F. M. KIRBY FOUNDATION SOLICITATION EVALUATION FORM

DATE: November 12, 2024 **REQUEST DATE:** October 28, 2024
Program Area: Health
Grant Type: Board Grant

APPLICANT:
Rockefeller University
1230 York Avenue, Box 164
New York, NY 10065-6399

CONTACT: Ms. Maren Imhoff, Senior Vice President for Development

AMOUNT REQUESTED: $114,200
BUDGETED AMOUNT: $125,000

NATURE OF REQUEST: Support of equipment purchases for research on hearing loss

GRANT HISTORY

SUPPORT: 1994-2023

 # OF APPROVED GRANTS: 23 **TOTAL DOLLARS:** $11,554,000

LAST GRANT DATE: 12/08/2023 **LAST GRANT AMOUNT:** $120,000

FYE DATE: 06/30 **AFS DATE:** 11/08/2023

Year Approved	Approved Amount	Approval Date	Grant Purpose
2023	$120,000	12/08/2023	Support of the purchase of a new lattice light sheet microscope
2022	$115,000	12/12/2022	Toward the purchase of a multimode microplate reader and a dedicated plate stacker
2021	$125,000	12/20/2021	Toward construction of a next-generation light-sheet microscope
2020	$125,000	04/29/2020	Toward the purchase of a scanning electron microscope
2018	$125,000	04/23/2018	Toward the purchase of an ultrafast laser scanning resonant confocal microscope

LAST SITE VISIT DATE: August 9, 2021

APPLICANT: Rockefeller University

ENDORSEE: N/A

FINANCIAL ANALYSIS COMMENTS: The FY24 operating budget for Rockefeller University is projecting a $7.7M surplus. Expenditures are expected to decrease by 5% due to decreases in laboratory operations, facilities, and energy expenses. Revenues, too, are anticipated to decrease marginally (3%). FY24 unaudited actuals show a slight (relative to the budget size) surplus of $82K. In FY24, Rockefeller expended $43.5M in debt service, representing approximately 10% of total expenses. The included audit is from FY23. As of June 30, 2023, Rockefeller had total assets of $3.9B, with investments totaling $2B and a cash position of $31M. Net assets without donor restrictions totaled $169M. Total liabilities were $1.4B, the majority of which ($986M) was long-term debt. FY23 saw a $145M deficit. At FYE, Rockefeller had $776M in liquid assets available to meet expenditures within one year. The F. M. Kirby Fund for Regenerative Neuroscience Endowment had a market value of $2.1M as of June 30, 2024. The F. M. Kirby Postdoctoral Fellowship Endowment had a market value of $2M as of June 30, 2024.

ORGANIZATION DESCRIPTION: Rockefeller University was founded as the first institution in the United States devoted exclusively to biomedical research, and we look forward to celebrating our 125th anniversary, in 2026, as one of the world's leading institutes of research and education in biomedical sciences. We strive to understand life’s fundamental processes and promote their translation into therapeutics. Our seventy-two independent laboratories conduct research with implications for deciphering the causes of a range of human health conditions, including vision and hearing disorders, infectious diseases, cancer, heart disease and stroke, autoimmune disorders, Alzheimer's, Parkinson's, and other neurodegenerative disorders, and many others. Research by Rockefeller scientists continues to contribute to the development of drugs, vaccines, and diagnostic tools that help populations in need the world over.

GINA BEVIGLIA COMMENTS: Since 1994, FMKF has supported sensory neuroscience research at Rockefeller University with 23 grants totaling $11.5M. Of these 23 grants, 15 have been dedicated to supporting the purchase, customization, and installation of highly specialized machinery. Rockefeller does not have departments and instead allows each lab to operate as an independent entity. This model promotes collaboration across disciplines and maximizes the usage of each of these pieces of equipment. Of course, many of the capital requests FMKF receives from Rockefeller are reflective of the needs of Dr. A. James Hudspeth, the F. M. Kirby Professor. Dr. Hudspeth and his team study the normal hearing process to understand the causes of hearing deterioration and to explore possibilities for hearing regeneration. The hearing loss experienced by most people is caused by damage to the sensory hair cells found in the inner ear, which are one of the few types of cells in the human body that do not regenerate. Studying the small, intricate structures of the inner ear requires investments in innovative microscopy technologies. This year, Rockefeller has provided updates on the customization of the lattice light sheet microscope supported by our 2023 grant and the collaborative research of the Hudspeth Lab. Additionally, Rockefeller is seeking a $114,200 grant to support the purchase of an optical coherence tomography system.

In 2023, FMKF awarded Rockefeller University with a grant of $120,000 in support of the construction of a lattice light sheet (LLS) microscope for shared use by several of the institution’s laboratories. LLS microscopy builds on the foundation of light-sheet fluorescent microscopy, which allows for the cross-imaging of live cells and tissues by shining planes of light through them, producing high-resolution three-dimensional images. LLS microscopy expands on these abilities, manipulating planes of light to capture images of subcellular structures as they function in vivo, in real time. This machine is an impressive amalgamation of hardware and software components, requiring collaboration across University departments and with partner institutions. Optical engineer Dr. Behzad Khajavi has overseen the construction of custom components in the University's Precision Instrument Technologies Resource Center and the high-energy physics machine shop; ordered manufactured parts that were purchased with funds from the FMKF grant; and continues to align and test the microscope's various optomechanical components. Final testing procedures are still underway to ensure that the microscope's hardware components are in alignment with the correlated data acquisition software. Dr. Khajav is also working on a further custom addition to the LLS microscope that will make it effective for imaging beyond a single layer of cells, deeper into tissue. This addition, a technique known as adaptive optics, will be particularly useful for Dr. Hudspeth's lab, as they examine the very small subcellular structures of hair cells in zebrafish. **(JJK: I was not aware of how intricate the assembly of this microscope would be. Wow.)**

We also received a very exciting update on the progress of Dr. Hudspeth's research. The Hudspeth Lab has been exploring how to harness the regenerative potential of the Hippo signaling pathway, which acts as an evolutionary "emergency brake" that prevents the excess growth of tissue or the development of cancer in the body. Temporarily removing this brake in a controlled manner, however, can allow for the positive regeneration of cells within organs that cannot typically heal themselves, such as the retina, heart, and ear. In collaboration with research institutions across the country, Dr. Hudspeth has identified a small molecule that inhibits this Hippo signaling pathway, thus introducing the possibility of positive regrowth. In experimentation, this compound and its derivatives have shown potential for use in regenerative therapies. In human-derived retinal organoids, this molecule fostered extensive cell proliferation. Administration of this substance in mice successfully activated genes that encourage cell division in the heart, liver, and skin. In models studying cardiac wound healing, like those following a heart attack, the compound initiated the proliferation of cardiac muscle cells. While this is early, basic research, the successes of these compounds in the lab are incredibly exciting. Beyond their therapeutic potential for vision loss, hearing loss, and cardiac recovery, these compounds are being studied by many researchers across the world for their potential clinical applications for a vast range of health conditions – prostate cancer, breast cancer, chronic myelogenous leukemia, iron-induced kidney cell death, Ebola, C. difficile, ischemic stroke, and muscular dystrophy, just to name a few. **(JJK: What a powerful example of how scientific discovery in one defined area can often unlock mysteries or problems in others.)**

In 2024, Rockefeller University is seeking a $114,200 grant to purchase a new optical coherence tomography system and accompanying equipment for use in sensory neuroscience discovery. The meeting of two light beams of the same wavelength, known as interference, is the basis for all optical imaging, including that which happens in our eyes and in microscopes. While traditional microscopy technologies have serious limitations on their resolution, optical coherence tomography (OCT) uses a broad band of light beam wavelengths to overcome these limitations. OCT systems can image at a single-cell resolution, can measure movements at frequencies as great as 20,000 cycles per second, and can register motions as small as the size of an individual atom. Using commercially available OCT systems, the Hudspeth Lab has successfully imaged sensory receptors dissected from gerbils and mice. In order to image these cells with the OCT, the cells must be isolated from the ear, as the bone around the cochlea is too dense to permit microscopic observation. Because the cells have undergone dissection and have been removed from the living animal, their quality, and therefore the images, are diminished. To remediate this, Rockefeller hopes to purchase a more custom OCT system that uses much longer wavelengths of light, allowing for the imaging of cells within living animals. The particular OCT system in which the Hudspeth Lab is interested would allow them to identify the basis of the ear's active process: hair cells amplify their inputs, sharpen their frequency discrimination, and extend the range over which they can accommodate sound stimuli. This is the process that fails when a person experiences hearing loss; using imaging made possible by the OCT system, the Hudspeth Lab hopes to gain insight into how damage to this system might be prevented or repaired. The $114,200 grant request includes the cost of the OCT system, a data acquisition computer, a data analysis computer, and advanced ethernet jacks.

Beyond just imaging the complex inner ear structures of small live animals, Dr. Hudspeth is also endeavoring to overcome the challenges of imaging the cochlea of a living person. The density of the bone in the human ear scatters the OCT's light waves, rendering the technology ineffective. This prevents the OCT system from being used in clinical diagnosis or in surgery. In coordination with prestigious otolaryngologists (ENTs) in Japan, Dr. Hudspeth has identified a chemical compound that safely renders human bone more transparent and more amenable to study with the OCT. Because the compound is already FDA approved for use as a contrast agent in the diagnosis of a cerebral stroke, the Hudspeth team is hopeful that this method will move into clinical practice quickly.

Our long history of supporting innovative microscopy technologies at Rockefeller University has the dual benefit of bolstering the work of Dr. Hudspeth, the F. M. Kirby Professor, and that of sensory neuroscience researchers across the institution. It is wonderful to read of such important progress in Dr. Hudspeth's lifelong commitment to curing hearing loss, and the implications that it may have across an array of research areas. I hope to make it to Rockefeller for a site visit in early 2025, to see these remarkable machines and to hear more from Dr. Hudspeth about the recent breakthroughs in his work. I recommend the requested $114,200 in support of the purchase of an optical coherence tomography system and accompanying equipment.

RECOMMENDATION: I recommend a grant of $114,200, payable over 1 year designated for support of the purchase of an optical coherence tomography system and accompanying equipment.

JUSTIN J. KICZEK COMMENTS: As we enter a new era of artificial intelligence — when human understanding has progressed so far that we now have in our pockets access to unfathomable quanities of data — it can be surprising to realize that there is still much we do not know about how organs like the ear work, simply because the organ itself is so fine and so delicate. While the Hudspeth Lab continues to help build our basic understanding of the ear, through the slow but steady accretion of knowledge, the Lab is also, as evidenced by this request, advancing therapeutic solutions that might help reverse hearing loss — and potentially help other irreperable organs heal as well. How exciting to see that Hudspeth has isolated small molecules that hold promise to help these cells regnerate.

APPLICANT: Rockefeller University

Rockefeller's proposal and report are noteworthy for lucidly explaining Hudspeth's research without over simplifying.

Due to the the lack of departments at RU, in favor of labs that share resources and learn from one another, we know that there is an increased "return on investment" when we help purchase highly specialized equipment at this particular institution, as pieces like the OCT system are likely to help researchers in other labs as well.

RECOMMENDATION: I recommend a grant of $114,200, payable over 1 year designated for support of the purchase of an optical coherence tomography system and accompanying equipment.

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DISPOSITION:

( ) Declination

( ) Hold for review on/about:

(**X**) Approval for: **$114,200**

( ) Recommended Grant Payment(s):
2024:
2025:
2026:

(**X**) Hold for Board Review: **December 13, 2024**

( ) Payee Other Than Addressee:

( ) Other:

Initials: JJK Date: October 28, 2024

Check #____________ Date:____________