Approved by the Regents
May 19, 2016

PROMOTION RECOMMENDATION
THE UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL
DEPARTMENT OF PEDIATRICS AND COMMUNICABLE DISEASES

Jordan A. Shavit, M.D., Ph.D., assistant professor of pediatrics and communicable diseases, Department of Pediatrics and Communicable Diseases, is recommended for promotion to associate professor of pediatrics and communicable diseases, with tenure, Department of Pediatrics and Communicable Diseases, Medical School.

Academic Degrees:

2000	M.D./Ph.D.	Northwestern University
1992	B.S.	University of Michigan

Professional Record:

2009-present	Assistant Professor of Pediatrics and Communicable Diseases, University of Michigan
2006-2009	Clinical Lecturer, Department of Pediatrics and Communicable Diseases, University of Michigan

Summary of Evaluation:

Teaching: Dr. Shavit provides instruction on multiple levels throughout the Medical School and university, in both didactic and practical training. During his clinical time, he teaches medical students, residents, and fellows in both outpatient and inpatient settings, as well as didactic lectures and small group discussions. Dr. Shavit has received the "Top Resident Teacher Award" from the Department of Pediatrics for excellence in education. Through his research activities, Dr. Shavit has served on preliminary examinations and dissertation committees for students in the Program in Biomedical Sciences (PIBS) and Cellular and Molecular Biology (CMB) Program. The bulk of his teaching occurs in the laboratory where he has served as the primary mentor to undergraduate, graduate, and medical students, technicians, as well as postdoctoral and clinical fellows. Dr. Shavit has mentored several undergraduate students and technicians who successfully applied for graduate level study at peer institutions, and one postdoctoral fellow and medical student who were awarded mentored American Society of Hematology Training Grants. In particular, Dr. Shavit's expertise in the genetics of hemostasis and thrombosis is integral to the educational aspect of our academic mission.

Research: Dr. Shavit's research is clinically-directed basic science in the field of blood clotting disorders. The overarching goal is to identify the modifier genes and pathways responsible for the gaps in our understanding of clinical presentations of patients with coagulation factor deficiencies. His first major contribution was to demonstrate in mice that it takes a combination of variants in von Willebrand factor (VWF) and distinct modifier loci to regulate blood plasma VWF levels. After realizing the benefits of aquatic models, Dr. Shavit demonstrated that

coagulation is functionally conserved in zebrafish and successfully imported genome editing technologies to the University of Michigan in the early days before they were widely available, and used them to produce multiple models of coagulation disorders, as well as assist colleagues across numerous departments. His clotting deficiency models demonstrate the expected phenotypes of pathologic bleeding and clotting, but have also provided unexpected insight into coagulation factor function in fish and humans. Dr. Shavit's research impact is demonstrated through his publications invited reviews, and external speaking invitations at peer institutions and international conferences. Increasingly he has been recognized in both the hemostasis/thrombosis and zebrafish communities for his work at the interface of these two fields. He has obtained extramural support from various sources, including the NIH (PI on an NHLBI-funded R01), American Heart Association (fellow to Faculty and Innovative Research Grant Awards), and American Society of Hematology (faculty scholar and mentored Trainee Research Awards). Now that he has developed and characterized clotting models in fish, he is now using them to perform high throughput genetic and small molecule screens. This will lead to discovery of genetic modifiers and novel compounds with the potential for translation to humans and subsequent diagnostic and therapeutic advances. Dr. Shavit has a well-funded laboratory with support from the NIH as well as multiple foundation sources and he is continuing to expand his core staff and trainees to work in this vibrant environment. Dr. Shavit's research grants support 90% of his faculty effort. He is a key faculty member in the advancement and success of his Division's scholarly mission.

Recent and Significant Publications:

Shavit JA, Manichaikul, A, Lemmerhirt HL, Broman KW, Ginsburg D: Modifiers of von Willebrand factor identified by natural variation in inbred strains of mice. *Blood* 114:5368-5374, 2009.

Ghosh A, Vo A, Twiss BK, Kretz CA, Jozwiak MA, Montgomery RR, Shavit JA: Characterization of zebrafish von Willebrand factor reveals conservation of domain structure, multimerization, and intracellular storage. *Adv Hematol* 2012:1-9, 2012.

Vo A, Swaroop A, Liu Y, Norris ZG, and Shavit JA: Loss of fibrinogen in zebrafish results in symptoms consistent with human hypofibrinogenemia. *PLOS One* 8:e74682, 2013.

Liu Y, Kretz CA, Maeder ML, Richter CE, Tsao P, Vo AH, Huarng, MC, Rode T, Hu Z, Mehra R, Olson ST, Joung JK, and Shavit JA: Targeted mutagenesis of zebrafish antithrombin III triggers disseminated intravascular coagulation and thrombosis, revealing insight into function. *Blood* 124:142-150, 2014.

Huarng, MC and Shavit JA: Simple and rapid quantification of thrombocytes in zebrafish larvae. *Zebrafish* in press.

Service: Dr. Shavit serves his discipline in many capacities. On the Medical School level, he was on the Cellular and Molecular Biology admissions committee and a faculty coordinator for graduate student recruitment. Within the Department of Pediatrics, he serves on the Research Advisory and NIH K12 funded Children's Health Research Center Advisory Committees. He

has reviewed grant and fellowship applications for the Cardiovascular Center and Department of Pediatrics, as well as other internal medical school reviews through the Office of Research Discovery and Biomedical Research Council. On a national level, he is a member of the editorial board for *Pediatric Blood & Cancer* and has performed manuscript review for multiple journals, including *Science Translational Medicine*, *Molecular and Cellular Biology*, *Blood*, *Genome Research*, and *Arteriosclerosis, Thrombosis, and Vascular Biology*. Dr. Shavit is a permanent member of an American Heart Association study section, and performed ad hoc review for three NIH study sections, as well as NSF, AAAS, and National Hemophilia Foundation review panels. He also serves on committees for two international organizations relevant to his research, including the American Society of Hematology and Zebrafish Disease Models Society.

External Reviewers:

Reviewer A: "Dr. Shavit then moved to the zebrafish model, where he has become internationally recognized for his pioneering work in using this organism to understand the pathogenesis underlying childhood bleeding disorders....Dr. Shavit is exactly the type of individual that I hope and encourage my resident research trainees to aspire to be. He has developed a unique research niche in which he is leading the field by conducting exciting novel discovery-based work that is not 'me-too science.'"

Reviewer B: "There are less than a handful of pediatric coagulation physician-scientist in the US who have the credentials, productivity, and recognition that Dr. Shavit has already garnered. I would recruit Jordan in a heartbeat."

Reviewer C: "In the application of zebrafish genetics to problems in hemostasis/thrombosis, I would rank Dr. Shavit as *first* among his peers. He has gained outstanding national and international peer recognition for his application of mouse and, especially, zebrafish genetics."

Reviewer D: "Dr. Shavit's independent work has established him and his laboratory as an international center of excellence in this approach to evaluation of hemostasis and thrombosis. The approach offers substantial promise of new insights that may lead to better therapies for hemophilia and other bleeding diseases as well as for thrombotic disorders."

Reviewer E: "Over the past decade, Dr. Shavit has established a national and increasingly international reputation for high quality scholarly work relating to the mechanisms regulating hemostasis. His recent initiation of studies utilizing the zebrafish model has already yielded novel findings, and along with the incorporation of new genome editing approaches promises to be an exciting area for future discovery."

Reviewer F: "He is one of the most creative, ambitious, and innovative scientists I know. Jordan has made major contributions and is now the top international leader in the analysis of coagulation and hemostasis using the zebrafish model....Given the considerable momentum of his research progress at this time I believe his future accomplishments will be very remarkable, and that he should definitely be promoted to Associate Professor with Tenure."

Summary of Recommendation:

Dr. Shavit has developed a world class research program on the genetics of coagulation using novel animal models and technical approaches. He has proven his commitment to excellence in the areas of scholarship, clinical service, teaching and administrative service and in particular has been a key faculty member in promoting novel insights into important problems in hemostasis and thrombosis on an international scale. I strongly recommend Jordan A. Shavit, M.D., Ph.D. for promotion to associate professor of pediatrics and communicable diseases, with tenure, Department of Pediatrics and Communicable Diseases, Medical School.

Marschall S. Runge, M.D., Ph.D.
Executive Vice President for Medical Affairs
Dean, Medical School

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