Scholarships for PhD study on demyelinating disease

A project investigating the pathophysiology of a demyelinating disease in mice and treatment by two novel anti-inflammatory compounds is available for 2008/9.

Funding is available for eligible applicants from the Multiple Sclerosis Research Association and NHMRC.

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Testing compounds which may enhance survival of myelin producing cells and reduce the severity of myelin damage in a mouse model of demyelination.

Demyelination is a feature of many neurodegenerative diseases of animals and man, including inherited myelin damage and acquired disorders such as Multiple Sclerosis. The cellular and molecular events leading to oligodendrocyte death and microglial activation are central to understanding and treating demyelination and can be investigated in animal models such as the *twitcher* mouse. This study will analyze the roles that a key inflammatory mediator, prostaglandin D₂ and protective factor, growth arrest specific protein 6, play in the delicate balance between myelin damage and repair. We will use a well characterized *twitcher* mouse model of toxic and inflammatory myelin damage where oligodendrocytes undergo apoptosis when signalled by cytokines and chemokines from activated microglia. Activated microglia release tumour necrosis factor (TNFα) and prostaglandin D₂ which contribute to programmed oligodendrocyte death in the *twitcher* mouse, leading to progressive myelin loss. Recent studies demonstrate reduced oligodendrocyte apoptosis by inhibitors of TNFα and prostaglandin D₂ in this model of demyelination.

This study tests the effects of two promising compounds which protect oligodendrocytes from apoptosis using the *twitcher* mouse model of inherited neuroinflammation. Growth-arrest specific protein (Gas) 6 reduces oligodendrocyte death in other models of demyelination, e.g. cuprizone demyelination, but has not been tested in *twitchers*. Recombinant human Gas6 will be tested alone and in combination with an inhibitor of prostaglandin D₂ mediated inflammation, HQL-79, which reduces *twitcher* demyelination. This will determine if they work synergistically in protecting oligodendrocytes, reducing microglial activation and astrocyte responses that are features of *twitcher* disease. We will evaluate clinical, behavioural, molecular and pathological changes and changes in gene expression during *twitcher* demyelination and oligodendrocyte loss. This is of wider relevance to myelin disorders, particularly MS. These studies are significant to understanding of the key players in oligodendrocyte death and survival and the clinical effects of treatment which may assist development of therapies for demyelinating diseases.
Scholarship details

Postgraduate Scholarships are available for a graduate to undertake full time study for three years towards a higher degree (PhD or a Masters degree).

In a unique partnership arrangement, the National Health & Medical Research Council (NHMRC) and Multiple Sclerosis Research Australia (MSRA) have agreed to jointly fund a number of Betty Cuthbert Postgraduate Scholarships. To be eligible, applicants must submit applications to both NHMRC and MSRA.

The Trish MS Research Foundation consults with MSRA to fund the best Young Scientists undertaking a MS research project. If your application is not successful with the NHMRC, it will be considered for a Trish MS Research Foundation Scholarship. MSRA Postgraduate Scholarships are awarded to the best remaining applications.

The Multiple Sclerosis Research Australia (MSRA) Research Management Council will not consider applications for Scholarships in the absence of reports from Referees, without pending ethical approval, where applicable and without the application being signed by the supervisor or Head of Department.

CLOSED DATES
Please note that your institution’s Research Office may have an earlier closing date. Late or incomplete applications will not be accepted.

- Postgraduate Scholarship Application & Referees Reports by 30th June 2008
- Full ethical approval by 31st October 2008.