

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.
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NAME Mak, Tak W.	POSITION TITLE Director, Senior Staff Scientist, University Professor		
eRA COMMONS USER NAME (credential, e.g., agency login) TAKMAK			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY
University of Wisconsin, Madison, Wisconsin	B.Sc.	06/67	Biochemistry
University of Wisconsin, Madison, Wisconsin	M.Sc.	06/69	Biophysics
University of Alberta, Edmonton, Alberta	Ph.D.	06/72	Biochemistry

A. PERSONAL STATEMENT

My research interests center on immune recognition and regulation as well as cell survival and cell death in normal and malignant cells. I was the leading scientist of the group that first cloned the genes of the human T cell antigen receptor. My more recent work includes leading the creation of a series of genetically altered mice that have proved critical to unraveling intracellular programs governing the development and function of the immune system, and the dissection of signal transduction cascades in various cell survival and apoptotic pathways. My laboratory team is also expert in basic cancer research both in vitro and in vivo. We have published numerous scientific papers on cancer biology, including the initial discovery that the breast cancer susceptibility genes BRCA1 and BRCA2 are related to DNA repair. More recently, we have determined that IDH mutations are involved in cancerogenesis and alterations of epigenetics. In addition to my academic credentials, I have extensive industrial and commercialization experience. Numerous highly respected researchers and scientists in both academia and industry, in Canada as well as around the world, have trained in my laboratory.

B. POSITIONS AND HONORS

Positions and Employment

1974-present Senior Scientific Staff - The Ontario Cancer Institute, Toronto, Ontario
1984 Professor, Department of Med Biophysics, & Immunology, U. of Toronto, Toronto
1979-present Member, Institute of Medical Science, University of Toronto, Toronto
1991-1993 Head, Division of Cellular and Molecular Biology, Ontario Cancer Institute
1993-2002 Founding Director, Amgen Institute, Toronto, Canada
1995-2001 Graduate Secretary, Dept of Med Biophysics, University of Toronto, Toronto
2002-present Director, Advanced Medical Discovery Institute, University Health Network, Toronto
2004-present Director, The Campbell Family for Breast Cancer Research Institute, Princess Margaret Hospital, University Health Network

Committees, Advisory Boards, and Other Professional Activities (selected)

1987-present Fellowship Panel, Cancer Research Institute, New York
1989-2000 T Cell Sciences, Cambridge, Massachusetts
1989-1991 Hong Kong Institute of Biotechnology, Hong Kong
1989-present Cancer Research Inc. New York
1990-1992 Northwestern University, Cancer Center, Chicago
1990-1994 General Motors Award Assembly, New York, N.Y.
1990-1993 R.W. Johnson Research Institute
1990-1993 Allelix Biopharmaceuticals, Canada
1992-present Scientific Advisory Council, Cancer Research Institute, New York
1994-present Induced Mutant Resource at The Jackson Laboratory, Bar Harbor, Maine
1994-present Member of the Advisory Council of the General Motors, Cancer Res Foundation, N.Y.

1995-2003 Lombard Odier Bank, Geneva, Switzerland
 1995-present Honorary Member, The Scandinavian Society for Immunology
 1997-2000 Advisory Board on Cancer Genetics, National Cancer Institute (US)
 1997-2000 Board of Directors, Rigel Inc., California, USA
 1997-present Ad hoc Member, National Cancer Institute (US) Breast Cancer Think Tank
 2002-2005 Board of Directors, Affinium Pharmaceuticals
 2002-2006 Scientific Advisory Board, Institute of Molecular & Cellular Biology, Singapore
 2002 Scientific Advisory Board, Kalypsys Pharmaceuticals
 2003-2006 Boards of Directors, Miikana Therapeutics, Fremont, Calif.
 2003-2006 Chief Scientific Officer, Miikana Corporation, Fremont, Calif.
 2004 Scientific Advisory Board, Affibody, Inc., Stockholm, Sweden
 2002 Scientific Advisory Board, Ohio State University Comprehensive Cancer Center, Ohio
 2006 Scientific Advisory Board, CBR Institute for Biomedical Research Harvard Medical School, Boston, Mass
 2006 Scientific Advisory Board, International Scientific Committee of the Fundacion Caubet-Cimera Illes Balears, Mallorca, Spain
 2006 Chairman, Scientific and Clinical Advisory Board, EntreMed Inc., Rockville, Maryland
 2006 Scientific Advisory Board, Ontario Institute for Cancer Research, Toronto
 2006 Trustee, The Croucher Foundation, Hong Kong
 2007 Scientific Advisory Board, Mayo Clinic Cancer Center, Rochester, MN
 2007 Scientific Advisory Board, Lymphoma Program, MD Anderson Hospital, Houston, Texas
 2007 Scientific Advisory Board, Singapore Health Services Pte Ltd ("SingHealth"), Singapore
 2008 Scientific Advisory Board (Founder), Agios Pharmaceuticals, Cambridge, Mass. USA
 2008 Scientific Advisory Committee, Stand Up To Cancer, American Association for Cancer Research, USA
 2008 Scientific Advisory Board, Immune Disease Institute Inc., Children's Hospital Harvard Medical School, Boston, Mass
 2008 Scientific Advisory Board, European Union Program on Diet, Microbes, and Immunity
 2009 Scientific Advisory Board, MD Anderson Hospital, Houston, Texas

Editorial Boards

Past and present include *Scandinavian Journal of Immunology*, *Immunology Letters*, *Biosciences Report*, *FASEB*, *International Journal of Immunology*, *Cancer Research*, *Cellular Immunology*, *JEM*, *Immunologist*, *Current Opinion in Immunology*, *Cancer Cell PNAS*, *Cell Death Differentiation*, *Nature Press*, *Oncogene*, *Journal of Clinical Immunology and Immunopathology*, *Cancer Cell*, *Expert Reviews in Molecular Medicine*.

Honors

1989 Gairdner International Award, Gairdner Foundation
 1994 Fellow of The Royal Society of London
 1995 King Faisal International Prize for Medicine
 1996 Sloan Prize, General Motors Cancer Research Foundation
 1998 Novartis Immunology Prizes, Novartis, Inc. Basel, Switzerland
 2000 Order of Canada, Governor General of Canada
 2002 Foreign Associate, National Academy of Sciences (US)
 2004 Paul Ehrlich Prize Ludwig Darmstaedter Prize, Republic of Germany
 2005 Member, American Academy of Arts & Sciences, USA
 2007 Premier's Summit Awards in Medical Research, Ontario
 2008 Order of Ontario, Canada
 2008 University of Alberta Alumni Recognition Award
 2009 2009 Inductee to Canadian Medical Hall of Fame, Canada
 2013 Inductee, Fellow of AACR Academy
 2014 Dr. Chew Wei Memorial Prize in Cancer Research, University of British Columbia Faculty Medicine
 2015 Medicine Doctor Honoris Causa, Karolinska Institutet, Stockholm, Sweden

2016 Honorary Medal 2016 of the German Signal Transduction Society/Cell Communication and Signaling (STS/CCS)
2016 6th Anthony Cerami Award in Translational Medicine, USA

C. SELECTED PEER-REVIEWED PUBLICATIONS (*selected from 879*)

1. Vasseur S, Afzal S, Tardivel-Lacombe J, Park DS, Iovanna JL, **Mak TW**. (2009). DJ-1/PARK7 is an important mediator of hypoxia-induced cellular responses. *PNAS* **106**: 1111-16
2. Pellegrini M, Calzascia T, Elford AR, Shahinian A, Lin AE, Dissanayake D, Dhanji S, Nguyen LT, Gronski MA, Morre M, Assouline B, Lahl K, Sparwasser T, Ohashi PS, **Mak TW**. (2009). Adjuvant IL-7 antagonizes multiple cellular and molecular inhibitory networks to enhance immunotherapies. *Nature Med.* **15**: 528-36.
3. Tusche MW, Ward LA, Vu F, McCarthy D, Quintela-Fandino M, Ruland J, Gommerman JL, **Mak TW**. (2009). Differential requirement of MALT1 for BAFF-induced outcomes in B cell subsets. *JEM* **206**: 2671-2683
4. Kamizono S, Duncan GS, Seidel MG, Morimoto A, Hamada K, Grosveld G, Akashi K, Lind EF, Haight JP, Ohashi PS, Look AT, **Mak TW**. (2009). Nfil3/E4bp4 is required for the development and maturation of NK cells *in vivo*. *JEM* **206**: 2977-2986.
5. Berger T, Cheung CC, Elia AJ, **Mak TW**. (2010). Disruption of the Lcn2 gene in mice suppresses primary mammary tumor formation but does not decrease lung metastasis. *PNAS* **107**: 2995-3000.
6. Gross S, Cairns RA, Minden MD, Driggers EM, Bittinger MA, Jang HG, Sasaki M, Jin S, Schenkein DP, Su SM, Dang L, Fantin VR, **Mak TW**. (2010). Cancer-associated metabolite 2-hydroxyglutarate accumulates in acute myelogenous leukemia with isocitrate dehydrogenase 1 and 2 mutations. *J. Exp. Med.* **207**: 339-44.
7. Wilhelm MT, Rufini A, Wetzel MK, Tsuchihara K, Inoue S, Tomasini R, Itie-Youten A, Wakeham A, Arsenian-Henriksson M, Melino G, Kaplan dR, Miller FD, **Mak TW**. (2010). Isoform-specific p73 knockout mice reveal a novel role for {Delta}Np73 in the DNA damage response pathway. *Genes Dev* **24**: 549-560.
8. Cairns RA, Harris IS, **Mak TW**. (2011). Regulation of cancer cell metabolism. *Nat. Rev. Cancer* **11**: 85-95.
9. Zaugg K, Yao Y, Reilly PT, Kannan, K, Kiarash R, Mason J, Huang P, Sawyer SK, Fuerth B, Faubert B, Kalliomäki T, Elia A, Luo X, Nadeem V, Bungard D, Yalavarthi S, Gowney JD, Wakeham A, Moolani Y, Silvester J, You Ten A, Bakker W, Tsuchihara K, Berger SL, Hill RP, Jones RG, Tsao M, Robinson MO, Thompson CB, Pan G, **Mak TW**. (2011). Carnitine Palmitoyltransferase 1C Promotes Cell Survival and Tumor Growth under Conditions of Metabolic Stress. *Genes & Dev* **25**: 1041-1051.
10. Sasaki M, Knobbe CB, Munger JC, Lind EF, Brenner D, Brüstle A, Harris IS, Holmes R, Wakeham A, Haight J, You-Ten A, Li WY, Virtanen C, Reifemberger G, Ohashi PS, Barber DL, Figueroa ME, Melnick A, Zúñiga-Pflücker JC, **Mak TW**. (2012). Idh1-R132H mutation increases murine haematopoietic progenitors and alters epigenetics. *Nature* **488**: 656-659.
11. McIlwain DR, Lang PA, Maretzky T, Hamada K, Ohishi K, Maney SK, Berger T, Murthy A, Duncan G, Xu HC, Lang KS, Häussinger D, Wakeham A, Itie-Youten A, Khokha R, Ohashi PS, Blobel CP, **Mak TW**. (2012). iRhom2 Regulation of TACE Controls TNF-Mediated Protection Against *Listeria* and Responses to LPS. *Science* **335**: 229-232.
12. Brüstle A, Brenner D, Knobbe CB, Lang PA, Virtanen C, Hershenfield BM, Reardon C, Lacher SM, Ruland J, Ohashi PS, **Mak TW**. (2012). The NF- κ B regulator MALT1 determines the encephalitogenic potential of Th17 cells. *J. Clin. Invest* **122**: 4698-709.
13. Lang KS, Lang PA, Meryk A, Pandya AA, Boucher LM, Pozdeev VI, Tusche MW, Göthert JR, Haight J, Wakeham A, You-Ten AJ, McIlwain DR, Merches K, Khairnar V, Recher M, Nolan GP, Hitoshi Y, Funkner P, Navarini AA, Verschoor A, Shaabani N, Honke N, Penn LZ, Ohashi PS, Häussinger D, Lee KH, **Mak TW**. (2013) Involvement of Toso in activation of monocytes, macrophages, and granulocytes. *PNAS* **110**: 2593-8.
14. Reardon C, Duncan GS, Brüstle A, Brenner D, Tusche MW, Olofsson P, Rosas-Ballina M, Tracey KJ, **Mak TW**. (2013). Lymphocyte-derived Ach regulates local innate but not adaptive immunity. *PNAS* **110**: 1410-5.
15. Gorrini C, Harris IS, **Mak TW**. (2013). Modulation of oxidative stress as an anticancer strategy. *Nat. Rev. Drug Discovery* **12**: 931-47.
16. Gorrini C, Baniyasadi PS, Harris IS, Silvester J, Inoue S, Snow B, Joshi PA, Wakeham A, Molyneux SD, Martin B, Martin B, Bouwman P, Cescon DW, Elia AJ, Winterton-Perks Z, Cruickshank J, Brenner D, Tseng A, Musgrave M, Berman HK, Khokha R, Jonkers J, **Mak TW**, Gauthier ML. (2013). BRCA1 interacts with Nrf2 to regulate antioxidant signaling and cell survival. *J. Ex. Med* **210**: 1529-1544.

17. Inoue S, Hao Z, Elia AJ, Cescon D, Zhou L, Silvester J, Snow B, Harris IS, Sasaki M, Li WY, Itsumi M, Yamamoto K, Ueda T, Dominguez-Brauer C, Gorrini C, Chio II, Haight J, You-Ten A, McCracken S, Wakeham A, Ghazarian D, Penn LJ, Melino G, **Mak TW**. (2013). Mule/Huwe1/Arf-BP1 suppresses Ras-driven tumorigenesis by preventing c-Myc/Miz1-mediated down-regulation of p21 and p15. *Genes Dev* 27: 1101-1114.
18. Lin AE, Ebert G, Ow Y, Preston SP, Toe JG, Cooney JP, Scott HW, Sasaki M, Saibil SD, Dissanayake D, Kim RH, Wakeham A, You-Ten A, Shahinian A, Duncan G, Silvester J, Ohashi PS, **Mak TW**, Pellegrini M. (2013). ARIH2 is essential for embryogenesis, and its hematopoietic deficiency causes lethal activation of the immune system. *Nature Imm* 14: 27-33.
19. Reardon C, Duncan GS, Brustle A, Brenner D, Tusche MW, Olofsson PS, Rosas-Ballina M, Tracey KJ, **Mak TW**. (2013). Lymphocyte-derived ACh regulates local innate but not adaptive immunity. *PNAS* 110: 1410-1415.
20. Brenner D, Brustle A, Lin GH, Lang PA, Duncan GS, Knobbe-Thomsen CB, St Paul M, Reardon C, Tusche MW, Snow B, Hamilton SR, Pfefferle A, Gilani SO, Ohashi PS, Lang KS, **Mak TW**. (2014). Tso controls encephalitogenic immune responses by dendritic cells and regulatory T cells. *PNAS* 111: 1060-1065.
21. Inoue S, Tomasini R, Rufini A, Elia AJ, Agostini M, Amelio I, Cescon D, Dinsdale D, Zhou L, Harris IS, Lac S, Silvester J, Li WY, Sasaki M, Haight J, Brüstle A, Wakeham A, McKerlie C, Jurisicova A, Melino G, **Mak TW**. (2014). TAp73 is required for spermatogenesis and the maintenance of male fertility. *PNAS* 111: 1843-1848.
22. Gorrini C, Gang BP, Bassi C, Wakeham A, Baniasadi SP, Hao Z, Li WY, Cescon DW, Li YT, Molyneux S, Penrod N, Lupien M, Schmidt EE, Stambolic V, Gauthier ML, **Mak TW**. (2014). Estrogen controls the survival of BRCA1-deficient cells via a PI3K-NRF2-regulated pathway. *PNAS* 111:4472-7.
23. Mason, J.M., Lin, D. C-C., Wei, X., Che, Y., Yao, Y., Kiarash, R., Cescon, D.W., Fletcher, G.C., Awrey, D.E., Bray, M.R., Pan, G., and **Mak, T.W.** (2014) Functional Characterization of CFI-400945, a PLK4 Inhibitor, as a Potential Anticancer Agent. *Cancer Cell* 26: 163-176.
24. Cescon, D.W., Gorrini, C., and **Mak, T.W.** (2015) Breaking up Is Hard to Do: PI3K Isoforms on the Rebound. *Cancer Cell* 27: 5-7.
25. Harris, I.S., Treloar, A.E., Inoue, S., Sasaki, M., Gorrini, C., Lee, K.C., Yung, K.Y., Brenner, D., Knobbe-Thomsen, C.B., Cox, M.A., Elia, A., Berger, T., Cescon, D.W., Adeoye, A., Brustle, A., Molyneux, S.D., Mason, J.M., Li, W.Y., Yamamoto, K., Wakeham, A., Berman, H.K., Khokha, R., Done, S.J., Kavanagh, T.J. Lam, C.W., and **Mak, T.W.** (2015) Glutathione and Thioredoxin Antioxidant Pathways Synergize to Drive Cancer Initiation and Progression. *Cancer Cell* 27: 211-222.
26. Afzal, S., Hao, Z., Itsumi, M., Abouelkheer, Y., Brenner, D., Gao, Y., Wakeham, A., Hong, C., Li, W.Y., Silvester, J., Gilani, S.O., Brustle, A., Haight, J., You-Ten, A.J., Lin, G.H., Inoue, S., and **Mak, T.W.** (2015) Autophagy-independent functions of UVRAG are essential for peripheral naïve T-cell homeostasis. *Proc Natl. Acad. Sci. USA* 112: 1119-1124.
27. Brenner D, Blaser H, **Mak TW**. (2015) Regulation of tumour necrosis factor signalling: live or let die. *Nat Rev Immunol.*; 15(6):362-74
28. Inoue S, Li WY, Tseng A, Beerman I, Elia AJ, Bendall SC, Lemonnier F, Kron KJ, Cescon DW, Hao Z, Lind EF, Takayama N, Planello AC, Shen SY, Shih AH, Larsen DM, Li Q, Snow BE, Wakeham A, Haight J, Gorrini C, Bassi C, Thu KL, Murakami K, Elford AR, Ueda T, Straley K, Yen KE, Melino G, Cimmino L, Aifantis I, Levine RL, De Carvalho DD, Lupien M, Rossi DJ, Nolan GP, Cairns RA, **Mak TW**. (2016) Mutant IDH1 Downregulates ATM and Alters DNA Repair and Sensitivity to DNA Damage Independent of TET2. *Cancer Cell.*; 30(2):337-48
29. Dominguez-Brauer C, Hao Z, Elia AJ, Fortin JM, Nechanitzky R, Brauer PM, Sheng Y, Mana MD, Chio II, Haight J, Pollett A, Cairns R, Tworzanski L, Inoue S, Reardon C, Marques A, Silvester J, Cox MA, Wakeham A, Yilmaz OH, Sabatini DM, van Es JH, Clevers H, Sato T, **Mak TW**. (2016) Mule Regulates the Intestinal Stem Cell Niche via the Wnt Pathway and Targets EphB3 for Proteasomal and Lysosomal Degradation. *Cell Stem Cell.*; 19(2):205-16
30. Lemonnier F, Cairns RA, Inoue S, Li WY, Dupuy A, Broutin S, Martin N, Fataccioli V, Pelletier R, Wakeham A, Snow BE, de Leval L, Pujals A, Haioun C, Paci A, Tobin ER, Narayanaswamy R, Yen K, Jin S, Gaulard P, **Mak TW**. (2016) The IDH2 R172K mutation associated with angioimmunoblastic T-cell lymphoma produces 2HG in T cells and impacts lymphoid development. *Proc Natl Acad Sci U S A.*; 113(52):15084-15089
31. Ye J, Gu Y, Zhang F, Zhao Y, Yuan Y, Hao Z, Sheng Y, Li WY, Wakeham A, Cairns RA, **Mak TW**. (2016) IDH1 deficiency attenuates gluconeogenesis in mouse liver by impairing amino acid utilization *Proc Natl Acad Sci U S A*. 2016 Dec 23.