Approved by the Regents
May 15, 2014

PROMOTION RECOMMENDATION
UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL
DEPARTMENT OF NEUROSURGERY
DEPARTMENT OF CELL AND DEVELOPMENTAL BIOLOGY

Xing Fan, M.D., Ph.D., assistant professor of neurosurgery, Department of Neurosurgery, and assistant professor of cell and developmental biology, Department of Cell and Developmental Biology, Medical School, is recommended for promotion to associate professor of neurosurgery, with tenure, Department of Neurosurgery, and associate professor of cell and developmental biology, without tenure, Department of Cell and Developmental Biology, Medical School.

Academic Degrees:

Ph.D.	2002	University of Navarre, Pamplona, Navarre Spain
M.D.	1994	Tianjin Medical University, Tianjin, China

Professional Record:

2008–present	Assistant Professor of Neurosurgery, University of Michigan
2008–present	Assistant Professor of Cell and Developmental Biology, University of Michigan

Summary of Evaluation:

Teaching: Dr. Fan's teaching activities focus largely on his mentoring of residents within the Department of Neurosurgery. He has also trained several medical students in the laboratory as well as two neurosurgery residents, both of whom have been successful in obtaining outside funding for their research. He meets with these students regularly and has been successful in helping them to be productive and develop their own meaningful research programs. In addition, he has given classroom instruction in neuropathology, teaching diseases of the nervous system. Dr. Fan also provides teaching within the molecular and cell biology course, CDB530, leading a discussion session with Dr. Billy Tsai. Although his classroom instruction is somewhat limited, he receives excellent evaluations for these instructions. He regularly lectures for the Department of Neurosurgery about basic science concepts and also receives strong evaluations from these lectures. His supervision of graduate students in the laboratory has also been extensive. He has mentored ten graduate students (two of whom have gone on to do Ph.D. theses within his laboratory), fifteen undergraduate students, and three post-doctoral fellows. Dr. Fan has also served on several dissertation committees and has been an evaluator for graduate student presentations in cancer biology, neuroscience and the CDB graduate program.

Research: Dr. Fan's research interest focuses on targeting of cancer stem cells in glioblastomas and medulloblastomas. He has been focused on blocking signaling pathways that regulate cancer stem cell self-renewal, including Notch, hedgehog, and P13K/Akt pathways. He has also been examining the way in which Notch signaling pathways may regulate self-renewal of cancer stem

cells in brain tumors. Most recently, he has been examining genomic alterations that exist in medulloblastomas. For his research, Dr. Fan has been successful in obtaining funding from outside agencies. At present he has an R01 relating to cancer stem cell niche in brain tumors, which expires in 2016. He has a second R01 which is investigating cancer stem cells/niche interactions in brain tumors. He is a co-investigator with effort on another R01 which examines differential mapping of stem cells in tumors. He has a foundation grant from the Motor City Golf Classic in which he is looking at novel therapies for glioblastomas and has been a mentor on a grant looking at Notch signaling pathways in glioblastomas. Dr. Fan has been quite aggressive in submitting additional grants and has held a series of grants in the past that have helped fund his laboratory efforts along with funding from the Department of Neurosurgery. He received an American Association of Cancer Research Scholar in Training Award, and has also received an American Brain Tumor Translational Research Award, as well as a Voices Against Brain Cancer Research Award. He has been invited to give multiple outside presentations on his research, including several at national and international neuro-oncology meetings. He has 35 peer-reviewed publications and has articles in such prestigious journals as the *Journal of Neuro-Oncology*, *Nature*, *LANCET Oncology*, and *Neurology*. He has been a corresponding and senior author on a considerable number of these publications. Dr. Fan has a very strong research background and has been recognized for his efforts, not only through invited presentations and publications, but also with a solid long history of grant funding.

Recent and Significant Publications:

Fan X, Eberhart CG: Medulloblastoma stem cells. *Journal of Clinical Oncology* 26:2821-2827, 2008.

Fan X, Khaki L, Zhu TS, Soules ME, Talsma CE, Gul N, Koh C, Zhang J, Li YM, Maciaczyk J, Nikkhah G, DiMeco F, Piccirillo S, Vescovi AL, Eberhart CG: NOTCH pathway blockade depletes CD133-positive glioblastoma cells and inhibits growth of tumor neurospheres and xenografts. *Stem Cells* 28:5-16, 2010.

Zhu TS, Costello MA, Talsma CE, Flack CG, Crowley JG, Hamm LL, He X, Hervey-Jumper SL, Heth JA, Muraszko KM, DiMeco F, Vescovi AL, Fan X: Endothelial cells create a stem cell niche in glioblastoma by providing NOTCH ligands that nurture self-renewal of cancer stem-like cells. *Cancer Research* 71:6061-6072, 2011.

Dai L, He J, Liu Y, Byun J, Vivekanandan A, Pennathur S, Fan X*, Lubman DM* (* Corresponding Author): Dose-dependent proteomic analysis of glioblastoma cancer stem cells upon treatment with γ-secretase inhibitor. *Proteomics* 11:4529-4240, 2011.

He J, Liu Y, Zhu T, Zhu J, Dimeco F, Vescovi AL, Heth JA, Muraszko KM, Fan X*, Lubman DM* (*Corresponding Author): CD90 is identified as a candidate marker for cancer stem cells in primary high-grade gliomas using tissue microarrays. *Molecular & Cellular Proteomics* 11: M111.010744, 2012.

Service: Dr. Fan participates in all of the activities within the Department of Neurosurgery. He has been particularly strong in the educational area, helping residents create and define their research goals during their residency. He is a member of all major professional societies related to neuro-oncology. He also is on the editorial board, as an associate evaluator, for the *American Journal of Stem Cells*. He has served on the Ohio Cancer Research Associates Ad Hoc Advisory Committee, and on the NIH Cancer Molecular Pathobiology Study Section. He has also been involved on an international level with the Canada Research Chairs Program and the Spanish National Evaluation and Foresight Agency. He is an ad hoc reviewer for multiple journals. Dr. Fan has also served as a mentor for a large number of students, postdoctoral fellows, residents and house officers, as well as a significant cadre of undergraduate students. Within the Department of Neurosurgery, he has been crucial in helping recruit medical students to a neurosurgical career at the University of Michigan. He is also involved in student recruiting at the University of Michigan Medical Scientist Training Program as well as the Program in Biomedical Sciences. Dr. Fan has helped write and design the Curriculum Handbook of Graduate Program in Cancer Biology at the University of Michigan. In all, Dr. Fan's service to the Department of Neurosurgery has been primarily to draw both attending and resident staff into the laboratory and help explain some of the newest developments in cancer cell biology. His service in this area has been exceptional and he is viewed as one of the more accommodating scientists with respect to neurosurgery clinicians.

External Reviewers:

Reviewer A: "Over the past 5 years, Dr. Fan has published several important papers pertaining to the possible role of developmental pathways in CNS malignancies, with a specific focus on the role of these pathways in maintaining cancer stem cells."

Reviewer B: "Dr. Fan has an excellent history of success with grant funding from the NIH and to date has had a very successful career....He serves as an ad-hoc reviewer for many significantly high profile journals and has had a very successful career teaching graduate students, medical students, post-doctoral fellows, as well as residents and undergraduate students."

Reviewer C: "...it is clear that Xing has had a continuous record of making important discoveries and maintaining focus on interesting and related problems....his trajectory for research accomplishment is continuing to ascend and more discoveries of impact will inevitably follow."

Reviewer D: "... he is a rapidly rising star in the field of neuro-oncology as it pertains to the study of signaling in cancer stem cells....This is a highly competitive and promising area of research with likely translational components for therapy and Dr. Fan is establishing himself as one of the leaders in the field."

Reviewer E: "Dr. Fan has clearly developed a focused area of research and a specific scholarly/professional niche, which has tremendous potential for future development and growth. He is currently well-funded to conduct his research investigations, and will undoubtedly continue to make further contributions to new knowledge in the area of cancer stem cells in brain tumors."

Reviewer F: "Importantly, his findings have had a major translational impact, leading to two successful clinical trials in a group of diseases that present major clinical challenges. His work is well-known worldwide in the cancer stem cells field. Particularly in the realm of neuro-oncology, Dr. Fan's research on Notch and CSC is at the very cutting edge of the field. I would rank him in the top 5% or better."

Reviewer G: "Dr. Xing Fan's research has had a significant impact on neuroscience/neuropathology research. His publications on the NOTCH signaling pathway and stem cell biology have been ground breaking....Dr. Fan has established both a national and international reputation as an investigator. He is involved in numerous organizations, serves as a grant reviewer in both the U.S. and internationally, is a highly respected reviewer for numerous scientific journals, and has presented his work at meetings around the world."

Reviewer H: "He has demonstrated effectiveness in teaching at multiple levels, his research program is strong and thriving as measured by peer reviewed grants as Principal Investigator from the NIH, and by his publication of high impact papers in the basic science and in neuron oncology literatures. He has also been an invited speaker to numerous venues and programs around the world. Finally, he has provided ample evidence of service work in the review of manuscripts for peer reviewed journals, and as a member of local institutional committees."

Summary of Recommendation:

Dr. Fan has demonstrated significant scientific prowess in developing an understanding of the Notch signaling pathways with respect to tumor development. His expertise with respect to stem cells and their importance in brain tumor biology is demonstrated by a series of publications, awards, and grants that he has already received. He is viewed as a strong member of the research community in stem cells. I strongly support the promotion of Xing Fan, M.D., Ph.D. to associate professor of neurosurgery, with tenure, Department of Neurosurgery, and associate professor of cell and developmental biology, without tenure, Department of Cell and Developmental Biology, Medical School.

James O. Woolliscroft, M.D.
Dean
Lyle C. Roll Professor of Medicine

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