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January 5, 2012

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

Re: Promotion of Dr. Douglas N. Robinson to the rank of Full Professor

Dear Dr. Miller,

It is with great enthusiasm that I nominate Dr. Douglas N. Robinson for promotion to the rank of full professor, full time, in the Department of Cell Biology. Dr. Robinson's current rank is Associate Professor at Johns Hopkins School of Medicine, and he holds a primary appointment in the Department of Cell Biology with secondary appointments in the Department Pharmacology and Molecular Sciences and the Department of Chemical and Biomolecular Engineering in the Whiting School of Engineering. Dr. Robinson has developed an extensive scholarship record of high quality primary research and review articles in his research area of cytokinesis and cell shape change and he has proven his commitment to excellence in education of graduate and medical students through teaching and course direction. Moreover, he has contributed to the community and to Baltimore City through his outreach program for underprivileged high school youths.

Dr. Robinson has distinguished himself among a large international contingent of investigators of cytokinesis by demonstrating the importance of mechanical force in this process. He has initiated this conceptual framework and become the leader in an emerging area he has help create. Cytokinesis, as the final step in the process of cell division, is critical for numerous cell physiological processes. Abnormal cytokinesis is observed in important diseases including cardiac myopathies and cancer.

Dr. Robinson is one of the most knowledgeable investigators of the cytoskeleton at the Medical School. He carried out doctoral thesis research in Lynn Cooley's lab in the Department of Genetics at the Yale University School of Medicine. He made several important contributions to *Drosophila* egg chamber development by demonstrating how the actin-rich ring canals, which are remnants of aborted cytokinesis, form and maintain stable connections between the nurse cells and oocyte. He also showed how kelch proteins function as actin organizers at a time when this large family of important proteins was barely known. Dr. Robinson then moved to James Spudich's lab in the Department of Biochemistry at the Stanford University School of Medicine as postdoctoral fellow. There, he established a robust and powerful new genetic system for conducting interaction genetics in the simple model system *Dictyostelium discoideum*. Using this genetic system, Dr. Robinson identified novel proteins, including dynacortin that are involved in cytokinesis and cell mechanics. This launched Dr. Robinson's research on the

mechanics of cytokinesis, which has been a major focus of his work here at Hopkins. Based upon his achievements and the promise of his program, Dr. Robinson was hired in the Department of Cell Biology as an Assistant Professor in November, 2001. In April, 2008, he was promoted to Associate Professor.

RESEARCH SCHOLARSHIP:

Dr. Robinson has been interested in cell shape control and morphogenesis because it is fundamental for all of multi-cellular development and critical for healthy function of many organ systems. Further, many pathological states such as hypertension, asthma, and cancer can trace their defects to problems in cell shape control. To have a simple model system for the investigation of cell morphology, Dr. Robinson chose cytokinesis of the amoeba *Dictyostelium discoideum*. Cytokinesis is a simple cell shape change because of its highly stereotypical nature, occurring in a precise location and at a specific time in a cell's life. *Dictyostelium* is a tractable model system because it offers a broad range of experimental techniques and molecular control while having a relatively simplified genome and well-defined cytoskeletal system.

Dr. Robinson has approached the investigation of cytokinesis from a novel perspective. He theorized that cell division is a cell mechanical process mediated by forces generated by actin polymerization and myosin II-based contraction. These forces then act upon the cross-linked actin network that forms the cortical actin cytoskeleton. His goal is to explain the mechanism of cell division quantitatively by elucidating how these force-generating and mechanical systems are derived from biochemical reactions.

Initially, it was essential to define the mechanics of a dividing cell: how soft or stiff the cell is, how the cell deforms over time, and how much active force is present in the actin network. Dr. Robinson applied micro-rheology (tracking the motions of particles bound to the cell surface) and micropipette aspiration (gentle pulling on localized regions of on the cell) to over 30 different *Dictyostelium* strains, including wild type and single and double mutant combinations. Based on these studies, he derived a detailed understanding of the cell's viscoelastic properties and the pathways controlling these properties. To summarize a very large body of published work, he found that actin cross-linkers define the deformability and the contractility of the actin network and that myosin II alters the character of and can increase the tension in the network. Key publications include: Girard et al. *EMBO J*. 2004; Girard et al. *PNAS* 2006; Octtaviani et al. *Mol. Biol. Cell* 2006; Reichl et al. *Curr. Biol.* 2008; Zhou et al. *Curr. Biol*. 2010; Kee et al. *Mol. Biol. Cell* in revision; and several review articles.

The next major effort was to link these mechanical features to the dynamics of cytokinesis. With physicist Wendy Zhang, an expert in nonlinear dynamics and fluid mechanics, Dr. Robinson determined that the decrease in furrow diameter as a function of time was an intrinsic property of the cell and distinct for each genetic mutant. They worked out a first generation analytical model for the fluid dynamics of cytokinesis (Zhang and Robinson, *PNAS* 2005). To build upon this modeling framework, Dr. Robinson worked with Pablo Iglesias, a computational biologist from the Department of Electrical and Computer Engineering. This model draws upon measured values of cortical tension and viscoelasticity for wild-type and mutant cell-lines, myosin II chemistry, friction/adhesion, protrusion, and curvature. The results of simulations are compared

to measured shape change parameters. The major advantage of this approach is that the force-generating systems of the cell can be separated to assess their specific contribution to cell division. Two papers have emerged from this work, including Yang et al. *BMC Systems Biol.* 2008 and Poirier et al. *PLoS Comp. Biol.* under revision.

Another major contribution from Dr. Robinson's research explains how cells sense and respond to mechanical inputs. The core component of cytokinesis machinery is the force generating molecule, myosin II. The field has understood for ~90 years from classic experiments that muscle myosin II functions differently depending on whether the muscle contracts with or without a load. Dr. Robinson reasoned that sensing and adjusting to mechanical force would be a significant factor in ensuring robustness of cytokinesis. He and his students used micropipette aspiration to apply physiologically relevant pressures over a well-defined surface area. They discovered that dividing cells were indeed exquisitely sensitive to mechanical forces, relocating myosin II and a specific actin crosslinker, cortexillin I, to the site of the externally imposed stress. This system has the hallmark of a cell division check point in that it slows cell division progress until the deformation is fixed. Upon examining unperturbed cells, they discovered that cells spontaneously relocate myosin II to correct shape irregularities. Dr. Robinson's group then conducted a detailed structure-function analysis of myosin II and cortexillin to determine how the system operates. They found that sensing is performed by a three-part sensor, including force amplification through the myosin II lever arm, myosin bipolar thick filament assembly/disassembly, and dynamics and actin filament anchoring by cortexillin I. This work has been published in three papers: Effler et al. *Curr. Biol*. 2006; Effler et al. *Cell Cycle* 2007; and Ren et al. *Curr. Biol*. 2009.

Dr. Robinson's group has developed a multi-scale model that explains how force-sensing by the myosin II motor and lever arm can regulate myosin II bipolar thick filament assembly. This model can account quantitatively for the amounts of myosin II that accumulate in response to applied stresses (Luo et al. *Biophys. J.*, in revision). Dr. Robinson's lab has also demonstrated how this mechanosensory system functions as a component of a control system that tunes the level of myosin II accumulation at the cleavage furrow under diverse mechanical constraints. (Kee et al. *Mol. Biol. Cell*, in revision; Dr. Robinson is the senior author).

Dr. Robinson has been curious how the mitotic spindle contributes to the dynamics of the cortex. To approach this question, Dr. Robinson conducted a genetic suppression screen for genes that would protect cells from the microtubule depolymerizing agent, nocodazole. They found that over expression of 14-3-3, a major regulator of a wide variety of cellular processes, could provide resistance to nocodazole. At the biochemical level, 14-3-3 does this by directly binding myosin II heavy chain and modulating its assembly into bipolar thick filaments, the functional contractile unit of myosin II. This work was described in two publications: Zhou et al. *Curr. Biol*. 2010 and Robinson *Small GTPases* 2010.

To determine how the principles uncovered in *Dictyostelium* apply to other systems, Dr. Robinson has been working with Janice Evans to study the mechanics of mouse oocytes as they mature and ultimately undergo a highly asymmetric cell division of polar body cytokinesis. They discovered that the mouse oocytes undergo a dramatic mechanical transformation as they mature from the germinal vesicle intact stage (GVI; *i.e.* upon ovulation) to metaphase II, which

is the point when the egg is typically fertilized. At metaphase II, the egg establishes a 2.5-fold mechanical differential between the so-called amicrovillar and microvillar cortical domains. The amicrovillar region is the region of increased cortical tension and myosin II concentration and where the spindle migrates, setting up the site of polar body emergence. Thus, in order for the egg to undergo the highly unfavorable shape transformation to form the polar body, the egg establishes a mechanically distinct domain, which isolates the polar body from the rest of the egg cortex. This work has been published in two papers: Larson et al. *Mol. Biol. Cell* 2010 and Evans and Robinson *Mol. Reprod. Dev*. 2011.

TEACHING SCHOLARSHIP:

Dr. Robinson has taught for nine years in the Cell Physiology block in Scientific Foundations of Medicine (SFM) course and organized by the Cell Biology Department. The course consists of 19 lectures, seven discussions and five virtual microscopy (VM) laboratory sessions. Dr. Robinson delivers five of the lectures including the Introductory, Cytoskeleton, Cell Division, Muscle and Review lectures. Dr. Robinson has received consistently strong positive feedback from the student evaluations of his lectures and discussion sections.

For graduate student teaching, Dr. Robinson presents annually two lectures, one on Cytoskeletal Filaments and one on Motors. Both now classic lectures are extremely well received by the students.

Dr. Robinson has presented lectures for other groups such as the engineering students at the Homewood campus. He was invited by Wolfgang Losert to present on the mechanics of cell division in Cancer Biophysics, a course for graduate students and postdocs at the University of Maryland, College Park. Dr. Robinson was invited to lecture based on the interdisciplinary nature of his research and teaching.

ORGANIZATIONAL AND ADMINISTRATIVE ACTIVITIES:

During Dr. Robinson's tenure as Cell Physiology block director, the entire SFM course was overhauled from the old Molecules and Cells format. Dr. Robinson oversaw the transition, including ensuring that appropriate *horizontal strands* were developed by each faculty lecturer. Dr. Robinson facilitated other aspects of the new SFM course for our block, such as the transition to electronic testing. He also initiated the inclusion of faculty from the Department of Pathology in the virtual microscopy laboratory sections of the course and recruited the faculty participants. This program has greatly enriched the experience for the Medical students.

Due to his example and encouragement, most faculty discussion leaders in Cell Physiology now use the *faculty facilitator* model. In this model, the faculty leader divides the students into groups and each group is assigned responsibility for leading an individual session. This approach creates a comfortable environment for the students to work in groups and to join into a whole group discussion. In this mode, the students teach and learn from each other, fulfilling one of the missions of the first-year curriculum, which is to promote *team-based learning*, a skill found essential for the later years of the students' medical education.

Community Outreach Program: Dr. Robinson has established a program that targets underprivileged high school students from inner city Baltimore. The objective of his high school program is to expose disadvantaged youth to modern scientific research combined with additional tutoring to help fortify and/or remediate basic academic skills. The rationale is that these youths will benefit from experiencing environments where creative and critical thinking skills are emphasized, where being smart and working hard are considered "cool", where substantial academic accomplishment is celebrated, and where colleagues collaborate to help when one needs it. University research laboratories are naturally constructed with this type of environment. Therefore, he has sought to leverage this environment and to utilize science in an additional way in outreach to a younger group of students. While research universities already have many outreach programs, most target the undergraduate and post-baccalaureate levels. Here, he strives to target this younger age group in a very focused and intensive manner, allowing for substantial impact on the students' lives. To accomplish this program, he developed a partnership with Boys Hope Girls Hope of Baltimore (BHGH; http://www.bhghbaltimore.org/) so that he can have home support and follow-up after the students finish the program. He has his technician Cathy Kabacoff who is a retired school teacher lead the summer program. The program just completed its third year and its first two graduates began college this fall. At least one is interested in pursuing a career in the medical sciences.

Overall, the program is rewarding for all involved. Faculty and student mentors report in end-of-summer evaluations a high level of fulfillment from the program (and all want to be repeat participants). This sort of direct involvement has benefited our scientific community by motivating our trainees to commit to the greater good. Graduate students have indicated that they hope in their career to conduct top-notch science and to develop their programs in multiple ways to contribute to the greater good too. This is a terrific mindset to instill in all of our Hopkins trainees.

CITIZENSHIP/COMMITMENT TO JOHNS HOPKINS:

Dr. Robinson has displayed excellent citizenship and commitment to the Department of Cell Biology, the School of Medicine, Johns Hopkins University and the greater community of Baltimore (through the BHGH summer program detailed above). He participates fully in every aspect of the community of our institution. He has served on more than 30 graduate thesis and postdoctoral committees, several Departmental committees, several admissions committees for summer programs, a website committee for the Center for Cell Dynamics, the Medical School Council, an exploratory committee to establish a Henrietta Lacks Memorial Scholarship, will serve (if funded) as a Pre-collegiate Director for a new proposed NSF-funded Engineering Research Center, and will serve (if funded) as the Outreach Coordinator for a proposed Systems Biology Center.

NATIONAL/INTERNATIONAL RECOGNITION:

Dr. Robinson has received several awards, including the Damon Runyon-Walter Winchell and the Leukemia Research Fund postdoctoral fellowships. He was a recipient of the Burroughs Wellcome Fund Career Award in the Biomedical, a Beckman Young Investigator Award and an American Cancer Society Research Scholar Grant. His research has been supported by an NIH R01 grant, a multi-PI NIH R01 he holds jointly with Pablo Iglesias, and an NSF grant. Dr. Robinson has presented over 50 invited seminars. Among these, he has co-chaired a Minisymposium at the 2009 American Society for Cell Biology (ASCB) Annual Meeting and presented a plenary lecture at the 2011 Biophysical Society Annual Meeting. He proposed and organized (with Ulrike Eggert of Harvard and now King's College London as co-organizer) a Special Interest Subgroup Meeting he entitled "Frontiers of Cytokinesis" at the 2010 ASCB meeting. He hopes to make this a biannual event.

This year (2011), Dr. Robinson organized (with Miho Iijima) the annual international *Dictyostelium* Conference, here in Baltimore, MD in August, 2011. This is an important service effort for the *Dictyostelium* research community and helps establish Dr. Robinson as a leader in *Dictyostelium* research.

Dr. Robinson serves on the editorial boards of two top-tier journals. One is the high profile journal *Current Biology*, which publishes cutting edge research across a broad range of biology disciplines, but with an affinity towards quantitative cell biology. In this role, Dr. Robinson is often contacted to comment on the appropriateness of papers for the journal as well as to provide reviews of papers. Dr. Robinson is also on the editorial board of the *Biophysical Journal*, the top biophysics-focused journal. Dr. Robinson oversees the review of ~30 papers per year and makes the decisions of whether to accept or reject the papers for publication.

There are several other indicators of Dr. Robinson's national and international reputation. He has been asked to write several review articles for a range of journals and books. These have targeted a variety of audiences, including the cell biology and engineering fields. Dr. Robinson has been invited to serve on a pre-tenure committee for a staff scientitist of the National Heart, Lung, and Blood Institute at the NIH and has been on an NIH Quad Annual Review. Internationally, Dr. Robinson has been invited for seminars at the Max Planck Institute in Dresden, at the 2011 EMBO Meeting in Vienna, and at the Technische Universität Munich. In 2007, by presenting four and a half hours of lectures, he helped teach the first biannual Curie Course on Cell Shape Changes, which was organized by Cécile Sykes and Julie Plastino and held in Paris. He was also invited to the Supervisory Board for a proposed European Union-funded training network. Though not funded in the first pass, this training network would have included ten faculty members across the European Union and four other international faculty, companies and institutions as associate partners. The focus of the proposed training network is on mitotic cell mechanics, and I believe the lead investigators plan to resubmit the proposal in the next year.

In a current project, Dr. Robinson is guest editing (along with Joe Sanger, Mohan Balasubramaniam, and William Bement) a special issue of the journal of *Cytoskeleton* on the topic of cytokinesis in memory of Ray Rappaport (d. 2010), the father of modern cytokinesis research. The editors will contribute articles along with 28 other leading international authors of

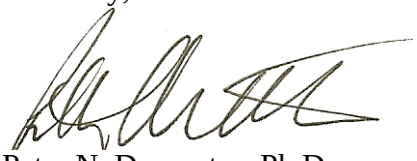
cytokinesis research that the guest editors selected. Tom Pollard has been invited to prepare an "In Memoriam" for the special issue.

ANTICIPATED FUTURE PROGRESSION:

With the completion of the three papers that are currently "in revision" at different journals, Dr. Robinson expects to greatly broaden his research program. In the first eleven years, Dr. Robinson has been extremely focused on understanding the molecular basis of the mechanics of cytokinesis using the model system *Dictyostelium discoideum*. In the next phase, Dr. Robinson will seek to work out much more of the molecular interactions of these cellular mechanical and mechanosensory systems he has defined. He will also expand his research dramatically to study how these principles uncovered with the *Dictyostelium* system apply to a host of other cell-types in different contexts. Several areas are underway already and can be seen in his recent publications on mouse oocyte maturation with Janice Evans (described above). He is also collaborating with Robert Anders in Pathology to look at the role of Hippo pathway genes in cell mechanics and cytoskeletal function of primary hepatocytes. He has a few new exploratory collaborations underway. With Ramana Sidhaye in Pulmonology, they are examining the role of aquaporins in microtubule stabilization and possibly cellular mechanosensing in asthma models. With Marcel Jacobs Lorena (JHU School of Public Health), they are looking at the role of certain genes in *Plasmodium* in red blood cell (RBC) mechanics. Other systems of exploration will include cell mechanics in the context of tissue morphogenesis. In one area with potential long term impact, Dr. Robinson is working to leverage his understanding and tools of *Dictyostelium* to identify small molecule modulators of the contractile machinery. His lab has already found one compound that appears to shift myosin II onto the cortex and a second compound that acts as a cytokinesis inhibitor. In this area, he expects to find compounds that will be useful small molecule modulators of cell mechanics that may be useful research tools and perhaps one day prove to have some medical value. His system is also primed to help with the identification of novel anti-amoeboid compounds, which may be useful for amoeboid parasitic infections that are particularly common in developing countries.

In conclusion, I am respectfully requesting your favorable consideration of my nomination of Dr. Robinson for promotion to Full Professor in the Department of Cell Biology. I have the utmost regard for his scholarship and integrity and give him my highest possible recommendation. I am happy to answer any questions or provide any further required information.

Sincerely,



Peter N. Devreotes, Ph.D.
Professor and Director