

F.M. KIRBY FOUNDATION SOLICITATION EVALUATION FORM

DATE: March 13, 2020

REQUEST DATE: January 30, 2020

Last grant acknowledgement: Yes

Program Area: Health

APPLICANT:

Yale University
School of Medicine
PO Box 2038
New Haven, CT 06521-2038

SEND CHECK TO:

Yale University
Office of Development
Contribution Processing
P.O. Box 2038
New Haven, CT 06521-2038

CONTACT: Dr. Patricia E. Pedersen, Associate VP, University Director of Corporate and Foundation Relations

PHONE: 203-436-8518

PAYEE OTHER THAN ADDRESSEE:

AMOUNT REQUESTED: \$200,000
support of the CNRR Imaging Facility

NATURE OF REQUEST: For general operating

GRANT HISTORY

LAST GRANT DATE: 4/15/2019

FYE DATE: 6/30/2019

LAST GRANT AMOUNT: \$100,000

AFS DATE: 10/22/2019

2015	\$200,000	4/13/2015	Toward the CNRR Imaging Facility Capital Equipment Fund-\$75,000
2016	\$150,000	4/4/2016	Toward operational costs of the CNRR Imaging Facility
2017	\$140,000	4/28/2017	Toward operational costs of the CNRR Imaging Facility
2018	\$140,000	4/23/2018	Toward operational costs of the CNRR Imaging Facility
2019	\$100,000	4/15/2019	Toward operational costs of the CNRR Imaging Facility

See Site Visit Report attached.

DLK COMMENTS: Financial analysis attached. Really nothing to add to Justin's comprehensive comments and our site visit report!

JJK COMMENTS: In 2016, Yale University President Peter Salovey identified science as a top academic priority in the coming years, and following suit, the School of Medicine elevated neuroscience as one of its priorities, given the way in which the field intersects with many disciplines. Fortunately, the Program in Cellular Neuroscience, Neurodegeneration and Repair, founded in 2005 by Drs. Pietro De Camilli and Stephen Strittmatter, was poised to lead this effort. As a result, the CNRR continues to attract more research funding and publish new findings. Research funding ticked up to \$23M in 2019 (from \$20M in 2018), while CNRR associated scientists authored 46 new publications in 2019, including new articles in *Cell*, *Science*, and *Nature Neuroscience*. Additionally, there are currently 41 active NIH R01 grants or equivalent, up from 23 in 2018.

The request itself reveals the interdisciplinary, collaborative nature of the Program in Cellular Neuroscience, Neurodegeneration and Repair. A look at the nine primary faculty members of the

APPLICANT: Yale University/School of Medicine

program reveals their associations with five different departments of the university: cell biology, neurology, neuroscience, genetics, and cellular and molecular physiology.

Operating at this nexus of scientific and medical research, the CNNR core facility makes available the equipment and technology needed to bring so many lines of inquiry together. This proposal requests support for the operational costs of the imaging facility, which requires the expertise of a scientist trained in microscopy, neuroimaging, and computer software. Given the collaborative nature of the CNNR, the facility manager also plays a crucial role as liaison between different disciplines and methods of inquiry. On our 3/4/2020 site visit, we gained both an appreciation for the collaboration between scientists as well as a chance to witness the ways in which microscopy technology and imaging is harnessed by researchers.

In 2019, FMKF's grant of \$100K makes up 43% of CNNR Imaging Core Facility operational costs and 26% of total operational costs for the CNNR. The 2020 budget shows a 7% increase in total operational funding and a decrease of 26% (from \$273K to \$201K) in Yale institutional support for the program.

We dropped Yale from \$140K to \$100K between 2018 and 2019. Given our targets for docket, I recommend keeping them at \$100K.

SDK COMMENTS: We have often read about the overlay of basic research that has direct application to Parkinson's and Alzheimer'.

Good comparison/contrasts in the site visit report between Children's Hospital/Boston and Yale School of Medicine.

FM KIRBY FOUNDATION
Financial Statement Analysis

Grantee Name: Yale University **Date:** 3/2/2020
Prepared By: DLK

Grant Request Amt.	\$ 200,000	Type of Financial Report Submitted	Audit
Budgeted Amt.	\$ 100,000	Period Covered in Financial Report	FYE 6/30/19
Audit Firm	PricewaterhouseCoopers LLP	Date of Report Issuance	10/22/2019
Opinion	Present fairly		
Basis of Acctg.	GAAP		

Current Ratio (Liquidity Ratio/Working Capital Ratio)	3.65	Amount of Unrestricted Net Assets (Operating Reserve)	\$ 5,892,315
			(in thousands)

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.

Allocation of Functional Expenses	6/30/2019	%	Must Read Financial Statement Notes
A. Programmatic Support	\$ 2,728,814	90%	Ideally program expenses should be at least 70% of total budget.
B. Patient Care	\$ 873,763	9%	
C. Administration/ Inst. Support	\$ 270,104	1%	
D. Total Expenses	\$ 3,872,681	100%	

(in thousands) Note 13 in Audit

Comments/ Notes:

Budget - Consistent with the 2019 request, the budget submitted is for general operating support of the CNNR. The \$200K requested is 50% of the total CNNR Program Budget and 42.4% of the total annual infrastructure expenses. The Total CNNR program budget is projecting a 4.9% decrease (\$1.0M) over 2018/19, all in the research funding area.

Audit - There was a \$271M operating surplus as of June 30, 2019 (vs \$190M in 2018). Net tuition represented 9.4% of the university's operating revenue. 71% of university eligible students received some type of student aid in the form of scholarships and/or loans. Grant and contract income represented 20% of the university's operating revenue and the federal government funded 74% of that income. The University had \$30.9B in investments, of which \$30.3B was endowment-related. Endowment revenue provided \$1.4 billion or 33% of the university's operating revenue. Overall, there were no red flags as a result of my review.

SITE VISIT REPORT

Report No: 10

Grantee:

Yale University/School of Medicine
PO Box 2038
New Haven, CT 06521-2038

Program Area: Health

Most Recent Grant Amount and Date: \$100,000.00 - 4/15/2019

Primary Contact: Dr. Patricia E. Pedersen, Associate VP, University Director of Corporate and Foundation Relations

Phone: 203-436-8518

Met With: Patty Pederson, Ph.D., Associate VP for Development; Pietro De Camilli, Director of the CNNR; Stephen M. Strittmatter, MD, PhD, Director of the CNNR; Sreeganga Chandra, Deputy Chair, Department of Neuroscience; Shawn Ferguson, PhD, Associate Professor of Cell Biology and of Neuroscience; Marc Hammarlund, PhD Associate Professor of Genetics and of Neuroscience; Stacy Wilson, Ph.D., Facility Manager of CNNR

Location: 333 Cedar Street, New Haven, CT

Date Visited: March 4, 2020

F. M. Kirby Foundation Representative: Justin J. Kiczek, Executive Vice President; Diana L. Kostas, Treasurer/Secretary

Site Visit Guide: Matrix Score [Rating Scale from a high of 4 to a low of 1]

	'20	'18
<i>A. Personnel: Turnover, Professional Development and Career Advancement</i>	3.50	3.50
<i>B. Board: Involvement, Development, and Training</i>	N/A	0.0
<i>C. Financial: Net Assets, Fundraising Performance and Capacity</i>	3.75	3.75
<i>D. Strategic Planning, Review and Implementation</i>	3.50	3.25
<i>E. Program Evaluation and Quality Assurance</i>	3.50	3.50
Total:	14.25	14.0
Average Score:	3.56	3.5

Comments: Patty Pederson, our primary contact at Yale picked us up at the New Haven train station. I mention this because, en route to the Yale School of Medicine campus, she pointed out a glass-walled building (Alexion Pharmaceuticals) as the future home of the Cellular Neuroscience, Neurodegeneration, and Repair program. The building is centrally located between the medical campus to the south and non-medical campus to the north. This new location will consolidate CNNR activities, for their labs and equipment are now spread out across a few floors of the School of Medicine building. It will also expand space for microscopy. The Anlyan Center ("below the neck research") and psychology will also be housed there. They faculty meets weekly to discuss layouts/co-location and Drs. Strittmatter and De Camilli meet bi-weekly with the architects. Dr. Strittmatter referred to the building as a CNNR neighborhood.

We eventually arrived at the School of Medicine, walking through the Hall of Deans, which was full of portraits of white men. This is worth noting because Yale has recently appointed Nancy Brown, its first female Dean; this news was a source of much excitement for several of the faculty members we spoke to. Once we settled in our conference room at the School of Medicine, we were joined by Pietro De Camilli, MD and Stephen Strittmatter, MD, Ph.D.

Drs. De Camilli and Strittmatter underscored that CNNR flips the ordinary model of medical research. While it is conventional to study the basic functions of cells in order to understand disease, at CNNR, when it comes to neuroscience, they are just as often trying to study disease in order to understand the basic science of the cell. Thus, the neurodegeneration field requires the expertise of cell biologists, who can best investigate cell function and dysfunction.

Dr. Strittmatter shared that he has recently brought two projects to clinical trial. The first trial, which will hopefully aid in neural repair of spinal cord injuries (SCI), involves a particular molecular pathway that was identified after genetically introducing lesions resembling SCI in mice and observing in vivo. Ideally a therapeutic regimen can clear the pathway of debris and allow for neural repair to take place. The second trial involves a potential oral solution that prevents the binding of particular proteins and peptides together to rescue synapses and memory function in Alzheimer's disease models. The journal Cell Reports referred to it as a "drinkable cocktail of designer molecules that interferes with a crucial first step of Alzheimer's".

We were soon joined by faculty members Sean Ferguson, Ph.D., who is working at the intersection of cell biology and neuroscience; Mark Hammerlund, Ph.D., a specialist in genetics and neuroscience, and Sreeganga Chandra, Ph.D., who studies synaptic cell biology in neurodegeneration. Dr. Hammerlund claimed that the CNNR is one of the world's top centers for cellular neuroscience, crediting this distinction to the collaborative atmosphere that brings together people with different levels of expertise and interests (to that point, Dr. Ferguson later commented on how much he learned about his colleagues' work just from their presentations to us!). The team also credited the technology and assistance available at CNNR as being critical to their success; as one put it, rather than designing experiments to fit the equipment they have, the CNNR faculty can pursue what most interests them and use the equipment available to support them.

The following hour was a fascinating crash course in cell biology, as each faculty member shared with us his or her current work. Drs. Ferguson and Hammerlund were quite good at "translating" their work into laymen's terms. Dr. Ferguson has been studying the role of the lysosome in Alzheimer's. It is now well understood that there is a relationship between amyloid "plaques" and the development of Alzheimer's. Ferguson is focusing on a related symptom, which is the clustering of the lysosome organelles in the neural axons in proximity to amyloid plaques. In other words, Ferguson is trying to understand if axonal lysosomes are important contributors to Alzheimer's disease brain pathology.

Dr. Hammerlund quickly followed by sharing his research on the role of healthy mitochondria in neural axon maintenance and repair. Since mitochondria are essential to the healthy function of both neural synapses and axons, Hammerlund, who is also a

geneticist, is experimenting with blocking axon degeneration through gene editing involving mitochondria.

DLK and I had a bit harder time following Dr. Chandra, who was more prone to using specialized terminology than the others. Chandra is studying the aggregated presence of the alpha-synuclein protein in patients with Parkinson's disease. She noted that 20% of Parkinson's patients have the same genetic mutation. There are currently 24 disease-causing genes for Parkinson's, with some having a much higher risk factor than others. She has contributed to understanding of how a molecule known as Hsp110 can ameliorate the aggregation of the alpha-synuclein protein in neural synapses.

Throughout the hour, Patty Pederson was an excellent moderator, always bringing back the scientists to the impact of the CNNR on their work. Each faculty member is leading a team of researchers in carefully studying different organelles of the neuron in order to better understand the interplay between genetics, cell function, and neurodegeneration. With the assistance of a high-powered, spinning-disc microscope, we were able to watch how organelles move around both human and worm neurons. Their work has implications for Parkinson's, Alzheimer's, and spinal cord injuries.

Upon the conclusion of this presentation, we were brought to the actual CNNR, which does not necessarily have the distinguishing presence of the Kirby Center for Neurobiology. Here, we were joined by Stacy Wilson, Ph. D., who serves as chief facilitator of the CNNR. Stacy oversees scheduling, maintenance of equipment, training, and repair. In the previous year, she had to oversee 139 scientists who logged 11,597 hours of equipment use! It should be noted here that FMKF support of the CNNR largely goes to supporting Stacy Wilson's position. Like the others we met that morning, she was friendly, down-to-earth, and funny. Stacy allowed us to peek into a couple of very darkened rooms, where scientists were hunched over microscopes. At current moment, she is operating six microscopes, each costing between \$500K and \$700K. While they seem satisfied with the equipment they have, on their wish list for their new location would be microscopes that have better resolution. Additionally, demand for the microscopes is high and researchers are currently having to come in all hours of the night to gain access to the microscopes.

Given that this visit quickly followed our visit to Children's Hospital, it might be worth pointing out salient similarities and differences. Contact persons at both Yale and BCS put together great agendas; in both cases, we were privileged to hear from some of their best and brightest scientists, and the visits were handled with the utmost professionalism. Both institutions are deeply invested in understanding neuroscience on at a cellular level, utilizing stem cell technology and CRISPR gene editing to help them achieve their goals. As for differences, whereas as the Yale faculty seem more invested in *understanding*, the BCS team appears more invested in translational research (though surely Yale engages in this too). BCS, given its larger budget, boasts almost three times the number of faculty and certainly appears to enjoy more cutting-edge equipment. Yale did not yet appear to be using AI or machine learning in its research, whereas BCS has.