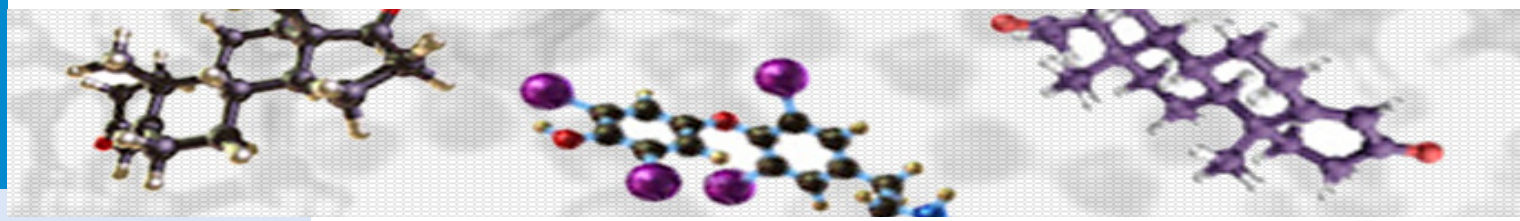
esa
endocrine society of australia
newsletter
april 2014



Important Items in this edition

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from the president

I have just returned from the Annual Meeting steering Group Meetings for ENDO 2014 and ENDO 2015 in Leesburg, Virginia. At the meeting, Kristy Brown from PHMRI-MMRI (who was accompanied by her beautiful new daughter) and I were able to successfully nominate 9 Australian speakers for the ENDO 2015 symposia programme. This means Australia will be third after USA and UK with the most numbers of speakers; a great outcome.

ESA Council is seeking nominations for ESA Council and Council office bearers, including the important role of President-Elect. I encourage you all to consider nominating; it is both an important and rewarding way to serve your society. Another ESA initiative achieved for 2014 via a joint letter with the ANZBMS to Professor Warwick Anderson AM, CEO of NHMRC, has been to form two grant review panels that combine the disciplines of endocrinology, diabetes, musculoskeletal diseases and gastroenterology. As there is much overlap between these disciplines, we hope this allows for more informed peer-review of endocrine-related grants. Thanks also to those who self-nominated for serving on GRPs and good luck to all!

ESA continues to be in sound financial shape, meaning we will continue to offer ESA Postgraduate Scholarships and Fellowships. Our total net assets are now nearing $2 million at over $1,900,000. The generous benefaction from the estate of ESA Founder, Dr Ken Wynne, of $541,320, has been be "ring-fenced", and currently provides an annual return exceeding the $25,000 Ken Wynne Memorial Scholarship. I am also pursuing additional clinical research funds by forming a partnership the RACP Research and Education Foundation. The good financial status of ESA means we have been able to add value to our Society for minimal cost by establishing partnerships with endocrine scientific Journals, details of which follow.

Benefits continue to flow from the ESA's decision to adopt Clinical Endocrinology (CEN) as the official Society's Journal.

1. All ESA members have free access to the online version of the Journal via the ESA member site, and for those wanting a print version, there is a substantial ESA discount. Print subscriptions cost 50 GBP per year.
2. The ESA is now well represented on the CEN Board with the recent appointment of Warrick Inder, Helena Teede and Christine Rodda, who now join Peter Ebeling and Fergus Cameron.
3. The CEN Board has approved priority access for publication of the best case presentation at the ESA Clinical Weekend meeting. This may be submitted as a case presentation with discussion or where appropriate as a Review of the topic supporting the case report.
4. In March 2014, the Journal is beginning a new initiative by providing an educational module based on a recent paper published in CEN. This will be linked to the RACP Advanced training curriculum and come with a hot link access to the paper, some Commentary and Background to the topic, 3 Multiple Choice Questions in the RACP format and with some historical context. This will be made available without charge to all members of the ESA during the first year. Thereafter, once its value can be assessed, it will require modest financial support (~£6000 annually), which it is hoped will come jointly from the Society for Endocrinology and ESA / RACP.
5. The Journal is keen to attract original articles and reviews from clinical members of the ESA.
6. The ESA's Logo is now prominently displayed on the front cover of the Journal.

ESA Council has recently approved similar collaborations with two Journal published by BioScientifica, Journal of Endocrinology and Journal of Molecular Endocrinology, so that basic and translational members of the ESA also benefit from Journal associations,. Journal of Endocrinology is currently 32nd of 121 in its category with an impact factor of 4.06; Journal of Molecular Endocrinology is currently 43rd of 121 at 3.58. Their scopes are distinct and complementary, covering all of the basic sciences in endocrinology. ESA members will receive electronic access to both Journals via the ESA website and the ESA logo will displayed prominently on the covers of both Journals. Bioscientifica will also sponsor a 'How to get published' education session at the ESA conference each year, on the Wednesday morning where overlap with the ADS ASM occurs. This is in addition to the ESA collaboration with Bioscientifica, whereby ESA members are also

eligible for a special discounted publishing fee when publishing case reports in the open access publication, Endocrinology, Diabetes & Metabolism Case Reports (submit online via www.edmcasereports.com).

The parallel Basic Science Weekend continues to evolve and the ESA Seminar Weekend, targeted towards early career researchers, is being held on May 2014 in Hobart. Associate Professors Don McLeod and Belinda Henry are the Clinical and Basic Co-Chairs, respectively, and promise a great weekend with an adrenal steroid hormone theme. Professor William Young, from the Mayo Clinic and a former President of the US Endocrine Society, is the keynote speaker and national experts, including Professor Peter Fuller, will also contribute. The planning for the ESA Annual Scientific Meeting in Melbourne from Sunday August 24th through to Wednesday August 27th, 2014, is almost complete thanks to Ann McCormack and her team. Professor Sundeep Khosla, an international expert in bone and mineral metabolism from the Mayo Clinic, will be the Keith Harrison Lecturer, while Professor John Wass from the University of Oxford, will be the Pincus Taft Lecturer. Professor Adrian Clark AM from the University of London will deliver the ESA/ADS plenary. Professors Khosla and Wass will also participate in the preceding Clinical Weekend from Friday August 22nd to Sunday August 24th at the Sands resort in Torquay, which is being organized by Shane Hamblin and his team. These meetings represent a winning "trifecta" and I encourage you to support ESA by attending.

ESA has really advanced over the last year and now has an increased international profile together with a "new look".

I thank all ESA Board members, Committee members, and ESA Scientific Programme and Local Organising Chairs for 2014 for their time as well as their expertise in making this possible. In closing, I look forward to seeing you at our ESA meetings later in the year.

Professor Peter Ebeling

MEDICAL AFFAIRS COMMITTEE ANNUAL REPORT

The Medical Affairs sub-committee continues to receive a number of requests for input into position statements and policy decisions from a range of health-related organisations including making recent contributions to the national antenatal care guidelines and the RANZCOG and ADIPS national consultation process. We are continuing to review approaches to stream line our workflow.

One issue of major interest is the criteria for androgen replacement in Australia. This has been raised by the PBAC who are concerned about a substantial increase in numbers of testosterone prescriptions in Australia and recent studies reporting a possible association between testosterone replacement and cardiovascular events. We are in the process of establishing a working group comprising experts in andrology from throughout Australia to consider relevant evidence and current clinical practice in order to formulate recommendations for:

1. A working definition of androgen deficiency in men.
2. Thresholds for abnormal testosterone concentrations in men across ages.
3. Indications for testosterone supplementation.
4. Precautions and monitoring for testosterone supplementation.

ESA receives a number of requests from individual patients for advice regarding Endocrinologists with expertise in a particular area of endocrinology or from patients from remote areas regarding local availability of Endocrinologists. We are developing a directory on the ESA website for clinical ESA members to self-nominate their areas of expertise and provide their practice location if they choose to. This information will be available to the public and may facilitate appropriate referral patterns. Provision of practice information is voluntary and it will be clear on the website that this does not represent an endorsement by ESA of an individual's practice.

Dr Morton Burt (Acting Head, Medical Affairs Subcommittee) on behalf of Prof Helena Teede (Head), Associate-Professor Warrick Inder and Prof Bu Yeap

IMPORTANT DEADLINES:

Life member nominations	**9 May 2014**
ESA Mid Career Award	**16 May 2014**
Council nominations	**23 May 2014**
Abstract deadline	**6 June 2014**
Novartis Junior Scientist Award	**6 June 2014**
Servier Award	**6 June 2014**
ESA Bryan Hudson Clinical Endocrinology Award	**6 June 2014**
ESA Travel Grants	**6 June 2014**
ESA IPSEN International Travel Grant Award	**1st August 2014**

NOMINATIONS FOR ESA COUNCIL 2014-2018

Nominations are now called for election to membership of the Council of the Endocrine Society of Australia.

At the 2012 election the following were elected for four years until 2016:
Warrick Inder, Tim Cole, Ashim Sinha and Morton Burt.

Council members reaching the end of their terms in 2014 are Peter Ebeling (who will stay on for the next year in the role of past-president), Bu Yeap, Nicolette Hodyl, Belinda Henry and Chen Chen. These members can stand for re-election if they wish.
Helena Teede will take on the role of President for two years, then past-president for one year.

Therefore, in the 2014 election, those elected will stay on ESA Council for 4 years until 2018. At least 4 states must be represented on the Committee.

A nomination form is included below for any ESA member wishing to nominate for election to ESA Council for 2014-2018. Nominees must be a financial member of the Society, and be nominated by two financial members of ESA. The primary requirement of a committee member is an interest in assisting with the work of ESA in promoting endocrine research and practice in Australia.

Nominations for election to the Society must reach the secretary of the ESA, A/Prof Tim Cole, 145 Macquarie Street, Sydney, NSW 2000 by 5:00 pm, Friday 23rd May 2014.
Further details regarding the Committee of ESA, and procedures for elections to the committee can be found at the ESA website: http://www.endocrinesociety.org.au/constitution.htm

Download nomination form from the ESA homepage:
http://www.endocrinesociety.org.au/

ESA LIFE MEMBERS

Criteria for ESA Life Membership:

- Age over 55.
- Member of ESA for 25 years or more.
- May have served on ESA Council, but have been off Council for a minimum of 2 years.
- Has made an outstanding contribution to research or clinical practice in the field of endocrinology in Australia.
- Is recognised as a high quality mentor/teacher through either supervision of higher degree candidates and/or clinical advanced training in endocrinology.

Nomination for Life Membership:
Nomination by any ESA member (of at least 5 year membership), to be seconded by another ESA member and accepted by the nominee (via a nomination form).

Considered and approved by a Council vote at the May/June ESA Council meeting. Life Membership will normally be limited to one recipient per year.

Download nomination form from:
http://www.endocrinesociety.org.au/life-members.asp

Add: Deadline Friday 9th May 2014

REMINDER TO PAY YOUR SUBSCRIPTION DUES

ESA membership subscriptions are now due. Please ensure that the Secretariat has all the correct mailing and contact details, particularly email addresses, as we rely on these to
maintain contact with you and keep you informed of ESA activities.

Membership to the ESA permits access to all meetings, obtaining membership registration, opportunity to apply for the various ESA awards/Travel Grants and the ESA newsletter.

Please renew your subscription by logging in at
www.endocrinesociety.org.au and selecting Subscription Renewal from the menu.

ESA Clinical Weekend

endocrine society of australia

22 - 24 AUGUST 2014 PEPPERS THE SANDS RESORT, TORQUAY, VIC

Registrations are now open for the ESA Clinical Weekend to be held at Peppers The Sands Resort Torquay, Friday August 22 - Sunday August 24 2014. We are fortunate to have excellent speakers in Prof John Wass (Oxford) and Prof Sundeep Khosla (Mayo Clinic) as guest plenary lecturers this year. Once again our advanced trainees will present interesting clinical cases in group settings with plenty of time for general discussion. We are now calling for cases to be submitted by advanced trainees (submissions close 16 May 2014).
Please refer to http://www.esaclinicalweekend.org.au/ for details.

Endocrine Trivial Pursuit will be held at the Friday welcome dinner (this year led by the reasonably capable Duncan Topliss). There are a variety of optional social activities on the Saturday afternoon and the Saturday evening dinner will feature Matt Parkinson (comedian, actor and radio presenter) as our guest speaker.

Shane Hamblin
Chair ESA Clinical Weekend
Organising Committee

The Annual Scientific Meeting of the Endocrine Society of Australia and the Society for Reproductive Biology

24th - 27th August, 2014
Melbourne Convention & Exhibition Centre, VIC

The 57th ESA and 45th SRB Combined Annual Conferences are being held at the Melbourne Convention and Exhibition Centre from Sunday 24th until Wednesday 27th August 2014. The aim of these joint conferences is to showcase the breadth of Reproductive Biology and Endocrinology research occurring within Australia and around the world.
Plenary and invited speaker lists are now available on the website http://esa-srb.org.au/

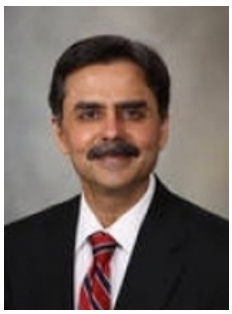
We look forward to seeing you in Melbourne!

Ann McCormack (ESA POC chair)
Rebecca Robker (SRB POC Co-chair)
Kaye Stenvers (SRB POC Co-chair)

ESA SPEAKERS

Adrian Clark
Deputy Principal and Dean of Research and Enterprise St George's, University of London, UK

Benita Katzenellenbogen
Department of Molecular and Integrative Physiology, University of Illinois and College of Medicine, USA



Sundeep Khosla
Mayo Clinic, USA

John Wass
Professor of Endocrinology, Oxford University, UK

ESA AWARDS Website: http://www.endocrinesociety.org.au/awards-and-grants.asp

ESA SENIOR PLENARY AWARD

This award recognises an outstanding research career in the field of Endocrinology in Australia. The award comprises a plaque and a plenary lecture at the Annual Scientific Meeting, and complimentary meeting registration.

Eligibility:
Active ESA member with extensive research experience, output and impact in any field of Endocrinology post-higher degree (PhD, MD or FRACP). The awardees must attend the ASM to present their lecture.

Applications Close: 6 June 2014

ESA MID-CAREER RESEARCH AWARD

This award is designed to recognise an outstanding mid-career researcher in endocrinology. The award comprises a plaque and 20-minute lecture at the Annual Scientific Meeting, and complimentary meeting registration.

Eligible applicants are active ESA members with five to 12 years' research experience post-higher degree (PhD, MD or FRACP) at the deadline of application (exceptions can be made for career interruptions). The winner must attend the ASM to present their lecture. The award will be made by a selection committee comprising the ESA Council members and the Chair of the ESA POC.

Applicants will be notified at the close of abstract submissions for the ASM, and the winner will be asked to provide an abstract for their lecture within three weeks of notification, to be included in the ASM Proceedings.
The ESA encourages all eligible members to apply for this new award.

Application Deadline: 16 May 2014

BRYAN HUDSON CLINICAL ENDOCRINOLOGY AWARD

The Bryan Hudson Clinical Endocrinology Award will recognize the best clinical research presentation at the Annual Scientific Meeting by an active member of the Endocrine Society of Australia early in their career. It will be made on an annual basis.

Eligibility:
Society members who are less than 45 years of age, or are within 10 years of obtaining professional qualifications and who are current financial members of at least 12 months standing.

Applications Close: 6 June 2014

ESA TRAVEL GRANTS TO ATTEND THE ASM

The ESA will provide funds to support travel to the 2014 Annual Scientific Meeting of the Endocrine Society of Australia, to be held 24-27 August 2014, Melbourne, Australia. The amount of funding and the individual success of applicants will be decided by Council. Preference will be given to full time students funded by a scholarship and presenting an abstract at this meeting.

Applications Close: 6 June 2014

ESA / IPSEN INTERNATIONAL TRAVEL GRANT AWARD

Aim: To support younger members of the society to travel to international meetings, laboratories and/or clinics to further their training and knowledge in Endocrinology.
Awards:
One award of $3500 will be granted to assist with the costs of international travel.

Deadline: 1 August 2014
Further information: http://www.endocrinesociety.org.au/awards-and-grants.asp#esa

WE / ESA AUSTRALIAN WOMEN IN ENDOCRINOLOGY (AWE) 2014 TRAVEL AWARDS

Purpose: To provide financial support to younger women involved in Endocrine-related training and/or research who are presenting an abstract at the ENDO Meeting in Chicago, 21-24 June 2014 Website: https://www.endocrine.org/endo-2014#/nav/

Eligibility: Preference is given to Postdoctoral trainees (first three years) and PhD students in their 3rd or 4th year of training at an Australian or New Zealand-based Institution. Depending upon sponsorship levels, applications will be considered from Post-Doctoral Trainees up to 5 years and PhD students.

Applicants must be the presenting author on an abstract accepted for presentation at the Endocrine Society meeting (USA).

Applicants must be current members of the Australasian Branch of Women in Endocrinology, with either financial membership of the ESA or NZSE.

For full information download Application form 2014
Deadline: 24 April 2014

ESA-NOVARTIS JUNIOR SCIENTIST AWARD

The ESA-Novartis Junior Scientist Award is given for the best presentation at the Annual Scientific Meeting by an advanced trainee or a person enrolled for a higher degree (PhD, MD, FRACP). Applicants will be judged initially on the basis of their Abstracts and a short list of applicants will be chosen to present in a special session. Applicants will be informed of the session in which they are to present when acceptances of Abstracts are sent out.

Eligibility:
Nominees must be members of the Endocrine Society of Australia and be an advanced trainee or a person enrolled for a higher degree (PhD, MD, FRACP).

Application Deadline: 6 June 2014

ESA AWARDS Website: http://www.endocrinesociety.org.au/awards-and-grants.asp

SERVIER YOUNG INVESTIGATOR AWARD

The Servier Award is made annually to recognise the best scientific paper published in the 12-month period preceding the closing date for abstracts for the Annual Scientific Meeting by an active member of the Endocrine Society of Australia early in their career.

The award is given for a single publication although up to two additional papers may be submitted in support of the application.

Eligibility:
Society members who are within 8 years of having obtained a higher degree or diploma (i.e. PhD, MD, FRACP) and who are currently financial.

Application Deadline: 6 June 2014

ESA WOULD LIKE TO THANK ESA AWARD SPONSORS

Ipsen Pty Ltd

Novartis Pharmaceuticals Australia Pty Ltd

Servier Laboratories (Australia)

ESA PARTNERSHIPS

ESA adopts Clinical Endocrinology as its Society Journal

Clinical Endocrinology is published monthly by Wiley-Blackwell. It is a high profile international journal with an Impact Factor of 3.396. It is the affiliated journal of the UK-based Society for Endocrinology and now, as a result of a decision by the ESA Council, it has also been adopted as the official journal of the ESA. The ESA President. Peter Ebeling has become a member of the Clinical Endocrinology Board and he will replace Stephen Judd as editor in 2014.

A number of benefits have already flowed as a result of this affiliation:

- All ESA members have free electronic access to the Journal, through the Society's website. This includes all the original scientific papers, the two Review papers in each issue and the Clinical Questions. This access extends to all previous papers published since 1972.
- Members also have access to the Journal's virtual issue of Clinical Questions from previous years, which provide expert opinions about specific clinical issues – a very popular component of the Journal.
- In addition, ESA members have access to a virtual issue of the most downloaded papers published in 2012, including many Reviews, the Editors' Choice papers and some Society Guidelines. Further compilations of articles are planned to assist trainees with Journal Club presentations etc.
- Wiley-Blackwell will publish the abstracts of the Annual Scientific Meeting, giving these recognition as a publication.
- There will be a greater level of recognition for clinical members of the ESA, as invitees for submission of Reviews and Clinical Questions, Commentaries etc.

Other benefits are likely to result as the partnership evolves:

- Clinical Endocrinology has a proposal for the ESA Council to provide a prize for the best clinical case presented by a trainee at the Clinical Weekend meeting. This offers the opportunity for a trainee to see their presentation in print.
- A number of other proposals are in the pipeline, which are designed to provide benefit to members of the ESA in the broader educational area.
- Closer liaison between ESA and SfE, particularly in sharing educational, CPD and training material.

To access the journal:
Use the member log-in on the homepage:
http://www.endocrinesociety.org.au/
Go to membership then Clinical Endocrinology Journal

Australian Endocrinology Research Review

Australian Endocrinology Research Review is an independent medical update. Each edition features 10 key medical articles from globalendocrinologyjournals with commentary fromProfessorCres Eastman and Professor Duncan Topliss on why it matters to Australian practice.

It is free to receive for allAustralian health professionals and is delivered by email as a PDF attachment.**Sign Up here** to receive the publication on a regular basis.
Website: http://www.researchreview.com.au/au/Clinical-Area/Internal-Medicine/Diabetes-Obesity/Endochrinology.aspx

EDM Case Reports

Endocrine Society of Australia is delighted to announce a collaboration with Bioscientifica on their new open access publication, *Endocrinology, Diabetes & Metabolism Case Reports*.

Members of ESA receive a 20% discount on the open access publishing when publishing case reports in the open access publication; ***Endocrinology, Diabetes & Metabolism Case Reports***(submit online via **www.edmcasereports.com**).

Endocrinology, Diabetes & Metabolism Case Reports is a unique, open access resource that publishes and links together case reports, enabling practitioners to communicate findings, share knowledge and convey medical experiences efficiently and effectively; furthering both medical education and clinical practice. The search and browse functionality enables fluid navigation between case reports, facilitating discovery, connections and comparisons; making it the go-to resource across all the many disciplines intersecting with endocrinology, diabetes and metabolism.

ANNUAL GENERAL MEETING

The Annual General Meeting of ESA will be held at
Melbourne Convention Centre on

Tuesday 26th August 2014
All members are encouraged to attend this meeting.

HOT TOPICS

The exceptionally high calibre of research conducted by our members is once again evident in the number of recent articles published in high impact, international, peer reviewed journals. Here we highlight recent outstanding publications by our members.

Whole exome sequencing is an efficient and sensitive method for detection of germline mutations in patients with phaeochromcytomas and paragangliomas

Clinical Endocrinology, 2014, 80, 25-33

McInerney-Leo A, Marshall MS, Gardiner B, Benn DE, McFarlane J, Robinson BG, Brown MA, Leo PJ, Clifton-Bligh RJ & Duncan E.

And

Whole exome sequencing is an efficient, sensitive and specific method of mutation detection in osteogenesis imperfecta and Marfan syndrome

BoneKEy Reports, 456 (2013) doi:10.1038/bonekey.2013.190

McInerney-Leo AM, Marshall MS, Gardiner B, Coucke PJ, Van Laer L, Loeys BL, Summers KM, Symoens S, West JA, West MJ, Wordsworth BP, Zankl A, Leo PJ, Brown MA & Duncan EL

These publications demonstrate the clinical utility of whole exome sequencing for genetic disorders. The Clinical Endocrinology paper uses this technique in patients with phaeochromocytomas or paragangliomas, conditions that may arise from mutations occurring on one of over a dozen genes making screening very costly by conventional methods. This paper attracted editorial comment (Toledo & Dahia, Clin Endo, 80, 23-24). The second paper, in BoneKey, demonstrates the utility of this approach in patients with osteogenesis imperfecta or Marfan's syndrome. In these conditions, the common causative genes (COL1A1 and COL1A2 for Osteogenesis imperfecta, FBN1 for Marfan's syndrome) are impracticably large for efficient screening by conventional sequencing technologies. Both studies show that whole exome sequencing is efficient, sensitive and specific; however, the choice of platform for exome capture can affect the sensitivity of the approaches. The challenge now is to see if this can translate to a timely and effective clinical service for patients.

A novel serogenetic approach determines the community prevalence of celiac disease and informs improved diagnostic pathways

BMC Medicine, 2013, 11, 138

Anderson RP, Henry MJ, Taylor R, Duncan EL, Danoy P, Costa M, Addison K, Tye-Din JA, Kotowicz MA, Knight RE, Pollock W, Nicholson GC, Toh B, Brown MA & Pasco JA.

In this publication the authors explore the value of genetic screening in celiac disease. This is a common concern in the community and results in many people excluding wheat from their diet and/or gastroscopy after positive TG2-IgA serology; however, TG2-IgA as a screening test for celiac disease has high false positive rates resulting in a large number of unnecessary gastroscopies. This paper showed, firstly, that essentially all patients with Coeliac disease have a common genotype (HLA-DQ2.5, DQ8, DQ2.2) and whilst this genotype is not rare the negative predictive value was >98%. Further, a combination of genotyping and more sophisticated serology resulted in a much more efficient and cost-effective means of diagnosing coelaic disease, and reduced the number of gastroscopies required for diagnosis by 40-70%, a huge cost-saving for Australians. The study also determined the population prevalence of celiac disease (1.15% in men, 1% in women). Approx. 9% of the Australian population currently restrict wheat from their diet for various reasons, at an average cost of 2.4x the cost of a non-wheat-exclusion diet disease. For many of these people there is no critical medical reason to do so (as is the case for patients with celiac disease); this too represents a huge potential saving for patients.

Fertility in Turner syndrome

Clinical Endocrinology (2013) 79, 606–614

Hewitt JK, Jayasinghe Y, Amor DJ, Gillam LH, Warne GL, Grover S & Zacharin MR.

This manuscript outlines the magnitude of fertility impairment and the significant risks of pregnancy in women with Turner syndrome. Pregnancy-associated mortality in Turner syndrome is often underappreciated by adult endocrinologists and fertility specialists, and this paper provides some guidelines for the consideration of both child bearing and fertility preservation techniques in this population.

Metastasis of ovarian cancer is mediated by kallikrein-related peptidases.

Clin Exp Metastasis 31:135–147, 2014.

Dong Y, Loessner D, Irving-Rodgers H, Nicklin JL, Obermair A, Clements JA.

This review is an overview of the role played by the Kallikrein-related (KLK) peptidases in serous epithelial ovarian cancer. Metastasis and chemoresistance are the key events associated with the tumor microenvironment that lead to a poor patient outcome. The KLK proteases are aberrantly expressed, in particular, in the more metastatic Type-II tumors. High KLK levels are differentially associated with the prognosis of ovarian cancer patients, suggesting that they not only have application as biomarkers but also function in disease progression, and therefore are potential therapeutic targets. Recent studies have demonstrated the function of these proteases in promoting and/or suppressing the invasive behavior of ovarian cancer cells in metastasis in vitro and in vivo and in chemoresistance.

HOT TOPICS

Secretome and degradome profiling shows that kallikreins 4, 5, 6, 7 induce TGF-1 signaling in ovarian cancer cells.
Mol Oncol. 8(1):68-82, 2014.

Shahinian H, Loessner D, Biniossek ML, Kizhakkedathu JN, Clements JA, Magdolen V, Schilling O.

Kallikrein-related peptidases, in particular KLK4, 5, 6 and 7 (KLK4-7), often have elevated expression levels in ovarian cancer. In OV-MZ-6 ovarian cancer cells, combined expression of KLK4-7 reduces cell adhesion and increases cell invasion and resistance to paclitaxel. The present work investigates how KLK4-7 shape the secreted proteome ("secretome") and proteolytic profile ("degradome") of ovarian cancer cells. Expression of KLK4-7 predominantly affected the abundance of proteins involved in cell-cell communication including increased levels of transforming growth factor b-1 (TGFb-1) and other factors in the TGFb-1 pathway and increased proteolytic maturation of TGFb-1. These data were corroborated in vivo in an ovarian cancer xenograft model. KLK4-7 have a pronounced impact on the secreted proteome, with a strong association between these proteases and TGFb-1 signalling in ovarian tumor biology.

A humanized tissue-engineered in vivo model to dissect interactions between human prostate cancer cells and human bone.
Clin Exp Metastasis. 2014 Feb 8. [Epub ahead of print]
Hesami P, Holzapfel BM, Taubenberger A, Roudier M, Fazli L, Sieh S, Thibaudeau L, Gregory LS, Hutmacher DW*, Clements JA*. *joint senior authors

Currently used xenograft models for prostate cancer bone metastasis lack the adequate tissue composition necessary to study the interactions between human prostate cancer cells and the human bone microenvironment. We introduce a tissue engineering approach to explore the interactions between human tumor cells and a humanized bone microenvironment. Scaffolds, seeded with human primary osteoblasts in conjunction with BMP7, were implanted into immunodeficient mice to form humanized tissue engineered bone constructs (hTEBCs) which consequently resulted in the generation of highly vascularized and viable humanized bone. At 12 weeks, PC3 and LNCaP cells were injected into the hTEBCs. Seven weeks later the mice were euthanized. Micro-CT, histology, TRAP, PTHrP and osteocalcin staining results reflected the different characteristics of the two cell lines regarding their phenotypic growth pattern within bone. Taken together, a highly reproducible humanized model was established which is successful in generating LNCaP and PC3 tumors within a complex the conditions seen clinically more closely than any other model described in the literature to date and hence represents a powerful experimental platform that can be used in future work to investigate specific biological questions relevant to bone metastasis.

PITX2 and non-canonical Wnt pathway interaction in metastatic prostate cancer.
Clin Exp Metastasis 31:199–211, 2014
Vela I, Morrissey C, Zhang X, Chen S, Corey E, Strutton GM, Nelson CC, Nicol DL, Clements JA & Gardiner EM.

The non-canonical Wnt pathway, a regulator of cellular motility and morphology, is increasingly implicated in cancer metastasis. In a quantitative PCR array analysis of 84 Wnt pathway associated genes, both non canonical and canonical pathways were activated in primary and metastatic tumors relative to normal prostate. Expression of the Wnt target gene PITX2 in a prostate cancer bone metastasis was strikingly elevated over normal prostate (over 2,000-fold) and primary prostate cancer (over 200-fold). The elevation of PITX2 protein was also evident on tissue microarrays, with strong PITX2 immunostaining in prostate cancer skeletal and, to a lesser degree, soft tissue metastases. PITX2 is associated with cell migration during normal tissue morphogenesis. In our studies, overexpression of individual PITX2A/B/C isoforms stimulated PC-3 prostate cancer cell motility, with the PITX2A isoform imparting a specific motility advantage in the presence of non canonical Wnt5a stimulation. Furthermore, PITX2 specific shRNA inhibited PC-3 cell migration toward bone cell derived chemoattractant. These experimental results support a pivotal role of PITX2A and non-canonical Wnt signalling in enhancement of prostate cancer cell motility, suggest PITX2 involvement in homing of prostate cancer to the skeleton, and are consistent with a role for PITX2 in PCa metastasis to soft and bone tissues.

Species-specific homing mechanisms of human prostate cancer metastasis in tissue engineered bone.
Biomaterials. 2014 Feb 14. [Epub ahead of print]
Holzapfel BM, Wagner F, Loessner D, Holzapfel NP, Thibaudeau L, Crawford R, Ling MT, Clements JA, Russell PJ, Hutmacher DW.

The development of effective therapeutic strategies against prostate cancer bone metastases has been impeded by the lack of adequate animal models that are able to recapitulate the biology of the disease in humans. Bioengineered approaches allow researchers to create sophisticated experimentally and physiologically relevant in vivo models to study interactions between cancer cells and their microenvironment under reproducible conditions. In this study, transplantation of biodegradable tubular composite scaffolds seeded with human mesenchymal progenitor cells and loaded with rhBMP-7 resulted in the development of a chimeric bone construct including a large number of human mesenchymal cells which were shown to be metabolically active and capable of producing extracellular matrix components. Further, the newly formed ossicle recapitulated the morphological features of a physiological organ bone with a trabecular network surrounded by a cortex-like outer structure. This microenvironment was supportive of the lodgement and maintenance of murine haematopoietic cell clusters, thus mimicking a functional organ bone.

HOT TOPICS

Bioluminescence imaging demonstrated that luciferase-transduced human PC3 cells reproducibly homed to the humanized tissue engineered bone constructs, proliferated, and developed macrometastases. This model allows the analysis of interactions between human prostate cancer cells and a functional humanized bone organ within an immuno-incompetent murine host.

Aberrant GDF9 expression and activation is *associated with common human ovarian disorders*
J Clin Endocrinol Metab, Jan 2014, [Epub ahead of print]
Simpson CM, Robertson DM, Al-Musawi SL, Heath DA, McNatty KP, Ritter LJ, Mottershead DG, Gilchrist RB, Harrison CA*, Stanton PG*

Growth differentiation factor 9 (GDF9) is an oocyte-secreted protein belonging to the TGF-□ superfamily, and is a critical determinant of granulosa cell function and essential for ovulation, oocyte quality and embryo development. Mutations in human(h)GDF9 have been implicated in premature ovarian failure (POF) or polycystic ovarian syndrome (PCOS), as well as in mothers of dizygotic (DZ) twins. In this study, 14 hGDF9 variants were generated by site-directed mutagenesis and expressed from mammalian cells to determine their effects on GDF9 protein production and GDF9 bioactivity.. All 14GDF9 mutations resulted in a significant reduction in growth factor secretion with variants P103S, P374L and S428T being the most disruptive. Of these, mutations observed in mothers of DZ twins (P103S and P374L) completely abrogated GDF9 expression, suggesting that women heterozygous for these mutations would have a 50% reduction in GDF9 levels. Of particular significance, we discovered 3 POF mutations (S186Y, V216M and T238A) that activated the normally latent hGDF9 molecule by decreasing the affinity of the prodomain for its mature growth factor. All three mutants increased granulosa cell proliferation and are presumed to increase the number of developing follicles thus leading to premature depletion of the ovarian reserve. Homology modelling suggests all mutations lie in structurally-important regions of GDF9, hence this study provides evidence that defective GDF9 production and/or activation may contribute to the several common ovarian pathologies in humans.

In older men an optimal plasma testosterone is associated with reduced all-cause mortality and higher hydrotestosterone with reduced ischemic heart disease mortality, while estradiol levels do not predict mortality
J Clin Endocrinol Metab 99: E9–E18, 2014

Yeap BB, Alfonso H, Chubb SAP, Handelsman DJ, Hankey GJ, Almeida OP, Golledge J, Norman PE & Flicker L.
Testosterone (T) levels decline with age and lower T has been associated with increased mortality in aging men. However, the associations of its metabolites, dihydrotestosterone (DHT) and estradiol (E2), with mortality are poorly defined. Participants were community-dwelling men aged 70 to 89 years who were residing in Perth, Western Australia. Plasma total T, DHT, and E2 were assayed from 3690 men, and deaths were obtained by data linkage. Men who died had lower baseline T, DHT and E2. After allowance for other risk factors, T and DHT were associated with all-cause mortality. Higher DHT was associated with lower IHD mortality. Optimal androgen levels are a biomarker for survival because older men with mid-range levels of T and DHT had the lowest death rates from any cause, whereas those with higher DHT had lower IHD mortality.
The importance of this work was recognised and highlighted in the editorial comment (J Clin Endocrinol Metab, January 2014, 99(1):70–72).

Do you have a publication hot off the press?
To have it included in the next Hot Topics!, please forward a pdf of your manuscript and a short (~150 word) summary to the newsletter editor, Nicolette.hodyl@adelaide.edu.au

DATES FOR THE DIARY

2014

15-17 May 2014
Controversies to Consensus in Diabetes, Obesity and Hypertension (CODHy)
Bangkok, Thailand
Website: www.codhy.com/AP

21-24 June 2014
ICE/ENDO 2014
Chicago, USA
https://www.endocrine.org/meetings/ice-endo-2014/endo-2014#/nav/

20 23 July 2014
ISPD
Brisbane
http://www.ispdhome.org/2014/brisbane.shtml

25-28 August 2014
ESA/SRB ASM
Melbourne Convention Centre
http://www.esa-srb.org.au/

27-29 August 2014
ADS/ADEA ASM
Melbourne Convention Centre
www.ads-adea.org.au

7-10 September 2014
ANZBMS ASM
Queenstown, NZ
Website: http://www.anzbmsconference.com/

25-27 September 2014
14th International Workshop MULTIPLE ENDOCRINE NEOPLASIA and other rare endocrine tumours. Vienna
Website: www.worldmen2014.

15-18 October 2014
7th International Congress of the GRS and IGF Society
Singapore
http://www.grs-igf2014.org/default.aspx

14-16 November 2014
IOF 5th Asia Pacific Osteoporosis Meeting
Chinese Taipei
Website: http://iofbonehealth.org/taipei-2014

5-7 December 2014
The 2nd World Congress of Clinical Lipidology
Vienna, Austria
Website: www.clinical-lipidology.com

2015

5-8 March 2015
ENDO 2015
San Diego, CA, USA
https://www.endocrine.org/meetings/endo-annual-meeting-related-pages/past-and-future-endo-meetings

21-23 August 2015
ESA Clinical Weekend
Adelaide
Website: http://www.esaclinicalweekend.org.au/

23-26 August 2015
ESA-SRB ASM
Adelaide Convention Centre
Website: http://www.esaseminar.org.au/

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