PROMOTION RECOMMENDATION THE UNIVERSITY OF MICHIGAN MEDICAL SCHOOL DEPARTMENT OF SURGERY

Approved by the Regents May 21, 2015

<u>Theodore H. Welling, M.D.</u>, assistant professor of surgery, Department of Surgery, Medical School, is recommended for promotion to associate professor of surgery, with tenure, Department of Surgery, Medical School.

Academic Degrees:

M.D.

2009

University of Michigan Medical School

B.S. 1991

University of Michigan

Professional Record:

2007-present 2005-2007

Assistant Professor of Surgery, University of Michigan

Clinical Lecturer, Department of Surgery, University of Michigan

Summary of Evaluation:

<u>Teaching</u>: Dr. Welling's teaching activities include undergraduates, medical students, residents, transplant surgery fellows, mid-level providers and practicing community physicians. In his role as codirector of the Multidisciplinary Liver Tumor Program, Dr. Welling gives lectures to community physicians at CME courses on the topics of liver transplantation and surgical treatment of hepatobiliary malignancies. He gives regular lectures to medical students and instructs undergraduates in reading and evaluating peer reviewed literature through the University of Michigan's Undergraduate Research Opportunity Program (UROP). Dr. Welling provides opportunities for training and instruction for physician assistants and nursing personnel in the Multidisciplinary Liver Tumor Program, The Transplant Center, and the University of Michigan Hospital Operating Rooms.

Research: Dr. Welling's research interests span both basic and clinical research associated with liver cancer and liver transplantation. He has developed a clinical and translational research program that seeks to advance therapies for hepatocellular carcinoma (HCC). Dr. Welling's HCC research efforts include multidisciplinary, team based clinical trials (industry and investigator initiated) as well as more individual efforts based within his laboratory that seek to identify new targets for therapeutic intervention. Dr. Welling was the institutional PI on a clinical trial evaluating the role of Soranfenib as adjuvant therapy for HCC following surgery or ablation. He leveraged his laboratory work with PD-1 inhibition to help develop a phase I multicenter clinical trial evaluating the novel immune check point inhibitor (anti-PD-1 antibody (Nivoluman)) which targets TAM/effector T cell interactions, and he serves as the institutional PI for this trial. He is also actively involved in the development of a phase IB/II trial of therapy designed to disrupt TAM cytokine signaling to HCC CSC expansion. Dr. Welling's research has led to over 30 peer-reviewed manuscripts, 11 book chapters and numerous invitations to present his work at national meetings. In addition to securing funding from industry, Dr. Welling has been successful at obtaining peer-reviewed funding including a GI SPORE career development award from the NIH/University of Michigan entitled "Hepatocellular cancer stem cells and microenvironmental influence of immune cell subsets," as well as K08 award from the National Cancer Institute entitled "Immunosuppressive network of human hepatocellular carcinoma." Work on this latter project has generated preliminary data to support Dr. Welling's R01 grant submission "Microenvironmental influence on HCC cancer stem cell and EMT function," that is currently under review. Dr. Welling's is an ad hoc reviewer for several high impact journals such as American Journal of Gastroenterology and

Annals of Surgical Oncology and serves as an editorial board member of the World Journal of Gastroenterology.

Recent and Significant Publications:

Wu K, Kryczek I, Chen L, Zou W, Welling TH: Kupffer cell suppression of CD8+ T cells in human hepatocellular carcinoma is mediated by B7-H1/PD-1 interactions. *Cancer Res* 69:8067-8075, 2009.

Mathur AK, Ghaferi AA, Osborne NH, Pawlik TM, Campbell DA, Englesbe MJ, Welling TH: Body mass index and adverse perioperative outcomes following hepatic resection. *J Gastrointest Surg* 14:1285-1291, 2010.

Welling TH, Fu S, Wan S, Zou W, and Marrero JA. Elevated serum IL-8 is associated with presence of hepatocellular carcinoma and independently predicts survival. *Cancer Invest* 10:689-697, 2012.

Welling TH, Feng M, Wan S, Hwang, SY, Volk ML, Lawrence TS, Zalupski MM, Sonnenday CJ. Neoadjuvant stereotactic body radiation therapy (SBRT), capecitabine, and liver transplantation for unresectable hilar cholangiocarcinoma. *Liver Transpl* 20:81-88, 2014.

Wan S, Zhao E, Kryczek I, Vatan L, Sadovskaya A, Ludema G, Simeone DM, Zou W, Welling TH: Tumor-associated macrophages produce interleukin 6 and signal via STAT3 to promote expansion of human hepatocellular carcinoma stem cells. *Gastroenterology* 147:1393-1404, 2014.

Service: Dr. Welling actively serves on the American Society of Transplant Surgeons Scientific Studies Committee. Appointment to this committee is competitive and reflects peer recognition. He has served on both the Research Committee and the Program Committee for the American Hepatico-Pancreatico-Biliary Association. He is a member of numerous professional societies, such as the American Association for the Study of Liver Diseases, International Liver Cancer Association and American Society of Transplant Surgeons. Through participation in inaugural Leadership Development Program, organized by the Department of Surgery and University of Michigan Business School, Dr. Welling led a pilot program to study and provide targeted community outreach to potential referring specialty physicians involved in the multidisciplinary care of hepatobiliary malignancies. Dr. Welling is one of two liver transplant surgeons at the University of Michigan that specialize in hepatobiliary surgery. He is an active member of both the Transplant Center and Comprehensive Cancer Center. Dr. Welling is the co-director of the Multidisciplinary Liver Tumor Program. In this role, he has worked to improve the quality, volume, and development of novel treatment strategies for patients with hepatobiliary malignancies. As one example of his innovative efforts he helped foster the Tele-Tumor Board which is now actively engaged with an oncology group in Northern Michigan.

External Reviewers:

Reviewer A: "Dr. Welling's scholarly output has been impactful on the field. He and his collaborators have made several seminal observations related to our field of hepatic surgery and hepatic malignancy. Several of these have practical value for the daily practice of surgery and I anticipate several others will lead to novel trials for the treatment of hepatic malignancies."

Reviewer B: "I think his achievements should be taken in the context of the demanding work in transplantation and hepatobiliary surgery. His multiple grants on the subject compliment his commitment and success in the field. Having a solid academic priority in addition to his clinical skills makes him extremely competitive for promotion at most universities in the United States...Dr. Welling's surgical

innovations alone have made him one of the most prominent liver transplant surgeons in the country. He is a rising star with great potential for translational science."

Reviewer C: "I again know from personal contact with his colleagues that his students value his abilities to transmit difficult information in an understandable manner. His basic research has given him the opportunity to teach a number of undergraduate students, medical students and surgical residents of these techniques and transmit the intricate details of his discipline. From the provided material, it is easy to see that he has provided educational experiences not only at the home institution, but regionally, nationally and internationally."

Reviewer D: "He has a strong and continuous record of teaching, scholarship and research, and service. It is very difficult to maintain this type of career path with a busy clinical transplant surgery practice, but Ted seems to have accomplished this. These are the type of bright investigators [of his cohort] that we wish to foster and support in transplant surgery. I know that he will have a successful career in academic surgery."

Reviewer E: "Dr. Welling's research has been presented locally, nationally and internationally at prestigious scientific meetings within his field, and he has remained an active contributor to the editorial boards of numerous respected scientific journals since 2008. In summary, regarding Dr. Welling's scientific productivity, he is at the extreme end of the spectrum for his peer group."

Reviewer F: "His work includes both state-of-the-art research in basic science and clinical research. Most notable is his track record of close collaboration with his colleagues across a multitude of disciplines. Dr. Welling has been creative in his efforts to advance the state of transplantation and hepatobiliary and pancreatic surgery. He has taken on the challenge of liver transplantation for unresectable hilar cholangiocarcinoma which has required close collaboration with a multitude of specialists at the University of Michigan in addition to the responsibilities associated with taking care of a very challenging group of patients."

Summary of Recommendation:

Dr. Welling is well respected by his colleagues and considered to be an outstanding clinician and talented educator, who has also established himself as a respected leader in translational research for liver cancer. I am pleased to recommend Theodore H. Welling, M.D. for promotion to associate professor of surgery, with tenure, Department of Surgery, Medical School.

James O. Woolliscroft, M.D.

Dean

Lyle C. Roll Professor of Medicine

May 2015