



Highlights

- Prizes, prizes, prizes!!!
- Strong links have been forged between the AGTS & BSGT
- A New AGTS Travel Award

Editorial

Dear membership, the Australasian Gene Therapy Society (AGTS) Newsletter is a means to enrich your participation in our society. Please feel free to contact the AGTS secretary (d.wei@mailbox.uq.edu.au) or myself (r.martiniello@centenary.usyd.edu.au) with information that you would like to bring to the membership's attention in the next issue.

2005 welcomed a new AGTS executive committee including Dr Gerry Both (now President), Dr Ming Wei and Prof Ann Simpson in their previous positions as Secretary and Treasurer respectively as well as newly elected members A/Prof Steve Wilton (Vice President), and committee members A/Prof Donald Anson, Dr Jim Vadolas and myself giving the AGTS Australia-wide representation. Over the last year we have been committed to developing stronger international links with other gene therapy societies and preparing for the 5th biennial meeting April 18-20 2007 at the Shine Dome, Australian Academy of Sciences, Canberra and I would encourage you now to place the dates in your diary (see page 6). The conference theme is "Gene Delivery and Control". We have put together an exciting line-up of international and national speakers and the program includes diverse aspects of gene therapy including: the current status of gene therapy/the successes and challenges; targeted vectors for gene delivery; chromosomal gene delivery and control; new approaches to gene therapy/ RNAi, anti-sense oligonucleotides, DNA; preclinical and translational research and clinical trials. In 1997 the Boden Research Conferences together with funds raised by the Organising Committee lead by Gerry supported the first AGTS meeting and now 10 years later we have again received Boden support for the meeting and venue.

I urge all members in particular the students and young investigators to submit an abstract and come and participate. In recognition for their excellence in research at the 2005 meeting eight students were awarded prizes for "Best Abstract by a Student" and Dominic Glover, a PhD student from Monash University received the "Panos Ioannou Young Investigator Award". The closing date for abstract submission is Friday 2nd March 2007. All registration, abstract submission and membership information is found on the AGTS website <http://www.agts.org.au>.

INSIDE THIS ISSUE:

Editorial	1
"Best Gene Therapy Paper" Award	2
AGM President's Report	3
AGM Treasurer's Financial Statement	4
5th AGTS Conference 2nd Announcement	5-6
Establishing links with other gene therapy societies and "Conference Travel Awards"	7-8

This issue showcases the efforts of the AGTS committee to forge stronger links with various international gene therapy societies (see page 8). We are now advertising on the AGTS website the web-links and conference information for the Israeli (ISGT), Japanese (JSGT), British (BSGT) and American (ASGT) Societies for Gene Therapy. To encourage collaboration between AGTS and BSGT members, these two societies have established a new travel award to exchange a speaker for their respective conferences. In September 2006, the BSGT awarded Dr Suzy Buckley from the Imperial College London a Travel Award (flights, registration & accommodation) to attend the 5th AGTS meeting in 2007. **The AGTS is now offering a similar award to one of our members to attend the 5th BSGT conference in Edinburgh 2008 (see details page 8).** Get your abstracts in now with an indication that you wish to be considered for the travel award. The winner will be announced at the 2007 AGTS meeting. I look forward to seeing you at the next meeting.

Rose
(Rosetta Martiniello-Wilks, PhD)

Prize for the “Best Gene Therapy Paper” by an AGTS Member



In the last AGTS Newsletter issue, the establishment of a new prize to encourage our early career scientists to disseminate information among our members was announced. The AGTS Executive is offering two \$250 awards in each 6 month period of a calendar year to the first author of a gene therapy publication judged by the Executive as the best for the previous period. Only current AGTS members may apply and the award is open to all AGTS members (the young as well as the wise).

The AGTS executive is pleased to announce our first prize winner Mr Keefe Chng. Keefe is a qualified veterinary surgeon (University of Sydney) who is currently completing his PhD in the Gene and Stem Cell Therapy Program head by Prof John Rasko at the Centenary Institute of Cancer Medicine and Cell Biology in Sydney.

Keefe has recently had his first author paper accepted by the Journal of Gene Medicine and is entitled “Specific adeno-associated virus serotypes facilitate efficient gene transfer into human and non-human primate mesenchymal stromal cells.”

Abstract

Mesenchymal stromal cells (MSCs) show great promise for *ex vivo* gene and cell-mediated therapies. The immunophenotype and *in vitro* differentiation capacity of primary baboon MSCs was demonstrated to be near-identical to that observed in human MSCs. To optimize gene transfer efficiency, we compared the efficiency of serotypes 1, 2, 3, 4, 5, 6, and 8 of adeno-associated virus (AAV) vectors for their ability to mediate transduction of human and baboon MSCs. AAV serotype 2 vectors were the most efficient in transducing MSCs from humans and baboons. As a reference, human Ad293 cells were transduced with these seven AAV serotypes, and were found to have the highest transduction levels followed by baboon MSCs, and then human MSCs. The order of increasing transduction efficiency for the serotypes tested was similar for human and baboon MSCs, but was different for human Ad293 cells. The transduction efficiency of MSCs isolated from different individuals was comparable within the same species. We also demonstrated that baboon MSCs transduced with AAV serotype 2 vectors retain their potential to differentiate into adipocytes *in vitro*, and can incorporate into injured muscle tissue of a NODSCIDmouse *in vivo*. We detected β -galactosidase reporter gene expression in host muscle tissue for up to 9 weeks in this study, indicating engraftment of transduced baboon MSCs and sustained transgene expression *in vivo*. Copyright 2006 John Wiley & Sons, Ltd.

“Please forward your accepted paper details to
r.martiniello@centenary.usyd.edu.au
and a copy to
d.wei@mailbox.uq.edu.au”

Keefe met all the selection criteria of being: the first author; a current AGTS member; and the paper was submitted and accepted for publication at the time the prize application was made. The AGTS committee wish Keefe every success in his research.

Please forward your paper details once the paper is accepted with the Editor’s notification to r.martiniello@centenary.usyd.edu.au and a copy to Dr Ming Wei, d.wei@mailbox.uq.edu.au. The title and abstract of each submission will be included in the next issue of the AGTS Newsletter.

AGTS Annual General Meeting: President's Report



President's Report: I am pleased to present my report on AGTS activities for 2006.

Meetings: The Executive Committee met five times by teleconference over the last year with regular participation by members when they were not travelling. I thank Executive Members for their considered inputs, opinions and assistance.

Links with Other Societies: One of the key things we have tried to do this year is to forge stronger links with other gene therapy societies. The AGTS now has a reciprocal display of website links with the US and British Gene Therapy Societies. In addition, the first notification of our forthcoming meeting in April 2007 was circulated electronically and by a flyer that we commissioned for satchels at the ASGT meeting in Baltimore last June.

More significantly, we invited societies to participate in a scheme where we would exchange speakers, with local costs to be covered by each society and travel by the overseas society. We are delighted that the British Society enthusiastically adopted our proposal and conducted a competition to choose a candidate with a key selection criterion being to encourage collaboration between groups in the UK and Australia. Dr Suzanne Buckley who is collaborating with Dr Don Anson (Adelaide) was the successful applicant. We look forward to welcoming her in April next year and hearing firsthand about that exciting an innovative project.

In return the AGTS will run a competition for the Panos Ioannou Memorial prize for best science/best presentation at our meeting in April. Details have recently been circulated to members as part of our preparations for that meeting. **This year the winner will receive sponsorship to visit the UK, either for a seminar tour or to attend the next BSGT meeting.** Please tell your associates.

NH&MRC Research Panels: In an effort to support the scientific process in Australia and to improve the chances of obtaining funding several individuals were successfully nominated by the AGTS for appointment to the assessment panels for grant applications.

Newsletter and Prizes: In December last year we provided a comprehensive newsletter as a way of communicating with members. We announced two prizes of \$250 for the best gene therapy papers submitted in 2006. Members are reminded to submit their abstracts if they hope to collect the money.

April 2007 Biennial Meeting: Planning for our meeting in Canberra is well advanced. The Committee has worked hard to obtain sponsorship and to assemble an exciting line-up of international speakers. I am pleased to report that our application to the Boden Research Conferences, Australian Academy of Science for core sponsorship of \$10,000 was successful. This sponsorship also brings with it the use of the Academy as a venue for the meeting. It is noteworthy that it will be ten years since our gene therapy meeting at Thredbo in 1997 which predated the formation of the AGTS but which also received Boden sponsorship. We are also very appreciative of the continuing support of the Murdoch Children's Research Institute and the Children's Medical Research Institute for our meeting. Additional corporate sponsorship is also being sought to support seven international and one prominent Australian who will present the Greg Johnson Memorial Oration. Details will be circulated shortly with registration and abstract submission details. We strongly encourage members to renew their memberships, register and submit abstracts.

Conclusion: Although small by international standards, the AGTS is well founded and supported and in a stable financial position. I commend the Executive committee for their diligent contributions this year and submit this report for the consideration of Members.

Gerald W Both, PhD

President

Dec 11th 2006

**"Please forward your
comments via the
AGTS Secretary,
d.wei@mailbox.uq.edu.au"**

AGM Treasurer's Report



ABN 84 866 293 264

INCOME AND EXPENDITURE STATEMENT Year Jan 1, 2005 – December 31, 2005

Income

Annual Subscriptions (Including journal subscription)	\$	6,000.00
Bank Adjustment	\$	13.55
Conference Dinners	\$	4,340.00
Conference Registrations	\$	18,180.00
Interest	\$	682.69
Sponsorships	\$	16,087.00
TFN Refund	\$	104.00

Total Income **\$ 45,407.24**

Expenditure

Account fees	\$	45.00
Conference Dinner	\$	7,410.20
Conference Photo	\$	165.00
Conference Satchels	\$	832.50
Conference Speaker Gifts	\$	196.96
Conference Venue & Catering	\$	12,138.80
Dept of Fair Trading Fee	\$	41.00
Domain Name Registration	\$	88.00
Insurance	\$	2,257.08
Journal Subscriptions (John Wiley & Sons)	\$	1,050.00
Local Meeting - Adelaide	\$	427.40
Merchant fees	\$	1,117.65
Printing	\$	5,936.82
Reimbursements	\$	417.10
Student Prizes	\$	1,940.00
Teleconferences	\$	717.31
Travel	\$	238.06

Total Expenditure **\$ 35,018.88**

Society Funds

Surplus from previous year	\$	20,386.37
Surplus/ -deficit for the year	\$	10,388.36

Total Surplus **\$ 30,774.73**

Current Assets

Cash at bank- Commonwealth (Premium Business A/c)	\$	10,774.73
Cash at bank- Commonwealth (Term Deposit A/c)	\$	20,000.00

Total Funds **\$ 30,774.73**

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**The President's Invitation:
5th Australasian Gene Therapy Society
Meeting
April 18-20th 2007
Academy of Science, Canberra, Australia
Core Sponsor: Boden Research Conferences**

Dear Colleagues,

On behalf of the Executive Committee I cordially invite you to attend AGTS 2007, the 5th biennial Conference of the Australasian Gene Therapy Society. The conference will be held at the Academy of Science, Canberra. A select group of international and national speakers will cover key areas in gene therapy research, including several new approaches involving novel vectors and reagents. We are expecting up to 200 professionals to attend the conference, providing an excellent opportunity to network and develop collaborations.

We look forward to seeing you in Canberra.

Regards,

Gerald W Both, PhD
President

The closing date for abstract submission is Friday 2nd March 2007.

REGISTRATION IS NOW OPEN! - Register now to take advantage of the Early Bird rate. Early Bird closes on Friday 2nd March 2007.

ABSTRACTS SUBMISSION DEADLINE - Friday 2nd March 2007

**All registration, abstract submission and membership information is found on the AGTS website
<http://www.agts.org.au>.**

SUBMISSION of ABSTRACTS

Abstracts for all AGTS Conference presentations will be published in the Journal of Gene Medicine, the official journal of our society. The Organising Committee will select some oral presentations from the submitted abstracts and will notify those authors directly by March 23rd 2007.



Sydney Harbour Bridge

Sydney Opera House

Second Announcement

5th Meeting Australasian Gene Therapy Society

www.AGTS.org.au

April 18-20th, 2007

Academy of Science, Canberra, Australia
Core Sponsor: Boden Research Conferences



Academy of Science,
Canberra



Uluru,
Northern Territory

Theodore Friedmann,
Ian Frazer,
André Lieber,
Robert Kotin,
Jozef Anné,
Patrick Iverson,
Ken Barton,
Suzanne Buckley,

USCD, La Jolla, USA
CICR, Brisbane, Q
U. Washington, Seattle, USA
NIH, Bethesda, USA
Rega Institute, Louven, Belgium
Avi Biopharma, Portland, USA
HFHS, Detroit, USA
Imperial College, London, UK

Great Barrier Reef
Queensland

Wineglass Bay,
Tasmania



Establishing links with other gene therapy societies

The AGTS committee has this year forged stronger links with various international gene therapy societies. We are now advertising on the AGTS website <http://www.agts.org.au> the web-links and conference information for the Israeli (ISGT), Japanese (JSGT), British (BSGT) and American (ASGT) Societies for Gene Therapy.

To encourage collaboration between AGTS and BSGT members, these two societies have established a new travel award to exchange a speaker for their respective conferences.

In September 2006, the BSGT judging panel made up of John Fabre, George Dickson, Andy Baker, Chris Boyd, Vivien Mautner, Richard Wade-Martins and Len Seymour (President BSGT) and Gerry Both and Rosetta Martiniello-Wilks from the AGTS awarded Suzy Buckley from the Imperial College London a Travel Award (flights, registration & accommodation) to attend the 5th AGTS meeting in 2007. Find Suzy's 1 page abstract and a 1 page justification for attendance below.

The AGTS is now offering the same award to one of our members to attend the 5th BSGT conference in Edinburgh 2008 or for a seminar tour preceding the meeting. Get your abstracts and justification for attendance (1 page each) in now with an indication that you wish to be considered for the travel award. The winner will be announced at the 2007 AGTS meeting.

ABSTRACT: SUZY BUCKLEY

“Get your applications for the AGTS Travel Award to the BSGT conference in Edinburgh 2008 in now”

Significant lung transduction after *in utero* and neonatal administration of lentiviral vectors. Suzanne M. K. Buckley¹, Steve Howe², David W. Parsons³, Don S. Anson³, Adrian J. Thrasher², Charles Coutelle¹, Simon N. Waddington⁴ & Tris McKay⁵.

¹ Department of Molecular and Cellular Medicine, Imperial College, Exhibition Road, South Kensington, London, SW7 2AZ, UK.

² Molecular Immunology unit, Institute of Child Health, 30 Guilford Street, London, WC1N 1EH, UK.

³ Department of Genetic Medicine, Women's and Children's Hospital, 72 King William Road, Adelaide, South Australia, 5006.

⁴ Department of Haematology, Haemophilia Centre and Haemostasis Unit, Royal Free Hospital, Pond Street, London, NW3 2QG, UK.

⁵ Cancer Research UK, Department of Medical Oncology, Patterson Institute for Cancer Research, Christie Hospital NHS Trust, Wilmslow Road, Withington, Manchester, M20 4BX, UK.

Gene therapy for cystic fibrosis airway disease has been hampered by the lungs' innate refractivity to pathogen infection. To overcome this, various viral vector systems have been used to target the immune privileged developing airways. Furthermore, early intervention could avoid the relative inaccessibility of the diseased lung due to mucus obstruction in adult life. CFTR expression is significantly higher *in utero* than it is in adult life and so a fetal gene therapy strategy could benefit prognosis and potentially target abundant stem cells. Previously, we have shown that adenoviral vectors can be used to transduce the fetal/neonatal airway but expression is transient. Here, third generation HIV vectors pseudotyped with either the baculovirus GP64 envelope glycoprotein or with vesicular stomatitis virus glycoprotein (VSV-G) were compared after fetal intra-amniotic injection or neonatal intra-nasal administration. Vectors were administered to the murine fetus (at 16 days *post coitus* via intra-amniotic injection) or neonate (at 1 day post birth via intra-nasal instillation) and airway tissue was harvested 2 weeks after injection. Lung tissue was analysed by macroscopic examination, GFP ELISA, TaqMan qPCR and immunohistochemistry. Macroscopic imaging revealed widespread and intense GFP fluorescence throughout the lungs (see Figure 1), which was confirmed by GFP ELISA. Co-localisation studies with a marker for ciliated cells (b-tubulin IV) showed that GP64/HIV transduced both ciliated and non-ciliated airway epithelia with great efficiency when administered either *in utero* or to neonates. In conclusion, to our knowledge, this is the first instance of substantial airway transduction of fetal and neonatal mice using a lentivirus vector and may be an excellent therapeutic strategy for gene therapy of cystic fibrosis and other lung disorders.

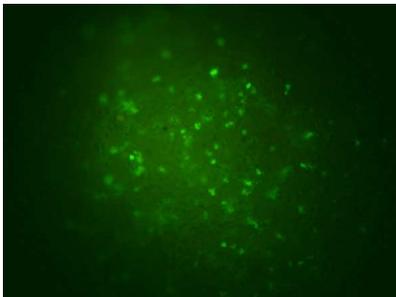


Fig A

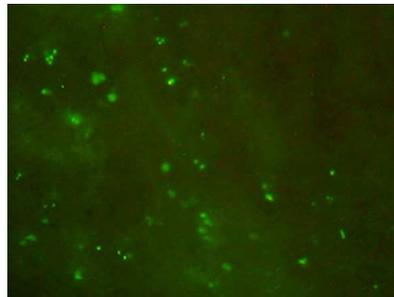


Fig B

JUSTIFICATION: SUZY BUCKLEY

Collaboration proposal

Preliminary studies have revealed a pseudotype specific, developmentally associated protocol for efficient transduction of the conducting airways in the murine lung. We have good evidence of efficient transduction of both ciliated and non-ciliated lung airway epithelium using GP64 pseudotyped HIV lentivirus administered to the fetus by intra-amniotic administration. We plan to repeat these experiments with a lentiviral construct expressing the CFTR gene to provide mammalian proof of concept data for pre-clinical safety and efficacy. To this end, we propose to collaborate with Dr. David Parsons and Dr. Don Anson at The Women's and Children's Hospital in Adelaide, South Australia. Dr. Parsons and Dr. Anson originally provided us with the baculovirus GP64 envelope plasmid used in these experiments and they have vast experience in the field of cystic fibrosis gene therapy, particularly in the use of lentiviral vectors and end-point analyses in CF null mice (Limberis, Anson et al. 2002; Koldej, Cmielewski et al. 2005; Parsons 2005; Anson, Smith et al. 2006).

Proficiency in the technique of intra-amniotic injection requires significant training and practice. I have been performing this technique on a variety of mouse strains for the past 8 years both during my PhD and subsequent post-doctoral position (Waddington, Buckley et al. 2004; Buckley, Waddington et al. 2005). In addition, high titre lentiviral preparations are essential to obtain the degree of gene expression observed in these experiments. It is well known that freeze/thawing substantially reduces lentiviral titre and so we have used fresh viral preparations in the described experiments. Dr. Parsons and Dr. Anson also have a colony of CF null mice (*cfr^{tm1Unc}*) that could be time-mated to provide pregnant dams. If possible, I would then perform the intra-amniotic injections with fresh lentiviral preparation in their laboratory in Adelaide. The mice would then be analysed for CFTR gene expression and appropriate correction studies.

Cystic Fibrosis gene therapy is widely studied in Australia and attendance at the Australian Gene Therapy Society would allow me to discuss future projects with a number of experts in the field in addition to the experiments outlined above.

- Anson, D. S., G. J. Smith, et al. (2006). "Gene therapy for cystic fibrosis airway disease- is clinical success imminent?" *Curr Gene Ther* **6**(2): 161-79.
- Buckley, S. M., S. N. Waddington, et al. (2005). "Factors influencing adenovirus-mediated airway transduction in fetal mice." *Mol Ther* **12**(3): 484-92.
- Koldej, R., P. Cmielewski, et al. (2005). "Optimisation of a multipartite human immunodeficiency virus based vector system; control of virus infectivity and large-scale production." *J Gene Med* **7**(11): 1390-9.
- Limberis, M., D. S. Anson, et al. (2002). "Recovery of airway cystic fibrosis transmembrane conductance regulator function in mice with cystic fibrosis after single-dose lentivirus-mediated gene transfer." *Hum Gene Ther* **13**(16): 1961-70.
- Parsons, D. W. (2005). "Airway gene therapy and cystic fibrosis." *J Paediatr Child Health* **41**(3): 94-6.
- Waddington, S. N., S. M. Buckley, et al. (2004). "Reduced toxicity of F-deficient Sendai virus vector in the mouse fetus." *Gene Ther*.