

FRAXA Grants & Fellowships Available

FRAXA Research Foundation funds basic and clinical research leading to treatments and a cure for Fragile X Syndrome. We anticipate funding \$500,000 to \$1 million at each funding cycle. Upcoming application deadlines: May 1, 2004; December 1, 2004; May 1, 2005.

Awards Available

- Postdoctoral Fellowships of up to \$40,000 per year (salary plus fringe benefits and/or travel to meetings and/or a budget for consumable supplies).
- Investigator-initiated research applications for innovative pilot studies aimed at developing and characterizing new therapeutic approaches for the treatment and ultimate cure of Fragile X. There is no funding limit to this category of grant, but typical grants are \$30K - 60K per year.

Fellowships and grants are generally awarded for one year. Based on reasonable progress, awards may be renewable for a second year. Renewal applications are also due on May 1 or December 1, at least three months before the second year of funding is needed.

FRAXA's goal is to bring practical treatment into current medical practice as quickly as possible; therefore, preference will be given to research projects that have a clear practical application and the results of which will be shared with other qualified researchers in a timely fashion.

Background on Fragile X

Fragile X Syndrome is the leading inherited cause of mental retardation, affecting about 1 in 4000 males and 1 in 6000 females and carried by 1 in 400 females and 1 in 1000 males. Symptoms are cognitive delay, hyperactivity, autistic-like behaviors, and in some cases, seizure disorder. There is currently no effective treatment.

Fragile X is caused by a triplet repeat expansion in the 5' untranslated region of the FMR1 gene, resulting in methylation of the promoter and a resulting lack of transcription of the gene.

The protein encoded by the FMR1 gene, FMRP, is an RNA-binding protein that associates with translating polyribosomes and modulates the translation of its mRNA ligands. FMRP is believed to function as a regulator of protein synthesis; it is located at the synapse and its absence alters synaptic plasticity. As synaptic plasticity has been implicated in learning and memory, further studies of fragile X should be enlightening.

Special Request for Applications 2004

Two strategies for drug discovery have emerged from recent research:

2) The MAP1B connection

Convergence of several studies published in *Cell* (Nov. 2001) points to overproduction of MAP1B as a prominent factor in the pathophysiology of Fragile X. FRAXA is interested in pursuing drug discovery projects which may utilize inhibition of MAP1B as a primary therapeutic strategy. There is some evidence that MAP1A and MAP2 may also be involved, so further work in delineating the precise defect resulting from over-expression of this family of proteins is also a high priority.

2) The mGluR hypothesis

It has recently been reported that fragile X knockout mice have excessive hippocampal long-term synaptic depression (LTD) (PNAS, April 24, 2002). The particular type of LTD involved requires protein synthesis and is mediated by group I metabotropic glutamate receptors (mGluRs). mGluR5 appears to account for most of this mechanism, although the contribution of mGluR1 requires further elaboration. The group I metabotropic glutamate receptor antagonists are an exciting near-term therapeutic possibility. Further research to follow up this lead is FRAXA's highest priority at this time.

How to Apply

No specific application format is required, but an abbreviated NIH R01 or R03 proposal is acceptable. For complete details, see www.fraxa.org or contact

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