



SOCIETY FOR FREE RADICAL
RESEARCH
(Australasia)



NEWSLETTER March 2000

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This is the first Newsletter from the Australasia branch of SFRR for the new millenium. The Executive would like to thank all those researchers who have contributed to this issue of the Newsletter and wish all SFRR(A) members the very best in their continuing research. As always, the Executive will continue to up-date members of recent and up-coming events in Australasia and elsewhere around the globe. For example, this issue includes a diary listing future meetings covering areas related to free radical research. To aid the transfer of information we have set up an e-mail address book with the current financial members listed. If you have not previously received electronic mail from SFRR(A) and/or have recently changed your electronic address please forward your (new) e-mail address to the Secretary, Dr Paul Witting. We continue to distribute hard copies of this Newsletter to members without e-mail access, although we aim at reducing the mailing of hard copies to a minimum to lower our overhead costs. In this context, the Executive would like to thank The Heart Research Institute for the generous support provided for copying and mailing materials to the members of SFRR(A). 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).

From the President

Dear Fellow Radicals,

It's an absolute privilege to be president of SFRR (Australasia) and a pleasure to serve the society in this position. Please feel free to contact me if you have ideas on various initiatives that you think may benefit the society. Since its inception over ten years ago, SFRR (Australasia) has gained a justifiable reputation for providing friendly forums in which new members are welcomed and the quality of research is consistently high. In the next two years I would like to work for the society to maintain these positive attributes and attract new members to our fold so that we can continue to grow over the next decade. Our conferences have been the main focus of the society and the best vehicle for attracting new members. I expect that this will always be the case. However, with the advent of Redox Report becoming the official journal of SFRR (Australasia) we have a new avenue for promoting our society and the free radical research that is carried out in this part of the world. I encourage all our members to consider submitting research manuscripts to Redox Report. It is obvious when going to conferences in Europe and the USA that the quality of free radical research in Australasia is of the highest standard. I feel strongly that we should show our northern-hemisphere colleagues the strength and breadth of our research by collectively publishing in Redox Report. A solid Australasian presence in Redox Report should also attract other local researchers in free radical biology and chemistry to our society.

I would like to thank our Past President, Roland Stocker, for the considerable time and enthusiasm he put into the society over the last two years. Roland's two main initiatives of instigating a smaller meeting between our biennial conferences and aligning Redox Report with the society will undoubtedly prove to be very positive moves for SFRR (Australasia). The growth in our membership is a testament to Roland's hard work and commitment to the society. I only hope that Kiwi ingenuity is an adequate substitute for Swiss efficiency. I would also like to thank Paul Witting (secretary) and Mike Murphy (treasurer) for agreeing to continue to serve in their respective positions. These two characters do much of the donkey work that keeps the society ticking over and their efforts are much appreciated. I have already been impressed by Paul's ability to get me to deliver on time.

Many thanks should also be extended to Nick Hunt and his team for organising a very successful conference in Sydney at the end of last year. Nick had clearly put a big effort in the meeting and the concept of running it jointly with two other societies worked well. It was heartening to see many new people presenting their work. In particular, I thought that the student presentations were of a very high standard. I hope the society will be able to continue to support their efforts financially by helping them attend our local meetings as well as overseas conferences. The success of our students will very much determine our future as a society, so I think we need to look at all possible ways of supporting them and maintaining their interest in free radical research. For example, I encourage eligible members to apply to both the SFRR(A) and the Sydney Society for Free Radical Research (SFRG) for funding to attend international conferences in 2000 (see details on the application for these Travel Awards in this issue of the Newsletter).

Judy De Haan recently attended a meeting of the Australian Society for Medical Research. They are planning a big meeting to be held at the end of 2002 (Nov 25-28th tentatively) in Melbourne. They want as many societies to join with them as possible and expect approximately 1000 delegates. Your views on whether or not we should join with them would be appreciated and can be directed to the Executive via the Secretary at the address(es) shown on the opening page of this Newsletter.

I also would like to invite you to Wellington at the end of the year (see the "first announcement" in this issue of the Newsletter). We are organising a two-day symposium that will be run in conjunction with the joint meeting of the Australian and New Zealand Societies of Biochemistry and Molecular Biology. We hope that as many Australians as possible can cross the ditch and visit Wellington. There will be much excellent science to be had and the location of the meeting is superb. Wellington is now a showcase for New Zealand culture and its harbour setting is stunning. Please come and join us. I will be sending out full details of the symposium soon.

Finally, on behalf of the Executive I would like to congratulate the winners of the student prizes at the recent SFRR(A) meeting in Sydney (Anna Chapman, Christchurch School of Medicine 'best student presentation'; Mathew Sweeney University of Wollongong 'best poster presentation'; Lisa Israel University of NSW; Andrew Aquilina University of Wollongong and Sarah Potter University of Sydney, each receiving 'runners-up awards for poster presentations').

All the very best,

Tony

Minutes of the 8th Meeting of the Society for Free Radical Research (Australasia)

Venue: Veterinary Faculty Conference Centre, University of Sydney Main Campus

Date: 1pm Thursday December 2 1999

1. **Apologies:** Paul Witting, Mike Murphy, and Bob Anderson

2. **Attendees:** (If you attended the meeting but are not on the list please contact Tony Kettle so it can be corrected.); Michael Davies, Roland Stocker, Nick Hunt, Judy De Haan-Klein, Roger Dean, Wendy Jessup, Chris Easton, Ian Dawes, George Smythe, Lincoln Morton, Ora Lux, Ken Watson, Jack von Borstel, Mike Berridge, Mavis Abbey, Trevor Mori, Kevin Croft, Brett Garner, Mark Hicks, Steven Gieseg, Jan Gebicki, Sylvia Gebicki, Tony Kettle, Christine Winterbourn, Margret Vissers.

3. **Business Arising from Minutes of Previous Meeting:**

Roland Stocker presented the outcome on the ballot for the proposal that Redox Report should become the official journal of SFRR (A). There was overwhelming support (51 vs 8) for the proposal. However, the majority (30 vs 16) did not favour an automatic subscription to the journal, which would increase the membership fee by US\$66. The point was raised that it may be difficult to sustain the journal without subscriptions from members.

4. **President Report:**

Roland Stocker presented his final report as President which was included in the October Newsletter of 1999.

He commented on the success of the yearly meetings, which have helped to boost membership and have been excellent to facilitate scientific exchanges between Australasian researchers. He brought peoples attention to the website for SFRR (A), which will be maintained by Nick Hunt. Roland thanked Nick Hunt and Mike Davies for organising the Sydney meeting, and Mike Murphy and Paul Witting for support as treasurer and secretary, respectively. Roland informed the meeting of the disappointingly low number of subscribers to Redox Report. This situation is clearly not tenable for the publisher and a more satisfactory arrangement will have to be negotiated.

5. **Treasurers Report:**

Roland tabled the report submitted by Mike Murphy.

Mike reported that the financial position of SFRR (A) has remained stable since 1998. It was hoped that the 1999 meeting make a profit and would be able to payback the NZ\$1,840 invested by SFRR (A). A substantial profit (NZ\$3,500) remains from the Dunedin meeting the fate of which has yet to be decided. The report was accepted conditional on the decision regarding the profit from the Dunedin meeting.

Mike thanked Teena Joyce in the Biochemistry Department, University of Otago, for doing an outstanding job of controlling finances while he was on sabbatical.

6. **Secretaries Report:**

Roland tabled the report submitted by Paul Witting.

Paul thanked all those who had worked with him in the society over the last two years, including Roland, Nick, and Teena Rohmets (Dunedin) and Jacinta Letters (Sydney). He welcomed the move to electronic distribution of information to members and urged members to support Redox Report by subscribing to the journal.

7. **Election of Officers:**

At this point in the meeting Tony Kettle took over the chair from Roland Stocker. Tony thanked Roland for all the work he had put into the society over the last two years as well as Nick and his team for organising the Sydney meeting. He also thanked Mike and Paul for their work.

President Elect:

Mike Davies was nominated by Roland Stocker and seconded by Sylvia Gebicki. Mike was unanimously elected.

Secretary:

Paul Witting offered to remain in this position and there were no other nominations.

Treasurer:

ISFRR Representatives:

Christine Winterbourn nominated Tony Kettle and Roland Stocker. The nominations were seconded by Mike Davies and unanimously accepted.

Regional Representatives:

Discussion arose about the need for these positions because contact amongst members was now so easy via email. Tony Kettle proposed that these positions are eliminated and Christine Winterbourn seconded this. The motion was unanimously agreed upon.

8. Next Annual Scientific Meetings

It was decided that the next meeting would be held in Wellington in December 2000. The meeting will be organised by Tony Kettle.

The 2001 meeting will be held in association with SFRR (Asia) and will be organised by Roland Stocker.

The 2002 meeting was tentatively agreed to be held in Melbourne in association with the Australian Society for Medical Research.

9. General Discussion

It was agreed that Bruce Ames be added to the list of nominees for the ISFRR Trevor Slater Award.

SFRR (Australasia) Treasurer's Report (20/03/00)

Opening Balance	8,037.92 (Bank statement 20/10/98)
Income	
Subscriptions	3,419.89
Interest	<u>273.15</u>
	3,693.04
Expenditure	
Prof Packer's travel to AINSE/Rad '98 meeting	751.00
Resident withholding tax	90.12
Bank fees	0.75
Aus. Soc. Med. Res. Subscription	224.17
SFRR(Aus) meeting 1999	1,840.04
SFRR(Int) subscription	874.05
SFRR(Aus) meeting deposit for venue	<u>605.25</u>
	4385.38
Current balance	7345.58 (Bank statement 20/3/00)

Membership	<u>1999</u>	<u>1998</u>	<u>1997</u>
<i>Full</i>	60	63	48
<i>Student</i>	<u>14</u>	<u>11</u>	<u>8</u>
Total	74	74	56

Comments

Membership numbers and the financial position are stable. In addition, NZ\$3,000 from the SFRR(Aus) meeting in Dunedin will be paid into the society's accounts shortly. If there was any profit from the Sydney meeting then some of this may also be donated to the society in due course. It is hoped that profits from meetings will be ring fenced and used primarily for travel grants for those who have difficult obtaining such funds from elsewhere. Some subscriptions for 1999 are still outstanding and can be paid, along with your membership for 2000. Membership forms are attached as the last page to the Newsletter and annual subscriptions are due on or before the 31st of July, 2000.

Mike Murphy
Treasurer
SFRR(Australasia)

“Oxidative pathways in Health and Disease”

Incorporating the 8th Meeting of the Society for Free Radical Research (Australasia).

Clare Hawkins and Steve Leichtweis (The Heart Research Institute)

The 8th meeting of the Society for Free Radical Research (Australasia) was a joint meeting combined with the Australian Society for Experimental Pathology and the Australia and New Zealand Environmental Mutagen Society. The meeting was held in the very well-equipped Veterinary Faculty Conference Centre at the University of Sydney. The organising committee chaired by Nick Hunt (Sydney, Aus) did a very good job of assembling a programme which encompassed the interests of the representatives from each society. The meeting opened with a comprehensive overview of UVA damage to skin cells presented by Rex Tyrell (Bath, U.K.). Low doses of UVA radiation were shown to lead to an increase in the pool of labile iron in cells and a corresponding drop in the levels of intact heme proteins. The change in labile iron and heme release were found to be related to the activation of heme-oxygenase-1. Eventually an increase in ferritin synthesis is observed, but transient increases in free iron leaves cells vulnerable to oxidative damage. Other aspects of UV-induced damage to cells were explored in sessions devoted to photobiology and photoprotection.

Myeloperoxidase and HOCl

The role of myeloperoxidase and the oxidants derived from it was introduced by Tony Kettle (Christchurch, New Zealand). In his presentation, Tony described the preferred substrates of both myeloperoxidase and eosinophil peroxidase and the impact this may have on oxidative lung damage in asthma sufferers. Jay Heineke (St Louis, U.S.A.) gave an overview of the role of myeloperoxidase and hypochlorous acid (HOCl) in the oxidation of low density lipoprotein (LDL). Chlorotyrosine was established as a specific marker, and chlorination of tyrosine was proposed to be mediated by Cl₂, as opposed to HOCl. The use of both mono- and di-chlorinated tyrosine and protein carbonyls as markers for the detection of HOCl-modified proteins was subsequently discussed (Anna Chapman; Christchurch, New Zealand). Further product studies utilising electrospray mass spectroscopy to investigate the reaction of HOCl and S100 proteins were reported (Mark Raftery; Sydney, Aus). Electron paramagnetic resonance spectroscopy, with spin trapping, was used as a tool to investigate the formation of radical intermediates in the HOCl-mediated oxidation of human red blood cells (Clare Hawkins; Sydney, Aus).

Hydroperoxides

The formation and subsequent reactions of hydroperoxides with both lipids and proteins were the focus of a number of presentations. The formation of free radical-mediated regioisomeric cholesteryl linoleate hydroperoxides was investigated (Yorihiro Yamamoto, Tokyo, Japan) and Jan Gebicki (Sydney, Aus) discussed hydroxyl radical-mediated protein oxidation in blood serum during irradiation. Other presentations involving protein oxidation included a discussion of the role of protein hydroperoxides in oxidative DNA base damage and the formation of DNA-protein crosslinks (Catherine Luxford, Sydney, Aus). Michael Davies (Sydney, Aus) showed that initial radical reaction at side chain sites may give rise to both backbone cleavage and the loss of side chain sites on proteins and peptides.

Nitric Oxide

Guna Karupiah (Sydney, Aus) presented information on the contribution of NO to host defence against pathogens and how this is largely dependent on macrophage activation by gamma-interferon. Interferon-gamma and nitric oxide, and their immuno-regulatory role in an animal model of multiple sclerosis was discussed by David Willenborg (Canberra, Aus). Lincoln Morton (Perth, Aus) presented evidence that phenolic compounds may be preferentially targeted by peroxynitrate, thereby providing a potential antiatherogenic role for these dietary components.

New Technologies

Bob Armstrong (Sydney, Aus) described recent advances in vibrational spectroscopy that allows for in situ Raman spectroscopy to be performed in single living cells.

Atherosclerosis

Atherogenesis and the oxidative modification hypothesis was introduced by John Keaney (Boston, USA) who discussed the current difficulties in linking decreased LDL oxidation with a reduction in atherosclerosis. However, the involvement of vitamin E in maintaining vascular homeostasis and protecting against the endothelial dysfunction associated with atherosclerosis by preventing protein kinase C stimulation was highlighted. Roland Stocker (Sydney, Aus) further emphasised how atherosclerosis intervention studies with vitamin E have to date produced inconclusive results. Recent findings in his lab using atherosclerosis prone animal models have shown that inhibition of lipoprotein lipid oxidation is not always associated with a decrease in the extent of atherosclerosis, (and inhibition of atherosclerosis can occur without a concomitant inhibition of aortic lipid oxidation). Kevin Croft (Perth, Aus) presented information on recent studies looking at F2-isoprostane levels as a marker of in vivo lipid peroxidation. Results indicated that phenolic compounds present in wine did not reduce F2-isoprostane levels in vivo in smokers while de-alcoholised wine did reduce F2-isoprostane levels. However, they were unable to distinguish between the potential protective effect of phenolic compounds or a decrease in the ingestion of the pro-oxidant ethanol. Andrew Terentis (Sydney, Aus) discussed recent data on alpha-tocopherol oxidation products in human atherosclerotic lesions. His findings suggest that two-electron oxidants make a major contribution to alpha-tocopherol oxidation in the artery wall, particularly in the earlier stages of atherosclerosis.

Coenzyme Q

A symposium on Coenzyme Q₁₀, sponsored by the International CoQ₁₀ Association and co-chaired by Gian Paulo Littaru and Svend Mortensen, provided lively discussions. David Celermajer (Sydney, Aus) outlined the potential role of antioxidants on vascular reactivity. In recent studies in his lab, healthy subjects orally supplemented with coenzyme Q₁₀ had no significant effect on endothelium-dependent or smooth muscle-dependent arterial reactivity/function. Nicholas Bett (Brisbane, Aus) presented recent findings on oral coenzyme Q₁₀ supplementation of patients with chronic left ventricular dysfunction. His data indicated that 3 month of oral supplementation had no effect on resting left ventricular systolic function despite a more than two-fold increase in plasma coenzyme Q₁₀ levels.

Salvador Pepe (Melbourne, Aus) described recent findings in young and senescent rat hearts using an isolated, buffer perfused system. Prior coenzyme Q₁₀ supplementation diminished pre-pacing and post-pacing (stress) work parameters in the senescent rat hearts. Similar findings were presented in studies on human right atrial tissue, collected during elective heart surgery, subsequently subjected to in vitro contractile function tests.

Shane Thomas (Sydney, Aus) discussed the antioxidant properties of the reduced form of coenzyme Q₁₀, ubiquinol-10, for plasma lipoprotein lipids. He then reported on a recent study indicating that dietary supplementation of atherosclerosis prone apolipoprotein E knockout mice with coenzyme Q₁₀ could inhibit atherosclerosis. Perhaps more importantly, co-supplementation with coenzyme Q₁₀ and vitamin E more significantly inhibited the extent of atherogenesis than either supplement alone.

RESEARCH PROFILE

Dr. Dianne Watters. Current address: Dept. of Surgery, University of Queensland. Royal Brisbane Hospital. Formerly from The Queensland Institute of Medical Research.

Research Interests: The major areas of research focus on the role of oxidative stress in the disease ataxia-telangiectasia and how tumour cells become resistant to apoptosis (programmed cell death) induced by ionising radiation and chemotherapeutic drugs.

Ataxia telangiectasia project: Ataxia telangiectasia (A-T) is a rare human autosomal recessive disease affecting 1 in 100,000 live births. Approximately 1 in 400 people are heterozygous for the defective gene. A-T is a multisystem disorder characterised by increased sensitivity to ionising radiation, immunodeficiency and susceptibility to cancer. The major hallmarks of the disease are ataxia (abnormal gait resulting in confinement to a wheel chair by the early teenage years) and oculocutaneous telangiectasia (spidery veins on the whites of the eyes and facial skin often seen in people after radiotherapy). Other symptoms include oculomotor disturbances, premature ageing, clinical and cellular sensitivity to ionising radiation and radiomimetic drugs.

cerebellum), and susceptibility to infection. The two major causes of death, usually in the second decade of life, are lymphomas and respiratory infections.

Heterozygotes are intermediate in radiation sensitivity between normal and A-T homozygotes, and there is increasing evidence that heterozygosity for this gene may predispose to cancer, particularly breast cancer. The gene mutated in A-T was recently cloned and shown to code for a large protein (ATM, 350 kDa) with a domain homologous to the kinase domain of phosphatidylinositol (PI) 3-kinase. The mutations in over half of A-T patients are truncating mutations rendering the protein unstable. The other mutations result in loss of kinase activity. ATM is most closely related to proteins, which are involved in maintaining the integrity of DNA and/or cell cycle control in response to DNA damage. It is a protein kinase rather than a lipid kinase and some of its known substrates are p53, and BRCA-1 (the product of the breast cancer susceptibility gene) both of which are involved in DNA damage signaling. ATM is also involved in homologous recombination and *Atm* knockout mice are sterile due to aberrant recombination during meiosis. We have localised the ATM protein to the nucleus, as expected for a protein with these functions, and also unexpectedly, to peroxisomes and cytoplasmic vesicles (endosomes). While a role for nuclear ATM in DNA damage signalling in proliferating cells is well defined, it does not explain the etiology of the neurodegeneration. In terminally differentiated cells such as the Purkinje cells, ATM is almost exclusively outside the nucleus.

A-T cells appear to be in a state of oxidative stress as evidenced by indirect measures, which show that these cells behave as if they had already been irradiated. In addition genes which are up-regulated after irradiation in normal cells are already up-regulated in A-T cells in the absence of irradiation. We have found decreased activity of the peroxisomal enzyme catalase in cultured A-T cells and in the cerebellum but not the liver of ATM mutant mice. Consistent with these observations, we have found increased lipid hydroperoxides in A-T cells and others have found evidence of oxidative damage in tissues from *Atm* knockout mice. Interestingly this damage is present in the cerebellum but not in the liver. A-T cells display defective signal transduction in response to a number of different stimuli and there are also reports of altered lipid metabolism in A-T. Our current research is aimed at understanding the role of the ATM protein in peroxisomes and endosomes, in the maintenance of redox homeostasis, and the possibility that the signal transduction defects are related to oxidative damage/alterations of membrane lipids which are crucial for efficient functioning of cell surface receptors. Defining the role of ATM outside the nucleus will help explain aspects of A-T, such as ataxia and defective cell signalling, which have been difficult to explain by aberrant cell cycle checkpoint control after ionising radiation or defective recombination events.

Apoptosis project: We are interested in defining the molecular pathways leading to apoptosis induced by ionising radiation and how tumour cells develop resistance. Free radicals resulting from ionising radiation affect the cell membrane as well as the nucleus and there is some evidence that apoptotic pathways can be initiated at the level of the cell membrane, at least in some cell types. Ceramide generation as a result of sphingomyelin hydrolysis has been postulated to be an important mediator of apoptosis, however there has been considerable controversy on this topic. We are investigating the increasing evidence that lack of ceramide generation is an important feature of resistance in many tumour cells and the mechanisms by which ceramide is generated after ionising radiation.

Research staff and collaborators:

Dr Dianne Watters is a molecular cell biologist/ biochemist with a long standing interest in signal transduction and more recently, the role of ATM outside the nucleus.

Dr. Jeffery Smith is a biochemist with extensive experience in lipid research, particularly the pathophysiology of cholesterol-rich gallstones.

Nicole Irwin, an honours graduate from the University of Queensland has just been appointed as research assistant on the ATM project.

Collaborators: Prof. Martin Lavin, Dr. Philip Chen, Dr. Karen Keating, Dr. Kevin Spring, Sergei Kozlov QIMR. Assoc. Prof. Denis Crane, Griffith University, Nathan.

Professor Martin Lavin (head of the cancer unit at QIMR) is internationally recognised in the field of A-T research and has spent many years investigating this disease. His major focus is on the role of ATM in the response to DNA damage.

Dr. Kevin Spring has produced a mouse model of A-T in which a mutation found in human patients was

amino acids located outside the PI 3 kinase domain), resulting in near full length but inactive protein (kinase dead). Dr. Phil Chen is interested in radiosensitivity and chromosomal instability while Dr. Karen Keating is working on the regulation of ATM protein levels. Sergei Kozlov has recently completed his PhD thesis in the Department and is now pursuing research at QIMR on mechanisms controlling the nuclear/ cytoplasmic localisation of ATM. Assoc. Prof. Denis Crane is an expert in the peroxisome field and is providing valuable assistance with this aspect of the project. Recently graduated PhD students on the apoptosis project, Nigel Waterhouse and Julie Michael, are now engaged in post-doctoral research elsewhere. Nigel has just published a paper in the March 2000 issue of *Nature Cell Biology* on the kinetics of cytochrome c in apoptosis, emanating from his work in Dr. Douglas Green's laboratory, La Jolla, California.

Financial Support:

The group is currently supported by research grants from the National Health and Medical Research Council, the Queensland Cancer Fund and the A-T Children's Project (US). Enquiries from prospective PhD students are welcome at the address given above.

Recent Relevant Publications

- Watters, D., Khanna, K.K., Beamish, H., Birrell, G., Spring, K., Kedar, P., Gatei, M., Stenzel, D., Hobson, K., Kozlov, S., Zhang, N., Farrell, A., Ramsay, J., Gatti, R. and Lavin M.F. (1997) Cellular localisation of the ataxia-telangiectasia (ATM) gene proteins and discrimination between mutated and normal forms. *Oncogene* **14**, 1911.
- Watters, D., Kedar, P., Spring, K., Chen, P., Gatei, M., Birrell, G., Bjorkman, J., Srinivasa, P., Crane, D. and Lavin, M. (1999) Localization of a portion of extranuclear ATM to peroxisomes. *J. Biol. Chem.* **274**, 34277.
- Waterhouse, N., Kumar, S., Strike, P., Sparrow, L., Song Q, Dreyfuss, G., Alnemri E., Litwack G., Lavin, M.F. and Watters, D. (1996) Heteronuclear ribonucleoproteins C1 and C2, components of the spliceosome, are specific targets of ICE-like proteases in apoptosis. *J. Biol. Chem.*, **271**, 29335.
- Watters, D. (1999) Molecular Mechanisms of radiation-induced apoptosis. *Immunol. Cell Biol.* **77**, 263.
- Waterhouse, N., Finucane, D., Green, D.R., Elce, J., Alnemri, E., Litwack, G., Khanna, K.K., Lavin, M.F. and Watters D. (1998) Calpain activation is upstream of Caspases in radiation-induced apoptosis. *Cell Death and Differentiation*.**5**, 1051.
- Watters, D. and Lavin, M. (Eds) Signalling Pathways in apoptosis. Volume 5 of the series Modern Genetics (Series Ed. Rick Lathe) Harwood Academic Publishers, Amsterdam 1999. ISBN 90-5702-392-X.

Impressions of the 11th Gordon Research Conference on Oxygen Radicals in Biology

Christine Winterbourn

This conference is held in February alternate years in Ventura, California. This year's conference was up to the usual high standard and was judged by most attendees to be a success. Gordon Conferences, for those not familiar with them, are small, live in meetings (maximum number of attendees 150) with a standard format of morning and evening sessions, well-lubricated poster sessions, and afternoons free for recreation or informal discussion. There are relatively few speakers and generous time is allocated for discussion. The weather was kinder than usual this year (in my experience of previous meetings, floods in the Los Angeles area at this time are not unusual) and walking on the beach, volleyball and cycling were all popular.

The programme of the meeting included presentations on biomarkers, antioxidants, redox regulation and cell signalling, nitric oxide, oxidant generating enzymes, LDL oxidation, mitochondrial function and aging, and several poster discussion sessions. Rather than cover all the presentations, I thought I would try to convey my overall impressions of the science and what I considered to be highlights. In that vein, the points that remain in my memory are:

- The importance of biomarker assays for making links between oxidants and disease, but at the same time the extreme caution that must be taken in validating the methodology and carrying out appropriate controls with these assays (Andrew Collins, Larry Sayre, Garret Fitzgerald, Harry Ischiropoulos).
- The accumulating evidence for deterioration of mitochondria and oxidant leakage with age and the evidence from knockout mice of the importance of MnSOD in protecting iron-sulphur proteins from inactivation and

- The elegant dissection of the pathway leading to NF- κ B activation through a series of phosphorylation steps (Michael Karin). Although making a case against NF- κ B as a sensor for oxidative stress, he nonetheless showed the involvement of Michael addition to a specific cysteine residue in the inhibitory action of cyclopentenone prostaglandins on NF- κ B activation.
- The common chemical features of compounds considered as nutritional antioxidants and electrophiles that act as inducers of phase II detoxifying enzymes and increase GSH levels by upregulating -glutamylcysteine synthetase (Paul Talalay and Tim Mulcahy). Could any beneficial action of nutritional antioxidants involve the upregulation of these defence systems? Both these speakers commented on the emerging evidence that the inducers of Phase II enzymes act through KEAP1, a protein that contains 25 cysteine residues.
- Suggestive evidence for an NAD(P)H oxidase (MOX1), related to the phagocyte oxidase, being present in smooth muscle cells and generating oxidants on receptor-mediated activation (Kathy Griendling).
- The major confounding factors associated with interpreting results obtained with any of the methods available for measuring intracellular production of reactive oxidants (Ron Mason) and the crying need for a rigorous assay of this type.
- The potential benefits of consuming large quantities of kiwi fruit (Andrew Collins).

A particular highlight was the plenary lecture by Louis Ignarro, one of the 1998 Nobel Prize winners for his work on nitric oxide. We were privileged to hear Dr Ignarro's after dinner lecture in which he described his experiments leading up to the identification of endothelial derived relaxing factor as NO and also took us through the period from the announcement of the winners to the reception and presentation in Stockholm. We all felt the momentous nature of the occasion when he described his feelings as he added his signature to those of Rutherford, Einstein, Pauling and all the other Nobel Laureates.

In all, the meeting was a successful combination of good science and opportunities to revive old or make new contacts. I have the dubious honour of being co-chair of the next conference in 2002. Ann Aust and I aim to put together a stimulating programme and I hope to see a good representation of Australasian free radicals.

TOP NZ SCIENTIST SCOOPS "PRESTIGIOUS" PRIZE AT GORDON CONFERENCE (Michael Davies, HRI)

At the recent 11th "Oxygen Radicals in Biology" Gordon Conference held at Ventura, California, Dr Tony Kettle {SFRR(Australasia) president} was presented with the "Iron Bolt" award. This "prize" (literally an old iron bolt, found on the Ventura beach, mounted on a tasteful wooden plaque) is awarded at each conference to an attendee who in the eyes of the previous awardee(s) has either made a particularly noticeable contribution to the meeting, or who is felt to deserve it for other reasons.

The award of this prize to Tony is particularly memorable and notable as this is the first time that it has ever been awarded to a non US or European scientist. Previous illustrious holders of the award include Ed Copeland, Wilhelm Koppenol, Simon Wolff, Catherine Rice-Evans, and Gideon Czapski amongst others, so Tony is now is very good company and obviously destined for great things.

Tony was praised for his outstanding and memorable invited lecture at the conference on "Myeloperoxidase-induced oxidant generation by neutrophils" and in particular his splendid demonstration of the effects of the neutrophil-derived oxidant hypochlorite on complex lipid- and protein-containing tissues. This involved a glass, a large amount of "Chlorox" (a commercial disinfectant, containing ca. 400 mM HOCl at high pH) and a piece of bacon kindly donated by the hotel kitchen. The extent of decomposition of the bacon after this treatment was extensive, smelly, and messy, and gave the audience a wonderful example of the power of HOCl. It did little however for the consumption of bacon the following morning. The relevance of this model of tissue destruction to the situation within a phagocytic vacuole of a neutrophil was however questioned by a few members of the audience, though Tony's response to these challenges was both robust and forthright. His closing comment on the controversy, and which was undoubtedly instrumental in him being awarded "The Iron Bolt", was "I never

Congratulations Tony!!

Keystone Symposia January 9 – 15 1999

Type 2 Cytokines in Allergy and Helminth Infections / Asthma

Christine van Dalen (Christchurch School of Medicine)

In January I attended two concurrent symposia on Type 2 Cytokines and Asthma in the picturesque ski resort of Lake Tahoe, Nevada. I had chosen to attend these symposia as I am investigating eosinophil peroxidase and its role in asthma in my PhD studies.

The presentations covered a wide range of research in the fields of eosinophil biology and type 2 cytokines, and their roles in allergy and asthma pathology. In particular, the areas covered in the asthma symposium were epidemiology of asthma, immunological features of the asthmatic process, mediators of pulmonary inflammation including viral and environmental factors, animal models of asthma, and asthma therapy. The emphasis of the cytokine symposia was the regulation of type 2 cytokines and their interaction with antibodies, receptors and inflammatory cells. Joint sessions were also held covering the role of cytokines in asthma pathology.

Many of the speakers at the conference are world leaders in their area of research and the standard of the presentation was excellent. Here are a few outlines of some of the talks that I particularly enjoyed. Dr Stephen Holgate gave a talk entitled, 'The Interaction Between Airway Inflammation and Tissue Remodelling in Chronic Asthma'. In this he proposed a mechanism to explain the increase in bronchial smooth muscle, thickening of the basement membrane and subepithelial fibrosis seen in the lungs of chronic asthmatics. He proposed that inflammatory mediators disrupt connections between respiratory epithelial cells so that the subepithelial layer becomes exposed to environmental factors. These damaged epithelial cells produce increased levels of growth factor which results in increased myofibroblast activity and elevated collagen production.

Dr Thomas Platts-Mills presented a very entertaining talk on asthma epidemiology drawing on data from studies in Africa and on activity profiles of children in developed countries to try to understand the increase in asthma prevalence since the 1950s. He did not make any definite conclusions as to why this increase has occurred but brought up some very interesting points such as the marked difference in childhood exercise between children in England and in Africa. He also pointed out that while the house dust mite is a common allergen in many western societies, in Sweden where there has been a similar increase in asthma, house dust mites are not found but cat, dog and birch pollens are the main allergens. This was a fascinating talk that showed that we are still a long way from understanding the many factors involved the development of asthma.

Dr Robert Lemanske gave a talk on the role of viral infection in early infancy and the development of asthma. He proposed that a difference in cytokine expression between individuals results in one person developing asthma and the other not. It appears that genetic differences determine whether a type I or type 2 cytokine profile develops in response to viral infection and this sets the ground for development of asthma. Using a rat model he has shown that treatment with an aerosol of interferon- γ , a type I cytokine, reduces bronchial inflammation and airways resistance.

I presented a poster of my work on eosinophil peroxidase substrate preference at one of the daily poster sessions. This was an interesting experience especially as I gained a perspective of where my research sits within the field of asthma research.

As a whole, this conference was very interesting and well presented and I gained valuable knowledge on asthma and eosinophil biology. I am very grateful to the Sydney Free Radical Group for providing funds for me to attend this conference which was a tremendous experience all round.

REDOX REPORT: The Official Journal of SFRR(A)

Last year the Society adopted Redox Report as its official scientific journal. So far the benefits that have accrued in both directions include the following:

1. Society members receive a reduced subscription rate (a 62% saving over the normal subscription rate).
2. The journal will publish, in 2 batches, about 40 “mini-papers” arising from the “Oxidative Pathways in Health and Disease” conference held in Sydney in December 1999. The papers were reviewed and amendments requested and made in the normal way, so they will be run in the journal as “Short refereed papers”. The papers are about 3 pages long and have appeared in volume 4, issue 6 (December, 1999) and the remainder will be in volume 5, issue 1 (March 2000). These short papers turned out very well and the overall quality was good. Both the journal and the contributors benefit from having novel findings published quickly.
3. The publishers of Redox Report, Maney Publishing, are always ready to listen to suggestions for publication of conference proceedings.
4. From time to time the Journal runs announcements about forthcoming events associated with the Society.

The subscription rates for the Journal to members of SFRR (Australasia) is UK£48 or US\$78. The institutional subscription rate is £274 or US\$428. The journal is now available on-line to subscribers.

As one of the Chief Editors of the Journal, can I urge you not only to subscribe but to submit your work to the journal. We are particularly interested to receive submissions in the following areas:

1. Normal research articles.
2. Review articles (we like to get a short synopsis before committing ourselves when the article is author-initiated). We would particularly like to encourage people to ask students who have recently submitted their PhD theses to consider re-vamping parts of their Introduction section into a review article. The supervisor might well wish to be a senior author, to help change the material from thesis style to review style. Few people read PhD theses, lots more read review articles, so it seems sensible to get the students to take advantage of the often substantial amount of work they have put into their Introductions and get them published.
3. “Classic Redox” articles. Here someone undertakes to review, discuss or criticize a key publication, or group of publications, that have strongly influenced the free radical field. We are always looking for ideas for these – we don’t necessarily ask the person who came up with the idea to write the article, in case that is a deterrent !

On behalf of the journal, may I thank those members of the Editorial Advisory Board who live in our region for their services. We also greatly appreciate the reviewing expertise of members of SFRR (A).

Conference Travel Grants

- Travel grants will be provided each year on a competitive basis to the total value of A\$2000 for attendance at an international meeting related to free radical research within the same year. All financial members of SFRR (A) are eligible to apply and we welcome applications from Australia and New Zealand.
- Funds are available to those researchers aged 35 or less, except where a special case can be made to the Executive. Deadlines for applications are 1 January and 1 July of each year for meetings in the following 6 months. A nominated committee reviews all applications.

To apply submit a copy of the abstract for the conference to be attended, a Curriculum Vitae including a full list of publications, and two reprints to: Dr Roland Stocker, Secretary, Sydney Free Radical Group Inc., The Heart Research Institute, 145 Missenden Road, Camperdown, NSW 2050, AUSTRALIA

Collaborative Study Grants

SFRG, Inc. also provides support for collaborative studies in an overseas research laboratory for periods up to 3 months. The deadlines are as for the Conference Travel Grants. Applications must include a brief outline of and justification for the proposed research, a letter of support from the host laboratory, as well as a full CV of the applicant. Please submit applications to the Secretary, SFRG.

SFRR(A) Travel Award for attendance at the Xth International SFRR Meeting

A single travel grant will be provided on a competitive basis to the total value of NZ\$1500 for attendance at the Xth Biennial meeting of the International Society for Free Radical Research (ISFRR 2000) held in Kyoto, Japan. The award cannot be used to attend an alternate meeting.

The SFRR(A) Travel Award will be available to a financial member of SFRR (A) aged 35 or less. The Deadline for application is 1 July, 2000. A nominated committee reviews all applications. Proof of acceptance of the abstract may be requested at a later date prior to the recipient receiving the award.

To apply submit a copy of the abstract for the conference, a Curriculum Vitae including a full list of publications, and two preferred reprints to: Dr Paul Witting, Department of Biochemistry & Molecular Biology, Copp Building, 2146 Health Science Mall, University of British Columbia, Vancouver BC, V6T 1Z3 Canada.

Oxidants, Antioxidants and Nutrition



Wellington New Zealand, 9-11 December 2000

‘First Announcement’

A meeting of the Society for Free Radical Research (Australasia) to be held in conjunction with the Annual Meetings of the Australian and New Zealand Societies for Biochemistry and Molecular Biology.

Come and experience the best of New Zealand culture in the superb setting of Wellington Harbour

The symposium will start with a social function on the night of Saturday December 9. On Sunday, all sessions will be run by SFFR (Australasia). The sessions on Monday will be run jointly with ASBMB & NZSBMB. Full details of the conference and registration material will be available by May 1 2000. The closing date for reduced registration and abstracts is September 1 2000.

For more information please contact Tony Kettle (tony.kettle@chmeds.ac.nz)

Australian Institute of Nuclear Science & Engineering

RADIATION 2000

Venue: to be held at AINSE, Lucas Heights near Sydney, NSW, Australia

Sunday 26 – Tuesday 28 November 2000

In association with the Polymer Division, Royal Australian Chemical Institute
Incorporating the 20th AINSE Radiation Chemistry Conference
and the 17th Radiation Biology Conference

The conference topics will include

Radiation Chemistry	Radiation biology
Radiation and polymers	Radiation Oncology
Radiation Curing	Free Radicals and Oxygen
Plasma Chemistry/UUV	Protein Oxidation
Environment/dosimetry	Radiation sensitisation of DNA damage
Radiation Protection	Antioxidants in Biology
Nuclear Medicine	Radiopharmaceuticals

Deadlines

Paper titles with the name(s) of the author(s) and 7-line abstracts, together with an indication of preference for oral or poster presentation	15 May 2000
Advice to authors re acceptance of paper(s) for oral or poster presentation	8 June 2000
Distribution of Conference program and registration brochure	17 July 2000
Camera-ready, one page paper, including references and essential diagrams for inclusion in the Handbook	11 September 2000
Registration and payment of conference activities fee	11 September 2000

Paper Presentation

A Conference handbook containing one page papers will be distributed to delegates at the Conference. Authors will be allowed 20 minutes (including question time) during session times to present oral paper(s). A poster session will be held during the Conference.

For further information please contact

Irene Parker, Conference Co-Ordinator
RADIATION 2000

PMB 1, MENAI NSW 2234 Australia

Tel: (02) 9717 3436; Fax: (02) 9717 9268 Email: ainse@ansto.gov.au

WebSite <http://www.ansto.gov.au/ainse/ainse1.html>

For Your Diary

- 2000 -

April 15-18. Experimental Biology 2000, San Diego, California. Participating Societies: The American Physiological Society (APS), American Society for Investigative Pathology (ASIP), American Society for Nutritional Sciences (ASNS), American Association of Anatomists (AAA), The Biomedical Engineering Society (BMES), Society for Experimental Biology and Medicine (SEBM), American Federation for Medical Research (AFMR), The Microcirculatory Society (MCS), North American Society for Biorheology (NASB), Society for International Nutrition Research (SINR), American Society for Clinical Nutrition (ASCN). For further information: eb@faseb.org

May 18-19. 2nd International Conference on Superoxide Dismutase. Pasteur Institute, Paris, France. See www.isanh.com for more information.

June 4-8. ASBMB/ASPET Joint Meeting and Satellite Meetings Boston, Massachusetts Participating Societies: American Society for Biochemistry and Molecular Biology, The American Society for Pharmacology and Experimental Therapeutics, French Pharmacological Society, Pharmacological Society of Canada. The Call for Papers including electronic abstract submission information and Exhibit Brochure will be available on the Web in late October. For further information: drita@faseb.org

June 3-7. The First Biennial International Conference of the Nitric Oxide Society Hyatt Regency Hotel, San Francisco, CA. Contact: Krebs Convention Management Services 657 Carolina Street San Francisco, CA 94107-2725 Phone: 415-920-7000 FAX: 415-920-7001 or see the following website: <http://www.apnet.com/no/>

June 26-28. VIth Meeting of the Spanish Group on Free Radicals Cadiz, Spain Contact Person: Ana Navarro Arevalo. Tel: +34-956015231 fax: +34-956015230 E-mail: ana.navarro@uca.es

July 16-20. Sixth International Symposium on Biological Reactive Intermediates (BRI VI) Paris, France Contact: Patrick Dansette Universit Ren Descartes, CNRS URA 400 45, rue des Saits-Peres 75270 Paris Cedex 6 E-mail: dansette@diti2.fr

July 20-22. Liverpool 2000: Summer Meeting of SFRR Europe Contact Malcolm J. Jackson The University of Liverpool Department of Medicine The Duncan Building, Daulby Street Liverpool, L69 3GA Tel +44-151-706 4072 Fax +44-151-706 5802

July 27-30. Micronutrients and Health. Molecular Biological Mechanisms Island of Langkawi, Malaysia Contact: Augustine S.H. Ong Malaysian Invention and Design Society Tel 011-60-3-833-0703 Fax 011-603-754 9298 E-mail TSO@minds.org.my

August 28-September. International Society on Oxygen Transport to Tissue 27th Annual Meeting - Dartmouth College - Hanover, NH www.dartmouth.edu/~eprctr/ISOTT99/isott99.html Contact: Harold Swartz, MD PhD Dept Diagnostic Radiology Dartmouth Medical School 7785 Vail, Room 703 Hanover, NH 03755

September 3-8. The Peroxidase Superfamily II of Animal and Human Enzymes: Biochemical Basis and Clinical Application. Vienna, Austria. The tOrganizing Committee can be contacted at: myelo@edv2.boku.ac.at and at web page is accessible at : <http://www.boku.ac.at/pod2000/>

September 6-10. XIth International Vascular Biology Meeting Geneva, Switzerland. Contact: IVBM 2000, c/o-MCI Group SA, Rue de Lyon 75, 1211 GENEVA 13-SWITZERLAND, Fax: +41 22 340 2363. E-mail: anne-lise@mcitravel.com

September 19-22. Third European Symposium of the Protein Society, Garmisch-Partenkirchen, Germany Meeting Information Organizer: Wolfgang Baumeister, Max-Planck-Institut für Biochemie, D-82152 Martinsried. Contact: Third European Symposium of the Protein Society Meeting Office 9650 Rockville Pike, Bethesda, MD 20814-3998, USA, Telephone: 301-530-7010 Fax: 301-530-7014 Website: www.faseb.org/meetings/europro99, E-mail: europrot99@faseb.org

October 1-5. 7th International Symposium on Selenium in Biology and Medicine (SELENIUM 2000) Fondazione Giorgio Cini, Isola di San Giorgio Maggiore, Venice, Italy Contact: Prof Fulvio Ursini, Department of Biological Chemistry, University of Padova, Italy Tel +39-049-827-6104 Fax +39-040-8073310 E-mail ursini@civ.bio.unipd.it

October 16-20. Xth Biennial meeting of the International Society for Free Radical Research (ISFRR 2000). Kyoto International Conference Hall. Correspondence to SFRR 2000, C/o- JTB Communications Inc., Shin Kyoto Center Bldg. F5, Shiokoji Shinmachi, Shimogyo-ku, Kyoto 600-8216, Japan. Tel: +81 75 341 1618. Fax: +81 75 341 1917. E-mail: sfr2000@jtbcom.co.jp

November 16-20. 7th Annual Meeting of The Oxygen Society, Paradise Point Resort, San Diego, California USA. Registration information and abstract submission forms will be mailed in April 2000 to all persons on The Oxygen Society mailing list. If you are not a member and wish to receive this information via mail, please forward full address information

SFRR (Australasia) 2000 Membership Application Form (Subscription due date July 1, 2000)

Title: _____

Name: _____

Address: _____

Phone _____ Fax: _____

E-mail address: _____

Research Interest: _____

Annual Fees: (please tick the appropriate category)

Full Membership Aus\$30/NZ\$35 Student Membership Aus\$15/NZ\$17

Make a Cheque payable to **“Society for Free Radical Research (Australasia)”** in either Australian or New Zealand Dollars and send it to the following:

Dr Michael Murphy
Treasurer SFRR (Australasia)
Biochemistry Department
University of Otago
Box 56
Dunedin
New Zealand

Signed: _____ Date: _____

Student application only: Please ask your supervisor to complete the declaration below:

I confirm that the above applicant is at present a student under my supervision

Signed: _____ Date: _____