

PROMOTION RECOMMENDATION
UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL
DEPARTMENT OF BIOLOGICAL CHEMISTRY

Approved by the Regents
May 14, 2009

Roland P.S. Kwok, Ph.D., assistant professor of biological chemistry, Department of Biological Chemistry, Medical School, is recommended for promotion to associate professor of biological chemistry, without tenure, Department of Biological Chemistry, Medical School. [also associate professor of obstetrics and gynecology, with tenure, Department of Obstetrics and Gynecology, Medical School].

Academic Degrees:

Ph.D.	1991	University of Pittsburgh
M.S.	1985	University of Saskatchewan
B.S.	1985	Chu Hai College, Hong Kong

Professional Record:

2006–present	Associate Professor of Obstetrics and Gynecology, University of Michigan
2006-present	Research Associate Professor, Reproductive Sciences Program, Department of Obstetrics and Gynecology, University of Michigan
1998–present	Assistant Professor of Biological Chemistry, University of Michigan
1998–2006	Assistant Professor of Obstetrics and Gynecology, University of Michigan
1998-2006	Research Assistant Professor, Reproductive Sciences Program, Department of Obstetrics and Gynecology, University of Michigan

Summary of Evaluation:

Teaching: Dr. Kwok, since 2000, has been the course co-director of the Biological Chemistry's winter term Critical Analysis (BC597). It is a two-credit class that meets for 1.5 hours twice a week. This class teaches first year Biochemistry graduate students to read and analyze scientific papers. As the course co-director for BC597 (Critical Analysis), Dr. Kwok organized the schedule as well as arranged assignments, and attended all lectures. Dr. Kwok has also taught BC652 (Eukaryotic Gene Expression) from 2001 to 2003, and he has given four one-hour lectures. In 2005, Dr. Kwok gave one 1.5-hour lecture to students, and in 2006, he gave three 1.5-hour lectures in BC650 (Mechanism of Eukaryotic Gene Expression). To date, he has trained six post-doctoral fellows, two graduate students and eight undergraduate students. Dr. Kwok was a member of the thesis committee for seven graduate students, and is currently a dissertation committee member for four graduate students. He has been a member of the preliminary examination committee for nine graduate students and has served on a total of eleven dissertation committees. One of his postdoctoral fellows is a research associate in the Department of Pharmacology at the University

of Michigan, and another is an assistant professor at Brown University. Student evaluations available for all of these classes consistently rank Dr. Kwok's teaching as above average. Dr. Kwok also participates in departmental seminars and, since 1999, he has presented fifteen departmental seminars.

Research: Dr. Kwok's research focuses on the mechanism of gene activation and its regulation, including the cell's learning and memory, hormone production, and the proliferation and differentiation of cell expression. He is researching the roles of CBP in developing mouse oocytes, hoping to identify and characterize factors that interact with CBP in initiating gene activation and whether the interaction between Tax-1 and CBP is important for the pathogenic effects of HTLV-1.

While a postdoctoral fellow, he assisted with the discovery of a protein, CBP, which activates the cAMP dependent signaling pathway, a pathway used by many hormones and neurotransmitters to regulate cellular activities and gene expression. Subsequently, CBP and its homologue p300 were found to be universal coactivators of many classes of transcription factors. The functional roles of CBP in cells are highlighted by the finding that the CBP gene is mutated, causing a reduction in CBP levels in patients with Rubinstein-Taybi syndrome. Furthermore, CBP and p300 are now known to acetylate histones, a process linked to the chromatin remodeling and gene activation, signifying the roles of CBP and p300 in gene transcription. Dr. Kwok, along with Dr. Lundblad, shared the senior authorship of a paper that was the first to show that acetylation of lysine residues within the nuclear localization signal blocks nuclear trafficking of a protein.

Dr. Kwok's collaborative work with Drs. Valerie Castle and Tony Opipari focuses on how HDAC1 inhibitors induce apoptosis of neuroblastoma cells. They have demonstrated that HDAC inhibitors stimulate the release of Bax from the Ku70-Bax complex. His hypothesis is that acetylation of ku70 prevents its association with Bax. Based on these findings, he has been able to develop a model to evaluate the effectiveness of HDACIs as cancer treatment. Dr. Kwok's laboratory is also among the few laboratories in the field devoted to the study of interactions between acetyltransferases and deacetylases and the only laboratory at the University of Michigan specializing in the study of acetylation and deacetylation of proteins. Dr. Kwok and his colleagues were invited to submit a perspective description of their work in *Cell Cycle* and they are planning to submit an R01 application to continue this work. Dr. Kwok's work and collaborations have been published in high-ranking scientific journals.

Recent and Significant Publications:

Subramanian C, Jarzembowski JA, Opipari AW, Castle VP, and Kwok RPS: CREB-binding protein mediates apoptotic effects of a histone deacetylase inhibitor, Trichostatin A, on neuroblastoma cells. *Neoplasia* 9:495-503, 2007.

Kwok RPS, Liu X, and Smith GD: Distribution of co-activators CBP and p300 during mouse oocyte and embryo development. *Molecular Reproduction and Development* 73:885-94, 2006.

Subramanian C, Opipari AW Jr, Bian X, Castle VP, and Kwok RPS: Ku70 acetylation mediates Neuroblastoma cell death induced by histone deacetylase inhibitors. *Proc. Natl Acad Sci USA* 102, 4842-4847, 2005.

Lu Q, Hutchins AE, Doyle CM, Lundblad JR and Kwok RPS: Acetylation of CREB by CBP enhances CREB-dependent transactivation. *J Biol Chem* 278,15727-15734, 2003.

Madison DL, Yaciuk P, Kwok RPS* and Lundblad JR*: Acetylation of the adenovirus-transforming protein E1A determines nuclear localization by disrupting association with Importin- α . *J Biol Chem* 277:38755-38763, 2002. (*Kwok RPS and Lundblad JR contributed equally to this work.)

Service: From 2006-2008, Dr. Kwok served on the Department of Biological Chemistry's Preliminary Examination Committee. Also, from 1999-2000, Dr. Kwok was chair of the Department's seminar committee and also served as an Advisory Committee member to the chair. Dr. Kwok has been a member of the Program Committee and the Training Committee for the Reproductive Sciences Program (2000-2001 and 2007) and (2003-2004 and 2006), respectively. In 2007-2008, Dr. Kwok served as a member on the Student Biomedical Research Program Committee. From 2007-2008, he was director of the International Examination Committee for the Department of Obstetrics and Gynecology. Since 2005, Dr. Kwok has reviewed grants for the Department of Defense and the National Science Foundation.

External Review:

Reviewer A: "His contributions to others' studies have been reflected in his large amount of publications with him as the co-author. Hence, Roland has made important contributions to the field of CREB as well as other CBP-regulated areas. For his excellent work, he has gained several extra-mural grants including one R01 and one American Cancer Society grant and Leukemia Society of America research grant."

Reviewer B: "...it is no surprise that the published studies from his lab are solid, scholarly works. The studies add to the understanding [of] transcriptional regulation and contribute to a large body of work on acetylation and transcription....Overall there is evidence that his judgment and advice are sought at the local and national level....I was favorably impressed by the solid nature of publications from his lab and the pace of publication seemed to be accelerating."

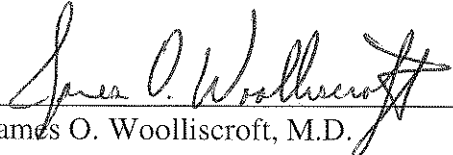
Reviewer C: "His 2003 paper (Lu *et al.*) nicely details the potential role of CREB acetylation by CBP/P300 in modulating CREB dependent transcription. His decision to continue along these lines should provide new insights into this system."

Reviewer D: "Dr. Kwok's research has made important and crucial impact on this field of study. Dr. Kwok is recognized nationally and likely internationally as an emerging and important leader in this scientific area."

Reviewer E: "Dr. Kwok has demonstrated the ability to establish an independent research program and has published a number of important manuscripts in high profile journals that reflects a highly focused body of research."

Summary of Recommendation:

Dr. Kwok has performed very well in teaching, service and research. He is making good progress as an independent investigator and is an excellent academic citizen. I enthusiastically support his promotion to associate professor, without tenure, in the Department of Biological Chemistry.



James O. Woolliscroft, M.D.

Dean

Lyle C. Roll Professor of Medicine

May 2009