

PROMOTION RECOMMENDATION
UNIVERSITY OF MICHIGAN MEDICAL SCHOOL
DEPARTMENTS OF INTERNAL MEDICINE AND OF PHARMACOLOGY
UNIVERSITY OF MICHIGAN COLLEGE OF PHARMACY
DEPARTMENT OF MEDICINAL CHEMISTRY

Shaomeng Wang, Ph.D., Associate Professor of Internal Medicine, with tenure, Department of Internal Medicine and Associate Professor of Pharmacology, without tenure, Department of Pharmacology, Medical School, and Assistant Professor of Medicinal Chemistry in the Department of Medicinal Chemistry, College of Pharmacy, is recommended for promotion to Professor of Internal Medicine, with tenure, Department of Internal Medicine, and Professor of Pharmacology, without tenure, Department of Pharmacology, Medical School, and Professor of Medicinal Chemistry, without tenure, in the Department of Medicinal Chemistry, College of Pharmacy.

Academic Degrees:

Ph.D.	1992	Case Western Reserve University
B.S.	1986	Beijing University, Beijing, China

Professional Record:

2006-Present	Associate Professor of Pharmacology, University of Michigan
2001-Present	Associate Professor of Internal Medicine, University of Michigan
2001-Present	Assistant Professor of Medicinal Chemistry, College of Pharmacy, University of Michigan
2000-2001	Associate Professor of Oncology, Georgetown University
2000-2001	Associate Professor of Neuroscience, Georgetown University
1996-1999	Assistant Professor of Neurology, Georgetown University

Summary of Evaluation:

Teaching: Dr. Wang has had considerable experience both as a didactic teacher and laboratory mentor. With respect to the former, since his move to the University of Michigan in 2001, Dr. Wang has been an active participant in the Bioinformatics Seminar Series having served as course Co-Director in 2003. He has also provided lectures for the Cancer Biology Seminar Series (2001) and the Breast Cancer Forum Seminar Series (2002). His scientific mentorship activities have included his service as thesis mentor for four graduate students in the Department of Medicinal Chemistry, College of Pharmacy, and as rotation supervisor for nine additional students in the College of Pharmacy. He also provides scientific mentorship for 12 postdoctoral fellows or research investigators and has served on the candidacy exam or thesis committees of nine graduate students in the College of Pharmacy.

Research: In July, 2001 Dr. Wang was recruited to develop a new program in anticancer drug discover within the University of Michigan Comprehensive Cancer Center. With a major investment of resources made by the Department of Internal Medicine and the Comprehensive Cancer Center as complemented by major extramural funding from the NIH, Department of Defense, and other granting agencies, Dr. Wang has assembled a large team of computational chemists, medicinal chemists, biochemists, structural biologists, cell and tumor biologists with a goal of creating “designer drugs” which target aberrant signaling pathways in cancer cells. Beginning with the three dimensional structure of cancer cell target proteins, the Wang laboratory uses innovated computer algorithms and databases to design and synthesize candidate small molecule inhibitors of target cell function, test candidate agents against cancer cells in vitro, and finally perform toxicology, pharmacology, and efficacy essays in animal models of human cancer. A major focus of the laboratory has been the design of agents which overcome apoptosis-resistance of cancer cells to other chemotherapy drugs and radiation therapy, including members of the Bcl-2/Bcl-xL and IAP protein family. Dr. Wang has made notable progress in the development of cell-permeable, small molecule inhibitors of the X-linked inhibitor of apoptosis (XIAP): in a screen of 8,000 natural herbal agents of defined molecular structure, a single agent, Embelin was found to overcome the inhibitory effect of XIAP resulting in inhibition of cancer cell growth and induction of apoptosis. Using a second approach, Dr. Wang and co-workers used a molecular modeling strategy to design and synthesize a class of small molecule mimetics of the second mitochondria-derived activator of caspase (Smac) that also target XIAP and other IAPs and induces cancer cell apoptosis. Furthermore, Dr. Wang and co-workers have designed and discovered several classes of novel inhibitors targeting Bcl-2 and Bcl-xL proteins and have performed extensive in vitro and in vivo evaluations for their therapeutic potential as a new class of anticancer agents. Another successful approach has been to target the endogenous cellular inhibitor of the p53 tumor suppressor, MDM2. Specifically, Dr. Wang and co-workers have designed non-peptide small molecule inhibitors of MDM2 which block the interactions of MDM2 and p53 which permits the proapoptotic activity of p53. Altogether, Dr. Wang’s bibliography includes 121 reports published or in press in the peer reviewed literature (46 of which have appeared during the four years in which Dr. Wang has been on the UM faculty). Complementing Dr. Wang’s productivity as an investigator is his remarkable success in accruing significant extramural support for his research efforts: he currently serves as principal investigator of 13 awards from federal, foundation, and industry sources, accounting for 96% of his professional effort; he also serves as a co-investigator on eight additional awards. Four federal awards are pending. Dr. Wang holds six issued patents, with an additional 18 patents pending. To capitalize on his exciting discoveries in the laboratory, Dr. Wang and his collaborators have formed a University of Michigan spinoff biotech company, Ascenta Therapeutics, Inc., which has received significant venture capital funding to sponsor phase I human clinical trials. Other measures of Dr. Wang’s national and international stature in his field are reflected by his extensive service to federal grant review study sections, and his demand as a lecturer both in the U.S. and abroad.

Recent and Significant Publications:

Ding K, Lu Y, Nikolovska-Coleska Z, Qiu S, Ding Y, Gao W, Stuckey J, Krajewski K, Roller P, Tomita Y, Deschamps J, Wang S: Structure-Based Design of Potent and Non-Peptide MDM2 Inhibitors. *J Am Chem Soc* 2005 (in press).

Wang R, Fang X, Lu Y, Yang C, Wang S: The PDBbind Database: Methodologies and Updates. *Journal of Medicinal Chemistry* 48(12):4111-4119, 2005.

Nikolovska-Coleska Z, Hu Z, Xu L, Tomita Y, Li P, Roller P, Wang R, Fang X, Lippman M, Zhang M, Yang D, Wang S: Discovery of Embelin as A Cell-Permeable, Small-Molecular Weight Inhibitor of XIAP through Structure-Based Computational Screening of Traditional Herbal Medicine Three-Dimensional Structural Database. *Journal of Medicinal Chemistry* 47(10):2430-2440, 2004.

Sun H, Nikolovska-Coleska Z, Yang C, Xu L, Tomita Y, Roller P, Wang S: Structure-Based Design, Synthesis and Evaluation of Conformationally Constrained Mimetics of the Second Mitochondria-derived Activator of Caspase (Smac) That Target the X-linked Inhibitor of Apoptosis Protein/Caspase-9 Interaction Site. *Journal of Medicinal Chemistry (Letter)* 47(17): 4147-4150, 2004.

Service: Dr. Wang provides extensive invited service to various NIH study sections and as an ad hoc reviewer to multiple journals within his field. His intramural activities include his co-direction of the Molecular Therapeutics Program of the University of Michigan Comprehensive Cancer Center as well as his service as Chair of the Bioinformatics Program Faculty Search Committee and the University of Michigan Medical School High-Performance Computing Subcommittee.

External Review:

Reviewer A: "Dr. Wang's expertise in medicinal chemistry as applied to small molecule therapeutics in oncology is a highly sought talent in Comprehensive Cancer Centers in the United States. If he were available...he would be at the top of my list for recruiting, and I would have no problem recommending him to be hired at the full professor level."

Reviewer B: "His publication record is extremely impressive, as is his list of invited lectureships. His publications are in respected journals, and the diversity of journals in which he publishes provides a testament to the breadth and dept of his research program. His research funding would be the envy of the laboratories of most senior researchers: he has multiple grants from the NIH and the Department of Defense, as well as foundations and industry."

Reviewer C: "...his work on the structure-based design of small-molecule inhibitors of several apoptosis-regulating proteins represents a major breakthrough in identifying novel anticancer agents....There is no doubt that Shaomeng is one of the leading investigators in the area of drug discovery in the US."

Reviewer D: “Let me state right up front that I think you have an enviably easy decision. There is no doubt that Shaomeng is already a star with an impressive level of accomplishment in structure-based small molecule drug design and even brighter future ahead of him...”

Reviewer E: “If anything, it seems to me that his promotion is a bit overdue, as Shaomeng has an outstandingly productive and well-funded research program...he is quite exceptional in having developed such strong research programs in both experimental and computational drug discovery.”

Reviewer F: “His real world impact is evident from his record of patents and patent applications currently being processed. The assessment of his peers is clear from the magnitude of grant support that he currently has and the consistency with which he has maintained strong funding. His academic participation is evident from his active role as a research and student advisor.”

Reviewer G: “Overall, I consider Prof. Wang to be one of the leaders in the application of computational approaches to drug discovery.”

Summary of Recommendation:

Dr. Wang’s recruitment to the University of Michigan represented a unique opportunity to spearhead a new program in rational anti-cancer drug design based upon the analysis of the three dimensional structure of target proteins. In pursuing this goal, Dr. Wang has exceeded our most optimistic expectations. He has assembled a large team of interactive scientists who have succeeded in developing multiple candidate small molecule inhibitors that attack various elements of the anti-apoptosis cascade. Several agents have reached the stage of phase I clinical testing. In this work, Dr. Wang has forged collaborations with multiple University of Michigan scientists and clinicians to the mutual benefit of all concerned. Dr. Wang’s extraordinary efforts over the past four years have put the University of Michigan “on the map” as a leading center in targeted drug therapy of cancer. He is certainly a most worthy candidate for promotion to Professor of Internal Medicine, Professor of Pharmacology, and Professor of Medicinal Chemistry.



Allen S. Lichter, M.D.
Dean, Medical School
*Newman Family Professor
of Radiation Oncology*



Frank J. Ascione, Ph.D., Pharm.D.
Dean, College of Pharmacy

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