



SOCIETY FOR FREE RADICAL
RESEARCH
(Australasia)



NEWSLETTER May, 2001

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The Executive would like to thank all those who have contributed to this first issue of the Newsletter for 2001. 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 the current 2000-2001 "Diary". This Newsletter will be sent via E-mail to the greater membership and only a few members without e-mail access will receive actual hard copies via surface mail. In an effort to cut overhead costs we urge all members to gain access to e-mail and please forward your e-mail address to the Secretary, Dr Paul Witting. 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). The Executive also take this opportunity to warmly thank Dr Michael Murphy for his service as Treasurer of SFRR(A) over the last 3 years and wish him all the very best in his new appointment in Britain.

From the President:***Dear Fellow Radicals***

The dust has settled slowly after our conference in Wellington but it is now time to look ahead and to establish a number of new initiatives for our society. These include expansion of our membership, fostering links with our Japanese colleagues, and making the society an incorporated organisation.

It was clear from the meeting in Wellington that we have a very solid but small core of enthusiastic members who maintain the vitality of the society. If our society is to grow and be actively involved at the leading edge of research, we must expand our core. We need more enthusiasts in diverse areas of free radical biology and medicine to become involved in the society. Nutrition is one area that we need to embrace and recruit new people from. There are obvious signs from the business world that antioxidants, either in foods or pills, are on an explosive growth curve. Yet it is equally clear that the science behind nutritional antioxidants is in its infancy. This situation presents the society with some golden opportunities. I am sure there are many nutritionists within Australasia who would like to link up with chemists and biochemists to understand how antioxidants work in our bodies. Paul Talalay, our plenary speaker in Wellington, was a shining example of how successful scientists can be when they use the best tools in biochemistry to explore curiosities in nutrition. Collaborations with nutritionists will also help attract business sector support to our research and the activities of the society. We must also entice more of our clinical collaborators along to our conferences. Through them we can convince the wider research community of the importance of reactive oxidants and of the need to apply solid science to clinical problems. I strongly encourage all our members to invite or coerce their contacts in related areas to participate in our conferences.

Our next meeting in Sydney will be an excellent platform for recruiting new members to the society. Roland Stocker and his team are doing an excellent job in organising this meeting. As society members the best way we can help them, and the society, is by dragging as many new researchers along as possible. The conference itself is a new initiative in that it is being run jointly with SFRR members in Japan. I am sure a successful meeting will forge stronger links with our Japanese colleagues, which will benefit us all in the long term. **Preliminary details for the meeting can be found in this Newsletter and I urge all members to consider attending what promises to be a great meeting.**

At this stage we have not finalized a location for our meeting in 2002. Please consider getting involved. Let me assure you that organising a meeting is a rewarding experience and is not as onerous as you might think. It could be a small focussed conference along the lines of the recent Wellington and Melbourne meetings.

The Society is looking at becoming an incorporated body primarily to minimize the financial risks associated with running our meetings. To date local organisers have been liable for any losses incurred. My personal experience is that this situation provides an overwhelming incentive to organise a successful meeting. However, it puts an unjust pressure on members who volunteer to host meetings for us all. Therefore, the secretariat will move as quickly as possible to become incorporated.

Finally, I would like to welcome Des Richardson as our new Treasurer. He is dead keen to get involved and is anticipating all those membership renewals that are about to be sent in. I wish you all the best for the year and hope that the joy of scientific discovery can still be placed high on your priority list.

Tony Kettle

Oxidants, Antioxidants and Nutrition: The 9th Annual Meeting of SFRR (Australasia)
Te Papa, Wellington NZ, 9-11 December 2000.

I would like to take the opportunity to reflect on our recent conference that was held at Te Papa in Wellington. I will not give a detailed account of the science presented except to say that the standard was very good with many high points and only a few lows. Rather, I would like to give some of my impression on organising the meeting.

The conference was well attended and there were many new faces amongst the delegates. Clearly, there is currently a new wave of interest in free radicals which is predominantly from the antioxidant area. It was great to catch up with all the Australians who crossed the ditch. Without you the conference would not have been the success it was. I can appreciate the expense required in coming to New Zealand and thank you for making the effort. For those who missed the meeting, I hope we can get together again in Sydney at the end of the year.

Running the conference in conjunction with ComBio2000 did not have the expected bonus of capturing more delegates to our meeting. Rather it created difficulties in obtaining sponsorship from traditional sources. This made us think laterally and seek sponsors who promote foods on the basis of their antioxidant content. There was an enthusiastic willingness of these commercial companies to support us as they could see real benefits in aligning their products with hard science. Our promotion of the conference in the media was greatly appreciated by the main sponsor. Paul Talalay, our plenary speaker, took to the media with style and did an entertaining job of promoting broccoli sprouts and SFFR. Keep an eye out for all those companies in Australasia who advertise the benefits of antioxidants in their products. They might like to help us one day!

The one distinct advantage of combining with ComBio 2000 was the great attendance we got at our Oxidative Stress Symposium that was held at the ComBio centre. All the talks presented in the symposium were excellent and the speakers showcased our society superbly. It was the best attended symposium of that day and demonstrated that there is a real interest in oxidative biochemistry throughout Australasia. The success of the joint symposium indicates that at some stage in the near future we should consider linking up with a major biochemistry/chemistry meeting in Australasia.

Finally, I would like to thank all delegates who attended the meeting and to acknowledge the great work done by Helena Parson-Muir and the rest of my team in organising the meeting.

Tony Kettle

Minutes of the 9th Annual Meeting of the SFRR(Australasia)

Venue: Te Papa, Wellington

Date: 11th Dec 2000

Present: Tony Kettle (President and Chair), Roland Stocker, Mike Murphy (Treasurer), Kevin Croft, Nick Hunt, Mike Davies (President-elect), Peter Southwell-Keely, Ian Dawes, Christine Winterbourn, Rex Munday, Bob Anderson, Steven Giesege, Margret Vissers, Mark Hampton, Roger Dean, Mike Berridge.

1. Apologies:

Paul Witting, Dedee Murrell, Jan Gebicki, Silvia Gebicki, Rheal Towner, Ian Gillam, Ian Clark, Anneke Blackburn, Adrienne Grant, Mark Baker, Garry Graham, Phil Burcham, Trevor Mori.

2. Business arising:None

3. President's Report:

Annual conferences: Tony strongly endorsed the concept of continuing to have annual meetings. Roland Stocker originally proposed that we move from biennial to annual meetings and he felt that this move has worked extremely well. The current conference has attracted ca. 85 registrants at this meeting, which was well beyond expectations. There is considerable interest in antioxidants from nutritional groups, and we should be in a position to benefit from this. Tony suggested that as a society we should endeavour to make more contact with those interested in nutrition so as to strengthen both our society and assist in promoting research collaborations.

Practicality of joint meetings: Having been the main organiser of the current meeting, Tony suggested that the Society think carefully about holding future meetings as satellites to major conferences. The original idea was that such joint meetings would help attract more delegates to the Societies meeting and bring in new members. However, these potentially positive aspects must be balanced against difficulties in obtaining sponsorship, suitable venues, and lack of flexibility in timing of the meeting.

Mike Murphy: Tony, on behalf of the whole Society, thanked Mike Murphy for the tremendous work he had done for the society over the last three years as treasurer. These efforts were very much appreciated. Tony also extended the Society's thanks to Teena Joyce of the Biochemistry Department at Otago University for assisting Mike in his role as treasurer.

Redox Report: Tony endorsed the move to have Redox Report as our official journal. It has the potential to be an ideal flagship for the SFRR(A) and helps promote free radical research in this part of the world.

Membership renewal: A number of active members in the society have not renewed their membership. Tony commented that he will work with the new treasurer over the next year to ensure that all active members pay their fees. The Society will also endeavor to increase membership by targeting those who are involved in the wider area of free radical biology to join the society.

Thank you: Tony extended his thanks to Paul Witting for his excellent work as secretary, and his willingness to continue in this role. Tony also thanked Nick Hunt for maintaining our web page, and Roland Stocker for attending SFRR(A) meetings as our representative and for taking up the organisation of our next meeting.

Treasurer's Report: Mike Murphy presented a report on the current status of the Society's bank account that is in a healthy state, having a balance of NZ\$20 529.81. There were a small number of outstanding bills to be paid including our dues to the International Society. The latter need to be paid soon by the incoming Treasurer. Tony Kettle reported that the Wellington meeting should break even and may even make a small profit, though this would depend on the size of outstanding bills.

Secretary's Report: Paul thanked all those who have contributed to SFRR(A) [particularly to the Newsletter] over the last year, and commented that the Executive will endeavour to continue to keep SFRR(A) members informed via the Newsletter. The society has moved almost completely to email as the avenue for distribution of the Newsletter. All members are urged to gain access to e-mail and forward their address to Tony Kettle. Paul encouraged the membership to visit the SFRR(A) web-site for on-line information on the free radical society and its associated branches world-wide. The web-site

(<http://www.med.usyd.edu.au/path/society2.htm>) also contains useful links to a wide range of information as well as a calendar of up-coming events.

Paul encouraged the members of the society to submit relevant articles and news to the Secretary, so that they can be made available to the SFRR(A) membership. Paul commented, that though he was currently in Canada (until February 15), he would be moving shortly thereafter, and will notify the membership of his new address.

Election of Treasurer: As a result of Mike Murphy's imminent departure for a new position in Cambridge, a replacement Treasurer was required. Two candidates were nominated and seconded for the position: Dr. Des Richardson and Dr. Steven Gieseg. Dr. Des Richardson was elected to the position on a show of hands. Both candidates were thanked for their interest in the position.

Travel Awards: As a result of the relatively sound current financial situation of the Society a question was raised as to whether the Society should maintain the current surplus as a capital reserve, or whether it should allocate some of these monies for further student travel awards. After some discussion, in which a number of different options were canvassed, it was agreed that the Society should allocate a further sum of up to \$2000 for student travel / conference registration for the alternate years between those containing an International meeting (where one, or more, awards to a total value of \$2000 had previously been agreed). This sum would be used to fund either one, or multiple, awards at the discretion of the awards committee.

Subscription to Redox Report: Prof. Nick Hunt addressed the meeting on the subject of the proposed link between subscription to the Society and subscription to the journal Redox Report. A previous canvass of the members had resulted in feedback to the President that the majority of the members would only support such a motion if postgraduate students and junior post-docs were omitted from this requirement. After further discussion in which various arguments both in favour, and against, such a link were aired it was agreed that the inclusion of a subscription to Redox Report with the Society membership would need to be investigated further, as it was felt that the resulting increased cost of membership might exert a further negative effect on fully-paid membership of the Society and that the resulting benefit to the publisher, and the journal, would be small. It was therefore agreed that Prof. Hunt should negotiate further with the publisher of Redox Report to see whether a reduced rate, electronic access, subscription might be available, as this might be more attractive to the membership of the Society. This subject would be re-examined at the next AGM.

Future Annual Meetings: The next meeting of the Society would be in Sydney over the period 1-4th Dec. 2001. For 2002 it was agreed that Melbourne would be a suitable venue, though this is dependent on the availability of suitable local organisers. Tony Kettle would approach potential people. In the absence of any suitable organisers, Perth (Kevin Croft et al) would be approached. For 2003, Dr Bob Anderson raised the possibility of a joint meeting (or an associated satellite meeting) with the large International Congress on Radiation Research that would be held in Brisbane in mid-August 2003. As there are likely to be both positive and negative aspects of such a joint meeting (e.g. cost, loss of autonomy, a lesser or more broad program, larger number of international speakers), Dr. Anderson was asked to investigate the potential links more closely and liaise with the Society executive.

Other Business: The role of the Society in underwriting meetings of the Society was discussed (partly arising out of item 7.) as the organisers of the Society meetings to date had been under pressure to accept financial liability. This was a major risk for the individuals involved and might prove to be a negative factor. As such it was agreed that the Society should move, as soon as possible, towards becoming an incorporated body (in Australia, as this has a more advantageous tax regime) with public liability, which would minimise such risks to the organising committee. The new Treasurer and the executive were asked to progress this matter. The President of the Sydney Free Radical Group (SFRG) - Prof. Roger Dean - commented that this organisation had already got such incorporated status and that there might be advantages in either using this company as the organising body, or amalgamating the resources of these two bodies. Prof. Dean agreed to bring this matter to the attention of the members of the SFRG and determine their reaction.

It was also mentioned that the International SFRR committee was encouraging each of the member organisations to adopt their own constitution and rules. It was agreed that this might be most easily achieved by adapting the current constitution of the International organisation. The executive agreed to progress this matter.

The members of the society at the meeting thanked Dr. Tony Kettle and Ms. Helena Parsons-Mair for their tremendous efforts in organising a highly successful and enjoyable meeting.

“Redox Processes in Chemistry, Biology and Medicine”

November 30th - December 4th 2001

Joint meetings of:

**The Society for Free Radical Research (Australasia) &
The Society for Free Radical Research (Japan)**

Venue: The Veterinary Faculty Conference Centre, University of Sydney, Sydney, Australia.

Sponsored by: Unilever
Linus Pauling Institute
Sydney Free Radical Group Inc.

First announcement of a major international conference of interest to all researchers working in the area of redox reactions, oxidative stress, free radical chemistry and biochemistry, and the role of oxidative damage in experimental pathology and mutagenesis.

Topics to be covered by the conference include:

- Ageing,
- Apoptosis and Necrosis
- Cancer
- Inflammation
- Markers of Oxidative Stress/Damage
- Metal Ions and Redox Chemistry
- Microorganisms, Immune Responses

- Peroxidases, Cytochrome P-450 and Oxidative Strength
- Photo- and Radiation Biology
- Plants, Plant-derived and Other Natural Antioxidants
- Polymerization, Catalysis and Inhibitors
- Radicals in Chemical Synthesis
- Reactive Nitrogen Species
- Redox Control of Activity of (Metal-Free) Proteins
- Redox Regulation of Cellular Function
- Redox Processes in Cardiovascular Diseases
- Relationship between Markers of Oxidative Damage and Disease
- Singlet Oxygen
- Synthetic Antioxidants, Pharmaceuticals, Vitamins and Coenzymes

The conference will include sixteen lecture and two poster sessions.

Approximately half of the oral presentations will be selected from submitted abstracts.

Keynote and invited speakers

Kevin Croft

Ian Dawes

Chris Easton

Jason Eiserich

Balz Frei

Junichi Fujii

Phillip Hogg

Tony Kettle

Satoshi Kokura

Martin Lavin

Michael Murray

Yasukazu Nakagawa

Hajime Nakamura

Futoshi Okada

Salvatore Pepe

Makoto Suematsu

Shinya Toyokuni

Koji Uchida

Hideo Utsumi

Joe Vita

Christine Winterbourn

Yorihiro Yamamoto

General Information:**Venue and Travel**

The meeting will start at 5 pm on the 30th November and finish at ca. 5 pm on the 4th December. The conference venue is the University of Sydney Veterinary Pathology Conference Centre on the central campus of the University of Sydney, within easy reach of the city centre and airport.

Registration

Registration cost includes a mixer on the evening of Nov 30, morning and afternoon coffee and tea, refreshments and lunches on 1-4th December and two evening receptions associated with the poster sessions. Full details of costs will be given in the second announcement.

Accommodation

Three grades of accommodation have been pre-booked for delegates: University Halls of residence (Womens College, Sydney University A\$37-70 per person), the Centra Hotel (A\$126 per person) and the Mercure Hotel (A\$126 per person). The first two are within easy walking distance of the venue, the latter is on a major bus route (or ~25 minutes walking distance).

Deadlines

Deadline for registration and receipt of abstract submissions is: *Oct 1st 2001*.

Further details on the submission of abstracts and registration costs will be given in the second announcement and posted on the conference web site:

<http://www.med.usyd.edu.au/path/society2.htm>

Further Information:

If you would like further information about the conference please complete the following form and return it by post or email to:

Kaylene Thomas,
Redox Processes in Chemistry, Biology and Medicine,
The Heart Research Institute,
145 Missenden Road,
Camperdown, Sydney, NSW 2050,
Australia

Or email to: sfrr.sydney.2001@hri.org.au

Please type or print in capital letters:

Family

name: _____

First

name: _____

Title: _____

Institution: _____

Address:

Postcode: _____

Country: _____

Email: _____

Telephone: _____

Fax: _____

RESEARCH PROFILE : Dr. Phil Burcham

Laboratory Address: Molecular Toxicology Research Group, Dept. Clinical and Experimental Pharmacology, Medical School, Adelaide University, North Terrace Campus, Adelaide, 5005. *Phone:* 08-8303-5287, *Fax:* 08-8224-0685, *Email:* philip.burcham@adelaide.edu.au

Research Staff (2001)

<u>Postdoctoral</u>	<u>Postgraduate Students</u>	<u>Honours Students</u>
Dr. Frank Fontaine	Lisa Kaminskas Suzanne Froscio	Rhoula Ghaoui

Research Interests

The long-term goal of this Group is to better understand the molecular toxicological properties of reactive lipid-derived intermediates, with a view to clarifying their role in the toxicity accompanying exposure to pro-oxidant xenobiotics. In recent years our emphasis has shifted from a focus on genetic damage by lipid peroxidation products to the role of protein modification by toxic aldehydes in oxidative cell injury.

Immunochemical Detection of Aldehyde-Modified Proteins in Hepatocytes.

Our present interests predominately revolve around the protein-damaging properties of two short-chain *2-trans*-alkenals, acrolein (*2-t*-propanal) and crotonaldehyde (*2-t*-butenal). These reactive compounds possess diverse toxicological properties and have long concerned toxicologists due to their presence as environmental contaminants in various settings. Somewhat surprisingly, comparatively little is known concerning their mechanism of toxic action at the molecular level. Our interest in these two toxic compounds is partly due to the fact that acrolein and crotonaldehyde have long been identified in peroxidised lipid mixtures, raising the possibility that they contribute to cell damage during oxidative stress. The discoveries in other labs during the mid-1990s that acrolein- and crotonaldehyde-derived DNA adducts are present in the human genome, presumably as a result of endogenous production, suggests these substances might also participate in damaging the proteome. However while the contribution of toxic aldehydes such as malondialdehyde and 4-hydroxy-2-nonenal to protein damage during oxidative stress is receiving attention in a number of laboratories, less is known concerning the significance of acrolein or crotonaldehyde production during oxidative cell injury. Using an immunohistochemical approach, Uchida and associates have established that acrolein-modified proteins are present in the affected tissues of patients with a number of degenerative conditions that are known to involve oxidative stress (eg. diabetic nephropathy, Alzheimer's, etc). At present, which cell proteins are involved in the formation of these adducts is not known. Thus one goal of work in our lab is to identify critical proteins that sustain damage during acrolein- and crotonaldehyde-mediated cell injury, in the expectation that such knowledge will illuminate the critical biochemical perturbations underlying the toxicity of these substances.

The main experimental approach we are using to detect damaged proteins during aldehyde-mediated toxicity involves the use of antibodies in Western blot procedures. In the past we have exploited the fact that Michael addition reactions (to form carbonyl-containing adducts) feature strongly during the reaction of *2-trans*-alkenals with proteins. Thus we have used an immunochemical assay based on derivatisation of

carbonylated proteins with 2,4-dinitrophenylhydrazine followed by immunodetection with anti-dinitrophenyl sera to detect modification of a wide range of proteins in the early stages of aldehyde-mediated toxicity in mouse hepatocyte monolayers.

To selectively study protein damage by acrolein and crotonaldehyde in isolated cells, we have explored the use of unsaturated alcohol precursors as a means to generate these aldehydes directly within the intracellular environment. This avoids the problem of side reactions between these reactive aldehydes and cell culture media components that confound experiments where reactive aldehydes are directly added to cells. Allyl alcohol, which undergoes rapid oxidation to acrolein via an alcohol dehydrogenase-dependent pathway, has enabled us to establish that extensive protein carbonylation precedes acrolein-mediated cell-killing in isolated liver cells. Furthermore, novel work conducted by Honours student Ms. Rachael Dunlop (recently commenced candidature as a PhD student at the HRI in Sydney) as well as Dr Frank Fontaine established that *2-trans*-crotyl alcohol is useful for studying crotonaldehyde-mediated protein damage and toxicity in isolated cells. As with allyl alcohol, the toxicity of crotyl alcohol in isolated hepatocytes was completely abolished by 4-methyl pyrazole, while it was enhanced by the aldehyde dehydrogenase inhibitor cyanamide. This confirms that an aldehydic oxidation product (crotonaldehyde) was responsible for the acute toxicity of crotyl alcohol. This ability to control the generation of acrolein and crotonaldehyde directly within the intracellular environment of hepatocytes provides a powerful approach to comparing patterns of protein damage by these substances in a model where such damage can be carefully related to cytotoxicity and other biochemical end-points.

Recognising that protein carbonylation is a blunt tool for studying protein damage by unsaturated aldehydes, we have recently commenced production of polyclonal antibodies that recognise protein adducts formed by individual *2-trans*-alkenals, including acrolein and crotonaldehyde. This work is conducted primarily by Dr Fontaine as part of a NH&MRC-funded project. The first antibody produced during this effort recognises acrolein-modified lysine residues in proteins with high sensitivity. More importantly, cross-reactivity of this antibody with adducts formed by other endogenous aldehydes (such as malondialdehyde, methyl glyoxal or even crotonaldehyde) is essentially negligible, at least under conditions of an ELISA-based assay. Dr Burcham is currently optimising the use of the anti-acrolein sera in Western blot procedures during a sabbatical in the laboratory of Prof. Dennis Petersen at the University of Colorado Health Science Center. The preliminary data from this effort suggests that this approach provides more toxicologically-significant insights into protein damage during allyl alcohol toxicity than is provided by protein carbonylation assays.

Aldehyde-Trapping Compounds as Pharmacotoxicological Tools.

Concurrent with our efforts to characterise the role of reactive *2-trans*-alkenals during oxidative cell injury, we are also seeking to identify compounds with strong aldehyde-sequestering properties for use in our experimental models. To this end we examined the acrolein-trapping potential of various amine compounds with reported abilities to trap other lipid-derived aldehydes such as malondialdehyde and 4-hydroxy-2-nonenal (eg. aminoguanidine, carnosine, pyridoxamine, methoxyamine, etc). During this work, we found that compared to the aforementioned amine compounds, the phthalazine antihypertensive drug hydralazine possesses remarkable acrolein-trapping properties. In conjunction with Dr Simon Pyke in the Chemistry Department at Adelaide University, Dr Fontaine recently isolated and characterised a Schiff-base adduct that forms rapidly during reactions between hydralazine and acrolein. Micromolar concentrations of hydralazine also strongly protected hepatocytes against acrolein-mediated cell killing. More recently, we

established that the di-substituted hydralazine analogue, 1,4-dihydrazinophthalazine (dihydralazine), exhibits even greater acrolein-trapping potential than hydralazine itself. In work that is partly funded under the ARC Small Grant Scheme and co-supervised by Dr Pyke, Lisa Kaminskas recently commenced a project that involves synthesis of various heterocyclic compounds that are chemically-related to hydralazine. We expect that this work will define the molecular features contributing to the pronounced reactivity of hydralazine with acrolein, and also inform as to whether this reactivity can be dissociated from other pharmacological and toxicological properties of hydralazine (eg. vasodilatory properties, immunotoxicity, etc).

Collaborative Interests.

We are actively involved in collaborative research with several other groups. In particular, work by a previous PhD student from the Group, Dr Felicity Nicholls-Grezemski (currently working at Washington State University) identified a new phenomenon that has attracted the attention of a number of groups worldwide. She established that pretreatment of mice with a diverse group of peroxisome proliferators (eg. clofibrate, silvex, dibutyl phthalate) afforded dramatic protection against the toxicity of a number of bioactivation-dependent hepatotoxic agents. Although the biochemical basis for this effect remains obscure, we have established that an enhanced resistance to oxidative stress accompanies the hepatoprotective phenomenon. The precise mechanisms underlying this response are under active investigation.

In work conducted in conjunction with Dr Betty Sallustio (Pharmacology & Haematology, The Queen Elizabeth Hospital, Adelaide), we also described pronounced DNA-nicking properties for a reactive class of Phase II drug conjugates, the acyl glucuronides. In on-going work, Ms. Rhoula Ghaoui is seeking evidence for such damage in isolated cells treated with the parent aglycones.

Finally, in collaboration with Professor Ian Falconer (Emeritus, Adelaide University) and Dr Andrew Humpage (CRC Water Quality, Bolivar, S.A.), Ms. Suzanne Froscio is exploring the mechanistic aspects underlying the pronounced hepatotoxicity of the blue green algae toxin, cylindrospermopsin. Since the toxicity produced by this substance is preceded by disruption of thiol homeostasis, Ms. Froscio is exploring the role of oxidative stress in cylindrospermopsin hepatotoxicity.

Representative Publications.

- Nicholls-Grzemski, F.A., Belling, B.G., Priestly, B.G., Calder, I.C., and Burcham, P. C. (2000) Clofibrate-pretreatment in mice confers resistance against hepatic lipid peroxidation. *J. Molecular and Biochemical Toxicology*, **14**, 335-345.
- Nicholls-Grzemski, F.A., Calder, I.C., Priestly, B.G., and Burcham, P. C. (2000) Clofibrate-induced *in vitro* hepatoprotection against acetaminophen is not due to altered glutathione homeostasis. *Toxicological Sciences*, **56**, 220.
- Burcham, P. C., and Harkin, L. A. (1999) Mutations at G:C Base-Pairs Predominate After Replication of Peroxyl Radical-Damaged pSP189 Plasmids in Human Cells. *Mutagenesis*, **14**, 135-140.
- Burcham, P. C. (1999) Internal Hazards: Baseline DNA Damage by Endogenous Products of Normal Metabolism. *Mutation Research*, **443**, 11-36.
- Harkin, L. A., Butler, L. M., and Burcham, P. C. (1997) Role of G T transversions in the mutagenicity of alkylperoxyl radicals: Induction of alkali-labile sites in bacteriophage M13mp19. *Chemical Research in Toxicology*, **10**, 575-581.

Sallustio, B. C., Harkin, L. A., and Burcham, P. C. (1997) Genotoxicity of acyl glucuronide metabolites formed from clofibrac acid and gemfibrozil: a novel role for Phase II-mediated bioactivation in the hepatocarcinogenicity of the parent aglycones? *Toxicology and Applied Pharmacology*, **147**, 459-464.

Conference Report:

Oxygen Society Meeting: San Diego California, 16-20 November 2000

The 7th annual meeting of the Oxygen Society was held at Paradise Point resort San Diego CA, the conference centre being on the edge of beautiful Mission Bay and directly opposite Sea World San Diego. All abstracts submitted to the meeting are presented in mini-form in the Supplement to Free Radical Biology and Medicine (Vol 29, 2000). The meeting was preceded by a workshop broadly entitled "In vivo Assessment of Oxidative Stress and Antioxidant Status: From concepts to validation" that attracted a large number of delegates from all over the globe.

In keeping with the program of past meetings each day started with the Sunrise Free Radical School hosted by Master Teacher Dr Gary Beuttner. Overall, I found the discussions in this allotted time from 8.00 am to 9.30 am to be the most stimulating and provocative in terms of scientific content. Alberto Boveris started the first official day of the meeting (Friday) with an overview of free radical generation in mitochondria, focusing on mtNOS as a source of nitric oxide generated by mitochondria. This led onto a forum where the Role of Mitochondrial Oxidative Stress was the focus of the days presentations with speakers such as Guy Brown, Enrique Cadenas, Victor Darley-Usmar and Cecelia Giuvili presenting sub-plenary lectures before a crowd of ~600-700 delegates. The afternoon was dedicated to selected oral presentations and poster session that lasted well into the early evening: this program was repeated for each of the remaining days.

Saturday saw presentations based on cell signaling and redox-controlled cellular response. The highlight for me during the sub-plenary session was Dr Al Claiborne's (Wakeforest University North Carolina) presentation. Dr Claiborne illustrated that hydrogen peroxide is not necessarily only to be considered as a two-electron oxidant but rather proteins containing thiol moieties can yield a sulfenic acid in a reversible process that can ultimately modulate bio-activity of the protein.

The whole of Sunday was dedicated to nitric oxide and the day was started with an excellent presentation by Dr Jack Lancaster (Louisiana State University) speaking on the physical properties of NO. This was again followed by a variety of sub-plenary speakers discussing a role for NO in inflammation. Of particular interest was a presentation by Dr Paul Kubes (University of Calgary, Canada) who showed real-time video data illustrating leukocyte adhesion to micro-capillaries treated with chemotactic agents (from *in situ* microscopy on mesenteric capillaries) and the

subsequent infiltration of these cells to the interstitial space. The infiltrating cells were also activated to release oxidants as evidenced by parallel fluorescence microscopy using a redox sensitive probe on the same micro-capillaries.

Monday (the final day) was dedicated to the role of dietary antioxidants in disease. As a matter of interest, Dr John Erdman (University of Illinois) presented a lecture describing the “National Academy of Sciences” press release of guidelines for “Dietary Reference Intake of Antioxidants and other nutrients”. The report [found at www.nationalacademies.org/news.nsf (go to News Archives and Search April 10, 2000)] outlined recommended intakes of dietary nutrients for the North American population. Overall, the meeting was well attended and well organised, with the exception of some of the projectors locking up on certain slides (delegates experiencing projector problems were applauded for their efforts to continue regardless and maintain the schedule). I would like to thank the National Heart Foundation of Australia for providing funding that allowed me to both attend and present data at this meeting.

Paul Witting

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. Previous awardee winners should not reapply.

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.

Amgen Award for Research Excellence

Past Winners were: Ismail Kola (1995), Glenn Begley (1996), Seong-Seng Tan (1997), Mark Smyth (1998), and Doug Hilton (2000).

We are all acutely aware of the importance of bringing discoveries in medical research to the bedside. The Amgen Medical Researcher Award is aimed at supporting and encouraging those researchers with demonstrated independence, excellence, innovation and achievements in medical research, with evidence of translation from bench to potential for application, with particular emphasis on research of the last 2 years.

The criteria for the selection of the successful applicant are: Evidence of research excellence - publications, patents, clinical trial involvement; Ten years maximum since qualifying for a PhD or equivalent degree; Preparedness to communicate research achievements with the public and media; & achievements in translational research. The presentation of this second national award will take place in Sydney on June 5th 2001, at a specially convened luncheon to which key media and institute heads are invited and at which there will be an address by the recipient.

The award is an international return economy airfare to a medical research conference of the winners choice, plus registration and accommodation expenses (to a maximum of \$5,000), and airfare and accommodation for the award ceremony.

Application forms are available for download at <http://www.asmr.org.au/mrw/Amgen01.pdf>

Peter O'Loughlin (President, ASMR)

Catherine West Executive Officer

The Australian Society for Medical Research

145 Macquarie Street,

Sydney NSW 2000

Phone: 02 9256 5450

Fax: 02 9252 0294

Email: asmr@world.net or

Home email: cwest@froggy.com.au

Website: <http://www.asmr.org.au>

For Your Diary**- 2001 -**

May 16-19, 2001. Diet and Optimum Health. Marriott Hotel, Portland, Oregon, USA. This conference is organized by the Linus Pauling Institute at Oregon State University to commemorate the 100th anniversary of Linus Pauling's birth. Scientific and public sessions will explore the roles of micronutrients, vitamins and phytochemicals in cancer, heart disease, neurodegenerative disorders and aging. For more information, contact: Balz Frei, Linus Pauling Institute, Oregon State University, Corvallis, OR 97331-6512, USA. TEL: +1 541 737-5075; FAX +1 541 737-5077; E-MAIL: balz.frei@orst.edu; WEBSITE: www.osu.orst.edu/dept/lpi.

May 21-22, 2001. Orphan Nuclear Receptors: Biology and ligand identification. Radisson Inn, Sunnyvale, California, USA. Contact: The Knowledge Foundation Inc. 18 Webster St, Brookline, MA, USA. Tel: 1-617-232-7400, Fax: 1-617-232-9171, E-mail: custserv@knowledgefoundation.com

June 4-7, 2001. Second International Symposium on Natural Antioxidants: Molecular Biological Action Beijing, China Corresponding Organizer: Bao-Lu Zhao Academia Sinica 15 Datun Road Chaoyang District Beijing, 199191, China; Tel 8610-64888576; Fax 8610-64877837; E-mail xinzhsc@sun5.ibp.ac.cn

8 – 12 July 2001. 9th International Congress of Toxicology ICT-IX, , Brisbane AUSTRALIA. Registration Brochure and Call for Abstracts is available on the Congress website, www.uq.edu.au/ICT9/. Alternatively, a hard copy of the Registration Brochure and Call for Abstracts may be obtained from the Conference Secretariat: ICT9 Congress C/- Intermedia P.O. Box 1280 Milton, QLD 4064. The closing date for abstract submission is February 5, 2001. Tele 07-3858 5496; Fax 07-3858 5511; E-mail ictix2001@im.com.au

September 9-12, 2001. The XIV International Symposium on Drugs Affecting Lipid Metabolism. New York Hilton and Towers. XIV DALM contact: Giovanni Lorenzini, Medical Foundation, 6550 Fannin, Suite 1211, Houston Texas 77030, USA. Tel: 1-77030-2704, Fax: 1-713-796-8853, E-mail: dalm2001@bcm.tmc.edu

September 16-19, 2001. The Third International Conference on Oxygen/Nitrogen Radicals: Cell Injury and Disease Morgantown, West Virginia, USA This conference will bring together prominent investigators to present current research on the role of reactive oxygen/nitrogen species in the areas of cellular and molecular mechanisms of disease processes. For more information contact: Val Vallyathan, TEL: 1-304-285-5770, FAX: 1-304-285-5938, E-MAIL: vav1@cdc.gov

November 15-19, 2001. 8th Annual Meeting of The Oxygen Society Sheraton Imperial Hotel and Convention Center Research Triangle Park, North Carolina, USA. For further information, contact The Oxygen Society at info@oxygensociety.org or via phone at (925) 472-5900.

December 1-4. Joint meeting of the Societies for Free Radical Research Australasia and Asia. University of Sydney Vet. Science Conference Centre. University of Sydney, Sydney. Contact: Kaylene Thomas, The Heart Research Institute, 145 Missenden R'd Camperdown, Sydney, NSW, 2050. Tel: 61-2-9550-3560, Fax: 61-2-9550-3302, E-mail: sfrr..sydney.2001@hri.org.au

December 4-8. New Zealand Institute for Chemistry conference: Molecules for life: including the meetings of the ANZSMMB and BIOTENZ Societies. War Memorial Centre, Napier, New Zealand. Register online at: www.hort.cri.nz/nzic

July 17-21, 2002. XIth Biennial Meeting of the International Society for Free Radical Research Paris, France Contact: Catherine Pasquier Tel 33 01 44 85 62 11 Fax 33 0144 85 62 07 E-mail pasquier@bichat.inserm.fr

Society for Free Radical Research (Australasia)
2001 MEMBERSHIP APPLICATION/RENEWAL FORM: (Due date 31 July 2001)

Title: _____ **Name:** _____

Address: _____

Phone: _____ **Fax:** _____

e-mail: _____

Research Interests (short description for the 2000 membership directory):

Annual Fees:

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

Please tick the appropriate box above and send a cheque payable to "Society for Free Radical Research (Australasia)" in either Australian or New Zealand dollars to:

Dr Des Richardson, Treasurer, SFRR (Australasia)
The Heart Research Institute
145 Missenden R'd
Camperdown, NSW
Australia
2050

Signature: _____

Date: _____

(Student membership only - ask your supervisor to complete the declaration below)

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

Name:

Signature:

Institution:

Date:
