

Example of Chairman's letter recommending a candidate for promotion to Associate Professor who has scholarship in virology diagnostics, program building and teaching.

Dear Dean Miller

It is a pleasure to recommend Sarah Green, M.D., Ph.D. for promotion to Associate Professor, full time, salary.

Abstract

Sarah Green, M.D., Ph.D, has been full-time Assistant Professor in the Division of Medical Microbiology since July 1, 1999. She currently serves as Director of Molecular Microbiology and Director of Clinical Virology. **Promotion is proposed based on accomplishments as a clinician scientist and clinician who has built a large clinical reference laboratory specializing in clinical virology and molecular infectious disease testing and her contributions to teaching.**

Through her publications, invited talks, and clinical experience. Dr. Green has become a local, regional, and nationally recognized leader in clinical virology and molecular diagnostics for infectious diseases. Her research is broadly based due to the breadth of her clinical work. She has a research sub-focus in molecular assays for the detection and quantification of hepatitis C virus (HCV). She is a leader in this field and has contributed significantly to the HCV scientific community at Johns Hopkins and extramurally.

Her major research accomplishments are in the area of understanding infectious diseases (particularly HCV) through diagnostic methods development and diagnostic clinical trials. Specifically, she has 1) developed two hepatitis C virus assays 2) completed three clinical trials that provided data for FDA applications (one HCV product; one multiplex HCV, human immunodeficiency virus type 1 [HIV-1], hepatitis B virus [HBV] product; one human papillomavirus [HPV] product), and 30 completed pre- and post-market trials for HCV, HIV-1, HBV, and respiratory syncytial virus (RSV).

Dr. Green has made important contributions to clinical practice and research at the Johns Hopkins Medical Institutions. She has directed major clinical program development in the Clinical Virology and Molecular Microbiology Laboratories that has resulted in significant test menu expansion, test volume increase, and the development of critical infrastructure required for clinical service expansion (in hepatitis, solid organ transplantation, and oncology) and interdisciplinary clinical investigation. Her clinical services are regarded as among the premier hospital-based reference laboratories in the nation.

Introduction

Dr. Green received her Bachelor of Arts with Distinction from Brown University (1984) and her M.D. and Ph.D. degrees from the University of Iowa College of Medicine (1986 -1992) where she was supported by the Medical Scientist Training Program. She then successfully completed an internship (1992-1993) and residency (1993 - 1994) in Clinical Pathology at the University of California at San Diego. Her postdoctoral training includes fellowships in Molecular Virology at the Johns Hopkins Bloomberg School of Public Health (1994-1998) and in Clinical Microbiology at the John Hopkins Hospital and School of Medicine (1997 - 1998). Dr. Green joined the full-time faculty at the Johns Hopkins University School of Medicine in 1998 as an Instructor of Pathology. She was promoted to Assistant Professor of Pathology in 1999.

Research Scholarship

As detailed in her curriculum vitae, Dr. Green has authored 23 peer-reviewed publications and 4 book chapters. Her research career and publication record can be divided into two parts: manuscripts published during training in molecular virology, and those published as an independent investigator in the field of infectious disease diagnostics. She was consistently productive during her training, with 14 manuscripts, 7 of which were first author publications in high profile journals such as *Molecular and Cellular Biology*, *Journal of Infectious Diseases*, *Journal of Virology*, and *Proceedings of the National Academy of Sciences*. Her training and publication record provided a solid foundation in scientific methodology and virology that allowed her to become productive shortly after changing research focus from viral pathogenesis to infectious disease diagnostics in 2001. Despite significant clinical responsibility developing a molecular microbiology laboratory, shifting her research focus, and devoting only 40% effort to research, she has remained consistently productive as an independent investigator, with 8 manuscripts, 5 of which were senior author publications in high impact journals such as *Journal of Clinical Microbiology* and *Journal of Molecular Diagnostics*. Dr. Green has worked in the field of molecular infectious disease diagnostics for only a short period of time; however her significant contributions have been rapidly recognized through invitations to write chapters in authoritative texts. She has also authored 3 chapters (one as a single author, 2 as a senior author) in well-respected textbooks in the field of clinical microbiology (*Manual of Clinical Microbiology*) and molecular pathology (*Molecular Pathology for the Clinical Laboratorian*).

Advancement of clinical diagnostics is dependent upon investigators who draw upon their knowledge of disease pathogenesis to develop new assays, perform industry-supported clinical trials that supply data for FDA approval applications, and conduct pre/post-market studies to verify performance and demonstrate clinical utility of commercial assays. In the specific field of molecular diagnostics for infectious diseases, there are few FDA-approved, marketed tests. Clinical laboratorians who wish to perform these assays therefore rely heavily on information (methodologic protocols and performance descriptions) provided in published manuscripts and talks at specialty meetings. Due to the scope of her clinical practice, her research is broadly based but

contains a focus in HCV, a virus of considerable importance to the scientific community at Johns Hopkins. **Dr. Green has become a leader in clinical virology, molecular diagnostics for infectious diseases, and HCV diagnostics by performing studies in each of the three categories described above.** In the arena of methods development, Dr. Green pioneered a method of ultrasensitive PCR-based detection of HCV (18) and she was one of the first two groups to publish protocols for the use of commercial primers and probes in the latest generation HCV RNA assay marketed in the U.S. (19). Dr. Green's work demonstrated that this new assay was capable of revolutionizing the paradigm of HCV molecular testing from a two test format (qualitative detection to Achieve sensitivity required to assess end-of-treatment cure and quantitative measurement to monitor response during therapy) to a single quantitative assay with great sensitivity and broad dynamic range that can be used to monitor therapy and determine cure. Her protocol was used in a multi-center trial to determine the comparative performance of 4 different quantitative HCV RNA tests. Dr. Green played a key role in the experimental design, data interpretation, and manuscript writing for this trial. She is second author on this manuscript (23).

Dr. Green has demonstrated her leadership in infectious disease diagnostics by helping to bring cutting edge diagnostics into routine laboratory practice through the direction of FDA clinical trials. Dr. Green has directed two trials in her laboratory, one for a quantitative HCV RNA assay (Bayer Diagnostics Corp., received FDA approval in March 2003) and a second for a multiplex HCV/HIV-1/HBV nucleic acid detection assay (Gen-Probe, Inc.). This trial was a large, complex trial that enrolled 500 high risk subjects. Dr. Green directed all on-site aspects of this trial (IRB, patient recruitment, clinical testing). Her work successfully passed an on-site FDA audit and the trial data are currently under review by the agency. Finally Dr. Green was co-principal investigator on an FDA trial to determine the effectiveness of SurePath liquid cytology medium (AutoCyte Inc., now TriPath Oncology) in high risk human papillomavirus detection using the hCell assay (Digene, Inc.). The data for this trial are currently under FDA review.

As a leader in the field, Dr. Green is committed to ensuring that promising new assays using novel technologies are thoroughly investigated in the field before and after FDA licensure. To that end, she has directed pre-market studies on three different real time PCR assays (one each for HCV, HIV-1, and HBV; sponsored by Roche Molecular Systems) and a post-market analysis of a lateral flow rapid antigen detection test for respiratory syncytial virus in children and adults, which was recently published (22).

Programmatic growth under Dr. Green's direction has facilitated accomplishment of core Johns Hopkins Medicine missions including intramural interdisciplinary clinical investigation. Given that HCV is a recognized opportunistic infection in HIV, state-of-the-art molecular hepatitis testing initiated by Dr. Green has enabled collaboration with Dr. Susan Eshleman (an internationally recognized HIV antiviral resistance expert) and has resulted in successful funding of a Hopkins-based, AIDS Clinical Trials Group Virology Service Laboratory. This critical testing infrastructure was also key element of Dr. Water's soon to be awarded NIH application to serve as the central network

laboratory for the HIV-1 Prevention Trials Network, on which Dr. Green is co-investigator for the Virology Core Laboratory. In addition, introduction of BK viral load testing has led to a funded collaboration with Jeannette Carson, MD (Division of Infectious Diseases, JHH Department of Medicine) to investigate BK virus nephropathy in renal transplant patients. Expertise in respiratory virus testing has led to two interdepartmental collaborations, one funded (Efficacy of macrolide antibiotics in prevention of asthma, with Andrew Parks MD, Division of Pulmonary Medicine, Department of Medicine) and one pending (development of rapid, novel influenza virus diagnostic tests with Lola Brown, PhD, Division of Infectious Diseases, JHH Department of Medicine).

Teaching Scholarship

Dr. Green has made considerable contributions to intramural and extramural medical education. She teaches an extensive range of topics within the discipline of clinical virology and molecular infectious disease testing since she is one of a handful of practitioners on campus. Her largest classroom teaching commitment on an annual basis has been to the second year medical school pathology course in which she gives a lecture on negative strand viruses and teaches microbiology laboratory to one section of medical students (~20 students) for 20 laboratory sessions. Her lecture is highly regarded, and in 2004 she was the only Assistant Professor in the top 10% of course lectures. Her laboratory teaching commitment extends for 4 weeks and is significant. It includes laboratory teaching time (40 contact hours), assisting student with clinical cases (5 contact hours), and one contact hour for review at the end of the course. Dr. Green has also lectured on negative strand viruses for the Fundamental Virology course in the Department of Molecular Microbiology and Immunology graduate program at the Johns Hopkins Bloomberg School of Public Health (2000-2004) and directed seminars in viral pathogenesis (3 contact hours per year, 2000-2005) for the Introduction of Pathobiology course in the Pathobiology Graduate Program in the Department of Pathology, JHU School of Medicine.

Dr. Green has provided clinical instruction on multiple levels. She has given 3 CME courses at external venues in the area of her sub-specialization, HCV diagnostics. She taught selected topics in clinical virology and molecular infectious disease testing to infectious disease fellows and pathology residents from 1998-2005 (50 contact hours per year 1998-2002; 25 contact hours per year 2002-2005). She lectures on these topics annually to incoming infectious disease fellows during their orientation. For pathology residents, Dr. Green teaches an “unknown case conference: (one contact hour per year, 1998-2006), introductory lectures on molecular microbiology and clinical virology (3 contact hours per year, 1999, 2001, 2003, 2005), and principles of molecular assay verification (6 contact hours per year, 2004-2006). Dr. Green lectures regularly for various clinical services throughout the medical center on a diverse range topics including SARS (Grand Rounds for the Department of Pathology at JHH and the Kennedy Krieger Institute), atypical infectious meningitis, herpes simplex virus encephalitis, and CMV disease/diagnostic testing.

As director of Molecular Microbiology and Clinical Virology, Dr. Green is responsible for medical technologists' career development and advancement. To that end, she was the thesis advisor for Margaret Greer, a medical technologist in the laboratory who earned her Masters in Health Sciences from the Bloomberg School of Public Health in 2000. Dr. Green regularly mentors medical technologists on clinical scientific investigation through completion of studies and presentation of data in poster and manuscript format. Dr. Green has been senior author on 5 publications with JHH medical technologists.

Clinical Scholarship

As Director of the Molecular Microbiology Laboratory and Clinical Virology Laboratory, Dr. Green's role indicates responsibility for establishment/implementation of laboratory goals for test development, directing process improvement, and oversight of quality control/quality assurance for existing tests. Direction of these laboratories requires 45% of her effort. Under her leadership, the molecular infectious diseases testing panel has expanded dramatically from 10 assays (2001 status) to 21 assays (2006 status) for 16 different pathogens (including 13 viruses and 3 bacteria). She has concentrated on introducing state-of-the-art diagnostic testing that catalyzes programmatic growth (in both patient care and clinical investigation). As a result, Dr. Green has been a key contributor to the successful development of patient care programs that are vital to the expansion of clinical investigation and to the growth of an internationally renowned tertiary care, referral hospital such as Johns Hopkins. This clinical program growth is reflected in the 100% increase in clinical testing volume in Molecular Microbiology from 8,000 in fiscal year 2002 to over 18,000 tests in fiscal year 2006. The specific areas that she has chosen and that have demonstrated significant expansion include molecular testing programs in infectious hepatitis, transplantation (solid organ and bone marrow), and women's health. In infectious hepatitis, Dr. Green has implemented quantitative conventional PCR assay for HCV and HBV. As a direct outcome of her research, her laboratory was among the first clinical laboratories to offer new real-time homogeneous PCR assay for HCV and HBV quantification. She has also implemented HCV genotyping by gold standard methodology (direct sequencing of virus). In transplantation, Dr. Green has directed the implementation of quantitative molecular assays for BK virus, Epstein Barr virus, and cytomegalovirus. Finally, in the arena of women's health, Dr. Green has implemented high risk HPV testing from liquid-based cytology specimens and nucleic acid and amplification methods to detect *C. trachomatis* and *N. gonorrhoeae* in genital specimens. Molecular testing for *C. trachomatis* and *N. gonorrhoeae* is currently formally under the umbrella of the Bacteriology Laboratory in the Division of Microbiology, but it will transition to the Molecular Microbiology Laboratory in June 2006. At this time, the Johns Hopkins Molecular Microbiology Laboratory will be one of the largest, most diverse hospital laboratories in the nation with annual testing volume of >45,000 tests per year, on 18 different pathogens.

In the Clinical Virology Laboratory, Dr. Green's efforts have concentrated on implementing an algorithm for respiratory virus testing that decreases the time to result of the most common viruses (respiratory syncytial virus [RSV], influenza A/B [flu A/B]

viruses, parainfluenza types 1, 2, 3, and adenoviruses) and decreases laboratory cost. Rapid, membrane-based antigen testing is now available for RSV and flu A/B; turnaround time has decreased from 2 hours to 30 minutes for these results. Rapid testing (by immunofluorescence microscopy) for the remainder of the viruses is a new clinical improvement and these results are now available in <2 hours. Implementation of rapid culture for all these respiratory viruses now provides results in 48 hours. Cost savings of the respiratory algorithm was estimated to be \$20,000 per year (primarily in reagent costs).

Organizational and Administrative Activities/Program Building

Dr. Green has significant administrative responsibilities in directing the Clinical Virology and Molecular Microbiology Laboratories. The FTE's in the molecular program have expanded from 3 to 6 from 2001 - 2006 due to increased test volumes. A lead technologist position was recently created and filled in this area due to the demand for quality control/quality assurance oversight of the tremendously complex molecular test menu. The number and complexity of instruments has increased under Dr. Green's leadership from 6 conventional thermal cyclers, to an additional 6 real-time PCR instruments, 3 automated nucleic acid extraction instruments, and a capillary-based nucleic acid sequencer.

Given Dr. Green's extensive administrative service obligations and our desire to protect her time for research and clinical activities, she has not been asked to spend significant effort serving on department and institutional committees. However Dr. Green has found other ways to contribute to the success of the department and the institution. She has served on an ad hoc promotions committee within the Department of Pathology and regularly interviews pathology residency candidates and prospective fellows in molecular pathology and medical terminology. In addition, Dr. Green enthusiastically welcomes opportunities to participate in student committees. She has been a member of two thesis committees and one preliminary exam committee.

Citizenship/Commitment to Johns Hopkins

Recognition

Dr. Green curriculum vitae provide ample evidence that her research and reputation as a practitioner of infectious disease diagnostics are highly regarded. She has been invited to speak regionally (CDC Regional Consortium - Baltimore, MD; Washington G-2 Best Practices Symposium - Arlington, VA; Clinical Laboratory Managers' Association, Delaware Valley Chapter - Fort Washington, PA), nationally (Plenary session talk, Molecular Pathology; and Alabama State Society of Clinical Laboratory Scientists - Birmingham, AL) and internationally (meeting workshop, Asia-Pacific Association for the Study of Liver - Taipei, Taiwan; European Society for Clinical Virology - Geneva, Switzerland). She has been elected by her peers to serve as Chair of the Infectious Diseases Subdivision, Association for Molecular Pathology and has been asked to serve

on editorial boards of journals (Diagnostic Microbiology and Infectious Diseases) and textbooks (section editor, Manual of Clinical Microbiology). Dr. Green has served on study section (infectious diseases diagnostics proposals were reviewed for SBIR Study Section ZRG1 IDM-B (12)). Her research and expertise are highly regarded by industry. She has served on numerous industry-sponsored molecular infectious diseases diagnostics advisory panels advising companies on molecular diagnostic testing platforms and their design for the clinical market (Bayer Diagnostics, Gen-Probe, Roche Diagnostics Corporation). Her laboratory has become a sought-after for clinical trials (FDA trials, pre-market trials, and post-market studies).

Anticipated Future Progression

In the next phase of her career at Hopkins, I anticipate that Dr. Green will continue to expand her publication record in molecular hepatitis testing and develop internationally recognized expertise in this area. I expect that she will continue to develop a publication record with added depth in the other expansion areas in the Molecular Microbiology (transplantation diagnostics, women's health) and Clinical Virology (respiratory virus diagnostics). Sponsored support in molecular infectious diseases diagnostics is also expected to increase. Her two clinical laboratories will continue to expand their test menus and increase their test volumes, thereby continuing to provide crucial infrastructure for ongoing institutional programmatic growth. I expect that she will continue to teach extensively on local, national and (newly) international levels. She is also expected to successfully mentor technologist, students and fellows.

Summary Statement

After undergoing a career transition two years into her assistant professorship, Dr. Green has rapidly established herself as a leader in the field of molecular infectious disease diagnostics. She has built a respected research program and a clinical laboratory that is viewed as one of the premier molecular microbiology services in the country. Her work has substantially benefited research and clinical programs at John Hopkins Medicine. I support her promotion to Associate Professor of Pathology with great enthusiasm.

Sincerely

Chair,
Department of Pathology

