



Alex Greninger, M.D., Ph.D.
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I'm a third year resident in laboratory medicine at the University of Washington Medical Center. I received a BS and MS in Biological Sciences/Immunology and a BA in International Relations from Stanford University, a MPhil in Epidemiology at Cambridge University, and a MD/PhD from the University of California San Francisco. I'm interested in genomics of infectious diseases and metagenomics, especially expanding reference genome databases through first genomes of bugs and viral discovery and understanding the crazy evolutionary pressures we put on viruses in the clinic and the lab.

Nomination Letter

To the selection committee:

It gives me great pleasure to nominate Dr. Alex Greninger, a resident physician at the University of Washington, for an ASM/PASCV Young Investigator Award. Alex is an exceptional young scientist, and committed to a career in diagnostic virology. I hope I am able to convey the reasons behind my enthusiastic endorsement.

Alex joined our laboratory just over two years ago, coming to us out of an MD/PhD program at UCSF, where he had worked with Drs. Joe DeRisi and Charles Chiu. Alex was remarkably productive during his graduate training, publishing approximately 40(!) papers in the peer-reviewed literature. His main focus was the use of unbiased technologies such as next-generation sequencing and mass spectrometry with an emphasis on viral illnesses. His first first-author paper detailed the discovery of salivirus, a new picornavirus that is associated with up to 4% of pediatric diarrhea. He then went on to perform an affinity purification mass-spectrometry screen of all culturable picornaviruses to find novel host protein interactors. This work culminated in the discovery of a new host protein ACBD3 that acts as a hub for PI4KB recruitment by a wide-array picornavirus 3A proteins, including the enteroviruses and rhinoviruses. Four years later, the crystal structures of these complexes are just being completed and forming the basis for the development of broadly-active 3A inhibitors against enteroviruses and other picornaviruses, similar to the NS5A inhibitors for hepatitis C virus. In addition to this work, he also co-authored publications on the discovery avian bornavirus, Saffold virus, as well as the first RNA virus of ciliates among 20 others he found in the sewage of San Francisco.

While finishing medical school, Alex did a post-doc in the laboratory of Charles Chiu on the use of clinical metagenomics, publishing four first-author papers in the span of one year. One highlight was his 2015 first-author publication in *Lancet Infectious Disease* demonstrating an association of Enterovirus D68 with acute flaccid myelitis. He co-authored work on the "de-discovery" of so-called Hepatitis H virus as a likely contaminant of Qiagen extraction columns and discovered an additional novel human polyomavirus in stool. Alex's passion for sequencing first genomes carried over into other organisms, where he published the first draft genome of *Balamuthia mandrillaris* as well as the first genomes of many clinically relevant esoteric *Mycobacteria*.

Based on his impressive track record, we were very interested in Alex's application to our residency program. Upon meeting him we were immediately impressed, and recruited him very strongly. We were fortunate to succeed, and Alex has been remarkably productive in the lab already, coming in evenings and on weekends to help build our next-generation sequencing capabilities. Beyond his obvious intelligence, Alex is highly skilled in lab, has the ability to make difficult experiments and procedures "work", and communicates his knowledge to others efficiently. He is very goal-oriented, and is always motivated to get his work done and bring a project to completion as quickly as possible.

In his first two years, Alex has already published 30(!) papers with the University of Washington group. Many of these have had a substantial impact on the field. For example, Alex described the use of metagenomic next-generation sequencing to identify single-source transmission of RNA viruses during nosocomial outbreaks at Seattle Cancer Care Alliance and Seattle Children's Hospital (published in the Journal of Clinical Microbiology and the Journal of the Pediatric Infectious Disease Society). He subsequently used NGS to challenge the integrity of multiple international standards that are routinely used in clinical virology, including JC virus, BK virus, and human herpesvirus 6 (Clinical Chemistry, Journal of Clinical Microbiology, and Journal of Virology). He has completed a large-scale survey of >120 human herpesvirus 6 genomes and completely reannotated the viral genome based on comparative genomics and RNA-sequencing of the transcriptome (bioRxiv and submitted). Managing a team of just two undergraduates and a part-time tech, Alex has discovered over 50 new RNA viruses in animals from Washington state. He is currently sequencing all of our viral positives to prospectively identify transmission of viral infections in the Seattle area and to track viral evolution over time. At the same time, he has directed the development of informatics pipelines to automatically align, assemble, annotate, and deposit whole viral genomes into NCBI as soon as they pass quality-control measures. Through his efforts, our group has doubled the worldwide availability of whole genomes for several viral species in the NCBI database, including human coronaviruses and human parainfluenza viruses. On top of all this, Alex has co-authored multiple publications with my basic science lab on using next-generation sequencing to sensitively measure genome editing techniques as therapy for chronic viral infections.

In addition to his scientific skills, Alex has a number of personal qualities that contribute to his success. He is a great lab citizen, and is well liked by all the lab staff. Alex is very collaborative, always seeking input and new ideas, and always willing to consider new approaches to his work. He deals with everyone in a respectful, collaborative manner, and in every way is a joy to have in lab. He has already begun to make a name for himself at conferences, as an active participant in presentations, poster sessions, and post-talk question periods. Alex has even begun to provide service to our field, recently joining the ID Multiplex working group for the Association for Molecular Pathology.

To finish, I think Alex is exactly the type of young physician/scientist we need to attract into clinical virology - smart, ambitious, and comfortable with the latest technology and eager to apply it for clinical benefit of patients. I believe he will make a major mark during his career in virology. I can think of no one more deserving for the ASM/PASCV Young Investigator Award.

Sincerely,

Keith R. Jerome, MD, PhD
Professor and Head, Virology Division
Department of Laboratory Medicine
University of Washington
Member, Vaccine and Infectious Disease Division
Fred Hutchinson Cancer Research Center