

May 16, 2005

Edward D. Miller, M.D.
CEO, Johns Hopkins Medicine
Dean of the Medical Faculty,
Johns Hopkins University School of Medicine
Administration, Suite 100

Re: Andrea M. Corse, M.D.

Dear Dr. Miller:

This letter will propose Dr Andrea M. Corse for promotion to Associate Professor, full time, in the Department of Neurology, with a secondary appointment in Pathology. Dr. Corse is currently an Assistant Professor in the Department of Neurology, with a secondary appointment in Pathology. She is Director of the Johns Hopkins Neuromuscular Clinical Pathology Laboratory, a nationally recognized expert in clinical neuromuscular disease, and quite simply one of the finest clinician-educators in the institution. In this letter, I will outline her career in terms of her early basic and clinical research work that has evolved into her current roles in clinical research and care and as director of a clinical laboratory.

The Individual

Andrea finished University of Kansas School of Medicine in 1987 and came to Baltimore and Johns Hopkins as an Intern in Medicine on the Osler Medical Service. She completed Neurology Residency training, serving as Chief Resident in 1991. After Residency, she had a 2 year combined basic and clinical research fellowship in neuromuscular disease with Drs. Daniel B. Drachman, John W. Griffin, David R. Cornblath, Ralph W. Kuncl, and Jeffrey D. Rothstein.

Research Scholarship

Lab-based Research. Her post-graduate basic research work focused on motor neuron degeneration and glutamate excitotoxicity as a model of amyotrophic lateral sclerosis (ALS) and related neurodegenerative disorders. She was a key part of the group that developed organotypic culture techniques for studying postnatal motor neurons. Although embryonic motor neuron cell cultures were commonplace, postnatal motor neuron culturing had not previously met much success. This work was published by the CRC Press in 1995 and featured on their book cover (Book Chapter # 3 in CV). Using the organotypic culture technique, she then studied the role of growth factors as neuroprotectants of motor neurons in a unique model of chronic glutamate-induced excitotoxicity. Her papers on the role of IGF-I as a motor neuron protectant were published in the Journal of Neurobiology of Disease and the subject of their feature editorial (Reference # 13 in CV) and in Amyotrophic Lateral Sclerosis (Ref. # 15). These papers were cited by Cephalon during the FDA hearings supporting the role of IGF-I in arresting motor

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neuron cell death in ALS as part of their rationale for clinical development. The Cephalon trial had mixed results (the American trial was positive while the European trial was negative), IGF-I continues to be investigated as a potential therapeutic agent: a second large-scale, multi-center, IGF-I phase-III clinical trial is currently underway, and an IGF-I gene therapy trial is planned later this year.

She worked with Masako Bilak, Ph.D. a post-doctoral fellow, focusing on the role of pigment-epithelial-derived factor (PEDF) as a neuroprotectant that grew out of a collaboration Dr. Corse established at the National Eye Institute in 1998. Results of this work were published in the *Journal of Neuropathology and Experimental Neurology* (Ref. # 12), *Molecular and Cellular Neuroscience* (Ref. # 14), and the *Journal of Neurochemistry* (Ref. # 16).

A subsequent collaboration with Barbara Slusher, Ph.D. at Guilford Pharmaceuticals investigated the promising neuroprotective role of NAALADase inhibition of motor neurons in chronic glutamate-toxicity. This was published in the *European Journal of Pharmacology* (Ref. # 19).

Her basic research was funded initially by an intramural Richard S. Ross Clinician-Scientist Award (PI) for 1993-94, then an NINDS-sponsored KO8 award (PI) for 1994, followed by an NIH sponsored RO1 (Co-PI) for 1995-99 and a Muscular Dystrophy Association grant (Co-PI) for 1998-2001.

Dr Corse is an important member of the research team that helped to establish the Cal Ripken/Lou Gehrig Fund for Neuromuscular Research, an endowment from the Baltimore Orioles, community leaders, corporations, and individuals on the occasion of Cal Ripkin breaking Lou Gehrig's consecutive game record. These monies continue to go toward ALS research.

Clinical Research. Her clinical research career began with a project on multifocal motor neuropathy (MMN), a chronic, slowly progressive motor neuropathy that can be mistaken for ALS clinically. MMN is an autoimmune disorder responsive to certain immunomodulatory therapies (Ref. # 5-6). Detailed electrophysiological data she obtained from these patients provided clues to further understanding the pathophysiology of this mysterious disorder and distinguishing it further from motor neuron syndromes (Ref. # 7). Subsequently, she reported the presence of sensory nerve pathology in MMN, previously considered a pure motor disorder (Ref. # 9-10).

Her clinical research in ALS began in 1994. She was a Co-PI in a number of multicenter phase II and phase III clinical trials investigating ciliary neurotrophic factor, Rilutek, brain-derived neurotrophic factor, and a proprietary Sanofi Pharmaceutical compound. As her involvement in clinical research increased, she took further training in 1999 with the Bloomberg School of Public Health and Hygiene Graduate Summer Institute of Epidemiology and Biostatistics course "Clinical Research: An Introduction to Design and Analysis."

She has participated in a number of other clinical research studies mainly with the EMG/Neuromuscular Group (Ref. # 8, 11, 17, 18, 20).

Her growing interest and involvement in clinical trials work along with a growing regional and national recognition for providing clinical neuromuscular care lead her to

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concentrate on clinical care and clinical research. Complementary to this, she accepted the Directorship of the Neuromuscular Clinical Pathology Laboratory in 2001. Dr Corse has a unique combination of skills evidenced by Board Certification by the American Board of Psychiatry and Neurology in Neurology (1992) and Clinical Neurophysiology (1996), and by the American Academy of Neurology in Neuromuscular Pathology in Muscle and Nerve (1999).

Over the past decade, she has participated in seven multicenter national or international ALS clinical trials. She served as the Principal Investigator on the most recent of these trials, an international, multi-center, phase IIb trial sponsored by Novartis Pharmaceuticals investigating the role of the anti-apoptotic agent TCH346 in the treatment of patients with ALS. Currently, she is PI on two multi-center ALS clinical trials which are in the final planning stages, including a large Phase I/II trial entitled 'Clinical Trial of Ceftriaxone in Subjects with ALS' funded by the NINDS and tentatively scheduled to begin in 2005 and a smaller trial sponsored by Penn State Hershey Medical Center to establish validation of a new assessment tool for "Quality of Life in ALS."

Clinical Service. Her own neuromuscular clinical and histopathology practice is diverse. She provides particular expertise in the management of myasthenia gravis (MG), myositis, and ALS (Chapters # 1-2, 4-11). She is known regionally and nationally for her management of these disorders as evidenced by her referral base. Her international reputation is evidenced by her invitation as one of ten histopathologists worldwide to attend the 2005 Juvenile Dermatomyositis Biopsy Score International Consensus Process in London March, 2005.

In terms of her clinical service, her role as Director of the Neuromuscular Pathology Laboratory since July 2001 has had a very significant impact in the Department and the Hospital. From 1999-2001, she served as the Assistant Director of the Lab. After taking over Directorship, she increased productivity, added staff, integrated the reporting system with EPR, and importantly became profitable. Muscle and nerve pathology reports are now placed directly in EPR and hard copies often contain digital images. Laboratory specimen volume is increasing yearly. In 2003, the Lab became a primary referral laboratory for Quest Diagnostics and a number of hospitals in the Mid-Atlantic region. In 2002, the Lab provided nerve and muscle pathology interpretation to University of Utah when their personnel were unavailable.

Dr Corse is involved in a number of research collaborations which have grown out of the laboratory: with Drs. Antony Rosen and Livia Casciola-Rosen investigating auto-antigen expression in autoimmune myositis and its potential role in disease promulgation (Ref. # 21); with Dr. Neil Porter (University of Maryland) investigating gene expression in muscle of patients with fascioscapulohumeral muscular dystrophy; with Drs. Don Brown (Carnegie Institution) and Ralph Kuncel (Bryn Mawr College) investigating gene expression involved in muscle death during metamorphosis in tadpoles; and with Dr. Joseph Califano investigating histochemical analyses of mitochondrial abnormalities in head and neck cancers.

Teaching Scholarship

Student teaching. Dr. Corse is passionate about teaching. As a reflection of her commitment, she took *Designing an Effective Course* offered through the Johns Hopkins University Center for

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Training and Education. As this note will document, she has become one of the finest teachers in the School of Medicine. She has been Director of the second year medical students' Neurology Clinical Skills Course since 1999. This subspecialty Clinical Skills Course has been rated by the students one of the best, if not the best, of the subspecialty courses by the medical students for the past seven years. This rating reflects the intensive effort she puts into the course. She gives nine lectures to the students and organizes over 30 Neurology faculty as preceptors. A special aspect of the course is that she recruits over 60 volunteer outpatients with selected neurologic diseases to provide the students a unique, memorable, hands on, tutorial approach to learning neurology clinical skills. This requires a daunting effort, but it eliminates the randomness of teaching with inpatients, and allows students to understand the differences in upper motor findings, ataxias, movement disorders, and neuromuscular diseases. It is a remarkable experience for the students. I am, enclosing the student ratings.

Dr Corse is a clinical preceptor in the School of Medicine Introduction to Clinical Medicine Course. Since 2000, she has had first year medical students spend ½ day/week for 6 months in the EMG Laboratory in the Outpatient Center. She also teaches and supervises third and fourth year medical students on the Neurology in-patient and consult services and in her weekly outpatient Neuromuscular Clinic during their basic and advanced Neurology clerkship rotations.

Resident teaching. In recognition of her resident teaching, she was the 2004 recipient of the Department of Neurology's Frank Ford Teaching Award by the Neurology Residents. She regularly teaches Neurology, Neurosurgery, Medicine, and Pathology residents as well as Neuromuscular, Neuropathology, and Neurodevelopmental Fellows in the combined Kennedy Krieger/Department of Neurology Fellowship training program.

She teaches Medicine and Neurology residents weekly in her Neuromuscular Clinics, supervises Neurology and Neurosurgery residents as consult or ward attending, and lectures annually in both the Neurology Residents' Noon Lecture Series and the Neurophysiology Lecture series.

Dr Corse organizes and teaches the Friday morning Neuropathology Lecture Series for Neurology and Pathology Residents and medical students in Neurology and Pathology clerkships. Over the past dozen years, this lecture series grew out of informal monthly teaching sessions on peripheral nerve pathology at an antiquated microscope in the autopsy file room, to a well-attended lecture series covering central and peripheral nervous system pathology in a well-appointed conference room equipped with a multi-headed scope and three large video monitors. Half of these sessions are dedicated to Neuromuscular Pathology and half, directed by Dr. Barbara Crain in the Department of Pathology, to CNS Neuropathology. The Neuromuscular training is required training for Pathology Residents, and she truly appreciated for her efforts by the Pathology house staff.

She is also the primary trainer in the Department of Neurology's Neuromuscular Fellowship, the premier such training program in the country. It is a one-year clinical fellowship, and has produced a unique crop of academic Neuromuscular physicians. Many of the best have remained at Hopkins; the Neuromuscular group now has 14 neurologists, and is unquestionably

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the largest and finest on the planet. Make no mistake—much of the credit for this program belongs to Andrea and her tireless teaching efforts. To provide you with some feeling for her contributions I am enclosing comments from some of the prominent Neuromuscular physicians she has trained. She teaches in all aspects of the program, and makes a unique contribution as the teacher of muscle and nerve pathology. She signs out muscle and nerve pathology reports with the Fellows 6 months/year. As Director of the outpatient Muscle and Nerve Biopsy Service, she also trains each Fellow in these surgical procedures. The Fellows also spend 1 day/week with Dr Corse in the EMG lab.

Clinical Scholarship

Andrea is a major referral resource for difficult clinical Neuromuscular patients. She sees over 20 referral annually. She is also a skilled electrodiagnostician, and has a weekly EMG session. Both of these are used as teaching venues for students, residents, and fellows. She performs approximately 150-175 open muscle and nerve biopsies per year in the JHOC Surgical Center, and as noted is the Director of the Neuromuscular Clinical Pathology Lab.

Administrative Service

Dr Corse has been on the Johns Hopkins University School of Medicine Admissions Committee for the past six years. She has served on the Department of Neurology and Neurosurgery Appointments and Promotions Committee (1994-2000) and Finance Committee (1999-2000).

Summary

Andrea is quiet, modest, and understated, and she is all too happy to direct credit to others. I want to make it absolutely clear—she is the rock upon which much of the teaching effort in Neurology is based. She is anything but a failed lab researcher; rather, she found her true calling in teaching, and I am delighted she did. She inspires our other young teachers, and has a personal legacy in training some of the finest Neuromuscular physicians in the country. She is quite simply our best clinician-educator, and I cannot be more enthusiastic about her promotion.

Yours truly,

John W. Griffin, M.D.
Professor and Director,
Department of Neurology
Professor, Departments of Neuroscience
and Pathology

J. Brooks Jackson, M.D., M.B.A.
Baxley Professor and Director,
Department of Pathology