



Australasian Division of the
International Academy of Pathology Limited

Newsletters - 2008

Number Two

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Report from the President

One of the principal objectives of the Division is the fostering of education in pathology, and from feedback received this objective appears to have been well fulfilled by the 33rd Annual Scientific Meeting, held in Sydney on 30 May to 1 June 2008.

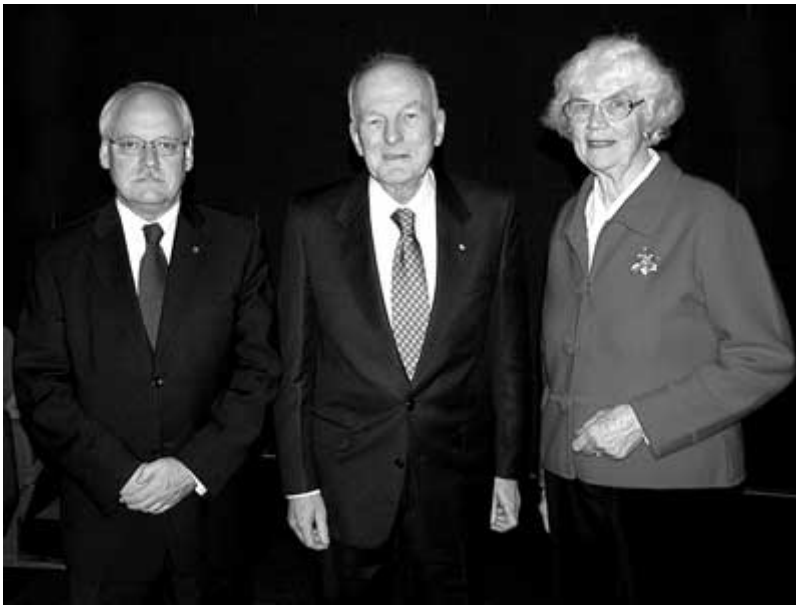
The keynote speakers for the weekend were Dr Zachery Goodman, from the Armed Forces Institute of Pathology, Washington DC and Professor Andrew Churg from the University of British Columbia, Vancouver, Canada,

On Friday, thirteen Companion clubs held their meetings and as usual a diverse and comprehensive fare was on offer with presentations by both senior pathologists and trainees. The highlight of the day was undoubtedly the keynote address by Dr John Rutherford, who recounted his first-hand experiences as Home Office Pathologist involved in the investigation of Dr Harold Shipman, Britain's most prolific killer.

The theme of the Saturday program was liver pathology and Dr Goodman presented lectures on tumours of the liver and hepatitis in the 21st century. These lectures were supplemented by a comprehensive slide seminar which covered the full spectrum of liver pathology. On Sunday the theme was pulmonary pathology with keynote presentations by Dr Churg focusing on malignant mesothelioma and pulmonary vasculitis, and again these were supported by an excellent case-based slide seminar.



Brett Delahunt presenting the Distinguished Pathologist Medal to Nobel Laureate (2006) Robin Warren



Brett Delahunt, Robin Cooke, (Robin Cooke Medal for meritorious service to the IAP), and Roma Cooke.

The Vincent McGovern Memorial Lecture has become an important component of the Saturday program and this year Professor C Soon Lee shared with us his considerable expertise relating to phyllodes tumours and fibroepithelial lesions of the breast. Following on from the success of the three Grey-Green Master Classes for Trainees that were established last year, trainee-focused seminars were presented on each of the days of the ASM. The theme for the Friday seminar was forensic pathology, presented by Dr John Rutherford, Regional Forensic Pathologist from Wellington, New Zealand. On Saturday the topic was neuropathology, with Professor Catriona McLean from the Alfred Hospital as guest presenter, while the final presentation on breast pathology was delivered on Sunday by Associate Professor Michael Bilous, Director of Tissue Pathology at the Institute of Clinical Pathology and Medical Research, Westmead Hospital. These presentations were of a uniformly high standard and were well received by the numerous trainees who braved the 7.30 am start-time.

An important component of our meetings has been the production of a comprehensive set of handouts that accompany the speakers' presentations and for our two main speakers this year,

electronic versions of these were prepared by Professor Robin Cooke. The Academy owes an enormous debt of gratitude to Professor Cooke for this sterling work and also for the seamless production of our newsletter, for which he acts as Editor. It is fitting, in recognition of this outstanding and sustained service, that the Academy has instituted an award for meritorious service in his name. It is further appropriate that the inaugural recipient of the Robin Cooke Medal was Dr Warick Delprado who has worked tirelessly to promote the field of diagnostic pathology and the aims of the Division. In addition to this award, the Academy annually recognises the achievements of a colleague who has made an outstanding and sustained contribution to the science and practice of pathology. This year, in recognition of his groundbreaking discoveries relating to our understanding of the role of *Helicobacter pylori* in the pathogenesis of gastritis and peptic ulcer disease, the 2008 Distinguished Pathologist Medal was awarded to Dr J Robin Warren.

An interesting and informative program has been planned for the 34th Annual Scientific Meeting which will be held on 12 - 14 June 2009. The keynote speakers will be Professor John R Srigley from McMaster University, Hamilton, Ontario, Canada and Dr Christopher Fletcher from the Brigham and Women's Hospital Boston, USA.

Professor Srigley, who is President-elect of the International Society of Urological Pathology and author of the AFIP fascicle on tumours of the male prostate, urethra and penis will speak on the general theme of testicular pathology. Dr Fletcher, who is well known to members of the Division through his previous visits to Australia, will present the Sunday program on soft tissue pathology.

Plan to attend the 34th ASM of your Division – we look forward to seeing you there.

Brett Delahunt
President

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Dermato- pathology Companion Meeting

The session was well attended and received. This year there were 7 speakers, presenting on a range of dermatopathology topics. The interesting case mix included case reports of newly described tumours, unusual stromal reactions in common tumours, old tumours for which there are new therapies (molecular target therapy) and clinical case presentations of patients presenting with dermatological manifestations of systemic disorders. This included a fascinating case presentation by Dr Venugopal of a patient with generalised skin colour change and dark urine as manifestations of advanced metastatic melanoma.

Dr Coleman gave a succinct and up-to-date presentation on premalignant disorders of the oral mucosa. While not strictly dermatopathology, it was a common addition to the case mix of the dermatopathologist.



Dermatopathology club: Squadron Leader Alan Lyons (RAAF-SR), Supriya Venugopal, Richard Bunter, Rooshdiya Karim, Dugald McCallum, Marcella Roman, Group Captain Greg Bruce (RAAF-SR), Vicki Howard, Hedley Coleman, Allan Cala, Squadron Leader Scott de Havilland (RAAF-SR).

A highlight of the session was a presentation by Dr Cala, RAAF-SR an amateur military historian on the topic of Dermatopathology of war and peacekeeping with conditions from "trench foot" to modern day problems of Leishmaniasis, a condition which is currently encountered in troops in Iraq. Three high ranking officers from the Royal Australian Air Force Specialist Reserve were in attendance. Group Captain Greg Bruce was given an opportunity to respond with interesting insights into skin conditions afflicting the military over the ages.

Vicki Howard
Convenor

Editor's Comment

I saw a few examples of Trench Foot when I visited a pathology museum in the University of Padua some years ago. The specimen jars were very murky and the feet were a homogenous white colour. They did not lend themselves to making a photograph that would be useful for demonstration of the subtle features of this historical condition.

Dr Cala mentioned during his talk that he thought that there might be at least one example of this in the Pathology museum at the Forensic Pathology Department at Glebe. Dr. Jo Duflou very kindly asked his photographer to take some photographs of the two amputation specimens they have, and he sent them to me. I then enhanced them, and I was pleased to see how much colour was restored with a minimum of tweaking. The blistered, necrotic skin, and even the light green colour of the gangrene can be seen.



Trench foot amputated in 1914. Note the blistering and the gangrene. (Courtesy of Jo Duflou and his photographer)

The illustration is one view of one of the feet. Of course the colour is not captured in the black and white reproduction.

Information obtained from the web:

Trench foot (now called non-freezing cold injury) appeared in the soldiers fighting in the trenches in the winter of 1914. One report says that there were about 77,000 casualties amongst the allied forces. The condition was characterised by pain, swelling and then numbness of the feet. Blisters appeared and secondary infection followed, especially fungal infections. This was followed by gangrene.

It was quickly recognised as being a new condition, and not frost bite because it occurred at temperatures of around 16 degrees Celsius. The possibilities were – exposure, diet and infection. Ultimately it was decided that it was caused by circulatory changes in the foot caused by cold, wet and pressure of tight fitting boots.

Conservative treatments were used, and by relieving the pressure and drying the feet, recovery occurred. Amputation was a last resort, and many amputations were done. Preventive measures were aimed at improving the foot wear and trying to keep soldiers provided with dry socks. The measures were considered to be successful because the prevalence of this condition was greatly reduced by 1917-1918.

Robin Cooke

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Paediatric club speakers Gareth Jevon, Susan Arbuckle, Adrian Charles, CW Chow, Shen Khor and Jill Lipsett.



Jack Kariks and Robin Cooke. Jack is now 82 and this will be his last meeting. He worked for many years in PNG as a medical officer, and later as a pathologist. He then went to Brisbane for a few years as pathologist at Wolston Park Hospital. Then to the Forensic Pathology Department in Sydney, and for some years after that he ran a small private practice in Sydney.



Michael Bilous with some registrars after his master class on Breast Pathology.



Board members May 29 2008 Kon Muller, Richard Jaworski, Gina Skuza, Stephen Fairy, Vicki Howard, David Ellis, Jane Nankervis, Brett Delahunt, Bastiaan De Boer, Soon Lee, Bob Eckstein, Peter Bethwaite, Jan Kencian, Robin Cooke, Jan McLean.



John Rutherford, the Keynote speaker.



Doug Henderson, Jennet Harvey, Marian Pryanthi, Benhur Amanuel.



Jenny Hamilton, Grace and Sutjahjo Endardjo (Sec of the Indonesian Division of IAP), Greg Manderson (Ventana).



Paediatric pathologists Jill Lipsett, Lynette More, Fiona Brown, Jane Dahlstrom, CW Chow,

Adrian Charles, Susan Arbuckle.



Warick Delprado, Robin Cooke, Zachary Goodman, Stephen Fairy, Brett Delahunt, Robin Warren.



Catriona McLean and students after her master class lecture on brain biopsy and its problems.



Brett Delahunt presenting the first Robin Cooke Meritorious Service Medal for the IAP to Warick Delprado.



Stephen Allpress, Cynric Temple-Camp, Jullie Beatson, Andrew Tie, Mike O'Sullivan (an engineer from NZ).



Graham Windrum, Jeffrey Searle, Afaq Khan.

Lentiviral-mediated RNA interference for type II TGF-beta receptor inhibits renal fibrosis

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AIMS

Our objective was to determine whether inhibition of type II TGF-beta receptor (TGF-beta_{II}) could reduce renal fibrosis in a murine model of chronic kidney disease (CKD). We used a lentiviral-mediated RNA interference (RNAi) strategy to target TGF-beta_{II} in the kidney of CKD mice. We found that TGF-beta_{II} RNAi significantly reduced renal fibrosis and improved renal function in CKD mice.

METHODS

The TGF-beta_{II} gene was cloned into a lentiviral vector and packaged into lentiviral particles. The lentiviral particles were used to infect CKD mice. The expression of TGF-beta_{II} was measured by RT-PCR and Western blotting. Renal fibrosis was measured by Masson's trichrome staining.

RESULTS

The TGF-beta_{II} RNAi significantly reduced TGF-beta_{II} expression (Figures 1-3). It also significantly reduced renal fibrosis (Figures 4-6) and improved renal function (Figures 7-9). The TGF-beta_{II} RNAi also significantly reduced the expression of TGF-beta₁ and TGF-beta₂ (Figures 10-12).

CONCLUSIONS

Inhibiting TGF-beta_{II} expression in CKD mice significantly reduced renal fibrosis and improved renal function. TGF-beta_{II} RNAi may be a potential therapeutic target for CKD.

DISCUSSION

Our findings suggest that TGF-beta_{II} is a potential therapeutic target for CKD. Inhibiting TGF-beta_{II} expression may reduce renal fibrosis and improve renal function in CKD mice. This may be a potential therapeutic strategy for CKD.

First prize for a registrar poster.

GARVAN INSTITUTE OF MEDICAL RESEARCH

Overexpression of Notch1 is an early event in the development of breast carcinoma and is associated with the Her2 subtype of breast carcinoma

Sarah J Zandewil, Sandra O'Toole, Ibrahim Zaidan, Ewan Miller, Duncan McLeod, Catherine Maher, Adrienne Morry, Paul Cres, Noam Murphy, Anne Hamilton, Andrew Spillane, C Soon Lee, Susan Hemshall, Robert Sutherland, Elizabeth Musgrove

Breast Cancer and Cell Cycle Groups, Cancer Research Program

Background

There is increasing evidence that deregulation of developmental pathways such as Hedgehog and Notch are involved in the progression and development of breast carcinoma. A greater understanding of these processes may identify new therapeutic approaches to the treatment and prevention of breast carcinoma, particularly women with pre-invasive and early stage disease.

The Notch signalling developmental pathway (Figure 1) is important for tissue development and homeostasis. Notch signalling is involved in breast organogenesis and is a regulator of mammary stem cells. Signalling through the Notch1 receptor has been previously linked with high grade, poor outcome breast carcinoma.

Figure 1: Delta and Jagged ligands bind to Notch receptors (Notch1-4) to cause receptor cleavage and translocation of the Notch intracellular domain to the nucleus where it facilitates down stream target genes.

Aim

To investigate Notch1 expression by immunohistochemistry in two patient cohorts with a range of breast lesions and correlate pathway activity with carcinoma progression, molecular sub-types and patient outcome.

Method

Immunohistochemistry (IHC) was performed on formalin fixed paraformaldehyde (FFPE) breast tissue of patients in two independent cohorts. The Garvan Royal Prince Alfred Hospital Progression cohort contains 222 patients with a range of normal ducts, usual ductal hyperplasia (UDH), ductal carcinoma in situ (DCIS) and invasive ductal carcinoma (IDC). The Garvan-St Vincent's Hospital Outcome cohort contains 292 patients with invasive breast carcinoma with median follow up of 64 months.

IHC was performed using a commercially available anti-Notch1 antibody (sc-9170). Notch1 cytoplasmic staining was scored for the percentage of tumour cells which stained and the intensity of the staining (Figure 1A). Endothelial cells were used as the positive control. Smooth muscle and a rabbit isotype IgG were used as negative controls (Figure 1B).

Notch1 over-expression was defined as cytoplasmic staining in >47% of tumour cells (n=94/228).

Figure 2: Notch1 cytoplasmic staining intensity and tissue controls.

Results

In the Progression cohort, IHC analysis showed an incremental increase in Notch1 expression from normal ducts to UDH, and from UDH to DCIS. A slight but significant decrease in Notch1 expression was observed between DCIS and IDC (Figure 3). There was a further progressive increase in Notch1 expression between grades of DCIS. No increase was observed between IDC grades. Notch1 expression also increased significantly between grade 2 DCIS and IDC and grade 3 DCIS and IDC (Figure 3B).

Figure 3: Garvan Royal Prince Alfred Hospital Cohort (n=222)

Figure 4: Garvan St Vincent's Hospital Cohort (n=292)

Notch1 expression	Her2 expression	Notch1 overexpression (%)
Low	Her2 negative	10.0
Low	Her2 positive	15.0
High	Her2 negative	20.0
High	Her2 positive	35.0

In the Outcome cohort, Notch1 overexpression was not prognostic for disease recurrence or patient death on Kaplan Meier analysis (Figure 4B, C) but strongly associated with the Her2 subtype of breast carcinoma as defined by overexpression of the Her2 receptor and loss of the oestrogen receptor by IHC (p=0.0122) (Figure 4A). No correlation was observed between Notch1 overexpression and clinicopathological parameters, cell cycle proteins or the remaining P53 subtypes.

Conclusion

Overexpression of Notch1 is seen early in breast carcinogenesis and shows a progressive increase with the development of atypia and malignancy and may contribute to the development of the Her2 subtype of breast carcinoma as there is an enrichment of tumours which overexpress Notch1 in the Her2 subtype (Figure 5).

Figure 5: Proposed mechanism for development of the Her2 subtype of breast carcinoma

First prize for a poster by a pathologist.

Pathology Update
2009 in conjunction
with
XXV WASPaLM



Ona Marie Faye-Petersen



Lester Thompson

Anatomical Pathology

In the anatomical pathology program, the range of topics has been designed to suit both the general anatomical pathologist as well as those with special interests, and includes symposia on breast, liver and lymphoma pathology. Of particular note, will be presentations given by US head, neck and endocrine pathology expert, Dr Lester Thompson, including a session on the challenges associated with diagnosing neoplasia of the salivary glands.

Dr Thompson will also present at one of the cross-discipline sessions, a feature of the WASPaLM programme. His talk entitled 'What is a small round blue cell tumour anyway?' will cater for those delegates with an interest in anatomical pathology and/or oral pathology.

Similarly, another session will see the interests of Anatomical and Paediatric pathology combined.

This session, featuring an approach to placental examination will be presented by the world-renowned, Associate Professor of Pathology and Obstetrics and Gynaecology at the University of Alabama, Ona Marie Faye-Petersen.

Associate Professor Faye-Petersen is well-recognised for her expertise in fetoplacental pathology and evaluation of pregnancy complication and loss, and her talk is expected to be a highlight of the anatomical pathology program.

Forensic Pathology

Forensic pathology is always a popular conference stream, and WASPaLM's 2009 line-up of sessions is unlikely to disappoint. Presentations include advances and controversies in

paediatric forensic pathology, pandemics and bioterrorism, recreational deaths, sudden death, and the use of CT imaging in forensics to name a few.

The Congress committee is especially delighted to have Dr Michael Pollanen, Chief Forensic Pathologist of Ontario, Canada as a speaker.

Dr Pollanen has been directly involved in forensic investigation of war crimes and miscarriage of justice including the appeal of the Steven Truscott case that resulted in a wide ranging review of the Canadian approach to forensic paediatric cases. Among other topics, Dr Pollanen will be discussing anthrax autopsies of which he has had personal experience.

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**IAP Australasian
Division
Scholarship
Programme**

The Australasian Division of the IAP is offering two scholarships which include the air fare and expenses (conference registration and accommodation) of pathologists or senior pathology trainees to attend the annual general meeting of the Division. This meeting is usually held on the first weekend in June. (in 2009 it will be held on the second weekend in June.)

The successful scholars will be able to spend one week either before or after the conference as an observer in a pathology laboratory in Australia.

Accommodation expenses will be covered for this week as well.

(Applicants need not necessarily be current members of the Australasian Division.

Nominations can be made by Members of the Division on behalf of overseas pathologists.)

Preference will be given to pathologists from the South Pacific Area who are working in relative isolation and who do not normally have the opportunity to attend such conferences.

The meeting lasts for 3 days. Day one (Friday) consists of a series of lectures on a wide range of subjects. The next two days each have a theme which is addressed by an invited international expert. Some of the subjects may be too specialized for the selected scholar but there are many topics of more general interest.

Applications and nominations must be received by February 1st, 2009.

For more information consult the web page.

Send all applications and nominations to
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Howden Medical Books

David Leask did not attend the IAP meeting in 2008 because of illness. This was the first meeting he has missed since the Division was founded. At the stand this year we were welcomed by his son, Tim, who has now taken over the running of the business. Welcome to the 'club' Tim. We wish David well.

The new address and contact details are as follows. Either Jane or Tim will answer the telephone.

Howden Medical Books
Postal Address: PO Box 2085, Rangeview VIC 3132
Phone: 02 6686 7302
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IAP ASM 2009

**34th Annual Scientific Meeting
of the Australasian Division of the International Academy of Pathology Limited**

Date: June 12-14, 2009

Venue: Sydney Convention & Exhibition Centre, Darling Harbour, NSW, Australia

Topics:

Testis - Presenter John Srigley, McMaster University, Ontario, Canada

Soft Tissue - Presenter, Christopher Fletcher, Brigham and Women's Hospital, Boston, USA

Further information:

E-mail: iap@rcpa.edu.au

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Tel: 61-2 8356 5898

PLEASE NOTE THE DATES FOR THIS YEAR ONLY, ARE THE SECOND WEEKEND IN JUNE. That is JUNE 12-14

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