To the NIGMS F32 study section:

I am writing in support of John Desmarais’ application for a Ruth L. Kirschstein National Research Service Award for an Individual Postdoctoral Fellowship (F32). Since 2018, I have collaborated with John on two projects and have had the chance to observe him as a scientist. I recommend him for this fellowship with great enthusiasm.

During our collaborations, John has displayed the skills and drive necessary to become a successful independent researcher. He has repeatedly demonstrated his skill in statistical methods, computational modeling, and science communication. Beyond this, John displays scientific integrity and collaborative spirit that will greatly aid his future endeavors.

As part of our response to the emergence of the SARS-COV2 pandemic, the Innovative Genomics Institute assembled an interdisciplinary team of researchers to investigate methods of improving CRISPR based diagnostics to meet the challenges of the time. This team included researchers from across a wide variety of specialties and from multiple institutions including UC Berkeley, UCSF, the Gladstone institutes, and others. John joined the team to lend his expertise in modeling, statistics, and data analysis. As part of this effort, he collaborated closely with researchers across multiple projects and specialties to analyze their experimental results, rapidly update our theoretical understanding of the system, and use that theory to guide new experiments to overcome limitations in our diagnostics. During this time, he demonstrated an ability to work quickly on fast moving projects and coordinate effort in large collaborations, all while also maintaining his independent thesis research.

During this collaboration, John demonstrated his science communication skills repeatedly. In order to maintain coordination on a team of this size, we organized weekly meetings where all collaborators would present their findings from the week to the entire team. These meetings required communicating to a large group of mixed experimentalists and theorists from across a variety of fields. John described complicated modeling and statistical results simply and made his findings accessible to the entire team. This enabled rapid incorporation of insights from the modeling into our experiments. For instance, after John’s modeling showed that stopping activator cleavage would dramatically improve detection characteristics, we were able to rapidly transition to using a chemically-modified, uncleavable, activator for csm6.

John also exhibited expertise in statistical methods and modeling. He developed data analysis and statistical protocols for identifying positive samples from one-off microfluidics time courses, while also optimizing sampling strategies with experimental collaborators to maximize statistical power and minimize time to detection. He wrote software for parsing plate reader data and provided training on its use to others on the team. He also performed kinetic modeling of enzyme reactions that provided insight into issues such as low sensitivity and high background in early diagnostic designs and helped to guide experiments to overcome these issues.

John is also a capable bench scientist. When my lab was characterizing CasX as a new RNA-guided CRISPR nuclease, we collected Cryo-EM data that revealed the presence of a domain with a potential zinc binding motif. In order to confirm that zinc was the bound metal, a graduate student in my lab at the time reached out to John, who was able to successfully confirm the presence of zinc with an x-ray spectroscopy experiment.

In summary, John’s willingness to collaborate, scientific ability, and skill at scientific communication make him outstanding collaborator. I have no doubt that he has the potential to become an exceptional independent researcher, and I most heartily recommend him for the Ruth L. Kirschstein National Research Service Award for an Individual Postdoctoral Fellowship.

Sincerely,

Jennifer Doudna, Ph.D.

Nobel Laureate

Professor of Chemistry

Professor of Biochemistry & Molecular Biology

Li Ka Shing Chancellor’s Professor of Biomedical Science

University of California, Berkeley