

<b>Centre</b>	DCRC – Assessment and Better Care
<b>Partner Institution</b>	
<b>Project ID</b>	PDCRC-CB59
<b>Project Name</b>	Genetic and environmental contributions to amyloid burden in older Australians: a PiB-PET imaging study of twins
<b>Date of Proposal</b>	5 Dec 2011

## 1. Investigator Details

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## Project Details

<p><b>Project Objectives (max. 2)</b></p>	<p>One hallmark of Alzheimer's disease (AD) is a build up of plaques in the brain, starting years before symptoms are observed. We will use PiB-PET brain scans to determine the degree of plaque build-up in pairs of twins at risk of developing AD, and calculate the heritability of these plaques. We will also be able to calculate (potentially modifiable) environmental factors that may be contributing to the relationship between plaques and cognitive function.</p>
<p><b>Project Description (200 words max)</b></p>	<p><math>\beta</math>-amyloid (A<math>\beta</math>) plaques are one of the hallmark neuropathologies of Alzheimer's disease (AD), yet their aetiology is not understood. Converging evidence from autosomal dominant mutations, study of Down's syndrome patients, family studies and the known risk of the APOE <math>\epsilon</math>4 allele suggests that genetic factors are important. However environmental factors appear to also make an important contribution.</p> <p>Amyloid burden can now be assessed in vivo using positron emission tomography with the Pittsburgh compound B ([<sup>11</sup>C]PiB-PET), making it possible to examine the relationship between A<math>\beta</math> burden and cognitive deficits in temporal proximity. Potential moderating factors such as genetics or environment need to be considered however.</p> <p>Twins offer a powerful strategy to differentiate the relative contributions of genetic and environmental factors, as monozygotic (MZ) twins share 100% of their genes while dizygotic (DZ) twins share only 50%. Our group has unique access to a cohort of elderly MZ and DZ twins who are participating in the longitudinal Older Australian Twins Study (OATS). This cohort has already had extensive medical, neuropsychiatric, and structural brain imaging assessments.</p> <p>We will invite a subset of this cohort to participate in a separate PiB-PET imaging study to determine their amyloid burden, and calculate the heritability of amyloid plaques. We will also calculate genetic and environmental factors that may be contributing to the relationship between amyloid burden and cognition. The current project will be a 10 twin-pair pilot study for this larger study, which is outlined in the Research Plan.</p>
<p><b>Research Plan</b></p>	<p><b>Please attach a Research Plan (2 - 5 pages, 12pt Arial font minimum) to this form which should include the following sections:</b></p> <p><b>(i) Aims of the project</b> List specific aims. Clearly state the research question and hypothesis (where applicable) to be tested, as well as rationale and objectives.</p> <p><b>(ii) Background and Significance</b> Summarise both your previous work and work reported by others. Include the proposed rationale, current state of knowledge and potential contributions and significance of the research to the field. Highlight why research findings are important beyond the confines of the specific research project and how research results can be applied.</p> <p><b>(iii) Research Strategy</b> Include a clear description of methods and design, including the following, if applicable: study design, subjects and sites, inclusion/exclusion criteria, measures, study procedures, other therapy, efficacy parameter(s), safety</p>

	<p>parameters, statistical rationale &amp; analysis, drug study regimens &amp; special equipment/measures and timeframe.</p> <p><b>(iv) References</b> Provide all references quoted in this application. Maximum of 20 references.</p>
<b>Ethics</b>	<p><b>Has this Project been approved by an ethics committee?</b></p> <p><input checked="" type="checkbox"/> yes   <input type="checkbox"/> no   <input type="checkbox"/> n/a – please say why</p> <ul style="list-style-type: none"> <li>• Austin Health H2006/02534</li> <li>• UNSW HC07001</li> <li>• Currently submitted to Melbourne Health</li> </ul>
	<p><b>If no, please indicate the current status of the application.</b></p> <p>.</p> <p><b>If yes, please give details (name of institution, date)</b></p>

## 2. Timetable

<b>Project Start Date</b>	<b>3 Jan 2012</b>
<b>Project End Date</b>	<b>31 Dec 2012</b>

<b>Milestones</b>	
<b>List a minimum of four milestones per year for progress reporting (e.g. completion of ethics, data collection, analysis, dissemination)</b>	
<b>First Milestone</b>	<b>NHMRC project grant application</b>
<b>Expected Completion</b>	<b>14/3/2012</b>
<b>Second Milestone</b>	<b>Pilot data collected</b>
<b>Expected Completion</b>	<b>1/6/2012</b>
<b>Third Milestone</b>	<b>Pilot data analysed</b>
<b>Expected Completion</b>	<b>1/7/2012</b>
<b>Fourth Milestone</b>	<b>Rejoinder submitted to NHMRC with pilot data included</b>
<b>Expected Completion</b>	<b>31/7/2012</b>
<b>Fifth Milestone</b>	
<b>Expected Completion</b>	
<b>Sixth Milestone</b>	
<b>Expected Completion</b>	
<b>Seventh Milestone</b>	
<b>Expected Completion</b>	

## 3. Proposed Project Outputs

<b>Academic Publications</b>	
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<b>Presentations</b>	
<b>Guidelines/Recommendations</b>	
<b>Capacity Building</b>	
<b>Leverage (grant applications)</b>	This project is a Goldstar-funded pilot project to leverage for an NHMRC project grant application. We intend to test 10 twin pairs as a “pilot project” for the larger application.
<b>Other</b>	

#### 4. Knowledge Translation

<b>How will you translate research findings into practice?</b>
Ultimately, we plan to provide recommendations for modification of environmental factors that contribute to amyloid deposition.

<b>How do the expected outcomes of this project have the potential to improve current practice? In what other ways can knowledge translation be enhanced for this project?</b>
Currently, there is a lack of understanding of the aetiology of amyloid plaques. By contributing to this knowledge, we may improve knowledge for development of therapeutic strategies.

#### 5. Linkages

<b>Please list any project or staff linkages within administrating DCRC</b>	N/A
<b>Please list any project or staff linkages between DCRCs</b>	N/A
<b>Please list any linkages beyond the DCRCs</b>	Linkage with the University of Melbourne and Austin Hospital

#### 6. Funding

<b>DCRC Funding for this project</b>	
<b>Salaries (itemised)</b>	Melissa Slavin’s salary is fully funded by the DCRC

<b>Other (itemised)</b>	
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<b>Please provide a brief justification for the above budget</b>

<b>Non-DCRC Funding for this project</b>	
<b>Salaries (itemised)</b>	
<b>Other (itemised)</b>	<b>Goldstar funding \$40,000 for 2012</b> PET scan      \$ 1,200.00 pp MRI scan      \$ 500.00 pp Travel         \$ 120.00 pp <hr/> pp charge     \$ 1,820.00 <hr/> <hr/> 20 people     \$ 36,400.00 <hr/>

<b>In-kind Contributions to this project</b>	
<b>Please list</b>	All other investigators' time

<b>If this project is part of a larger project, for which funding has been sought or applied for, please list details below (Funding Body, Project Name, Amount, Relationship between Projects)</b>
OATS, funded until end 2011 by NHMRC project grant. Re-applying for further funding in 2012. The current project will draw participants from this larger study.

<b>DCRC Management to complete</b>		
<b>DCRC-funded Project</b>	<b>DCRC-hosted Project</b>	<b>DCRC-supported project</b>
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

## 7. Project Proposal Assessment

<b>Depending on the nature of the project and the amount of funding sought, the DCRC might need to use an external reviewer. If so, we may contact you for suggestions.</b>