

F. M. KIRBY FOUNDATION SOLICITATION EVALUATION FORM

DATE: April 5, 2024
Program Area: Health
Grant Type: Board Grant

REQUEST DATE: February 26, 2024

APPLICANT:
Yale University School of Medicine
157 Church Street
New Haven, CT 06510

CONTACT: Ms. Nancy Brown, Dean, School of Medicine

AMOUNT REQUESTED: \$200,000
BUDGETED AMOUNT: \$125,000

NATURE OF REQUEST: Support of the CNNR Imaging Facility

GRANT HISTORY

SUPPORT: 2005-2023

OF APPROVED GRANTS: 15

TOTAL DOLLARS: \$1,769,750

LAST GRANT DATE: 05/01/2023

LAST GRANT AMOUNT: \$120,000

FYE DATE: 06/30

AFS DATE: 10/27/2023

Year Approved	Approved Amount	Approval Date	Grant Purpose
2023	\$120,000	05/01/2023	Support of operational costs of the CNNR Imaging Facility
2022	\$110,000	05/02/2022	Toward operational costs of the CNNR Imaging Facility
2021	\$110,000	05/03/2021	Toward operational costs of the CNNR Imaging Facility
2020	\$100,000	04/29/2020	Toward operational costs of the CNNR Imaging Facility
2019	\$100,000	04/15/2019	Toward operational costs of the CNNR Imaging Facility

LAST SITE VISIT DATE: January 25, 2024

APPLICANT: Yale University

ENDORSEE: N/A

FINANCIAL ANALYSIS COMMENTS: The FY24 expense budget for the program in Cellular Neuroscience, Neurodegeneration and Repair (CNNR) at Yale University's School of Medicine projects a 43% increase over the prior year actuals. Most of the increase is attributable to supplies and materials and equipment replacement and repair, which is unsurprising given their beautiful new lab spaces and imaging facility. The FY24 revenue budget projects a 37% increase over the prior year actuals. Please note that the CNNR brings in nearly \$26M in research revenue annually, which is not reflected in these percentages. The FY23 Yale University audit shows unrestricted net assets totaling \$9.1B, and a cash position of \$845.4M. Investments are valued at \$45.6B. Total endowment value is \$40.7B, a 2% decrease from FY22. Spending from the endowment, Yale's largest source of operating revenue, increased by 11.7% over FY22 to \$1.7B. Despite the decrease in endowment value, the University finished the year in a strong financial position, with an operating surplus of \$167M. Financial assets available for general expenditures within 12 months are \$4.7B. As per the FY23 audit, supporting services represented 30.1% of functional expenses. As of June 30, 2023, the University held long-term debt in the form of bonds and notes payable totaling \$5.1B. FMKF last approved a grant to CNNR in FY23. The amount accounted for 39.2% of total operating revenue.

ORGANIZATION DESCRIPTION: Neurodegenerative diseases affect millions of people worldwide, posing an urgent challenge for medicine and public health - if left unchecked, cases are expected to soar as the population ages. Alzheimer's Disease alone afflicts over 6M individuals in the US, and over 25 million worldwide, with these numbers expected to more than double by 2050 (this data point is also noted in the Alzheimer's Association EF). While mortality from many major diseases is decreasing, mortality from neurodegenerative diseases is accelerating due to an aging population, thus representing a tremendous societal burden. Despite more than 50 years of research, the underlying mechanisms of these diseases are still poorly understood, and there are no effective therapies for neurodegenerative disease today – though there are classes of drugs that have been shown to reduce the intensity of physical symptoms associated with some diseases. Situated within Yale University's School of Medicine, the Cellular Neuroscience, Neurodegeneration and Repair (CNNR) program was established to develop new knowledge on the mechanisms of neurodegenerative diseases such as Alzheimer's and Parkinson's and to aggressively translate findings into effective therapies. The program brings together researchers who study basic aspects of neuronal cell biology – neurons are nerve cells that send messages all over your body to allow you to do everything from breathing to talking, eating, walking, and thinking – with those who focus on neuronal disease toward accelerating the pace of Yale's research on neurodegenerative diseases and nerve injury and repair. CNNR also provides researchers with access to the tools and technologies required to advance their research through its Imaging Facility.

EMILY PRINCE COMMENTS: In FY24, Yale University is seeking a grant of \$200K in support of its CNNR Imaging Facility.

Thanks to transformative investments by the University and private philanthropy, nearly all the Department of Neuroscience has moved to new laboratories at 100 College Street as of the start of 2024. Integral to the Yale neuroscience mission, the CNNR Imaging Facility has relocated to an upgraded and newly renovated laboratory immediately adjacent to the 100 College Street site. I

APPLICANT: Yale University

recently had the opportunity to visit CNNR and the Imaging Facility in their new homes, the details of which are captured in a site visit report dated 2/14/2024. I will repeat some of those details here for reference. I was incredibly impressed by the work coming out of CNNR, the enthusiasm with which the staff shared their work, and the thoughtfulness behind the design of 100 College Street, which brings together neuroscience, data science, psychology, and others over several floors to work across disciplines and departments towards major scientific advancements focused on the mind and brain. CNNR occupies two floors of 100 College Street, spanning the East and West Wing – in total, Yale occupies 7 of the 13 floors. Just across the street, and accessible via a skybridge, is the Imaging Facility.

The CNNR is comprised of faculty with common research interests from multiple departments. It began with two faculty members, co-founders Drs. De Camilli and Strittmatter, in late 2005, and has since grown to 109 researchers – 9 Faculty, 54 Postdocs, 31 Ph.D. students, 7 techs, and 8 undergraduate students. Since 2008, primary CNNR faculty have published 611 peer-reviewed papers in leading journals such as *Nature*, *Science*, *Cell*, and *Neuron*. Faculty have published 70 new papers since January 2023. In the past year, CNNR scientists have successfully identified mechanisms underlying aspects of neurodegeneration as well as defining the underlying differential function of brain regions and the interactions between brain and hormonal responses, among other important findings. While visiting, I learned about some of this work firsthand from CNNR faculty like Dr. Hammarlund who is studying how neurons and neuronal circuits generate and maintain normal functioning in a type of roundworm when exposed to various scenarios like injury, disease, and age. The roundworm is an excellent study subject because of its size and anatomy which can be viewed easily when using fluorescence and the Imaging Facility's high-powered microscopes.

The Imaging Facility houses state of the art equipment for high-resolution, real-time, and in vivo cellular imaging, including three laser scanning microscopes, a light sheet microscope, and an internal reflection fluorescence microscope. The equipment is incredibly complex and requires training and usage certification, which is overseen by a full-time Ph.D. level facility manager, Stacy Wilson. To date, 152 scientists have been trained and become certified users. Scheduled usage during 2023 was 14,556 research hours, an increase over the previous year despite all instruments being offline several weeks in November and early December due to the move. The top 4 microscopes are used an average of 41-78 hours/week.

FMKF has supported Neuroscience at Yale since 2005, to the tune of \$1,769,750, but the last 10 years have been focused on CNNR's Imaging Facility specifically. The CNNR is funded through a mix of government grants, private philanthropy, and university contributions. Yale's President Peter Salovey announced that he will be stepping down from his position at the end of the 2023-24 school year, but I do not believe this has any significant bearing on our grant, as the Dean of the School of Medicine, Nancy Brown will remain in her role, as will the heads of the CNNR, Drs. De Camilli and Strittmatter. Funding the CNNR is an efficient way to foster intellectual exchange and spur scientific discovery across Yale's scientific community, since its Imaging Facility opens a world of otherwise out of reach, cutting edge equipment to every researcher regardless of discipline, seniority, or position. To make the Imaging Facility accessible, and keep it at the forefront of the field, the CNNR incurs significant costs associated with its operation and maintenance. These include service contracts and repairs, small part replacements, computer equipment, upgrading of sophisticated software as well as the salary and fringes of the manager.

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Support for this type of shared equipment is the most difficult to obtain from traditional sources, yet it represents a unique and exceptionally productive asset for the CNNR. It is this gap in support that FMKF has filled for the last 10 years, and which I am recommending the Board consider once more this year. Therefore, I am recommending a grant of \$125K in support of the CNNR Imaging Facility.

RECOMMENDATION: In FY24, I recommend a grant of \$125K in support of the CNNR Imaging Facility.

JUSTIN J. KICZEK COMMENTS: While our support keeps the engine of the CNNR running, it is of course the researchers themselves who propel the important discoveries. This year's report notes, in a rather understated fashion, a very important breakthrough made by Dr. Stephen Strittmatter, co-founder of the CNNR. Strittmatter, also chair of the Neuroscience department, and his lab have reached clinical trials in a neural repair therapy. The irreversibility of injury to the spinal cord is largely due to the irreparable nature of the neuron damage. As I learned in my own 2020 visit to the CNNR, the team here has been investigating the biomechanics behind some species' ability to regenerate damaged neurons. That research has now helped advance an important clinical trial: the Strittmatter lab used a pharmaceutical therapy to block inhibitors of axon growth in the human neuron, allowing for "axon sprouting and plasticity." In a two-part, double-blind control study, patients who received the AXER-204 treatment exhibited recovered motor strength and at the delivered dosage there were no deaths and no adverse effects beyond headaches. This project is years in the making and the fact that it has reached human populations for clinical trials is a major step forward, a great example of the way in which FMKF funds have propelled a major advance in spinal cord injury repair.

After a very positive site visit by ECP, I recommend continued support for the CNNR.

RECOMMENDATION: I recommend a grant of \$125,000 in support of the CNNR Imaging Facility.

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DISPOSITION:

- Declination
- Hold for review on/about:
- Approval for: **\$125,000**
- Recommended Grant Payment(s):
2024:
2025:
2026:
- Hold for Board Review: **April 26, 2024**
- Payee Other Than Addressee: **Yale University**
- Insert Information: **Support of the CNNR Imaging Facility**
- Other: **Include Support of the CNNR Imaging Facility on check memo**

Initials: JK

Date: 04/11/2-24

Check # _____

Date: _____