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February 7, 20[redacted]

Gilead Sciences Research Scholars Program in HIV

Dear Review Committee Members,

It is my pleasure to write in support of Dr. [redacted] application for the Gilead Sciences Research Scholars Program in HIV. I first met [redacted] at a Keystone Meeting on Intrinsic Cellular Defenses in 20[redacted], and then shortly thereafter I was excited to recruit her as a faculty member in the [redacted]. [redacted] is an exceptional young scientist who has already achieved recognition among the foremost HIV-1 biologists, and I have no doubt that she will quickly become a leader in the field herself. I have summarized the mentorship plan that [redacted] and I have created below. I have had the opportunity to train eight pre-doctoral students, seven postdoctoral fellows, and six clinical fellows. I have also recently taken on leadership positions in the School of Medicine as Director of the [redacted], where I am taking an active role in mentoring new faculty here. As such, I am committed to dedicating the necessary time to mentor Dr. [redacted] as part of this application.

Dr. [redacted] has received exceptional training in retrovirology. She completed her doctoral work in Microbiology at the [redacted] in the laboratory of Dr. [redacted] and received the Best Dissertation Award in the Biological Sciences Division. Her doctoral work focused on understanding how the innate immune system detects retroviral infection and initiates virus-neutralizing adaptive immune responses. She published three first author manuscripts as a doctoral student and made seminal contributions to our understating of retroviral pathogenesis including. Her work provided the first *in vivo* evidence of the requirement for [redacted] the detection of retroviral infection and subsequent activation of humoral immune responses. Additionally, she demonstrated that an orally transmitted retrovirus exploits the gut microbiota to counteract host immune responses. Together with Dr. [redacted], who showed that picornavirus and reovirus transmission also depends on the gut microbiota, this groundbreaking discovery established a new field investigating trans-kingdom interactions between viruses and bacteria in the gut and their influence on health and disease. During her time as a postdoctoral fellow [redacted] also continued management of an investigation initiated during her doctoral studies concerning a novel pathway for antiretroviral antibody production. These findings have been published with [redacted] as the corresponding author, and she has received funding from the [redacted] to continue this investigation. She has also obtained a secondary appointment in the Department of Immunology in order to capitalize on expertise and mentorship opportunities beyond the Infectious Diseases Division here [redacted]

For her postdoctoral training, [redacted] chose the laboratory of Dr. [redacted] at the [redacted] University. During her time in the [redacted] laboratory, she published three first author publications, obtained a [redacted] Award NIH F32, and was awarded the [redacted] Prize in Retrovirology in 20[redacted].

Her postdoctoral work focused on the identification and examination of genes with antiretroviral activity that comprise the “intrinsic” immune system that directly defends cells against infection. She a library of interferon-stimulated genes (ISGs) to test for antiretroviral activity against a variety of retroviruses including, lentiviruses, betaretroviruses, gammaretroviruses, and spumaviruses (foamy viruses). This approach revealed a number of genes with previously unknown anti-retroviral activity and work is ongoing to understand their specificity and mechanism of action. [redacted] has brought this library with her to the [redacted] and has established collaborations with me and with members of the [redacted] aimed at identifying ISGs with antiviral activity against other viruses. These collaborations have already proven fruitful in identifying novel antiviral genes as well as unexpected activities for known intrinsic immune effectors. As a postdoc, [redacted] also identified the interferon-induced GTPase, Mx2 as an inhibitor of HIV-1 nuclear import. Her comprehensive work investigating how previously unappreciated heterogeneity in nuclear pores influences both HIV-1 infection and the antiviral activity of Mx2 has proved to be a seminal contribution to the field. She is also now part of a multi-investigator project led by Dr. [redacted] at [redacted] investigations concerning HIV-host interactions during the early HIV-1 life cycle. Although these investigations will not directly overlap with this proposal, the techniques and tools developed therein will complement this proposal.

In conclusion, Dr. [redacted] already has an outstanding reputation among retrovirologists, and her expertise in retroviral biology, cellular nucleocytoplasmic trafficking, and immunity to retroviral infections has quickly made her a valuable asset to the research community here at the [redacted]. The research she proposes here will continue to advance our basic understanding of intrinsic defenses against HIV-1 infection.

Sincerely,

[redacted]

Mentoring Plan:

Eligibility.
Dr. [redacted] is a tenure-track Assistant Professor of [redacted] in her second year of her appointment. She has not received R01 funding.

1. Mentor Role. As the director of the [redacted] I recruited Dr. [redacted] to the university and have interacted with her continuously throughout the onboarding process and since her appointment in January 20[redacted]. In this capacity, I am highly invested in ensuring the success of Dr. [redacted]'s independent research career. Furthermore, given that our research interests are complementary, I am happy to serve as mentor on Dr. [redacted]'s Gilead Research Scholars in HIV research proposal. Dr. [redacted]s office and laboratory is in close proximity to mine, which has provided multiple opportunities for informal interactions and discussions concerning her research goals. In addition, as part of the mentoring plan, Dr. [redacted] and I will meet one on one monthly to discuss her new findings, as well as to provide her with the opportunity to solicit advice on her research, managing her laboratory, and navigating the university system. I will also monitor her compliance in her timeline for experimental studies, publications, and grant submissions.

2. [redacted] Scholars Program. The Department of [redacted] is committed to the mentorship of new faculty to monitor and guide them as they progress toward R01 funding and tenure. Tenure-track Assistant Professors at the [redacted] receive formal mentorship through the [redacted]. This program is directed by Dr. [redacted], chair of [redacted]; I also serve as Associate Director. Through the [redacted] program, [redacted] has access to funds for career development and travel, support for hosting visiting speakers, and access to funds for internal grants (which [redacted] has already been awarded). The program also facilitates an interactive and collaborate environment, with monthly seminars in which two [redacted] present their research and exchange ideas across different fields of research, and opportunities to present at the larger [redacted] series here at [redacted]. Finally, the [redacted] has initiated a grant review process for new faculty in which external grant submissions are reviewed by the research community at the [redacted] in a mock study section in order to provide detailed feedback and increase the chance of success in grant submissions.

3. Travel. In addition to support from the research community here in [redacted], travel to meetings is essential for networking and the cultivation of potential collaborations. [redacted] department is supporting her travel to meetings as part of her start up funding. In the coming year, [redacted] will attend the Cold Spring Harbor Laboratory Retroviruses meeting and West Coast Retroviruses meeting. In addition, [redacted] has been invited to speak in the AIDS Panel at the US-Japan Cooperative Medical Sciences Program's [redacted] International Conference On Emerging Infectious Diseases In The Pacific Rim this February.

4. Management Training/Support. The University [redacted] has developed a junior faculty career development program that provides junior faculty training in grant writing, management responsibilities, and navigating the university system as they approach tenure and promotion. [redacted] participates in this program as well as the Department of Immunology's Junior Academic Mentoring program. The university also has an excellent career development office, and seminar schedule to support junior faculty as they progress. I have encouraged [redacted] to take full advantage of these opportunities and I'm sure that she will continue to do so as her research program progresses, and her laboratory grows.

Research Resources and Facilities.
Funding: In addition to a competitive start-up package from the department, Dr. [redacted] is currently funded by an [redacted] Pilot Award investigating the genetic basic for a novel pathway for antiviral antibody production. She is also expected to receive funding this spring as a SubAward PI from a multi-investigator R01 grant on early events in the HIV-1 life cycle led by Dr. [redacted] (12th percentile, notice of award pending). The funding from the Gilead program would allow Dr. [redacted] to expand her current research understanding how the [redacted]

Laboratory, Office, and Departmental Resources: Dr. [redacted]'s laboratory is located in a state-of-the-art research building opened in 2008 and includes an "open space" main room with bench (four) and desk (four) space for laboratory personnel, and separate rooms for tissue culture (~400 ft^2) and BL2+ space (~300 ft^2), each containing

biological safety cabinets and CO_2 incubators. [redacted] has outfitted the laboratory with an Attune NxT flow cytometer coupled to an autosampler, a QuantStudio 3 qPCR machine, Li-Cor instruments for nucleic acid gel detection and chemiluminescent immunoblot imaging and quantification. as well as other miscellaneous small equipment. There are also shared equipment items such as high-speed and ultra-centrifuges and rotors, bacterial incubators and shakers, Nanodrop, UV-Vis spectrophotometer, autoclave, and ice supply. Core facilities also include molecular biology resources, with automated sequencing and oligonucleotide synthesis, a flow cytometry core, and a real-time PCR core.

Dr. [redacted] also has access to four inverted fluorescence microscopes in my laboratory. For routine microscopy (transmitted light and brightfield, phase contrast and epi-fluorescence techniques of cell culture specimens), there is a Zeiss Axiovert CFL inverted microscope equipped with 10x, 20x, and 40x objectives, filter sets (DAPI, FITC, and Texas Red), a Moticam 2300 high-resolution live imaging microscopy camera, and controlled by Motic Images Plus 2.0 software. For advanced microscopy, the laboratory is equipped with three high-resolution imaging microscopy systems. We have Olympus IX50, IX81, and IX83 inverted microscope equipped with 10x/0.40NA, 20x/0.75NA, 40x/0.95NA, 60x/1.45NA, and 100x/1.65NA objectives, filter sets (DAPI, FITC, Texas Red, Far Red), a cooled monochrome DP30 CCD camera (IX50), Hamamatsu Orca-R2 CCD camera (IX81), ORCA-Flash 4.0 CMOS Camera (IX83), Sutter Lambda 10-3 High Speed filter wheel system (IX81), and Prior Z-focus drive motorized XY-Stages (IX81, IX83), a DH-35i micro-incubation system (IX81) and Tokai Hit micro-incubation systems (IX83), a transmitted light differential interference contrast adaptor (IX81, IX83), and controlled by Olympus Slidebook 5.0 (IX50, IX81) and CellSens (IX83) advanced imaging software with deconvolution packages based on calculated point spread functions. In addition, for extended real-time imaging, the laboratory owns an Olympus VivaView imaging system in a fully temperature- and CO_2-controlled setting equipped with DAPI/GFP/RFP filters and a 40x/0.95NA air objective. This system can perform real-time imaging in living cells for several weeks, if necessary. The Department of Pediatrics also has a core microscopy facility located four floors away from the laboratory which contain three confocal microscopes (a Zeiss LSM 710 inverted LSM, a Leica TCS SP6 inverted microscope, and an Olympus spinning disk confocal microscope. Dr. Kane's laboratory can readily access these systems on a fee-for-service basis.

Dr. [redacted]'s office (~150 ft^2) is located down the hall from the laboratory. The PI has access to administrative services including accounting, budgeting and planning, policies, and human resources. In addition, Dr. [redacted] and her laboratory have a dedicated administrative assistant, employed by the [redacted]

Dr. [redacted]'s laboratory and office are fully equipped with two new Macintosh computers and a personal Macintosh laptop. In addition, a Macintosh computer loaded with Imaris Image Analysis software (Bitplane) is located in a shared space for common use and can accessed by all members of the laboratory. These computers are all equipped with network and internet connection and connected to scanners and/or color laser printers.

The laboratory has full access to all [redacted] library services, with on-line access to large collections of bioscience journals and textbooks. Electronic services at the Health Sciences Library System includes a full range of modern molecular biology resources and databases, including analysis software and databases for genomics, DNA and RNA tools, pathway analysis, genetic variations and diseases, molecular structure, immunology, microarrays, SAGE, gene expression analysis, organelles, protein sequences and proteomics.

Scientific Environment: The [redacted] is ranked #[redacted] in the nation in research dollars from the NIH and thus, serves as an excellent training ground for acquiring external research funding. The Department of [redacted] has a long research and education tradition in microbiology, virology, biochemistry and genetics. In addition to research on complex scientific problems, the department also emphasizes training the next generation of talented young scientists and physicians, providing outstanding mentoring to enable students and postdoctoral fellows.