



# The Society for Free Radical Research A U S T R A L A S I A

## NEWSLETTER March, 2005

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The Executive would like to thank all those who have contributed to this issue of the Newsletter. Special mention should be made to the efforts of the Organising committee for the successful 13<sup>th</sup> Annual Conference of SFRR(Australasia), held in Christchurch, New Zealand, Dec 2004 : details and reports on the event are enclosed in this Newsletter. As always, the Executive will continue to keep members informed of recent and up-coming events in Australasia and elsewhere around the globe via the current 2005 "Diary". Please feel free to submit relevant articles to the Secretary if you wish the information to be made available to the members of SFRR(A).

## **Membership Fee Changes**

It was decided at the 2004 SFRR(Australasia) AGM that the annual fee for membership of the Society, would be included in the cost of the registration to attend the annual conference. Therefore all delegates of the 13<sup>th</sup> Annual Meeting held in December 2004, in Christchurch, will now be financial members of SFRR(Australasia) for 2005.

To keep the collection of fees from non-conference delegates in line with this change, the annual membership fees will now be due in January (not July as previously).

The form to pay the 2005 SFRR(Australasia) membership subscription is included at the end of the newsletter. Please note that due to bank charges, cheques made payable in \$NZ are no longer accepted. However, electronic funds transfer from NZ accounts will be possible.

It is now possible to pay subscription fees by electronic bank transfer. For membership to be effective, and to receive a receipt for tax purposes, members opting to pay electronically must send the usual membership form to the Treasurer (Des Richardson). Contact Des for further details

## **Research Profiles added to SFRR(Australasia) Website**

Members may now have their Research Profile (typically 1 – 2 pages) added to the SFRR(Australasia) website. Please email your research profile, in the form of a PDF document, to the Secretary: [c.hawkins@hri.org.au](mailto:c.hawkins@hri.org.au)

# Minutes from the 2004 AGM

Held on 4<sup>th</sup> December 2004 at the Christchurch School of Medicine and Health Sciences, Christchurch, New Zealand.

Meeting opened at 5.15 pm –

The President Ian Dawes welcomed all the delegates attending the 13<sup>th</sup> Annual meeting of the SFRR(A) and thanked the members for giving their time to attend the AGM.

## (1) Apologies

- Silvia Gebicki and David Pattison

## (2) Matters arising from the previous minutes (published in the March 2004 newsletter)

- Previous minutes accepted as a true and accurate record of the events of the 2003 AGM by Des Richardson, seconded by Mike Davies.
- Membership – see below.
- Organisation of the biennial meeting of the SFRR(International)
  - Ian asked Des Richardson if he was still interested in organising the SFRR(International) meeting in 2008 or 2010. Christine Winterbourn queried whether we had the member base to support such a meeting. Steven Giesege added that the COMBIO meeting was to be held in New Zealand in 2009. After some discussion it was agreed that Sydney would be the most viable centre and that Ian Dawes would canvas opinion amongst Sydney-based researchers as to whether a bid should be made. Action : Ian Dawes

## (3) Reports from SFRR(A) Executive

### President's Report

Ian thanked everyone attending the AGM. He also thanked Tony Kettle and the organising committee (Christine Winterbourn, Mark Hampton and Steven Giesege) for all the hard work they had put into the organisation of a really great meeting. There were 115 attendees, the science presented was excellent, there was a great atmosphere and the meeting was likely to make a small surplus. Ian mentioned that the previous meeting was in Kyoto (Food Factors and Free Radicals), as a combined meeting with the Japanese branch of the society. As only 19 delegates were able to attend the Kyoto meeting, it was important to ensure a successful return this year.

Ian reported that the SFRR(A) website had been successfully transferred from the HRI to UNSW. He thanked Geoff Kornfield for the smooth transfer of the website and explained that the problems with the web server were due to UNSW and that this had now been fixed.

The 14<sup>th</sup> meeting of the SFRR(A) will be held at Griffith University, Gold Coast from 2 – 4 December, 2005. The organisation of this meeting is underway, and the committee is chaired by Jiri Neuzil. An invitation to attend the meeting will be extended to SFRR(Japan).

Ian reported that this year the society had invested in 11 scholarships for travel to the Christchurch meeting, and had supported 2 PhD students to attend the SFRR(International) meeting in Buenos Aires (May 2004). The heavy investment in student travel grants has improved the attendance at the meetings, which is great, but it has raised the issue of how the society can continue to finance travel grants. Ian stressed that those applying for SFRR(A) travel grants should be financial members of the society.

## **Secretary's Report**

Clare reported that the member email database has been updated by removing addresses as requested by prior members and also taking out addresses that bounce. She added that new members are added into the database when she is notified by the treasurer. This email list proved very useful in forwarding conference information and notices to SFRR(A) members.

The email addresses of financial members of the SFRR(A) were passed to the secretary of the SFRR(International) so that Australasian members will now receive notices and newsletters from SFRR(International) and be able to vote in the International society elections.

Clare also outlined that she communicates with the web manager (Geoff Kornfield) when updates and links need adding to the website and when problems occur.

## **Treasurer's Report**

### ***Summary of Accounts as of 2<sup>nd</sup> December, 2004***

***Opening Balance: (from last Treasurer's report of 2/12/2003) = \$ 55,488.66***

### **Current Financial Members as of 2/12/2004:**

(2004: 32 Australians and 6 New Zealander's; TOTAL = 38)

(2003: 33 Australians and 12 New Zealander's; TOTAL = 45)

### **Income:**

**1. Deposits in Cheque Account Bearing Interest Balance: \$14,076.53** (as of 2/12/2003)

Subscriptions : \$1035 + those promised at Christchurch conference

**Final Balance: as of 16<sup>th</sup> Aug: \$9843**

### **2. Term Deposit of \$10,000**

Interest Accrued to 7/9/2004 = \$350.65

**Total : \$10,818.67 (reinvested for 5 months on 7 Sept 2004)**

### **3. Term Deposit of \$30,000**

Interest Accrued Since Last Report = \$1641.56

**Total: \$32,585 (reinvested for 8 months on 23 Aug 2004)**

***Current Balance of all accounts (Including Term Deposits) as per last bank notifications:***

**\$ 53,246.67**

### **Expenditure:**

Public Liability Insurance –Austbrokers RWA Pty Ltd \$834.51

Affiliate Membership ASMR July 2004-June 2005 \$208.00

Two Competitive Travel Grants of \$2000 each to attend the \$4000

International Society of Free Radical Research, Buenos Aires

11 SFRR(A) Travel Awards to Christchurch \$9050

Account Service Fees (as of last Bank Statement) \$54.49

### **Comments:**

- Bank fees of \$10 AUS are charged for each subscription in New Zealand dollars. This needs to again be examined. This problem was noted in my last five Treasurer reports. Perhaps subscriptions can be merged with the conference attendance.
- Memberships should be paid by cheque or money order. Cash will not be accepted.

- A total of \$43,403.67 is in Term Deposit Accounts. This is to take advantage of the far greater interest offered. The money can be withdrawn at any time for a small fee.
- Profit will be returned from the Christchurch conference.

#### **(4) Membership**

##### **Membership fees and conference registration**

It was proposed that the membership fees for SFRR(A) will, as of the Christchurch meeting, be included in the registration costs for the annual conference. This means that all the delegates attending the 2004 meeting are financial members for 2005. Membership fees will now be collected in December and not July. Mike Davies proposed that anyone that has paid 2004-2005 membership and attended the 2004 annual conference and wishes to claim 50% of their membership fee back should contact Des Richardson.

For future meetings, there will be a reduced registration fee for non-Australasian delegates that does not include membership of the society.

However, we still need a mechanism in place to allow members not attending the annual conference to pay the SFRR(A) subscription fees. Members can send cheques / money orders directly to the treasurer, but cheques must be made out in AU\$ or a AU\$10 bank fee applies. Margret Vissers asked if members could be given the SFRR(A) bank details to enable the electronic transfer of membership fees – this would facilitate the collection of fees from New Zealand members, in particular.

(ALSO OUTLINED ON P.2)

##### **Student Travel Grant Subsidies**

This topic provided much discussion. In summary, it was agreed that the provision of 10 student travel grants by SFRR(A) was quite generous, especially given the size of the society. These grants were awarded this year to ensure that the 2004 annual meeting was well represented given the relatively few delegates able to attend the 2003 meeting in Kyoto. It was not expected that the society would offer this many travel grants to attend future meetings – to a maximum of \$5000, was proposed to be a more realistic option for future meetings. It was stressed that in future, applicants for the travel grant must be financial members before sending in applications for travel awards.

Roland Stocker proposed the motion that money to cover student travel awards is not required to come from the conference budget. This motion was seconded by Steven Gieseg. Several members agreed that the provision of student travel grants by the conference organisers would put too much pressure and stress on the committee organising the meeting, especially as it is difficult to know exactly how much money the conference will make until the conclusion of the meeting. Mike Davies mentioned that it has been possible previously to obtain sponsorship of travel awards from companies – companies will often contribute to a conference rather than to the society.

##### **New Members**

Ian reported that he had performed a search using Web of Science with the terms “Australian” and “oxidative stress” and “free radicals” and with Mike Davies had been trying to recruit potential new members / research groups to the society. He asked that if any members know of researchers that may be interested in SFRR(A) to pass on email addresses to the secretary (c.hawkins@hri.org.au).

### **(5) SFRR(A) Website**

It was suggested by Mike Davies that a good way to update the SFRR(A) website would be to include member research profiles as PDF documents. Any members interested should email Clare ([c.hawkins@hri.org.au](mailto:c.hawkins@hri.org.au)) a PDF file containing their research profile, this will be added to the website.

### **(6) Future Meetings**

2 – 4 December 2005, Griffith University, Gold Coast, Australia.  
Organisation for this meeting is underway.

Tony Kettle reported that he was organising the International Mammalian Peroxidase Conference in Queenstown, February 2007 and asked whether members would like SFRR(A) meeting to be incorporated into this conference. Ian was concerned that the Lorne conferences are also in February.

It was agreed that the 2006 meeting will be held in Perth, Kevin Croft to organise. Hopefully this will attract a number of delegates from SE Asia.

### **(7) Other Business**

None

Meeting closed at 6.00 pm –  
Clare Hawkins (Secretary)

## Conference Reports

### XII Biennial Meeting ISFRR, Buenos Aires, Argentina (5 – 9 May 2004)

**Rachael Dunlop** (pictured below with Angelo Azzi (left) and Kelvin Davies (right))



I have to admit, I was slightly nervous about travelling to South American having only been to Europe and Japan in my short travelling life. And considering my journey was to take me via Auckland, Chile then across the Andes to Buenos Aires...did I mention across the Andes? Have you not seen the film/read the book “Alive”? You know the one where survivors are forced to eat each other to survive? A classic tale of human endurance and absolute TERROR! And this from a girl who has a deep seated fear of flying so therefore logically, a morbid fascination with stories about plane crashes. Like that scene in Castaway when the plane goes down in spectacular fashion; but that’s just the movies right? Well at least according to the “safety card in your seat pocket”. You know those cute little cartoon pictures where the plane lands gently on the water, the chutes gently unfurl and we all take our high heels off to glide into the safety of the life raft – that is as long as you DON’T INFLATE YOUR LIFEJACKET UNTIL OUT OF THE AIRCRAFT. That’s what Tom Hanks did wrong...that must be it.

Suffice to say, I survived the crossing of the Andes and they were absolutely spectacular. In my haste to get the best view however, (hate aisle seats) I almost ended up in the laps of two gentleman who were also on their way to BA, had also originated their journey in Sydney and happened to be gainfully employed as nuclear scientists at Lucas Heights! What are the chances! They were to end their journey in a small town in the outskirts of BA to be trained in the fine art of operating the sister reactor to Sydney’s newest nuclear facility, recently christened OPAL. What luck I thought, after they offered me a ride to town in their chauffeured company cars, since according to my guide book the bus was to take over 2 h.

But back to the conference. My boss was also to attend, but he had to take the bus (sorry Ken). In fact the Australian contingent was small but very capable, consisting of Ralph Watts from CCIA in Sydney, myself and the aforementioned Dr Ken Rodgers, group leader of the Cell Biology Unit at the Heart Research Institute. I was rather excited at the prospect of meeting some of the greats of free radical biology and protein metabolism. All the big names were presenting, (however, at the risk of sounding like a desperate about-to-get-PhD-looking-for-overseas-postdoc-position they will remain anonymous). Both Ken and myself presented posters on our favourite subject, oxidised proteins. By some as yet unknown oversight, mine was awarded a gold star with “Young Investigator Award” stamped on it. (That’ll show those nuclear-scientist-physics-boffins). The conference ran in parallel sessions covering everything from iNOS, eNOS, protein degradation, mitochondria and apoptosis, with Free Radical School thrown in prior to the official sessions beginning (why did I have that last cerveza?!). The latter was particularly beneficial to brush up on those free radical concepts one may have neglected to remember and certainly furthered my appreciation for subsequent presentations. And of course, one can not give a conference report without mention of the conference dinner which was very lavish complete with an equally impressive tango performance. Another Argentinian speciality which we were also pleased to partake of was the delights of Argentinian beef, served up for lunch at various restaurants in close proximity to the conference venue (the impressive Crowne Plaza Panamericano with amazing views from the rooftop pool). All up, a very rewarding and stimulating conference, not just for the impressive science but also the opportunity to meet so many colleagues who’s work I have long admired. My only regret was not making it to Iguazu Falls, arguably the most impressive in the world. But not to worry, I will definitely be back to Argentina, just as soon as I stop reading all those stories about spectacular plane crashes. Because as they say in the airline business, it’s not flying people are afraid of, it’s crashing. Indeed.

**13<sup>th</sup> Annual Meeting of SFRR(Australasia),  
Christchurch, New Zealand (3 – 5 December 2004)**



## 13<sup>th</sup> Annual Meeting of SFRR(Australasia), Christchurch, New Zealand (3 – 5 December 2004)

### Vanessa Agon

The 2004 SFRR(A) conference was a great excuse for me to have my first visit to New Zealand, and to present my project as well. It has given me a chance to meet many scientists and extend my knowledge to a vast area of protein oxidation. The first day was a very busy one, consisting of a series of talks and of course, good food. Late in the afternoon was the first social event, the poster presentation. Good quality posters were on display that covered a range of topics including HOCl, myeloperoxidase, DOPA and other free radicals. The second day was just as busy as the first with more interesting oral presentations and a repeat of the poster presentation as well. After a hectic day, the conference dinner was highly anticipated. Everyone was allocated their seats which proved to be a very efficient way of us all interacting with other delegates. The buffet dinner was great and so was the presence of Santa Tony giving away gifts from sponsors. Towards the end of the dinner was a song number from Bo (and everyone else), who composed a free radical song. Finally, the last day of the conference arrived and after three eventful but worthy days, came to an end. I am really grateful to have been a part of such a successful conference.

### Geoffrey Kelso

The conference comprised an interesting series of communications and collection of posters on current free radical research from the clinic, molecular biology, biochemistry, food science and the chemistry laboratory. Oral presentations of particular interest included those by Professor Christine Winterbourn on the reaction of superoxide with tyrosine radicals, Lynette Ferguson on the antioxidant properties of an anthocyanin-rich New Zealand kumara and her personal experiments involving consumption of anthocyanin-rich flowers, Jiri Neuzil on the anticancer properties of  $\alpha$ -tocopherol succinate, Mike Berridge on a plasma membrane electron transport system, Ian Dawes on the response of yeast to oxidative stress and J Wu on nitrated  $\gamma$ -tocopherol. The poster sessions provided an opportunity to discuss research findings and ideas with a number of attendees who were all forthcoming about their work. To the delight of our group Frances Blaikie was awarded a prize for her poster on mitochondria-targeted spin traps. The conference also provided our group with the opportunity to meet with Jiri Neuzil and initiate a joint research project. I thank the organising committee for providing me with an opportunity to present some of my PhD research on mitochondria-targeted antioxidants and for a student travel grant.

### Gus Maghzal

The 13<sup>th</sup> SFRR Australasia conference was my first free radical conference. It was therefore a highlight to meet and discuss science with leaders in the free radical field in a very relaxed and informative environment. The oral presentations were of very high standard and were highlighted by Stan Hazen's talk on Myeloperoxidase as a susceptibility factor in the development of heart failure. The first day featured four very interesting sessions and the talks were wide-ranging, with the highlights for me being Michael Fenech's "Genome health nutrigenomics" and Sabina Belli's "protein oxidation in extracellular matrix stabilisation in a parasitic protozoan". This latter presentation probably had the most intriguing pictures, which demonstrated the autofluorescence of intact protozoan oocysts. The second day featured a lunchtime poster session with a large number of high quality posters. The day ended with the conference dinner, which provided one of the most entertaining moments of the conference (of course, Bo Åkerström's Free radical song). Overall, the meeting was very well attended and organised with all presentations running smoothly and to time, which left enough time for discussion. I would like to thank the society for providing funding that allowed me to attend and present data at this meeting.

### Robyn Midwinter

From the chemical to the clinical, the Society for Free Radical Research Conference held this year in rainy Christchurch had something for everyone. For such a seemingly specialized field, an extremely diverse range of talks was presented this year. The conference, which was both informative and interesting, had many dynamic speakers with a strong presence from the younger investigators along with some perennial attendees. From finally figuring out what everyone is talking about when they discuss the importance of DOPA, to some of the clinical aspects of MPO, the conference had something for everyone from the general to the detailed. I particularly enjoyed Prof. Hoggs' talk about how cross-strand disulphide bonds can act as switches. These switches act by forming or breaking a disulphide bond in a particular areas of the receptor to induce conformational changes, in such a way the receptors are able to rapidly respond to stimuli. He also indicated the possibility of a generic disulphide bond switch occurring in other cytokine receptors, and that oxidative stress may be the trigger for the disulphide switch. This was a wonderful opportunity to broaden my horizons a bit and to pick up some ideas that I could bring back to my own area of research. I would like to thank the SFRR(A) for their financial support for allowing me the opportunity to attend this meeting.

## Philip Morgan

I went to Christchurch in December  
To have a "radical" time  
The secretary said to write a report  
So here it is in rhyme

I went to talk on SLE:  
Systemic Lupus Erythematosus  
It's a chronic autoimmune disease  
But I don't know if they suffer from halitosis

I heard from experts in their field  
And many a talk was a winner  
Christchurch itself was very nice  
And there was a conference dinner...

My new knowledge of oxidants and disease  
Has given me more ideas  
I hope to attend the next conference too  
And share more results with my peers

A big thanks to SFRR(A)  
For the generous travel award  
To help me think in my PhD studies  
Instead of just getting bored



## Natalie Ward

The 2004 SFRR(A) conference in Christchurch provided me with my first and much anticipated trip to New Zealand. It also gave me a chance to put my society membership to use and actually attend one of the meetings! Despite not having enough time to tour around New Zealand, the conference did provide me with a chance to finally meet a lot of the people I have emailed, read or heard about over the years, and at last put some names to faces. I found the meeting to be extremely enjoyable and friendly, while also covering a wide range of topics in free radical research. Being allotted my talk in the first session enabled me to then relax and enjoy the rest of the talks (which thankfully all ran to time) as well as have a chance to look over the posters. Providing food and drinks during the breaks and posters sessions certainly made this easier to do. The conference dinner on Saturday night was great fun, and mixing up the seating plan gave us all a chance to meet even more people. Overall, I had a great time and certainly look forward to the next meeting in sunny Perth!

## Xiufang Wang

It was a rewarding experience to attend the 13th Annual Conference of the SFRR in 2004. Thanks to the effort of the conference organisers, this was a successful meeting. Many interesting talks, which encompass the diverse areas of free radical biology and chemistry, gave me a deep impression. I was especially interested in two of the nine sessions of the conference, which are "Cellular Oxidative Stress and Apoptosis" and "Mitochondria and Electron Transport", since there are strong links with my research area, which is focused on the role of mitochondria in apoptosis induced by anti-cancer drugs. Taking the advantage of the travel grant that the SFRR offered it to me, I had a chance to learn visit the beautiful New Zealand and meet the key people in free radical research from New Zealand and Australia. I especially enjoyed the plenary talk "Recent insights into the many links between myeloperoxidase-generated oxidants and cardiovascular disease" given by Stanley L. Hazen. Another lecture I would like to point out was given by Geoffrey Kelso and was titled "Mitochondria targeted derivatives of ebselen". Geoffrey Kelso comes from the laboratory of the University of Otago, who has developed the strategy of the use of mitochondria-targeted antioxidant to study mitochondrial function. Overall, I will utilise the new knowledge I acquired during the successful and high quality SFRR annual meeting, which I had the opportunity to take part in, in my own research.

## Alison Winger

It was clear from the moment I registered that I was in a strange place. Coming from a strong plant biochemistry background, listening to a large number of talks discussing oxidative stress in the pathology of atherosclerosis and various research involving neutrophils was, well, different! Although, isn't it surprising how easy it is to integrate a little 'plant' into ones presentation?! I thoroughly enjoyed the diversity of the oral presentations at the conference. I found the research on design of mitochondria-targeted chemicals, an exciting tool for studying mitochondrial function and potentially as a therapy for mitochondrial dysfunction, particularly interesting. And only in NZ could you get away with a triumphant display of the kiwis crushing the aussies (good on ya Wu). The conference dinner was a night to remember, with a fantastic array of food and side-splitting in-house entertainment provided by Bo and his illustrious back up singers. I would like to give a HUGE thanks to the conference organisers for the receipt of the travel award that made it possible for me to attend this conference, to congratulate them and all participants for a stimulating 3 days of science and to remind u all to eat your red kumara!

## Research Profiles

### Dr Jiri Neuzil : Apoptosis Research Group

Heart Foundation Research Centre  
School of Medical Science  
Griffith University Gold Coast Campus  
Southport  
Qld, Australia

**Group Leader:** Dr. Jiri Neuzil ([j.neuzil@griffith.edu.au](mailto:j.neuzil@griffith.edu.au))

**Current Research Group:** Dr. Lanfeng Dong, post-doctoral fellow  
Dr. Wenqiang Li, post-doctoral fellow  
Emma Swettenham, research assistant  
Xiu-Fang Wang, PhD student  
Ruth Freeman, PhD student  
Adisa Tomic-Vatic, honours student  
Renata Neuzilova, honours student  
Caroline Lidebjer, exchange student

### Research Interests

Anti-cancer activities of vitamin E analogues: The major thrust of our interest focuses on vitamin E (VE) analogues, epitomized by  $\alpha$ -tocopheryl succinate ( $\alpha$ -TOS), selective inducers of apoptosis and anti-cancer agents. We have shown that VE analogues induce apoptosis primarily by activating the intrinsic pathway and suppress cancer in pre-clinical models of colon and breast carcinomas as well as mesotheliomas, a fatal type of cancer. We study the molecular mechanism by which  $\alpha$ -TOS induces apoptosis and by which it sensitizes resistant cancer cells to other apoptogens, such as the TNF family members. We are synthesizing novel analogues of  $\alpha$ -TOS with higher apoptogenic activity and specificity for cancer cells, including specific adducts of the agents targeting malignant cells. We also investigate effects of VE analogues on signaling pathways that promote proliferation and/or survival of cancer cells, such as the FGF autocrine loop and the Akt pathway, including effects on transcriptional regulation of expression of key members. Further, we are interested in suppression of angiogenesis by VE analogues, since we found that  $\alpha$ -TOS causes apoptosis of proliferating (angiogenic) endothelial cells but not normal, arrested endothelial cells. Another focus of our studies is to understand the reasons for selectivity of VE analogues for malignant cells. We believe that in near future, we will be in a position to commence testing of selected VE analogues in human patients. This project is supported by grants provided by ARC, QCF and NBCF.

Role of mitochondria in apoptosis of heart muscle cells during myocardial infarction: During myocardial infarction, muscle heart cells die by apoptosis. This leads to major complications associated with the heart muscle insufficiency. We are interested in furthering our understanding of the processes that underlie this process. Current data strongly suggest that mitochondria may be the major organelle modulating cardiomyocyte cell death, but the precise mechanism is not well understood. We are interested in the molecular mechanism of apoptosis of cardiomyocytes in situation like ischemia/reperfusion (I/R). To study this, we use several models of I/R, including cultured cells, isolated mouse hearts and whole animal models. Our major interest here is to extend

the knowledge gained from cell culture studies to the in situ heart model and to the whole animal. We are studying not only the mitochondrial pathways of cell death in cardiomyocytes but also the alternative/parallel signaling pathways that may play a significant role, including the Daxx pathway. At present, we are establishing a method that allows studying apoptosis on the beating heart in a mouse model of myocardial infarction on the level of single cells, which will make it possible to study intervention that may protect the heart muscle from infarction-induced death. We hope that results of these studies may be used in the future for human patients. This project is supported by grants provided by NHMRC and NHF.

### **Selected Publications :**

1. Neuzil J, Weber T, Schröder A, Lu M, Ostermann G, Gellert N, Mayne GC, Olejnicka B, Nègre-Salvayre A, Sticha M, Coffey RJ, Weber C (2001) Induction of apoptosis in cancer cells by  $\alpha$ -tocopheryl succinate: Molecular pathways and structural requirements. *FASEB J* 15, 403-415.
2. Neuzil J, Schröder A, von Hundelshausen P, Zerneck A, Weber T, Gellert N, Weber C (2001) Inhibition of inflammatory endothelial responses by a pathway involving caspase activation and p65 cleavage. *Biochemistry* 40, 4686-4692.
3. Neuzil J, Kontush A, Weber C (2001) Vitamin E in atherosclerosis: Linking the chemical, biological and clinical aspects of the disease. *Atherosclerosis* 157, 257-283.
4. Weber T, Lu M, Andera L, Lahm H, Gellert N, Fariss MW, Korinek V, Sattler W, Ucker DS, Terman A, Schröder A, Erl W, Brunk U, Coffey RJ, Weber C, Neuzil J (2002) Vitamin E succinate is a potent novel anti-neoplastic agent with high tumor selectivity and cooperativity with tumor necrosis factor-related apoptosis-inducing ligand (TRAIL, Apo2L) *in vivo*. *Clin Cancer Res* 8, 863-869.
5. Neuzil J, Gellert N, Swettenham E (2004) Sensitisation of malignant mesothelioma to TRAIL apoptosis by inhibition of histone deacetylase: important role of Bcl-x<sub>L</sub> down-regulation. *Biochem Biophys Res Commun* 314, 186-191.
6. Jostarndt K, Rubic T, Kühn H, Anthonsen MW, Gellert N, Andera L, Trottmann M, Weber C, Johansen B, Hrboticky N, Neuzil J (2004) Enzymatically modified LDL upregulates CD36 expression in non-differentiated monocytic cells in a PPAR- $\gamma$ -dependent mode. *Biochem Pharmacol* 67, 841-854.
7. Neuzil J, Massa H (2005) Hepatic processing determines dual activity of vitamin E succinate. *Biochem Biophys Res Commun* 327, 1024-1027.
8. Stapelberg M, Gellert N, Swettenham E, Tomasetti M, Witting PK, Procopio A, Neuzil J (2005)  $\alpha$ -Tocopheryl succinate inhibits malignant mesothelioma by disruption of the FGF autocrine signaling loop: Mechanism and the role of oxidative stress. *J Biol Chem* (in press).

## **Dr Shane Thomas ([shane.thomas@unsw.edu.au](mailto:shane.thomas@unsw.edu.au))**

**Current position:** NHMRC CJ Martin Research Fellow.  
Currently establishing a research group and laboratory space that will initially consist of two research assistants and myself.

**Institution:** Centre for Vascular Research, University of New South Wales, Australia

### **Research Interests**

#### **Role of redox reactions in endothelial cell signaling and function**

The endothelium is critical for maintenance of vascular homeostasis. Central to this is endothelial-derived nitric oxide (EDNO), synthesized by the endothelial isoform of nitric oxide synthase (eNOS). Vascular diseases including atherosclerosis are characterized by endothelial dysfunction that is manifested as impaired EDNO bioactivity that may contribute to clinical events [1]. Considerable evidence indicates that endothelial dysfunction is due, in part, to vascular oxidative stress and there is great interest in defining the oxidative processes involved [1]. Diseased blood vessels produce increased amounts of reactive oxygen species, derived primarily from endothelial and smooth muscle cells and detected principally as superoxide anion radical ( $O_2^{\cdot-}$ ) and its dismutation product hydrogen peroxide ( $H_2O_2$ ) [2]. It is established that  $O_2^{\cdot-}$  rapidly reacts with nitric oxide (NO) to limit EDNO bioactivity. Increasing evidence indicate that  $H_2O_2$  also represent an important signaling molecule governing vascular cell phenotype and vascular tone [1, 2]. Our research focuses on defining to what extent and how  $H_2O_2$  impacts on endothelial function and phenotype and EDNO bioactivity during vascular disease. In collaboration with John Keaney and Kai Chen (Whitaker Cardiovascular Institute, Boston University, USA) to date we have discovered that  $H_2O_2$  activates eNOS by altering the enzyme's phosphorylation status [3]. We have also identified mitochondria as a novel target that mediates the proximal cell signaling events induced by  $H_2O_2$  in endothelial cells [4]. Currently we are investigating the effects of  $H_2O_2$  on EDNO bioactivity. Our recent data indicates that despite activating eNOS the oxidant can limit EDNO bioactivity by promoting oxidative inactivation of NO. We are in the process of characterizing the nature of the oxidative reactions limiting NO and the extent to which these processes are important for endothelial dysfunction during vascular disease states. Our research also focuses on determining the role of myeloperoxidase for endothelial dysfunction and redox control of cell signaling in endothelial cells stimulated with physiological agonists, in particular vascular endothelial growth factor.

#### **Roles and regulation of indoleamine 2,3-dioxygenase**

Indoleamine 2,3-dioxygenase (IDO) is an intracellular heme protein that catalyses the oxidative metabolism of L-Trp via the kynurenine pathway [5]. IDO is induced at sites of inflammation by interferon- $\gamma$  ( $IFN\gamma$ ) and is traditionally thought to function as an anti-microbial and anti-tumour effector of the cytokine. Recent groundbreaking studies have established that IDO also represents an important immune regulatory enzyme that inhibits T lymphocyte activation by reducing the local concentrations of L-Trp, the least abundant of all essential amino acids. Considerable evidence supports an IDO-based mechanism for immune suppression. For example, induction of IDO and inhibition of T cell activation protects against inflammatory disorders including colitis and collagen-induced arthritis in mice. We have discovered increased IDO expression in atherosclerotic lesions and have initiated a NHMRC funded project examining the role of IDO in this disease in which inflammation of the vascular wall represents an important pathogenic event. In light of the important immune regulatory role of IDO our research also focuses on determining the molecular mechanisms by which the enzyme is controlled. Together with Roland Stocker, we have previously described that IDO is inhibited by nitric oxide (NO) [6]. Currently we are investigating how NO inhibits IDO by characterizing the nature of the inactive NO-IDO heme adduct using Resonance

Raman Spectroscopy with Andrew Terentis (Florida Atlantic University, USA) [7]. We have also identified that IDO is subject to post-translational control and that this form of control may be subject to redox control [8]. We are in the process of extending these studies to determine the mechanisms by which IDO is subject to post-translational control and if these processes are important in the regulation of the enzyme's immune regulatory actions in innate immune cells.

#### **Selected Publications :**

1. Thomas SR, Chen K, and Keaney JF, Jr. 2003. *Antioxid Redox Signal* 5: 181-194.
2. Chen K, Thomas SR, and Keaney, JF, Jr. 2003. *Free Radic Biol Med* 35: 117-132.
3. Thomas SR, Chen, K, and Keaney, JF, Jr. 2002. *J Biol Chem* 277: 6017-6024.
4. Chen K\*, Thomas SR\*, Albano A, Murphy MP, and Keaney JF Jr. 2004. *J Biol Chem*. 279: 35079-35086. \*Co-First Authors
5. Thomas SR, and Stocker R 1999. *Redox Rep* 4: 199-220.
6. Thomas SR, Mohr D, and Stocker, R. 1994. *J Biol Chem* 269: 14457-14464.
7. Terentis AC, Thomas SR, Takikawa O, Littlejohn TK, Truscott RJ, Armstrong RS, Yeh SR, and Stocker R. 2002. *J Biol Chem* 277: 15788-15794.
8. Thomas SR, Salahifar H, Mashima R, Hunt NH, Richardson DR, and Stocker R. 2001. *J Immunol* 166: 6332-6340.

## Dates for your Diary

Date	Conference	Location	Contact / Details
18 – 21 May 2005	3 <sup>rd</sup> International conference on Diet and optimum health	Portland, Oregon, USA	<a href="http://lpi.oregonstate.edu/conf2005/">http://lpi.oregonstate.edu/conf2005/</a>
24 – 29 June 2005	SFRR(Asia) Natural antioxidants molecular mechanisms and health effects	Shanghai, China	<a href="mailto:wsy@moon.ibp.ac.cn">wsy@moon.ibp.ac.cn</a>
8 – 11 July 2005	SFRR(Europe) meeting	Leicester, UK	<a href="mailto:jl20@leicester.ac.uk">jl20@leicester.ac.uk</a> <a href="http://www.le.ac.uk/cm/sfrr/index.htm">http://www.le.ac.uk/cm/sfrr/index.htm</a>
4 – 8 Sept 2005	8 <sup>th</sup> International EPR spin trapping and 11 <sup>th</sup> in vivo EPR imaging	Columbus, Ohio, USA	<a href="mailto:Kuppusamy-1@medctr.osu.edu">Kuppusamy-1@medctr.osu.edu</a>
7 – 10 Sept 2005	Joint meeting of the Oxygen club of California and the University of Turin	Alba, Italy	<a href="mailto:Giuseppe.poli@unito.it">Giuseppe.poli@unito.it</a>
26 – 29 Sept 2005	SFRR(Africa) meeting	Tetouan, Morocco	<a href="http://vcampus.uom.ac.mu/sfinal/sf_home.htm">http://vcampus.uom.ac.mu/sfinal/sf_home.htm</a>
26 – 30 Nov 2005	Society for Free Radical Biology and Medicine, 12 <sup>th</sup> annual meeting	Austin, Texas, USA	<a href="http://www.sfrbm.org/">http://www.sfrbm.org/</a>
<b>2 – 4 Dec 2005</b>	<b>SFRR(Australasia)</b>	<b>Griffith University Gold Coast</b>	<b>Jiri Neuzil</b> <b><a href="mailto:j.neuzil@griffith.edu.au">j.neuzil@griffith.edu.au</a></b>
15 – 19 Aug 2006	XIII Biennial meeting of ISFRR	Davos, Switzerland	<a href="http://www.sfrr-congress.org">http://www.sfrr-congress.org</a> <a href="mailto:info@SFRR-Congress.org">info@SFRR-Congress.org</a>
15 – 19 Nov 2006	Society for Free Radical Biology and Medicine, 13 <sup>th</sup> annual meeting	Denver, Colorado, USA	<a href="http://www.sfrbm.org/">http://www.sfrbm.org/</a>

Useful websites for additional free radical meeting information :

<http://www.oxyclubcalifornia.org/>

<http://www.sfrr-europe.org/ExPage5.asp>