

F.M. KIRBY FOUNDATION SOLICITATION EVALUATION FORM

DATE: April 6, 2023

REQUEST DATE: March 10, 2023

Last grant acknowledgment: Yes

Program Area: Health

APPLICANT:

Yale University

School of Medicine

PO Box 2038

New Haven, CT 06521-2038

CONTACT: Ms. Melissa Hey, Associate Director, Corporate and Foundation Relations

PHONE: 203-436-8518

PAYEE OTHER THAN ADDRESSEE:

AMOUNT REQUESTED: \$200,000 **NATURE OF REQUEST:** For general operating support of the CNNR Imaging Facility

GRANT HISTORY

SUPPORT: 2005-2022 **# OF GRANTS:** 14 **TOTAL DOLLARS:** \$1,649,750

LAST GRANT DATE: 05/02/2022

LAST GRANT AMOUNT: \$110,000

FYE DATE: 6/30/2022

AFS DATE: 10/21/2022

2022	\$110,000.00	05/02/2022	Toward operational costs of the CNNR Imaging Facility
2021	\$110,000.00	05/03/2021	Toward operational costs of the CNNR Imaging Facility
2020	\$100,000.00	04/29/2020	Toward operational costs of the CNNR Imaging Facility
2019	\$100,000.00	04/15/2019	Toward operational costs of the CNNR Imaging Facility
2018	\$140,000.00	04/23/2018	Toward operational costs of the CNNR Imaging Facility

DLK COMMENTS: As the global population ages, the prevalence of neurodegenerative disorders, including Alzheimer’s disease (AD) and Parkinson’s disease (PD), is fast increasing. Notably, the number of cases of dementia in the developed world is projected to rise from 13.5 million in 2000 to 21.2 million in 2025, and 36.7 million in 2050. The number of deaths by AD is now on par with the number of deaths caused by stroke, which is the third leading cause of death in the world. Unfortunately, progress toward developing therapies or reliable early diagnosis markers is hindered by the limited understanding of the genetic and cellular mechanisms of AD and other neurodegenerative diseases. This is why the Cellular Neuroscience, Neurodegeneration and Repair (CNNR) program at Yale is so important.

Our history of funding the CNNR program dates back to 2005. Founders, Drs. Pietro De Camilli and Stephen Strittmatter, continue to lead the program which includes nine tenured faculty and over one hundred researchers. The highly anticipated move to 100 College Street, which will

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include the majority of the Department of Neuroscience, is finally taking place in Summer 2023. The new location will include new and improved laboratories, the WuTsai Institute, the Department of Psychology, and colleagues from more than a half dozen other departments. This represents an intentional collaboration in which research groups co-design experiments, approach neurodegeneration and repair from multiple perspectives, and bridge the gap between basic science and medical intervention. The CNNR Imaging Core will also be relocated adjacent to the 100 College Street site. **(JJK: Yes, a reminder that, in 2016, Yale President Salovey highlighted neuroscience as one of the major priorities for investment for the University.)**

The CNNR has an annual research budget of approximately \$27 million, and this work has generated over 500 peer-reviewed papers since 2008, many of which are published in leading, high-impact journals such as *Nature*, *Science*, *Cell*, and *Neuron*. CNNR has had 54 new publications since January 2022.

Recent research highlights include:

- Dr. DeCamilli's laboratory has established that the depletion of a particular gene, VPS13C, causes an accumulation of lysosomes with an altered lipid profile, in particular, one lipid biomarker associated with PD. The team also found that a second pathway implicated in PD is activated in these cells. This data reveals a link between subcellular organelles and innate immune activation in a model human cell line and place VPS13C in pathways relevant to Parkinson's disease pathogenesis.
- Dr. Strittmatter's laboratory has made progress in understanding the basis for the overaggressive synaptic pruning which leads to the development of cognitive impairments in AD. Research has shown that neuronal metabotropic glutamate receptor 5 (mGluR5) signaling plays a role in synaptic damage. Moreover, they found that treatment with the mGluR5 drug, BMS-984923, prevents abnormal synaptic signaling while preserving normal glutamate response. They used PET (positron emission tomography) scans to show that the drug effectively occupies brain mGluR5 sites at safe and well-tolerated doses. In two aged Alzheimer's mouse models, the treatment fully restored synaptic density, and the therapeutic benefit persisted after drug washout. It also reduced phosphor-Tau accumulation in the mice.

The CNNR Imaging Facility is a critical resource for the CNNR and contains state-of-the-art equipment for high-resolution, real-time, and in-vivo cellular imaging. The facility has three laser scanning Zeiss 800,880,900 microscopes, a total internal reflection fluorescence microscope, and two spinning disc confocal microscopes, to name a few. Over 134 scientists from CNNR laboratories have been trained to become certified users. Total scheduled usage during 2022 was 13,384 research hours (a 46.5% increase over 2021). Due to the advanced nature of the equipment, a full-time Ph.D.-level facility manager is required. The request of \$200K covers approximately 46% of the Imaging Core facility budget. We have increased Yale's budget to \$120K to bring it in line with funding at Cold Spring Harbor Laboratory, Rockefeller Institute, and Scheie Eye Institute. I recommend funding at the budgeted \$120K level.

Financial analysis attached.

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JJK COMMENTS: What Boston Children's Hospital and Yale University's Program in Cellular Neuroscience, Neurodegeneration, and Repair have in common is that both institutions are looking to develop and share a deeper understanding of the physiology of the nervous system and brain in order to advance therapies and improve quality of life. However, it is worth noting that the research at CNNR is more sharply focused on *cell* – neuron cells in particular – and their role in disease and degeneration. Thus, more typically, the findings of Yale are more directly related to diseases like Alzheimer's. Additionally, while our support to BCH goes directly into lab work and investigation, at Yale we have been supporting the Imaging Facility. The benefit of this is that, like our support for capital expenses at Rockefeller University, the chance to impact other research is multiplied, given the Imaging Facility's broad applicability to other research fields. As DLK notes, the 46.5% increase in usage tells us this facility has myriad utilities to the sciences at Yale – and is critical to the needs of the CNNR team.

There is a top-notch team at the helm here, as evidenced by the very strong record of publication and NIH funding.

Given the upcoming and highly anticipated move to 100 College St., I recommend a site visit to Yale in 2024. We were last there in 2020. It would be a good opportunity to meet our new contact, Melissa Hey, and to learn more about how the CNNR fits within the broader Department of Neuroscience at Yale.

I recommend \$120K, as designated below.

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FM KIRBY FOUNDATION			
Financial Statement Analysis			
Grantee Name:	Yale University	Date:	3/31/2023
Prepared By:	DLK		
Grant Request Amt.	\$ 200,000	Type of Financial Report Submitted	Audit
Budgeted Amt.	\$ 120,000	Period Covered in Financial Report	FYE 6/30/22
Audit Firm	PricewaterhouseCoopers LLP	Date of Report Issuance	10/21/2022
Opinion	Present fairly		
Basis of Acctg.	GAAP		
Current Ratio (Liquidity Ratio/Working Capital Ratio)	1.56	Amount of Unrestricted Net Assets (Operating Reserve)	\$ 8,594,216 (in thousands)
<p>Note: A current ratio measures an organization's ability to pay short-term and long-term obligations. The higher the ratio, the more capable the organization is of paying its obligations. A ratio under 1 indicates that the organization's liabilities are greater than its assets.</p>			
Allocation of Functional Expenses	6/30/2022	%	Must Read Financial Statement Notes
A. Programmatic Support	\$ 3,162,706	90%	Ideally program expenses should be
B. Patient Care	\$ 1,076,003	9%	at least 70% of total budget.
C. Administration/ Inst. Support	\$ 324,621	1%	
D. Total Expenses	\$ 4,563,330	100%	
(in thousands) Note 14 in Audit			
Comments/ Notes:			
<p><u>FY23 Budget</u> - Consistent with last year's request, the budget submitted is for general operating support of the CNNR. The \$200K requested is 46% of the total CNNR Program Facility Budget. Budgeted expenses are growing by \$118K (37%) over FY22. The expense growth is primarily in maintenance and repair of the research equipment (up \$78.6K) and operating costs (up \$22.5K).</p> <p><u>FY22 Audit</u> - The University had a \$269.8 operating surplus vs a \$377.6M operating surplus for FY21. Total net assets grew \$401.2M. Medical services income totaled \$1.3B in FY22, up 6% from FY21 and represented 27% of the university's operating income. Grants and contracts income (20% of the University's income - primarily research -related) grew 9.7%. 77% of grant income was from the federal government (NIH, National Science Foundation, Dept of Energy and Dept of Education). Net tuition, room and board totaled \$461.5M in FY22, an increase of 55.9% over the prior year as the vast majority of students who deferred have now matriculated or rejoined the campus. 74% of university eligible students received some type of student aid in the form of scholarships and/or loans. Gifts to Yale totaled \$614M for the fiscal year. The financial report noted investment returns of 0.8% (versus 40.2% for FY21). The University had \$44.2B in investments, of which \$41.1B was endowment-related. I did note that approximately 79% of Yale's investments (\$36.8B) fair values are based on NAV with venture capital, LBO and absolute return accounting for 77% of those investments NAV. Yale's endowment consists of approx. 8,000 funds established for a variety of purposes! Spending from the endowment was \$1.6M, an increase of 3.7% over the prior year. There were no red flags as a result of my review.</p>			

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DISPOSITION:

- Declination
- Hold for review on/about:
- Approval for: **\$120,000**
- Hold for Board Review
- Insert Information: **Toward operational costs of the CNNR Imaging Facility**
- Other:

Initials: JK

Date: 04/12/2023

Check #

Date: