PROMOTION RECOMMENDATION
UNIVERSITY OF MICHIGAN MEDICAL SCHOOL
DEPARTMENT OF RADIATION ONCOLOGY

Yi Sun, M.D., Ph.D., Associate Professor of Radiation Oncology, with tenure, Department of Radiation Oncology, Medical School, is recommended for promotion to Professor of Radiation Oncology, with tenure, Department of Radiation Oncology, Medical School.

Academic Degrees:

Ph.D.	1989	University of Iowa
M.S.	1986	Zhejiang Medical University
M.D.	1982	Jiangxi Medical College

Professional Record:

2003–Present	Associate Professor of Radiation Oncology, University of Michigan

Summary of Evaluation:

Teaching: Dr. Sun has become an excellent teacher. He has organized a course in advanced topics for radiation oncology residents, which is very well received. He lectures to students, residents and post doctoral fellows. He has been a guest lecturer at a number of prestigious universities as well as at scientific meetings. He has been a mentor to Ph.D. students and post doctoral fellows.

Research: Dr. Sun has mainly focused on two important and highly competitive areas of cancer research.

Project #1: E3 ubiquitin ligases

1.) SAG E3 ubiquitin ligase in regulation of apoptosis, hypoxia response, and carcinogenesis: SAG (Sensitive to Apoptosis Gene), originally cloned in Dr. Sun's laboratory, is a dual function protein with antioxidant activity when acting alone, or with E3 ubiquitin ligase activity when complexed with other ligase components. SAG promotes the ubiquitination and degradation of a number of cellular critical proteins, such as p27, caspase-3, HIF-1α, c-Jun, and IκBα to regulate cell proliferation, apoptosis, hypoxia response, and carcinogenesis. This work is supported by NCI grants, UM Munn Research Fund and Charlotte Geyer Foundation.

2.) TRAF2 (TNF Receptor-Associated Factor 2) E3 ligase in regulation of radiation resistance: Resistance of lung cancer to radiation therapy remains a significant therapeutic hindrance with mechanism still elusive. Dr. Sun's laboratory conducted a siRNA library screen and identified TRAF2, a RING-containing E3 ubiquitin ligase and a known cellular survival protein, as a target that sensitized lung cancer cells to radiation upon siRNA silencing. TRAF2 is over-expressed in lung cancer tissues. The work is supported by UM Cancer Center MUNN Idea Fund and Program Project Fund.

Project #2: p53 tumor suppressor in regulation of apoptosis and as a target for drug discovery
1.) RPS27L (Ribosomal Protein S27-Like) as a novel p53 target that regulates p53-induced apoptosis: RPS27L, an unknown gene, was identified by CHIP profiling in Dr. Sun's laboratory and was further characterized as a novel p53 target that mediates p53-induced apoptosis. Current work is to elucidate its function and mechanism of action in p53-mediated apoptosis and tumor suppression using both in vitro cell culture model and in vivo knockout model. This work is supported by the UM Cancer Center MUNN Research Fund and by the Start-Up Fund from Radiation Oncology. The first submission of this RO1 application was reviewed January 21, 2008. It received a priority score of 277 and percentile of 50.2.

2.) p53 synthetic lethal chemical library screen for small molecules and siRNA library screen for siRNA that selectively kill cancer cells with p53 mutation: Synthetic lethality is a situation where a cancer-associated mutation itself is non-lethal, but renders cancer cells susceptible to second hit that become lethal upon inactivation. Dr. Sun's laboratory conducted a synthetic lethal screen of a diversified NCI library (consisting of 3,100 compounds) and identified a lead compound. This preliminary work led to a successful application of an X01 grant (X01-06-4784). So far the Molecular Libraries Screening Centers Network at the NCI has completed HTS of 75,552 compounds. A total of 140 hits were cherry-picked and being counter-screened. Dr. Sun's laboratory has also performed the p53 synthetic lethal screen of a siRNA library and identified a few interesting potential targets, whose siRNA silencing selectively kills lung cancer cells with p53 mutation.

Recent and Significant Publications:

He H, Sun Y: Ribosomal protein S27L is a direct p53 target that regulates apoptosis. *Oncogene* 26:2707-2716, 2007.

Gu Q, Tan M, Sun Y: SAG/ROC2/Rbx2 is a novel AP-1 target that promotes c-Jun degradation and inhibits TPA induced neoplastic transformation. *Cancer Research* 67:3616-3625, 2007.

Gu Q, Bowden T, Normolle D, Sun Y: SAG/ROC2 E3 ligase regulates skin carcinogenesis by stage dependent targeting of c-Jun/AP-1 and IκB-α/NF-κB. *J Cell Biol* 178:1009-1023, 2007.

Tan M, Wang Y, Guan KL, Sun Y: PTGF-β, a type β transforming growth factor (TGF-β) superfamily member, is a p53 target gene that inhibits tumor cell growth via TGF-β signaling pathway. *Proc Natl Acad Sci USA* 97:109-114, 2000.

Duan H, Wang Y, Aviram M, Swaroop M, Loo JA, Bian J, TianY, Mueller T, Bisgaier CL, Sun Y: SAG, a novel zinc RING finger protein that protects cell from apoptosis induced by redox agents. *Mol Cell Biol* 19:3145-3155, 1999.

Service: Dr. Sun has served on departmental search committees. He has represented the Division of Cancer Biology in the planning and oversight for the construction of new departmental laboratories in Medical Science I. He serves on several editorial boards and has been a member of two NCI study sections.

External Review:

Reviewer A: "Dr. Sun has had a very significant impact on the cancer research community and it is clear that his productivity and contributions are continuing at a very high rate indicating that this promotion would indeed be very timely."

Reviewer B: "...Dr. Sun is an outstanding scientist, teacher, and mentor. He has carried important responsibilities for research, supervision, attracting outside funding, and organizing collaborative initiatives."

Reviewer C: "In the area of teaching, Dr. Sun's extensive involvement is demonstrated by the large number of graduate students and postdocs that he mentored, which is a direct outcome of his ability to run a large and productive research program."

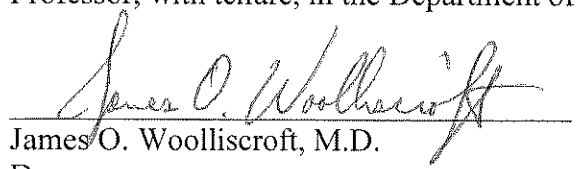
Reviewer D: "He has consistently made seminal contributions to the field of cancer research and investigators around the world are following his work....by all measures, his performance is consistent with and exceeding the requirement for a promotion to the rank of full professor at any major research university."

Reviewer E: "...[Dr. Sun] is precisely the sort of person who will bring successful and high-profile collaborations and funding opportunities to his parent institution."

Reviewer F: "Dr. Sun is an active participant and organizer of various national and international associations. I would like to mention that Dr. Sun's fair and thorough evaluation of NIH applications was very impressive to every member of the NIH Study Section. Taken together, I am certain that Dr. Sun will continue to be very productive and remain as a leader in the field."

Summary of Recommendation:

Dr. Sun left the pharmaceutical field to join our faculty in 2003. His productivity was already obvious before he came to the University (with approximately 100 publications). He has demonstrated stunning success in obtaining extramural funding, and quickly obtained two RO1 grants and an R21 grant in his first few years. Dr. Sun is now recognized internationally as a leader in the area of apoptosis and the role of E3 ubiquitin ligase. He has become an excellent teacher, and runs a very popular advanced topics course in radiation and cancer biology for radiation oncology residents. I enthusiastically support this very deserving promotion to Professor, with tenure, in the Department of Radiation Oncology.



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

May 2008