

December 2006

## The Motor Neurone Disease Research Institute of Australia Inc

was established in 1986 to promote medical and scientific research into motor neurone disease to work towards a world without MND. While the MND Associations have as their primary aim the promotion of the best possible care and support for people living with MND, the only way the future can be changed is through research. It is essential to ensure that people receive the best possible care while living with the disease, but support for research must also remain a top priority.

All funds available through the MND Research Institute come from contributions from Australian State MND Associations, bequests and donations. Each year, grants are advertised and applications are assessed by the Medical/Scientific Committee to determine which projects have the greatest merit. The Audit and Finance Committee meet to determine the level of funds available for distribution to support research in the following year. Final decisions are made at an annual Grants Allocation Meeting where members of the Medical/Scientific Committee meet in person or by teleconference to discuss the relative merit of competing applications. Grants are not given unless the applicant has an appropriate track record and the project is considered to have sufficient merit and relevance to MND.

After careful consideration, the Committee has allocated a total of \$370,000 for distribution by MNDRIA for MND research in Australia in 2007. \$185,000 will go to grants in aid, \$175,000 to postdoctoral Fellowships, and \$10,000 will support the Australian MND Registry (AMNDR). AMNDR will also be supported in 2008 and 2009.

MNDRIA extends thanks to Professor Norman Saunders who has resigned his membership of the Medical/Scientific Committee after ten years of untiring support. His contribution to the Committee has been greatly valued and we wish him well in his research at the University of Melbourne.

## Office Bearers and Members of the MND Research Institute of Australia for 2007

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**EXECUTIVE OFFICER:** Janet Nash

**AUDITOR:** C M Pitt & Co

## MND Research Institute of Australia Inc

### Annual General Meeting held on 1 November 2007 at Gladesville NSW

#### Chairman's address

Thank you all for attending today's Annual General Meeting. The last year has been a very successful one for the MNDRIA.

I would like to begin by thanking Janet Nash and Paula Trigg, who have put in a great deal of effort to the MNDRIA. Their organisational work has been superb. It has been a pleasure to work with them over the last year. I look forward to working with them next year. I would also like to thank Graham Opie, Ralph Warren and the MND NSW team for allowing us to use their facility today.

I would also like to thank David Lamperd in his role as the Treasurer, as well as Bob Howe, who has been invaluable on the newly formed Audit and Finance committee of the MNDRIA. The financial state of the MNDRIA is now very strong, especially with the fundraising initiatives of Janet and Paula, together with money from bequests. The philanthropy of our donors, both anonymous and identifiable, is remarkable. Strategically, the MNDRIA should have the ability to continue to fund research regardless of variations in funding streams, and we are working to achieve this goal.

I would like to thank the assessors from the Scientific Committee, who carefully reviewed the applications for Grants and the Bill Gole Fellowship. The effort that is taken to assess these applications is considerable, and the work of the Grants Allocation Committee is made easier by the efforts of all of the committee members.

The MNDRIA should be proud of the research and publications that have arisen from fellowship and grant in aid funding. I am looking forward to this afternoon's presentations of some of this work. It should also be noted, and congratulations extended to Dr Julie Atkin and Dr Peter Noakes who were successful in obtaining project funding this year from the NHMRC to continue projects initially funded by the MNDRIA. Julie's work focuses on the role of the endoplasmic reticulum in the pathway to motor neuron death, and Peter's group is looking at inhibition of complement pathways to slow the progression of MND. These successes follow the success of Dr Roger Pamphlett in obtaining an NHMRC enabling grant for his genetic work last year. The Scientific meeting this afternoon will be very interesting.

The primary motive for all at this meeting is to slow or stop MND. The only way for this to occur is by basic research. By understanding the biological mechanisms that are involved in MND, therapies able to slow or stop the disease will be developed. At the same time, it is important to perform clinical and translational research, so that more knowledge is attained regarding people with MND, and how to best care for them. Therefore specific funding is allocated for this form of research this year. I am very grateful to the MND Associations of Victoria and New South Wales for continued financial support of the MNDRIA, who have both encouraged this funding stream. It should be noted that applications are received from across Australia for grants in aid. The MNDRIA is a federal body. All states now have representation on the MNDRIA. The challenge for the MND Associations from each state is now to increase support for the MNDRIA so that our primary motive is achieved as soon as possible. It has been mooted that perhaps the way forward is by amalgamation of MNDRIA with the MND Association of Australia, to provide a unified, federal approach towards MND research and care. Discussions regarding this will occur over the next year, and if thought appropriate by the executive, will be formally considered at next year's AGM.

It was Plato who said: "Be kind, for everyone you meet is fighting a hard battle". In any organisation there are battles. No doubt there will be battles regarding the future of the MNDRIA, which has grown considerably over the last two years, and how it might be amalgamated with the MND Association of Australia. It is an interesting marriage proposition. The late American advice columnist, Ann Landers, commented: "All married couples should learn the art of battle as they should learn the art of making love. Good battle is objective and honest - never vicious or cruel. Good battle is healthy and constructive, and brings to a marriage the principle of equal partnership". It is important to remember that there is no battle as hard as MND.

*Dominic B. Rowe  
Chairman*

## Grants awarded for MND research in Australia in 2007

Researchers in Institutions all around Australia working in diverse fields of research are invited to apply for funding for MND research to ensure that every avenue is investigated. The majority of funded projects have been biomedical (laboratory based) research, focussing on understanding the causes or finding effective treatments or a cure for MND.

Recently the MND Associations have encouraged the support of health care research projects - research that will lead to better management and care of people living with MND. Specific funding for health care research has been contributed through the MND Associations of Victoria and NSW, and the MND Victoria Research Grant has been awarded for a health care project in 2007. Funding has also been allocated to contribute to support of the Australian MND Registry (AMNDR) over three years.

### Grants in aid

With limited resources, funding initially provided through the MND Research Institute was mostly for small grants in aid. These have been useful as top-up funding for larger projects funded through other sources, or often as seed funding that allows collection of data to provide the basis for applications for larger grants e.g. funding from the National Health & Medical Research Council (NH&MRC). It is difficult to attract this Government funding to MND research, but in the last two years, three projects supported by MNDRIA have resulted in significant grants being awarded by the NH&MRC: Assoc Prof Roger Pamphlett (Sydney) received \$750,000 for 2006 - 2010, Dr Peter Noakes (Brisbane) \$513,000 for 2007 - 2009 and Dr Julie Atkin (Melbourne) \$514,500 for 2007-2009.

### Fellowships

While grants in aid support MND *projects*, MND research fellowships support the *person* and aim to encourage young scientists to develop a specific interest in MND research. Receipt of a significant bequest allowed the introduction of the first MND Research Fellowship in 2001. Since that time, a further five two-year fellowships have been awarded and all these Fellows are continuing in their pursuit of unlocking the key to MND:

#### Sealey MND Research Fellowship

Dr Elizabeth Coulson, formerly from WEHI, VIC and now at the Queensland Brain Institute

#### MND Research Institute Fellowship

Dr Julie Atkin, Howard Florey Institute, Melbourne

#### Bill Gole MND Research Fellowships:

Dr Roger Chung, University of Tasmania

Valerie Hansen, University of Sydney

Dr Ian Blair, ANZAC Research Institute, NSW

Dr Julia Morahan, University of Sydney.

## Grants in aid

### Dr Gilles Guillemin

St Vincent's Hospital, Sydney

#### *Involvement of the kynurenine pathway in ALS*

We have identified a new neurotoxic mechanism involved in the neuroinflammatory disease. We propose to demonstrate that the tryptophan metabolism plays an important role in the pathogenesis of amyotrophic lateral sclerosis (ALS). Our main hypothesis is that a downstream tryptophan product, the neurotoxin quinolinic acid (QUIN), produced by activated immune brain cells (microglia/infiltrated macrophages) induces motor neuron dysfunction and activation of astrocyte (brain cells taking care of the neurons). This will open a new and important therapeutic door for ALS using different specific inhibitors already available from drug companies for other brain diseases.

### Professor Nigel Laing

West Australian Institute for Medical Research

#### *Whole genome amplification and PCR screening of a WA cohort of 97 familial and sporadic ALS patient DNA samples*

We are currently in possession of genomic DNA samples from a cohort of around 100 Western Australian familial and sporadic ALS patients that have tested negative for mutations in the SOD1 gene. These DNA samples are an invaluable resource for pursuing potential genes involved in the development of ALS. Due to the precious and finite nature of the patient DNA samples (as many of these patients have passed away) we are endeavouring to preserve these samples for current and future use. We aim to preserve these DNA samples by employing the technique of whole genome amplification. This technique has been used successfully in this lab to amplify other precious DNA samples used in the identification of disease-causing mutations. Amplification of the patient DNA samples will allow us to screen these DNA samples for mutations in genes other than SOD1, which have been implicated in the development of both familial and sporadic ALS. Due to the predominant Anglo-Celtic ethnic origins of Australia, the angiogenin gene (ANG), which is involved in blood vessel formation, is an important candidate gene to be screened in our ALS cohort after variations in ANG were associated with both familial and sporadic ALS earlier this year in predominantly Celtic pedigrees. Additionally, the gene VAPB has unequivocally been implicated in familial ALS and is therefore also an important candidate gene to be screened.

**Professor Grant Morahan**

West Australian Institute for Medical Research

*Discovery of novel genes causing MND*

We do not know what causes most cases of motor neurone disease (MND). Some people have mutations in a gene called *SOD1*. We propose that mutations in other genes that affect the levels of *SOD1* can also cause MND. It is impossible to identify these genes directly in humans. However, we can use a new system we have developed using mouse models to identify candidate genes. The human counterparts of these genes will then be tested using DNA samples from people with MND. If we find mutations in these genes, then we will have a better understanding of the causes of MND, and will be better placed to develop new ways to treat this disease. Our novel approach will streamline discovery of MND disease genes. If successful, it will lead to further funding proposals to NHMRC or NIH.

ZO-EE MND RESEARCH GRANT

**Professor James Vickers**

Menzies Research Institute, University of Tasmania

*Unravelling the cellular pathology underlying neuronal degeneration in MND*

Amyotrophic lateral sclerosis (ALS) is the major cause of motor neuron disease. There have been significant advances in the understanding of the underlying pathology of this progressive and degenerative condition, and yet the important links between potential causative factors have not been clearly established. One of the critical changes in motor neurons involves the abnormal accumulation of filamentous proteins in axons. This may be related to the blockage of flow of proteins down the axon, leading to impaired function of motor neurons and subsequent degeneration. We have recently derived preliminary data using cultured spinal motor neurons that links the overactivity of excitatory receptors with a pattern of axonal pathology that mimics ALS. This application explores this interrelationship further and also examines the potential role of known genetic causative factors. In addition, potential therapeutic approaches based on stabilizing axonal filamentous proteins will be investigated.

**Dr Bryce Vissel**

Garvan Institute of Medical Research, Sydney  
*The Effect of Kainate Receptor RNA editing in excitotoxic cell death of motor neurons in MND.*

Riluzole, the only approved therapy for MND,

directly or indirectly blocks molecules in the spinal cord called glutamate receptors. Blocking these receptors seems to slow motor neuron loss that leads to paralysis. However there are many types of glutamate receptors in the spinal cord and it is not yet known which of these are important for MND progression. We are systematically undertaking genetic studies in mice engineered with a gene that causes motor neuron disease. Our studies are directed to block each of the receptors one at a time. We hope to determine if blocking one of these receptors extends life of the mice we are studying. If we find that we can extend the life-span of the mice, that will indicate we may have discovered a new therapeutic approach for treating motor neuron disease.

**Dr Robyn Wallace**

Queensland Brain Institute  
University of QLD

*Assessing therapeutic peptides in a mouse model of MND*

The biological processes that lead to motor neuron disease are complex and multifactorial. Future treatment of MND is likely to involve a cocktail of neuro-protective compounds similar to the currently used chemotherapeutic combinations, which interfere with several molecular pathways. We propose using a multi-compound approach designed to target both the affected motor neurons themselves, and their supporting cells (astrocytes). We have developed two peptides for this purpose, one designed to promote nerve cell survival (p75-targetted) and one to prevent activation of astrocytes (EphA4-targetted). We will test these peptides separately and in combination in a mouse model of MND. These experiments may lead to a novel treatment for patients with MND.

MND VICTORIA RESEARCH GRANT

**Professor Kate White**

Faculty of Nursing & Midwifery  
University of Sydney

*Letter on future care: development of an individualised disease specific future care plan for MND*

The project aims to assist people with MND and their families to plan their future care, particularly in the later stages of the disease, in consultation with their health care team. The project aims to evaluate the implementation and documentation of an individualised disease-specific future care plan.

## Postdoctoral Fellowships for MND research

### Three MND Fellowships will be funded by MNDRIA in 2007

BILL GOLE MND RESEARCH FELLOWSHIP 2007-2008



**Dr Julia Morahan**

Department of Pathology, University of Sydney  
*Somatic mutations in motor neuron disease?*

The cause of sporadic ALS is not known but genetic abnormalities have long been suspected. Some gene mutations are only seen in certain tissues of the body and are not passed on to the next generation. We expect to find these mutations in the brain, but not blood or sperm cells, of people with sporadic ALS. Finding mutations in these genes would lead to an understanding of the cause of sporadic ALS and lead to more effective therapy.

### Continuing Fellowships

MND RESEARCH INSTITUTE FELLOWSHIP

**Dr Julie Atkin**

Howard Florey Institute, University of Melbourne  
*The mechanism by which hSOD1 mutations induce degeneration of NSC-34 motor neurons*

[The initial funding provided by MNDRIA has led to the award of an NH&MRC project grant of \\$514,500 over three years \(2007-2009\) to continue this study.](#)

This proposal aims to study the mechanisms that trigger degeneration of motor neurons in MND. Some forms of MND are inherited and linked to

mutations in a protein called SOD1, but how the mutations lead to cell death is unclear. However, SOD1 mutants are known to clump together in large aggregates and this is linked to toxicity. In a previous study, we found that normally SOD1 is secreted from the cell where it can protect the motor neuron from oxidative damage. However SOD1 mutants are not secreted as well as the normal protein, leaving the cell vulnerable to damage. In addition, the compartment of the cell responsible for secretion, the 'endoplasmic reticulum' (ER), is under stress due to secretory dysfunction of mutant SOD1. Our data suggest that this ER stress leads to the activation of 'cell suicide' pathways, leading to death of the motor neuron. However, very little is known about how molecular events in the ER lead to cell death in MND. This proposal will examine these processes in detail.

In other studies, we found that a molecule called 'PDI' inhibits mutant SOD1 from aggregation and is made in large quantities in our laboratory models of MND. This proposal will determine if PDI is potentially a new therapeutic target for MND due its ability to protect the cell from the toxic effects of SOD1 aggregation. Our findings are both novel and exciting and propose previously unexplored mechanisms of disease and new therapeutic targets. Once we understand the basic mechanisms occurring in the motor neuron, which we can design specific therapies to halt the progression of the disease and prolong the life of human MND patients.

BILL GOLE MND RESEARCH FELLOWSHIP 2006-2007

**Dr Ian Blair**

ANZAC Research Institute, Concord, NSW  
*Identification of novel genes involved in motor neuron degeneration*

We aim to identify new mutated genes responsible for disorders affecting motor neurones using genetic linkage studies in families with hereditary motor neuropathies (HMN). HMNs are slowly progressive, non-fatal disorders of motor neurones. Discovery of gene mutations in these families will tell us about the pathways leading to the death of motor neurons. This should ultimately lead to more effective diagnosis, and the development of drugs to prevent and treat both familial and sporadic forms of MND.

## Executive Report

### Summary of the year

A solid framework for the future growth of the MNDRIA has been established in the past year with the appointment of a part-time Executive Officer and provision of office space at the MND Association of NSW at Gladesville. Financial security has been provided through receipt of two bequests which came as an unexpected windfall. This will allow the Institute to use all other reserves for research in 2007, but still retain a 'safety net'. A number of enquiries have been received from donors and solicitors about provision of bequests in their wills.

Regular donors have been encouraged by provision of newsletters giving feedback about the way in which their funds are spent on research and information about the Institute.

The financial position of the Institute has been clarified by ensuring that all previously awarded grants have been claimed and used, so unclaimed grants are no longer a liability issue. Grants awarded for 2006 came with the conditions that they must be taken up before 30 June 2006, and funding for the second half of the grant will not be paid until a report on the first half-year's work has been received. All grants awarded have been taken up and all reports are up to date. The only outstanding liabilities are for grants awarded for a period of two years, and for the second half year payments for 2006 grants.

Following a suggestion at last year's Annual General Meeting, a Scientific Meeting was arranged to follow this year's Grants Allocation Meeting. All researchers funded by MNDRIA for 2006 were invited to make presentations and most of these were able to participate. PowerPoint presentations with recorded sound will be provided to MND Associations for distribution.

### Grant Applications

Research grants in aid and the Bill Gole MND Research Fellowship were advertised on the website ([www.mndresearch.asn.au](http://www.mndresearch.asn.au)) in May 2006 with a closing date of 25 August 2006. Additionally, research departments of major research facilities throughout Australia were notified, and an advertisement was placed in the Higher Education Supplement of The Australian newspaper.

Fifteen applications for grants in aid and two Bill Gole MND Research Fellowship applications were received for funding in 2007.

Six applications came from NSW, four from Western Australia, four from Victoria, two from Queensland and one from Tasmania.

### Fundraising

Appeal letters were sent out in December 2005 and May 2006. These were accompanied by newsletters to inform supporters about the work of the MNDRIA. Most donations come from loyal donors who continue to give year after year.

### Major Donors

**The State MND Associations** are the major contributors to funds for MND research. The NSW and Victorian MND Associations have significantly increased their level of financial support. Generous support has also been received from the Associations of South Australia and Western Australia. Provision of membership of the Institute for MND Associations has generated better communication between the Institute and the Association delegates.

**The Bill Gole MND Research Fellowships** are supported annually through the generosity of an individual donor. This has encouraged a number of excellent researchers to become established in MND research.

**The Henry Roth Charitable Foundation** continues in its support of selected projects.

**Bequests** come 'out of the blue' and give an unexpected boost to the resources of the Institute.

### Members of MNDRIA for 2006/7

New members welcomed to the Medical/Scientific Committee are Dr Susan Mathers from Bethlehem HealthCare Calvary, Victoria, and Professor James Vickers from the Menzies Research Institute, University of Tasmania.

New MND Association delegates are Tim Hynes and Lynette Willis from Tasmania, and Peter Whitehouse from South Australia.

*Paula Trigg*  
*Honorary Secretary*

*Janet Nash*  
*Executive Officer*

## Finance Report

Audited Financial Statements for the 12 months to 30 June 2006 are provided\* which reveal an improved and healthy financial position for the Institute. The following points assist to provide a summary of the financial year:

- Bequests received totalling \$422,874 influenced a 99.5% increase in the Institute's total revenue of \$802,143 from the previous 12 month period to 30 June 2005. Donations of \$82,719 (our highest recorded yearly amount) was a welcome improvement from the \$19,499 collected for the previous 12 month period due to the hard work of the Executive Officer via a newsletter and two appeal letters. State contributions received of \$275,472 were down from the \$343,746 collected to 30 June 2005 only due to a timing issue (receipt of funds after 30 June 2006).
- Total expenditure of \$389,610 comprised primarily of grants awarded of \$372,114. A further \$232,970 in grants have been committed over the next two years (please refer to Note 9 on page 6 of the Financial Statements). The remaining expenditure consist of administration and fundraising expenses and show that costs continue to be well managed and constrained.
- The resultant net profit of \$412,533 will provide an improved base to continue to support medical and scientific research into motor neurone disease.
- As at 30 June 2006 the Institute had total

savings of \$582,493 within three financially strong financial institutions (ING Direct: \$419,424, JB Were: \$41,085 and Macquarie: \$121,984).

- Other cash assets (CBA \$100,720) and receivables (\$9,500) give total assets of \$692,713.

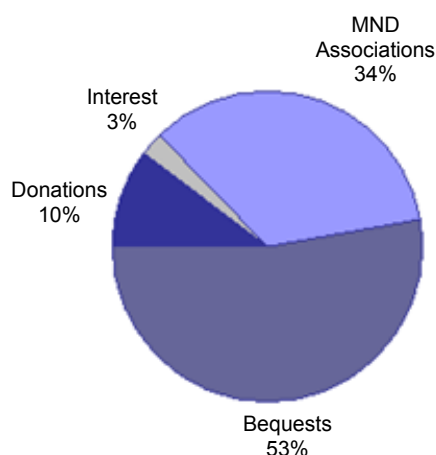
The MNDRIA Audit and Finance Committee met on 9 August 2006 and agreed that the \$422,874 in bequests received during the financial year be set aside for the establishment of a capital investment fund to provide income for future grants. At the same meeting the Committee also agreed to recommend that \$250,000 be allocated for the 2007 Grant in Aid applications. Together with two concurrent Bill Gole MND Research Fellowships and the continuing MND Research Institute Fellowship it is proposed that a total contribution of \$425,000 be provided towards research during the 2007 calendar year. This proposed expenditure will be assisted from the receipt of \$363,000 by the Institute since 30 June 2006.

In summary, the Financials to 30 June 2006 are a positive outcome of hard work, effective planning and also the continuing support from MND Associations and the Institute's members.

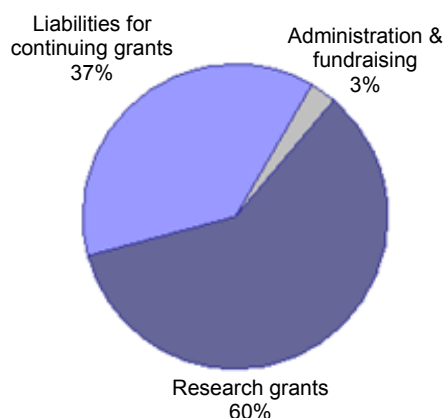
*David Lamperd  
Treasurer*

\* If you would like to receive a full copy of the audited Financial Statements, please contact Janet Nash at the MNDRIA.

**Income**



**Expenditure**



## MND Scientific Meeting - Hope for a Future 1 November 2006

Researchers who had received funding from the MND Research Institute during 2006 were invited to present the findings of their research at this special meeting which was held at the premises of the MND Association of NSW at Gladesville.

The meeting was sponsored by sanofi aventis and was an excellent opportunity for grant recipients to meet with MNDRIA members and to discuss their work with one another with a view to future collaborations.

The meeting was regarded as a great success and was very well attended by many of the NSW MND scientific community, as well as interstate attendees from Victoria and Queensland. We plan to make this an annual event and 2007 grant recipients have already been asked to prepare for the next MNDRIA scientific meeting in November 2007. They are also encouraged to present elsewhere and to publish their findings in relevant journals and, if possible, to attend the annual International Symposium on ALS/MND. The 17th International Symposium on ALS/MND is in Yokohama, Japan in December 2006, and the 18th Symposium will be in Toronto, Canada in December 2007.

Presentations from the *MND Scientific Meeting - Hope for a Future*, were recorded with sound to accompany the PowerPoint presentations so interested people who were unable to attend the meeting in Sydney can have the opportunity to view the presentations. These are available on CD through MND Associations in each State, or by contacting Janet Nash at MNDRIA on 02 8877 0990 or [info@mndresearch.asn.au](mailto:info@mndresearch.asn.au).

### Presentations

#### Jennica Winhammar

Royal North Shore Hospital & Prince of Wales Medical Research Institute, NSW

*Diffusion tensor imaging in motor neuron disease*

#### Dr Steve Vucic, MND NSW Clinical Scholar

Prince of Wales Medical Research Institute, NSW

*Cortical hyperexcitability in motor neuron disease*

#### Dr Robert Henderson

Royal Brisbane Hospital, QLD

*Assessing disease progression in motor neurone disease*

#### Dr Mark Bellingham

School of Biomedical Sciences, The University of QLD

*Glutamate receptors and ion currents controlling excitability of motor neurons susceptible to death in ALS*

#### Dr Ian Blair, Bill Gole MND Research Fellow

ANZAC Research Institute, Concord NSW

*Identification of novel genes involved in motor neuron degeneration*

#### Natasha Luquin

Depts of Pathology and Molecular and Clinical Genetics, The University of Sydney

*Somatic Mutations in Motor Neuron Disease:*

*An analysis of SOD1 exons and introns in MND brain tissue*

#### Assoc Prof Roger Pamphlett and Valerie Hansen

Depts of Pathology and Molecular and Clinical Genetics, The University of Sydney

*Whole genome scanning to detect differences in viral receptor (and other) genes in motor neuron disease*

#### Dr Julie Atkin (a recorded presentation was provided as Dr Atkin was unable to attend)

Howard Florey Institute, The University of Melbourne

*The mechanism by which hSOD1 mutations induce degeneration of NSC-34 motor neurons*

### Donations

Research funded by the MND Research Institute of Australia is dependent on donations. If you would like to contribute to this vital work, please send your gift to:

MND Research Institute of Australia  
PO Box 990, Gladesville NSW 1675

Donations can be made by cheque (payable to MND Research Institute of Australia) or credit card (Visa or MasterCard).

All donations of \$2 and over are tax deductible.

### Bequests

Your Will can provide an important way of making a gift that can have lasting influence on MND research and give hope for the future.

If you would like to consider the MND Research Institute of Australia in your Will by providing a Bequest from your Estate, please contact your solicitor.

For more details,  
phone Janet Nash, MNDRIA Executive Officer on  
02 8877 0990 or email [info@mndresearch.asn.au](mailto:info@mndresearch.asn.au).