OFFICE OF HIGHER EDUCATION

David J. Tomassoni ALS Research Grant Program Annual Report

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About the Office of Higher Education

The Minnesota Office of Higher Education is a cabinet-level state agency providing students with financial aid programs and information to help them gain access to postsecondary education. The agency also serves as the state's clearinghouse for data, research and analysis on postsecondary enrollment, financial aid, finance and trends.

The Minnesota State Grant Program is the largest financial aid program administered by the Office of Higher Education, awarding more than $224 million annually in need-based grants to Minnesota residents attending eligible colleges, universities and career schools in Minnesota. The agency oversees other state scholarship programs, tuition reciprocity programs, a student loan program, Minnesota's 529 College Savings Plan, licensing and early college awareness programs for youth.

About This Report

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Executive Summary

The David J. Tomassoni ALS Research Grant awards $19,600,000 to research institutions in Minnesota on a competitive basis to support clinical and translational research that leads to the prevention, functional improvement, and curative efforts for people ALS.

Key Takeaways:
- In fiscal year 2024, OHE awarded $4,341,910 to five grantees in alignment with legislative intent and industry standards and continues to administer them.
- OHE worked with legislators to revise language to reflect timeline and partnership opportunities in MN.
- OHE continues to collaborate with organizations such as ALS Association to plan for the future of the grants including awarding the remaining funds.

Per appropriation requirements, the Minnesota Office of Higher Education submits this report by January 15 to the legislature. The report includes, at minimum: (1) applicants receiving grants, (2) amount of each grant, (3) purposes for which the grant funds were used, and (4) amount of the appropriation that is unexpended. The report must also include relevant findings, results, and outcomes of the grant program.

Introduction

The 2022 Minnesota Session Laws, Chapter 42, Section 2 (https://www.revisor.mn.gov/laws/2022/0/Session+Law/Chapter/42) provided a one-time $20,000,000 appropriation from the State's General Fund to the Commissioner of the Minnesota Office of Higher Education (OHE) for the purpose of accelerating Amyotrophic Lateral Sclerosis (ALS) research.

Grant Program Development

OHE collaborated with Minnesota Department of Health (MDH) as well as the national Amyotrophic Lateral Sclerosis Association (ALS Association) to develop the Request for Proposals (RFP). The ALS Association is the largest philanthropic funder of ALS research in the world and has funded more than $120 million to worldwide research collaborations. The ALS Association currently funds close to 100 active research projects, selected through a peer review process involving top ALS scientists.

Through the initial proposal intake, OHE experienced delays due to a lack of institutional and scientific knowledge on ALS research. Recognizing the importance of specialized industry insight, OHE enlisted the American Institute of Biological Sciences (AIBS) through the state bidding process. AIBS, with over five decades of experience, assembled a panel of 19 experts in medical research and scientific fields. Reviewers included research scientists, professors in Neurology, and heads of neurological research institutes.

Fiscal Year 2024 Competitive Process

After conflict-of-interest vetting, the panel virtually reviewed proposals in late June 2023, leading to the

awarding of five proposals totaling $4,341,910 in July 2023. The 17% success rate aligns with industry standards, reminiscent of the NIH's 2022 research grant success rate of 20% (https://nexus.od.nih.gov/all/2023/03/01/fy-2022-by-the-numbers-extramural-grant-investments-in-research/). AIBS and the panel emphasized that unsuccessful applications often lacked sufficient research specificity, deviating from program criteria.

AIBS and panel feedback shared that many of the applications not suitable for funding were scored as such because they were not as research-specific and therefore didn't closely enough align with the program criteria to be considered.

Legislative Revisions

During the 2024 legislative session, OHE worked with legislators to revise the appropriation language. The updated language reflects the awards made to date and the collaboration between OHE and the ALS Association, as well as extends the timeline of the grants:

"Up to $15,000,000 may be used by the commissioner for grants to the Amyotrophic Lateral Sclerosis Association, Never Surrender, or other similar organizations to award and administer competitive grants to applicants for research into ALS under this section. This is a onetime appropriation. Notwithstanding Minnesota Statutes, section 16A.28, unencumbered balances under this section do not cancel until June 30, 2029." (https://www.revisor.mn.gov/laws/2024/0/Session+Law/Chapter/124/)

Fiscal Year 2024 Grantee Overview and Progress Reports

The grantees awarded in FY2024 have begun their work and made meaningful progress in the early months of their projects. See below for the overview and progress to date for the fiscal year 2024 Awardees:

Institution: University of Minnesota | Principle Investigator: Dr. Pramod Pisharady

Awarded: $1,437,644

Project: *Multimodal Longitudinal Imaging of Brain and Cervical Cord As A Disease Biomarker Using Microstructure Statistics And Morphometry*

A multimodal analysis of MRI biomarkers (microstructure and morphology) from the brain and spine to improve the sensitivity to detect disease-related changes for durations as low as 3 to 6 months. Hypothesizing that the improved effect size from the multimodal analysis will reduce the required cohort size and duration of clinical trials in ALS, uncovering important correlations between (changes in) MRI biomarkers and plasma neurofilament light (Nfl).

Outcomes to Date: From Grantee's June 2024 Interim Report:

> *UMN part of the study was received IRB approval on May 15th, 2024. We conducted our first MRI scan of a control participant on 4th June 2024 and subsequent scans are being scheduled. Our aims are focused on the longitudinal data, the first 3-month follow-up scan will be in September 2024.*

Institution: Mayo Clinic | Principle Investigator: Dr. Nathan Staff

Awarded: $1,125,337

Project: *Predicting The Clinical Response to Mscs: Analysis Of Biomarkers From A Phase 2 Clinical Trial*

To perform serial CSF cytokine, growth factor, and neurofilament analysis in pALS receiving intrathecal adMSCs and to develop a predictive model for response to adMSC therapy utilizing contemporary AI/ML approaches.

Outcomes to Date: From Grantee's June 2024 Interim Report:

> *The initial clinical trial results were presented in April 2024 at the American Academy of Neurology Annual Meeting in Denver, CO. These clinical trial data will serve as foundation for development of AI models supported by the David J. Tomassoni ALS Research Grant.*

Institution: Mayo Clinic | Principle Investigator: Dr. Divyanshu Dubey

Awarded: $793,008

Project: *Humoral Immunoprofiling and Proteomic Analysis Of Amyotrophic Lateral Sclerosis*

A deep analysis of the humoral immune response and cerebrospinal fluid exosomes in ALS will uncover a distinct biomarker signature that will reveal a new understanding of the disease pathogenesis and also enable better identification of ALS.

Outcomes to Date: From Grantee's June 2024 Interim Report, the grant has been included in the following publications:

> *Kherbek H, Itoh CY, Daley C, Eggers SD, Hinson S, Sarker P, Staff NP, Pittock SJ, Dubey D. Clinical and serological insights into paraneoplastic brachial amyotrophic diplegia. J Neurol. 2024 May 22. doi: 10.1007/s00415-024-12425-x. Epub ahead of print. PMID: 38772930.*

> *Rezk M, Pittock SJ, Kapadia RK, Knight AM, Guo Y, Gupta P, LaFrance-Corey RG, Zekeridou A, McKeon A, Dasari S, Mills JR, Dubey D. Identification of SKOR2 IgG as a novel biomarker of paraneoplastic neurologic syndrome. Front Immunol. 2023 Sep 18;14:1243946. doi: 10.3389/fimmu.2023.1243946. PMID: 37795104; PMCID: PMC10546397.*

Institution: University of Minnesota | Principle Investigator: Dr. Marija Cvetanovic Awarded: $495,000

Project: *Identification Of Protective Factors For Spinal Motor Neurons Using An Ipscs Model*

To create ALS and PLS human motor neurons from patient donated induced pluripotent stem cells (iPSCs), and study human motor neurons in culture as they provide several advantages; they model disease in the context of human genetic background and relevant disease-affected cell type.

Outcomes to Date: From Grantee's June 2024 Interim Report:

As planned in the proposal we have obtained fifteen iPSCs lines (five ALS, five PLS, and five control lines matched for sex, and age) from Cedar-Sinai. We have also identified female PLS patients and are in the process of obtaining sample to create female iPSCs lines. We are currently working on differentiating iPSCs into motor neurons.

Institution: University of Minnesota | Principle Investigator: Dr. David Walk Awarded: $490,921

Project: *Biorepository To Support ALS Research in Minnesota*

Funding the resources needed to proactively provide sufficient staffing and protocols to meaningfully increase the ability to contribute to basic ALS research.

Outcomes to Date: From Grantee's June 2024 Interim Report:

- *A universal informed consent document has been prepared for IRB*

  - *Includes post-mortem tissue donation consent from living donors*
  - *Includes opt-in options for blood, CSF, and skin biopsy donations*

- *Post-mortem tissue donation*

  - *Staff have been hired to assist in tissue collection*
  - *A new protocol has been developed to facilitate timely tissue collection*

- *A data collection process has been developed*

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