MEchanisms of cellular death in NeuroDegeneration (MEND) Request for Applications

A Global Funding Collaboration of the Alzheimer's Association, Alzheimer's Research UK and the Weston Brain Institute

Program objectives:
The "MEchanisms of cellular death in NeuroDegeneration' (MEND) funding program's overall goal is to discover and understand the mechanisms and pathophysiological processes by which brain cell loss is mediated in disease and thereby seek insights and potential targets for therapeutic interventions that would sustain healthy brain function.

Background:
The hallmark of many neurodegenerative diseases is the death of brain cells. Examples of neurodegenerative diseases include but are not limited to Alzheimer's disease, Lewy Body dementias and Frontotemporal Lobar Dementia. The loss of brain cells during disease progression, in many cases, leads to cognitive impairment and ultimately loss of function and death. Despite the critical importance of brain cell death in neurodegeneration, very little is understood about the processes and mechanisms of brain cell death.

The Alzheimer's Association, Alzheimer's Research UK and the Weston Brain Institute (Funding Partners) are jointly launching the MEND funding Initiative to target projects that address fundamental, unanswered questions such as:

- Are there common brain cell death pathways or do different diseases mediate brain cell death using distinct mechanisms?
- What is the role, if any, of the intracellular, abnormal protein deposits that are features of many neurodegenerative diseases?
- Does the inflammatory response seen in many neurodegenerative diseases protect or endanger brain cell health and functioning?
- Why are certain brain cell populations vulnerable to a given disease, but others are resilient?
- What is the role of aging in neurodegeneration? Why do some brain cells become more vulnerable to cell death processes with aging?

Potential Themes:
The MEND Initiative invites research proposals that will explore brain cell death mechanisms in neurodegenerative diseases. We seek proposals that have some, or preferably all of the following characteristics:

- Use *in vitro* models with high construct validity to the disease process, for example, iPSC brain cells harbouring autosomal dominant mutations that cause disease in humans.
- Involve *in vitro* phenotypic systems that have *in vivo* correlates allowing translational studies.
- Use technologies that might serve as target discovery engines with the potential to uncover signalling/ intracellular pathways that are activated during brain cell death.
- Provide model systems with the potential to test hypotheses: for example, the use of RNAi or compound screening.

- Use *in vivo* models that have face and construct validity to human diseases that are amenable to cell death pathway investigations.
- Include *in vivo* models that lend themselves to research technologies that permit unbiased investigations of brain cell death mechanisms, e.g., model organisms that can be genetically manipulated rapidly and at scale.
- Allow a multisystem interrogation of brain cell death, e.g., *in vitro*, to *ex vivo*, to *in vivo* investigations that permit the systematic translation of findings.
- Employ experimental paradigms that produce quantitative data that are highly replicable.

This MEND does **not** seek proposals that:
- Are focussed on ischemic neuronal cell death, as typified by stroke.
- Are focussed on neuronal cell death mediated by acute trauma.
- Are focussed on neuronal cell death mediated by autoimmune inflammatory processes, such as occurs in multiple sclerosis.
- Involve the extracellular or *in vivo* application of exogenous beta-amyloid peptide to cells.

General Considerations:
All proposals must clearly and explicitly describe whether specific hypotheses are to be investigated, the program of work, the methods for study, sample, outcomes, etc. The ultimate goal is to increase the understanding and knowledge of mechanisms of brain cell death in neurodegenerative diseases and develop novel model systems for further investigations.

Given the magnitude and complexity of the scientific challenge, the MEND Initiative strongly encourages submissions from global collaborative research teams that exemplify interdisciplinary expertise. In addition, while novel and creative ideas are sought, proposals also need to demonstrate feasibility. The funding organizations recognize the need to increase the range and diversity of scientific disciplines that might offer innovative techniques or solutions, and researchers that may not have a history of research in neurodegenerative diseases are encouraged to apply especially as members of consortia that have disease expertise.

Funding and Award Period:
The total sum available for this award program will be up to USD$1.25 million available over three years. MEND is looking to fund either a consortium of investigative teams or individual team-based projects ranging between USD$100,000-$1,250,000. The project budget should be in line with the proposed project goals with clear justification of the required resources to achieve those goals.

The funding partners seek proposals up to this amount with scientific quality, innovation, a resolute focus on goals of the MEND Initiative, and value for money being key parameters for success. Indirect costs are capped at 10 percent (rent for laboratory/office space is expected to be covered by indirect costs paid to the institution). Funding will be linked to milestones, as set forth in the application.

Eligibility:
Applications are encouraged from academic research laboratories or consortia of academic laboratories around the world. In addition, small biotech/small-medium enterprise organizations are eligible provided they are in collaboration with academic laboratories and the academic laboratory is the lead applicant.

Researchers with full-time staff or faculty appointments are encouraged to apply; post-doctoral fellows are eligible as co-applicants with an investigator who has a full-time faculty appointment (i.e. Assistant Professor or above; if your institution does not have Assistant Professor track, then you may be asked to supply appropriate documentation to confirm your employment status) as the lead applicant.

Submission and Review Process:
The application submission process will follow a two stage procedure. First, applicants will submit a pre-proposal or letter of intent (LOI). Submitted LOIs will be reviewed by the sponsor organizations and a select number of the LOIs fitting the funding priorities will be invited to submit full applications.

Full applications will be evaluated by a two-stage peer review process that engages an expert panel to review and evaluate each application. Final funding decisions will be made jointly among the funding organizations.

Both LOI and the full submissions will be reviewed based on:
1) Alignment with research priorities as outlined in this Request for Applications (RFA)
2) Demonstrable innovation/novelty of the proposed project
3) Collaborative approach of project design
4) Evidence of methodological rigor to address stated research question(s)
5) Impact

Deadlines and Award Timeline:
Letters of Intent (LOI) must be submitted through the *proposalCENTRAL* on-line application system at http://proposalcentral.altum.com, the site will open **Friday, February 13, 2015**.

Letters of intent must be received by 5:00 PM EASTERN STANDARD TIME, May 8, 2015. Letters of intent will not be accepted after this date. No exceptions will be made.

For those invited to submit a full application, **applications must be received by 5:00 PM EASTERN STANDARD TIME, June 30, 2015**.

The application materials, including the application format, templates, and instructions, will be available online at proposalCENTRAL after your LOI has been approved.

Scientific and technical review will be conducted from July – September 2015. Funding decisions will be shared with applicants by September 30, 2015

Mechanism of award, reporting requirements and allowable costs:
The mechanism of the award is the individual research grant. The maximum allowable duration is three years. Annual progress and financial reports are required. Continuation of the grant over the awarded duration is contingent upon the timely receipt of scientific and financial reports, and will be linked to specific project milestones (as mutually agreed upon at the time of award).

Budget and allowable costs:
A budget summary for the proposed research project is required and must be submitted with the application and within the allowable page limits. However, if the application is to be awarded, a more detailed budget will be required and must be approved before the disbursement of funds.

Your budget must not exceed the maximum amount of the award (USD$1.25million) although projects requiring significantly smaller amounts will be considered according to the above criteria. Applicants are required to contact grantsapp@alz.org prior to LOI submission to discuss an increased budget exception.

It is required that funds awarded under this Initiative be used for direct research support, with a maximum 10% of total award to be directed toward.

Allowable costs under this award include:
- Computer equipment if used strictly for data collection.
- Travel (up to USD$2,000 per year).
- Salary for the principal investigator (unless they receive a salary from their institution), scientific (including post-doctoral fellows) and technical staff (including interviewers, interventionists, data entry staff, technicians, and administrative support staff whose work is directly related to the funded project).
- Manual production/development/website, etc.

Not Allowable costs under this award include:
- Tuition
- Computer hardware or software for investigators
- Rent for laboratory/office space
- Construction or renovation costs

Questions?
Please contact grantsapp@alz.org for any questions regarding this program.