energetics by activation of poly(ADP-ribose) polymerase (PARP-1). Inhibition of PARP-1 attenuated the impairment of left ventricular function in this model. Targeting this pathway represents a potential therapeutic avenue for stress cardiomyopathy.

ABSTRACT 33

MEASUREMENT OF PSOAS MUSCLE CROSS-SECTIONAL AREA AT THE LEVEL OF THE L3 VERTEBRA IS REPRODUCIBLE BETWEEN OBSERVERS AND IS ASSOCIATED WITH POOR OUTCOMES FOLLOWING EVAR.

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Vascular Surgery Research Group, Dept of Surgery, University of Adelaide and The Queen Elizabeth Hospital

Pre-operative sarcopenia is an established risk factor for poor outcomes following surgery. Methods for assessing sarcopenia are either complex, time consuming or poorly validated. We aimed to assess the inter-observer reliability of scoring psoas area at the level of the L3 vertebra and to evaluate whether sarcopenia scored by this simple and rapid method impacted on mortality and length of stay (LOS) for patients undergoing endovascular infra-renal aortic aneurysm repair (EVAR).
We had access to 50 pre-operative CT scans of patients who underwent EVAR, together with 3 year follow up data. For each CT scan the axial slice at the most caudal level of the L3 vertebra was extracted. Three observers independently calculated the combined cross-sectional area of the left and right psoas muscle at this level. Inter observer variability was calculated by the method described by Band and Altman (Lancet, 1986). Psoas area was normalised for patient height and sarcopenia was defined as a total psoas area of <500mm2/m2. Presence or absence of sarcopenia was correlated with LOS >4 days and both 1yr and 3yr mortality using relative risk calculations as per Altman (1991).
Inter-observer reliability of scoring psoas area was good (reproducibility coefficient as % of the mean for each observer pair:7.92%,7.95%,14.33%; ANOVA of differences: p=0.82). Patients with sarcopenia had an increased risk of 3yr mortality (RR 5.25,CI:1.28-21.51,p=.021) and LOS >4 days (RR 2.33,CI:1.11-4.87,p=.025). There was no increased risk of 1yr mortality with pre-operative sarcopenia (RR 5.25,CI:0.36-75.6,p=0.22), but analysis was limited by only two deaths <1yr in our cohort.
Psoas area scoring has good inter-observer reliability. Pre-operative sarcopenia as defined by psoas area significantly increases the risk of 3yr mortality and LOS >4 days. Low incidences of 1yr mortality prevented this study from accurately assessing any impact of sarcopenia on 1yr mortality.

LAY DESCRIPTION

Outcomes following endovascular repair of abdominal aortic aneurysms are very good, but some patients have an increased risk of death at one year and of having a longer stay in hospital after the operation. Calculating muscle mass before the operation is a potential way of identifying which patients are more likely to have a worse outcomes. However, calculating total body muscle mass is difficult and time consuming. We have shown that we can reliably and quickly calculate the size of the psoas muscle in the back. If this muscle is smaller than a certain size then that patient has an increased risk of both death and a longer stay in hospital.

ABSTRACT 34

THE ASSOCIATION BETWEEN SARCOPENIA AND QUALITY OF LIFE IS DIFFERENT IN COMMUNITY DWELLING OLDER AUSTRALIAN MEN AND WOMEN

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Introduction : The impact of sarcopenia on health-related quality of life (HRQoL) in community dwelling older people in Australia is not known. The aim of this study was to evaluate the relationship between sarcopenia and HRQoL in older Australian men and women.
Methods: 367 men and 370 men aged 65 years and older from the North West Adelaide Health Study (NWAHS) study from Stage 2 (2002-2004). Sarcopenia was defined at baseline as the presence of low muscle mass and low grip strength. HRQoL was assessed using the Short Form-36 (SF-36) questionnaire: physical component summary (PCS) and mental component summary (MCS). Analyses were performed using multiple regression and adjustments were made for age, physical activity, smoking status, co-morbidity and depression.
Results: The prevalence of sarcopenia was 10.1% in men and 9.5% in women. Sarcopenia was significantly associated with the PCS score in the unadjusted model (P=0.012) and only model 1 adjusted for age (P=0.041). No significant association was noted in model 2 (model 1 + physical activity and smoking status) and model 3 (model 2 + Charlson co-morbidity index and depression). In men, a significant association between sarcopenia and MCS score was seen in the unadjusted model and all 3 adjusted models. No association was seen between sarcopenia and the PCS or MCS score in women for both the adjusted and unadjusted models.
Conclusion: After adjusting for multiple confounders, the association between sarcopenia only remained for the MCS score, in men. No association between sarcopenia and HRQoL was seen in women.

LAY DESCRIPTION

Sarcopenia is the age associated loss of muscle mass and function. The purpose of this study was to assess the relationship between sarcopenia and quality of life in older Australian men and women. 737 subjects aged aged 65 years and older from the North West Adelaide Health Study (NWAHS) study were included. In this study, the the prevalence of sarcopenia was 10.1% in men and 9.5% in women. After adjusting for multiple confounders, the association between sarcopenia only remained for the mental component summary score, in men. No association between sarcopenia and quality of life was seen in women.

TQEH Research Day Award Winners – 25 years

A full list of TQEH Research Day Award Winners can be found on the following pages.

20th Anniversary TQEH Research Day Award Winners – 2011 with TQEH Director of Research Professor Guy Maddern, Professor Basil Hetzel and Professor John Beltrame

10th Anniversary TQEH Research Day Award Winners – 2001

TQEH Research Day Award Winners – 25 years

2015	
Honours Student	Aashray Gupta
Junior Laboratory PhD Student	Bill Liapis
Senior Laboratory PhD Student	Aneta Zysk
Junior Clinical Researcher	Zoe Kopsaftis
Senior Clinical Researcher	Kristin Carson
Poster Prize	Ben Thurston
Best Lay Description	Kati Richter

2014	
Honours Student	Tammy Willsmore
Junior Laboratory PhD Student	Kati Richter
Senior Laboratory PhD Student	Bill Panagopoulos
Clinical Research Group 1	Shailaja Nair
Clinical Research Group 2	Harshani Jayasinghe
Poster Prize: Junior	Alice Du
Poster Prize: Senior	Helen Palethorpe
Best Lay Description	Aneta Zysk

2013	
Honours Student	Zacki Malik
Junior Laboratory PhD Student	Vikram Padhye
Senior Laboratory PhD Student	Amanda Drilling
Clinical Research Group 1	Tharshy Pasupathy
Clinical Research Group 2	Shailaja Nair
Poster Prize	Shalini Sree Kumar
Best Lay Description	Tamsin Garrod

2012	
Honours Student	Sathish Paramasivan
Junior Laboratory PhD Student	Erin Swinstead
Senior Laboratory PhD Student	Irene Zinonos
Clinical Research Group 1	Neil CW Tan
Clinical Research Group 2	Rachel Dreyer
Poster Prize	Michael Collins
Best Lay Description	Tessa Gargett

2011	
Honours Student	Sam Biermann
Junior Laboratory PhD Student	Amenah Jaghoori
Senior Laboratory PhD Student	Irene Zinonos
Clinical Higher Degrees	Elsa Dent
Clinical Research	Scott Graf
Poster Prize	Yang Du
Best Lay Description	Michael Djukic

2010	
Honours Student	Joshua Woenig
1st year PhD Laboratory	Camille Jardeleza
2nd year PhD Laboratory	Joshua Jervis-Bardy
3RD year PhD Laboratory	Sam Boase
Clinical Higher Degree	Rachel Dreyer
Poster Prize	Sumithra Krishnan
Best Lay Description	Chris Lauder

2009	
Honours Student	Raymond Yu
Junior Laboratory PhD Student	Kanchani Rajopadhyaya
Senior Laboratory PhD Student	Darling Rojas
Clinical Higher Degree	Andrew Foreman
Allied Health-Pharmacy	Nicole Such
Poster Prize	Shaundeep Sen
Best Lay Description	Michael Collins

2008	
Honours Group 1	Krishna Jeyaraman
Honours Group 2	Kanchani Radjopadhyaya
PhD Basic Science Jnr	Tyson Matthews
PhD Basic Science Snr 1	Christine Ball
PhD Basic Science Snr 2	Victoria Kopetz
Nursing & Allied Health	Hayley Vasileff
Higher Degrees Clinical	Rowan Valentine
Poster Prize	Andrew Foreman
Best Lay Description	Boris Fedoric

2007	
Honours student	Tyson Matthews
PhD Basic Science Jnr	Darling Rojas & Boris Fedoric
PhD Basic Science Snr	Nicola Leung
PhD Snr Clinical	Shilpa Prasad
Higher Degrees Clinical	Tong Le
Nursing & Allied Health	Hayley Vasileff
Undergraduates Vacation	Julia Kirby
Poster Prize	Alicia Chan

2006	
Honours student	Darling Rojas
PhD Basic Science	Deirdre Zander
PhD Basic Science	Christine Ball
PhD Clinical 1	Alkis Psaltis
PhD Clinical 2	Achim Beule
Nursing & Allied Health	Wendy McInnes
Undergraduates Vacation	Khanh Tran
Poster Prize	Rosanna Tavella

2005	
Honours Group 1	Boris Fedoric
Honours Group 2	Nick Mabarrack
PhD Junior Laboratory	Rebecca Dragovic
PhD Senior Laboratory	Theresa Hickey
PhD Clinical	Alkis Psaltis
Nursing & Allied Health	Peter Cheung
Undergraduates Vacation	Amellia Laidlaw
Poster Prize	Cadence Minge

2004	
Honours Group 1	Kara Cashman
Honours Group 2	Joanne Reed
PhD Junior Laboratory	Rebecca Dragovic
PhD Senior Laboratory	Harshita Pant
PhD Clinical	Wai Lim
PhD Population Health	Mark Kohler
Medical Student	Anthony Pisanello
Poster Prize	Theresa Hickey

TQEH Research Day Award Winners – 25 years

2003	
Honours Group 1	Maggie Centenera
Honours Group 2	Claire Seymour-Griffin
PhD Junior Laboratory	Ben Davies
PhD Senior Laboratory	Madelyn Zawitkowski
PhD Clinical	Jim Jannes
PhD Population Health	Katie Kandelaars
Poster Prize	Melanie Bagg

2002	
Honours	Deborah Marrocco
PhD Junior Laboratory	Ashley Newland
PhD Senior Laboratory 1	Cassandra Woithe
PhD Senior Laboratory 2	Madelyn Zawitkowski
Higher Degree Clinical	Matt Worthley
Higher Degree Surgical	Charles Morrison
Medical Student	Sasa Todorovic
Poster Prize	Lien Ho

2001	
Honours	Ashley Newland
Higher Degree Jnr	Cassandra Woithe
Higher Degree Snr	Al Truong Tran
Higher Degree Clinical	Matt Worthley
Higher Degree Surgical	Fiona Court
Advanced Fellowship Trainee	Anita Lee
Medical Student	Aiden Burrell
Poster Prize	Greg Roach

2000	
Honours Group 1	Ilse Dahn
Honours Group 2	Melanie Sutton
Higher Degree Group 1	Samantha Yates
Higher Degree Group 2	Tina Bianco
Higher Degree Clinical	Merlin Thomas
Nursing & Allied Health	Libby Birchmore
Medical Student	Victoria Tay
Poster Prize	Nicole Lamond

1999	
Honours	Tenielle Webb
Higher Degree Group 1	Ai Truong Tran
Higher Degree Group 2	Damien Hussey
Higher Degree Clinical	Denise Roach
Advanced Fellowship Trainee	Justin Evans
Nursing & Allied Health	Terry Jones & Dorothy Pannell
Medical Student	Edmund Tse & Ru-Siang Cheng

1998	
Honours	Ai Truong Tran
Higher Degree Group 1	Sarah Swinburne
Higher Degree Group 2	Damien Hussey
Higher Degree Clinical	Sarah Downie
Advanced Fellowship Trainee	Alan Wigg
Nursing & Allied Health	Robyn Clark
Medical Student	Rae-Wen Chang
Poster Prize	Lucia Sabordo

1997	
Honours	Samantha Yates
Higher Degree Group 1	Lisa Butler
Higher Degree Group 2	Michael Texler
Higher Degree Clinical	Dorothy Keefe
Advanced Fellowship Trainee	Andrew Luck
Nursing & Allied Health	Simon Stewart
Medical Student	Nan Williams

1996	
Honours	Anthony Kiosoglous
Higher Degree Group 1	Jennifer Hardingham
Higher Degree Group 2	Guy Patrick
Higher Degree Clinical	Christopher Zeitz
Advanced Fellowship Trainee	Alan Wigg
Nursing & Allied Health	Julie Lucker
Medical Student	Michael Osborn
Poster Prize	Matthew Callaway

1995	
Honours	Antiopi Varelias
Higher Degree Group 1	Guy Patrick
Higher Degree Group 2	Andreas Evdokiou
Higher Degree Clinical	Christopher Zeitz
Advanced Fellowship Trainee	Toby Coates
Medical Student	Rohini Sharma

1994	
Honours	Lucia Sabordo & Linda Dadds
Higher Degree Group 1	Rebecca Ritchie & James Moore
Higher Degree Group 2	Guy Patrick
Advanced Fellowship Trainee	David Campbell
Medical Student	I-Wen Chu

1993	
Basic Science	Dean Bacich
PhD/MD	Cui Lan Zhang
In Training	Jennifer Hardingham
Clinical	Dorothy Keefe
Medical Student	Kenneth Ooi

1992	
Basic Science	Yi Zhang
PhD/MD	Warwick Grooby
Clinical	David Campbell

Plenary Lectures – 25 years

2016: Professor Anne Kelso – NHMRC
"Medical research: why we mustn't stop now"

2015: Professor Steve Webb – Royal Perth Hospital, University of Western Australia & Monash University
"Pushing or pulling over the evidence-practice gap"

2014: Professor Brendan Crabb – Burnet Institute
"Malaria in the 21st century"

2013: Professor Tanya Monro – The University of Adelaide
"From theoretical physics to solutions in health and defence: a transdisciplinary journey"

2012: Professor Barry Brook – The University of Adelaide
"Future climate extremes and how to avoid them!"

2011: Professor Steve Wesselingh - SAHMRI
"Health Reform and Medical Research: Building better links between medical research and health care delivery to improve health outcomes"

2010: Professor David Allen - The University of Sydney
"Duchenne muscular dystrophy; connecting the gene to the disease"

2009: Professor David Vaux - La Trobe University
"Ten rules for the presentation and interpretation of data in publications"

2008: Dr Bob Irving - Nanotechnology Victoria
"Nanotechnology - Opportunities and Challenges at the Smallest Frontier of Science"

2007: Jenni Metcalfe - President Australian Science Communicators
"A Schizophrenic Life: the Career of a Science Communicator"

2006: Dr Rob Morrison - Science Communicator
"Trust me, I'm a Science Communicator"

2005: Professor Rob Norman - The University of Adelaide
"The reproductive revolution: How The Queen Elizabeth Hospital led the field"

Plenary Lectures – 25 years *(continued)*

2004: Robyn Williams - Australian Broadcasting Corporation
"How modern medicine changed the world - some anniversaries"

2003: Dr Sarah Robertson - The University of Adelaide
"Facing Challenges and Finding Solutions in Reproductive Medicine"

2002: Professor John Chalmers - The University of Sydney
"Enhancing Health and Medical Research in the Teaching Hospital Environment"

2001: Professor Peter Rathjen - The University of Adelaide
"Regenerative medicine using stem cells: Medicine for the new millenium"

2000: Professor Grant Sutherland - The University of Adelaide
"The human genome project: Applications to medical research"

1999: Dr Philip Reece - Biota Holdings
"Biota and Relenza: New drug discovery in Australia"

1998: Professor Colin Matthews (Moderator) - The University of Adelaide
Speakers: Dr Tim Kuchel, Dr David Turner, Dr John Chandler
"And Man made Dolly: The ethics of cloning"

1997: Dr Julian Cribb - CSIRO
"The origin of AIDS"

1996: Dr Deane Hutton - Science Communicator
"20:20 vision – Living in the 21st Century"

1995: Professor Mike Tyler - The University of Adelaide
"Frogs – the new frontier for natural products pharmacology"

1994: Dr Gael Jennings - Australian Broadcasting Corporation
"Communicating research via the medium of television"

1993: Dr Mark Wahlqvist - Monash University
"Salt intake and the non-pharmacological treatment of hypertension"

1992: Professor David Jarrett - The Queen Elizabeth Hospital
"The place of research in the face of a shrinking medical budget"