November 1, 2010

Edward D. Miller, M.D., Ph.D.
Dean of the Medical Faculty
Chief Executive Officer
Johns Hopkins Medicine
100 Medical Administration

Dear Dr. Miller:

I would like to request a promotion for Antonio C. Wolff, M.D. as a Professor in the Department of Oncology. Dr. Antonio C. Wolff has been at the rank of Associate Professor of Oncology since June 2005. He is Co-Chair of the Cancer Research and Review Committee of The Johns Hopkins Kimmel Cancer Center and Co-Chair of the Cancer Outcomes & Health Services Research Interest Group. I am now requesting his promotion to the rank of Professor of Oncology because of his evident accomplishments in the fields of predictive biomarkers in breast cancer, and in clinical practice guidelines in oncology, and in breast cancer survivorship.

Scholarship

Dr. Wolff is recognized for his contributions to the implementation of quality measures in biomarker testing and research, and for his abilities as a program builder, knowledge synthesizer, clinician, educator, and as a citizen in the academic oncology community. He has led international efforts to develop and implement clinical practice guidelines in oncology throughout the 2nd half of this decade. He led and co-chaired the first collaborations ever between the American Society of Clinical Oncology (AS CO) and the College of American Pathologists (CAP) on predictive biomarker testing in oncology, and served as lead author of an evaluation by a State of the Science Panel convened by the National Cancer Institute (NCI) on issues surrounding the use of preoperative systemic therapy as a research tool. Dr. Wolff is also a recognized educator with unique skills and ability to synthesize knowledge and disseminate information. He chaired the Breast Cancer track of the Education Program Committee of the 2010 ASCO Annual Meeting, and is a frequent guest speaker at international meetings. In the US, he leads the Translational Breast Cancer Research Consortium (TBCRC), a collaboration of all breast cancer SPOREs and major US academic breast cancer programs. He has built an international reputation in the clinical care of breast cancer, and serves as a resource for

patients and physicians from all over the world. He serves on the editorial board of the Journal of Clinical Oncology (JCO), and his work on predictive biomarker testing has been the focus of front-page stories in the New York Times and international news magazines.

In health services, Dr. Wolff has established important institutional efforts and guided ASCO efforts internationally. At Hopkins, he co-established and co-leads the Cancer Outcomes & Health Services Research (CO&HSR) interest group, a group that meets several times a year and has hosted annual visiting professorships since 2008. He collaborates with investigators from the Welch Center and from the School of Public Health. He established and leads an externally funded multidisciplinary team of researchers and clinicians from our Schools of Medicine and Nursing exploring new models of care for breast cancer survivors following completion of initial care. He served on and subsequently chaired ASCO's Health Services Research Committee. He is a founding member of ASCO's Quality of Care Committee, and has testified on behalf of ASCO to panels such as the Institute of Medicine's Committee on Comparative Effectiveness Research.

Accomplishments in Research

Dr. Wolff's involvement and expertise in clinical trials and predictive biomarker testing are a direct reflection of his clinical experience as a medical oncologist with a clinical practice fully devoted to the care of breast cancer patients. His initial work was devoted to clinical trials in developmental therapeutics, and his output gradually evolved from in-house phase IIII studies to multi-institutional phase II and randomized phase III collaborations that have significantly influenced the treatment of early stage breast cancer. These include two studies that confirmed the role of adjuvant chemotherapy in older women with early stage breast cancer and established weekly paclitaxel as a preferred standard in the adjuvant setting and were published in the New England Journal of Medicine. Today, he co-chairs the Developmental Therapeutics Working Group of the Eastern Cooperative Oncology Group and sits on the multi-national Executive Committee of the Adjuvant Lapatinib and/or Trastuzumab Treatment Optimization (ALTTO) trial, a study that will complete the accrual of 8,500 patients with HER2-positive breast cancer in late 2010.

Dr. Wolff is co-Principal Investigator with Dr. Sara Sukumar in one of the projects of the Johns Hopkins Breast Cancer SPORE. Their focus is on developing and testing DNA methylation signatures as a predictive/prognostic biomarker in breast cancer, alone or in combination with high-quality traditional pathology markers like tumor grade and biomarkers like ERlPgR and HER2. In a related project, they recently completed accrual to a prospective 180-patient study that was partly funded by the NCI. Preliminary data from the TBCRC 005 trial on developing a predictive model of outcome that integrates existing biomarkers like circulating tumor cells and CA-2729 were orally presented at a Clinical Science Symposium at the 2010 ASCO Annual Meeting, and his fellow received a Merit Award. Breast cancer is comprised of various phenotypes that influence treatment decisions. Throughout his early faculty years, Dr. Wolff identified significant deficits in the accuracy and quality of predictive biomarker testing in routine clinical practice worldwide. In 2005, trastuzumab was approved for the adjuvant treatment of human epidermal growth factor receptor 2 (HER2)positive early stage breast

cancer. Dr. Wolff proposed and led the development of an international multidisciplinary panel comprised of oncologists, pathologists, assay methodologists, regulatory experts, statisticians, and advocates with the goal of recommending and implementing large-scale and systemic measures to improve the accuracy of HER2 testing in clinical practice. He and colleagues conducted a systematic review of the available evidence and sought advice from government agencies such as the Centers for Medicare & Medicaid Services Clinical Laboratory Improvements Amendments (CMS CLIA) and the US Food and Drug Administration (FDA) and from industry such as drug/assay manufacturers and large commercial labs. On behalf of ASCO and the College of American Pathologists, Dr. Wolff led the development and was first author of a clinical practice guideline on HER2 testing in breast cancer that was jointly published in JCO and in Archives of Pathology and Lab Medicine after an extensive peer-review process. This was the 2nd most downloaded article in the JCO in 2007. Most important, the number of pathology labs undergoing annual proficiency testing to perform HER2 immunohistochemistry (IHC) testing in clinical practice increased 5-fold within a year as a direct result of this effort, and unpublished data from ongoing trials suggest an improvement in HER2 testing accuracy. An update of this guideline is now planned for 2011. The outcome of this first effort led Dr. Wolff and colleagues to propose a second effort, this time to address critical, long standing concerns following the widespread adoption of IHC testing for estrogen and progesterone receptor (ERlPgR) in the early 1990s. In collaboration with Cancer Care Ontario they conducted a systematic review of the literature and again sought external input from government and industry. In April 2010, the ASCO/CAP clinical practice guideline on estrogen and progesterone (ERlPgR) IHC testing in breast cancer was published with Dr. Wolff as senior author, and was the subject of intensive news coverage. Breast cancer is the most common cancer in women in low/middle income countries worldwide and ER-positive the most common phenotype. Therefore, the public health implications of accurate diagnosis are crucial especially as accurate ERlPgR testing is feasible and endocrine therapies like tamoxifen are relatively affordable.

Dr. Wolff has also collaborated with the Johns Hopkins Evidence-Based Practice Center, and published with Drs. Eric Bass and Steve Goodman the results of a systematic review on gene expression profiling assays in early-stage breast cancer and of a technology assessment on the impact of gene expression profiling tests on breast cancer outcomes. Dr. Wolff has established collaborative health services research bridges with investigators like Drs. Claire Snyder (a PhD-trained social scientist in health policy and management), Fred Brancati (Director, Division of General Internal Medicine - GIM), and Kevin Frick (Professor, Health Policy and Management). Drs. Wolff and Snyder have published 11 peer-reviewed manuscripts since 2007 (one in press) and share various grants. One of their projects used the SEER-Medicare to investigate the care provided to breast cancer survivors after completion of initial care, and this work has informed several ongoing survivorship projects in the Breast Cancer Program that are described below. Drs. Wolff and Brancati also assembled a group of investigators at Hopkins to examine the effects of pre-existing diabetes mellitus on long-term all cause mortality in cancer patients. Their group conducted a systematic review and meta-analysis of the published literature, and this work led to multiple abstracts and presentations at various internal medicine and specialty meetings, including five peer-reviewed manuscripts in various journals like JAMA and JCO. Their work is timely as the relationship between diabetes, insulin metabolism, and breast cancer is the subject of a just-activated North American prospective randomized placebo-controlled trial

examining the potential effects of metformin on recurrence and survival in non-diabetic patients with early stage breast cancer. Dr. Wolff will be the site PI at Johns Hopkins. His *curriculum vitae* lists 116 publications including 32 invited review articles, eight book chapters, and two letters to the editor. Among these 116 publications, 74 of them are peer-reviewed including 61 original science papers, 8 educational papers, and 5 editorials. His research funding includes awards from the NCI, the Avon Foundation for Women, The Breast Cancer Research Foundation, and Susan G. Komen for the Cure Foundation (National office and Maryland-affiliate). At Hopkins, he is the incoming chair of the Cancer Center Clinical Research Review Committee.

Accomplishments in Program Building

Dr. Wolff has an established record of program building at Johns Hopkins and at the national level. At Johns Hopkins, he played a critical role in creating the clinical research infrastructure of the breast cancer program, in co-establishing the Cancer Outcomes & Health Services Research interest group, and in the current effort to establish a survivorship program in breast cancer. Nationally, he helped create the Translational Breast Cancer Research Consortium and has led major initiatives at ASCO. In 2000, Dr. Wolff established in the Breast Cancer Program the first disease-specific clinical research infrastructure within the Division of Medical Oncology, a project he now co-leads with Dr. Vered Stearns. Research nurses and study coordinators dedicated to a single disease (breast cancer) develop clinical expertise and in-depth knowledge of a disease-specific research agenda, and work cohesively with the clinical research faculty. This model has proven successful and has since been adopted by the other disease-oriented programs in Medical Oncology. Dr. Wolff also implemented a new strategy of pre-screening all new patient records, a process now covered by study-specific HIP AA waivers. This allows the research staff to alert the clinician for possible trial eligibility, and facilitates a possible meeting of the research staff with potential study subjects during that same visit. Since then, we have consistently observed that half of all breast cancer patients who meet with a research nurse ultimately enroll on a clinical trial. Even more important, the percentage of minority patients seen as a new patient and then enrolled on studies is essentially the same, which suggests that the process he established may have eliminated potential barriers to the recruitment of minorities to clinical research studies, an issue frequently reported in the medical literature. Funding for clinical research infrastructure is limited and often project-specific, but Dr. Wolff has successfully retained continuous external funding for the last 10 years to exclusively support research personnel regardless of specific research projects. This has been critical to building a stable, knowledgeable, and cohesive research infrastructure. Dr. Wolff has also secured external funding to implement longitudinal data collection, allow the clinical annotation of biospecimens with appropriate consent, prospective collect patient-reported outcomes, and create an IRB-approved repository in the Breast Cancer Program available for future research use. Dr. Wolff co-chairs the CO&HSR interest group with Dr. Snyder. They established this group four years ago with support from Vice Dean Dan Ford, Cancer Center Director Marty Abeloff, and GIM Director Fred Brancati. The interest group was formed to connect researchers across the Schools of Medicine, Nursing, and Public Health who are working in the area of cancer outcomes and health services research. The purpose of the interest group is to identify who is doing research related to CO&HSR, learn about ongoing and

planned research projects, discuss opportunities for collaboration, and begin developing an infrastructure to support this area of research. The group has an electronic mailing list that reaches Cancer Center members and all interested faculty/staff, and meets 8-9 times per year for presentations by guest speakers. Drs. Wolff and Snyder have also established an annual visiting professorship in CO&HSR cosponsored by GIM and by the Cancer Center, and that has as its highlight a joint GIM Oncology Grand Rounds on day 2. Grant submissions and collaborations have resulted from this effort. Discussions within the CO&HSR interest group and the breast cancer program led Dr. Wolff to propose and establish a new effort in breast cancer survivorship. Two years ago, he and collaborators from the School of Nursing, the Division of GIM, and the Breast Cancer Program obtained external funding from Susan G. Komen for the Cure to launch the project *"A Survivorship Program for Breast Cancer: A Transition for Patients and Providers."* The goals are to develop an integrated multidisciplinary approach to survivorship care planning at Johns Hopkins that reflect the decreasing cancer-related mortality and growing ranks of breast cancer survivors, and to educate patients and providers at Johns Hopkins and elsewhere regarding survivorship care. He and collaborators have presented at meetings like the 2010 NCI *"Cancer Survivorship Research: Recovery and Beyond",* published a qualitative research study on perceptions regarding survivorship by patients, specialists, and primary care providers in the Journal of General Internal Medicine, and have organized panel discussions at various local and national meetings held by ASCO, Johns Hopkins/Harvard Medical School Pri-Med, and the American College of Physicians. A survivorship coordinator has been recruited and Dr. Wolff led the creation of a web site rich with patient material and video discussions for the Hopkins Breast Cancer web site, and that is also available on the YouTube channel of Johns Hopkins Medicine. They are currently establishing a consultative service for breast cancer survivors that will be staffed by advanced practice nurses and advised by a physician faculty group from the Breast Program and GIM. Web-based educational modules for medical and NP trainees are being developed. Many of these issues transcend breast cancer, and the work by his group will guide overall cancer survivorship efforts within our Cancer Center.

Dr. Wolff has been actively involved at ASCO during a period of evolution of the mission of ASCO's Health Services Research Committee, now more aptly known as Clinical Practice Guidelines (CPG) Committee. Consistently rated as one of the most valued services to its membership, ASCO guidelines are among the most accessed manuscripts in the JCO and are recognized by CMS as one of the key sources of evidence to support coverage decisions in oncology. Dr. Wolff served in that committee for six years, including three in its executive leadership (committee chair, 2006 - 2007). During that time, he oversaw the development process of many guidelines and also served as chair, co-chair, and member of various panels. In 2005, Dr. Wolff established the subcommittee now known as GuIDE (Guideline Implementation, Dissemination, and Evaluation). Adopting the concept of a "ToolBox", GuIDE is comprised of full time staff, advised by content experts, and charged with creating tools (e.g., slide sets, clinician summaries, patient summaries, and electronic forms) to improve the dissemination and adoption of guideline recommendations. Dr. Wolff also proposed the current process of creating guideline-derived measures that could then be used by the ASCO's Quality Oncology Practice Initiative (QOPI), and then feed back to the CPG Committee to assess the uptake of

guideline recommendations in clinical practice. He is a member of the Steering Group guiding the Komeni ASCO Foundation Breast Cancer Registry Pilot Program that is testing the implementation of treatment summaries and survivorship plans among breast cancer survivors. Dr. Wolff is also a founding member of the Translational Breast Cancer Research Consortium, and has served as its Executive Officer since 2006. The TBCRC is a collaborative group of patient advocates, clinical trialists, physician-scientists, and basic scientists from major academic breast cancer programs and all Breast Cancer SPOREs dedicated to innovative, high impact, biologically-driven translational and clinical research. TBCRC conducts clinical trials in the presurgical, neoadjuvant, post-operative adjuvant, metastatic, and preventive settings. Guided by a Steering Committee comprised of breast cancer leaders, he organized investigators, advocates, study coordinators, and institutional administrators to advance the science and infrastructure of the TBCRC. He also led the selection of the Hoosier Oncology Group as a 50lc3 academic partner to support TBCRC with clinical trial coordination efforts. A Central Office with dedicated staff has been established at Johns Hopkins. Dr. Wolff is a member of the TBCRC Steering Committee and Principal Investigator for its main supporting funding from the Avon Foundation for Women, The Breast Cancer Research Foundation, and Susan G. Komen for the Cure Foundation.

Accomplishments in Education

Dr. Wolff is an accomplished educator and has been involved in the mentoring and training of oncology fellows and junior faculty at Hopkins and elsewhere. Until 2005, he was co-director of the Medical Oncology Fellowship Program and worked closely with Dr. Ross Donehower on day-to-day operations of the fellowship program. Dr. Wolff was then instrumental in leading our fellowship program to become compliant with new regulatory requirements imposed by the Accreditation Council for Graduate Medical Education. Over the years, Dr. Wolff has mentored fellows in specific research projects that resulted in primary data manuscripts, posters and oral presentations, awards, and opportunities for scholarly work such as co-authoring editorials and review articles. Dr. Wolff has served as an advisor for various CME projects and was a member from 2007 to 2010 of the Steering Committee for the KomenlMedscape Breast Cancer Curriculum. Most recently, he was chair of the breast cancer track of the ASCO Education Program Committee and led the development of all breast cancer educational activities for the 2010 Annual Meeting. At Hopkins, Dr. Wolff serves as a member of the School of Medicine CME Advisory Board. He lectures annually to the fellows during the initial series of orientation lectures and has been invited several times to attend their board review sessions to provide content expert opinion. He routinely receives excellent reviews by the fellows and residents with whom he interacts in the hospital inpatient and consult services. In 2004, he established a monthly new patient clinic for first-year fellows to allow them greater exposure to breast cancer patients, and he now shares staffing responsibilities with Drs. Kala Visvanathan and Robert Miller. He frequently receives external trainees for short rotations in his outpatient clinical practice. Dr. Wolff is a frequent guest lecturer in graduate courses in the School of Public Health. In this current academic year, he has been invited to give Grand Rounds in the Departments of Pathology (Sep 2010) and Medicine (Bayview, Feb 2011).

Clinical Accomplishments

Dr. Wolff maintains a clinical practice dedicated exclusively to the care of patients diagnosed with breast cancer, and holds clinics two full days each week in East Baltimore (Weinberg Building) and at Green Spring Station (GSS). Dr. Wolff sees 4-6 new patients in his clinic each week and has developed the current guidelines for new breast cancer patient referrals in medical oncology. He is frequently contacted by cancer specialists from the US and overseas for advice on the management of patients with breast cancer. Dr. Wolff has attended on the inpatient solid tumor and hospital consult service consistently since 1998. His attending duties have gradually decreased from 8-10 weeks per year to 4 weeks per year over time in view of his other research and administrative responsibilities. He has consistently received high marks from the house staff and nursing staff. GSS is where most new breast cancer patients in medical oncology are now seen, and there he has led two important initiatives. First, he established GSS as a successful site for recruitment to breast cancer clinical trials, and research nurses and study coordinators are now present on all clinic sessions. Also, he successfully led the search committee that identified Dr. Robert Miller (a recent former member of the ASCO Board of Directors), and his recruitment has allowed the Breast Cancer Program to increase new patient volumes to fulfill its clinical research obligations.

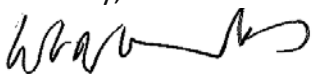
Evidence of National and International Reputation

Dr. Wolff is a recognized national and international thought leader whose clinical research interests and organizational activities are informed by an active clinical practice. He is a frequent guest at international meetings like the Milan Breast Cancer Conference. He has consistently served ASCO since 2002 in various committees, and in 2010 he received an ASCO Statesman Award in recognition for his contributions and leadership over the years. He is a recognized leader in quality initiatives regarding predictive biomarkers and has been asked to speak to the FDA and related organizations about these issues. On April 20, 2010, his work and that of collaborators was the subject of a front page article in the New York Times (http://www.nytimes.coml201 0/04/29/opinionllweb29cancer.html and http://www.nytimes.coml20 1 0/04/20lhealthiresearchl20cancer.html ?hp=&pagewanted=all), and one of his statements was selected as a NYT Quotation of the Day *("This is an issue that transcends breast cancer. A poorly developed test is potentially as dangerous as a poorly developed drug").* Dr. Wolff has also been recognized by his volunteer work with various breast cancer foundations. In 2007, he received a Cameo Award from Susan G. Komen for the Cure, and he was recently invited to join the Komen Scientific Advisory Council. He is a team player who practices the concept of collaborative work and team science. He has successfully led the Translational Breast Cancer Research Consortium since 2006. In 2008, he was selected by our Department to participate in the School of Medicine Leadership Development Program, and in 2009 he received an NCI Cancer Clinical Investigator Team Leadership Award. There are several other clinical leaders who have developed their careers along similar paths, achieved national and international recognition like Dr. Wolff, and have become full Professors. Examples might include: Julie R. Gralow, MD (Director of Breast Medical Oncology and Professor of Medicine at the University of Washington School of Medicine in Seattle) who is vice-chair of the Breast Cancer Committee of the Southwest Oncology Group and who in 2008 also received an ASCO Statesman Award; William J. Gradishar, MD (Professor of Medicine and Director of Breast

Medical Oncology at the Robert H. Lurie Comprehensive Cancer Center at Northwestern Feinberg School of Medicine in Chicago) who is Editor-in-Chief of Journal Watch Oncology & Hematology and Program Director of the Hematology/Oncology Fellowship Training Program; and Gary H. Lyman, MD, MPH (Professor of Medicine and Director of Comparative Effectiveness and Outcomes Research at Duke University) who is Associate Editor of ASCO's Journal of Oncology Practice. Like Dr. Wolff, all of them have had distinguished academic careers as breast cancer investigators in clinical trials, in clinical practice guidelines and health services research, in building programs, and in various leadership roles at ASCO.

In summary, Dr. Antonio Wolff has distinguished himself in the field of breast cancer predictive biomarkers through internationally recognized leadership, scholarship, mentoring, and research. In addition, he has also distinguished himself in quality of care initiatives centered around clinical practice guidelines and breast cancer survivorship. It is therefore, my privilege to enthusiastically support him for promotion to Professor of Oncology with the strongest recommendation.

Sincerely,



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