

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Margolis, Benjamin	POSITION TITLE Professor		
eRA COMMONS USER NAME (credential, e.g., agency login) bmargoli			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
University of Manitoba, Manitoba, Canada		1975-77	
University of Manitoba Medical School	M.D.	1977-81	Medicine

A. Positions and Honors.

Positions and Employment

1981-1982 Internship, The University of Texas Health Science Center
 1982-1983 Research Fellow, The University of Texas Health Science Center, Department of Medicine, Division of Renal Diseases
 1983-1985 Internal Medicine Resident, The University of Texas Health Science Center
 1985-1986 Clinical Nephrology Resident, The University of Toronto, Toronto General Hospital, St. Michael's Hospital
 1986-1988 Research Nephrology Fellow, The University of Toronto, Department of Medicine, Division of Nephrology
 1988-1989 Postdoctoral Fellow, Rorer Biotechnology, Inc.
 1990-1991 Instructor, Department of Pharmacology, New York University Medical Center
 1991-1995 Assistant Professor, Department of Pharmacology, New York University Medical Center
 1995-1998 Assistant Investigator, Howard Hughes Medical Institute
 1995-2000 Associate Professor, Departments of Internal Medicine and Biological Chemistry, University of Michigan Medical School
 1998-2005 Associate Investigator, Howard Hughes Medical Institute
 1999-2008 Co-Director, Cancer Center Cell Biology, University of Michigan
 2000-present Professor, Departments of Internal Medicine and Biological Chemistry, University of Michigan
 2006-present Associate Chair for Basic Research, Department of Internal Medicine, University of Michigan
 2008-present Director, Student Biomedical Research Program, University of Michigan Medical School

Honors

Lucille P. Markey Scholar
 Kaplan Scholar Award
 1997 American Society of Nephrology Young Investigator Award
 2001 University of Michigan Faculty Recognition Award

B. Selected peer-reviewed publications (from total of 109).

1. Blaikie P., Immanuel D., Wu J., Li N., Yajnik V. and **Margolis B.** A region of Shc distinct from the SH2 domain can bind tyrosine phosphorylated growth factor receptors. *J. Biol. Chem.* 269:32031-32034, 1994.
2. Bork P. and **Margolis B.** A phosphotyrosine interaction domain. *Cell* 80:693-694, 1995.
3. Ooi J., Yajnik V., Immanuel D., Buchberg A. and Margolis B. The cloning of Grb10 reveals a new family of SH2 domain proteins. *Oncogene* 10:1621-1630, 1995.
4. Yajnik V., Blaikie P., Bork P. and **Margolis B.** Identification of residues within the Shc PTB/PI domain crucial for phosphopeptide interaction. *J. Biol. Chem.* 271:1813-1816, 1996.
5. Borg JP., Ooi J., Levy E. and **Margolis B.** The PI domains of X11 and FE65 to distinct sites on the YENPTY motif of amyloid precursor protein. *Mol. Cell. Biol.* 16:6229-6241, 1996.
6. Blaikie P., Fournier E., Dilworth S.M., Birnbaum D., Borg JP. and **Margolis B.** The role of the Shc PI/PTB domain and tyrosine phosphorylation sites in polyoma middle T antigen-mediated cell transformation. *J. Biol. Chem.* 272:20671-20677, 1997.

7. Borg JP., Straight S., Kaech S.M., de Taddeo-Borg M., Kroon D.E., Karnak D., Turner R.S., Kim S.K. and Margolis B. Identification of an evolutionarily conserved heterotrimeric protein complex involved in protein targeting. *J. Biol. Chem.* 273:31633-31636, 1998.
8. Kamberov E., Makarova O., Roh M., Liu A., Karnak D., Straight S. and **Margolis B.** Molecular cloning and characterization of Pals, proteins associated with mLin-7. *J. Biol. Chem.*, 275:11425-11431, 2000.
9. Straight S.W., Karnak D., Borg J-P., Kamberov E., Dare H., Wade J.B. and **Margolis B.** mLin-7 is localized to the basolateral surface of epithelia via its amino-terminus. *Amer J. Phys.* 278/3:F464-475, 2000.
10. Doerks T., Bork P., Kamberov E., Makarova O., Muecke S. and **Margolis B.** L27, a novel heterodimerization domain in receptor targeting proteins Lin-2 and Lin-7. *TIBS* 25:317-318, 2000.
11. Borg JP., Marchetto S., Le Bivic A., Ollendorff V., Jaulin-Bastard F., Saito H., Fournier E., Adelaide J., **Margolis B.** and Birnbaum D. ERBIN: A basolateral PDZ protein that interacts with the mammalian ERBB2/HER2 receptor. *Nature Cell Biology* 2:407-414, 2000.
12. Verhey K.J., Meyer D., Deehan R., Blenis J., Schnapp B.J., Rapoport T.A. and **Margolis B.** Cargo of kinesin identified as JIP scaffolding proteins and associated signaling molecules. *J. Cell Biol.* 152:959-970, 2001.
13. Straight S.W., Chen L., Karnak D. and **Margolis B.** Interactions with mLin-7 alters the targeting of endocytosed transmembrane proteins in mammalian epithelial cells. *Mol. Biol. Cell* 12:1329-1340, 2001..
14. Roh M.H., Makarova O., Liu C., Shin KY, Lee S., Laurinec S., Goyal M., Wiggins R. and **Margolis B.** The Maguk protein, Pals1, function as an adapter linking mammalian homologues of Crumbs and Discs Lost. *J. Cell Biol.* 157: 161-172, 2002.
15. Roh MH, Liu CJ, Laurinec S and **Margolis B.** The carboxy-terminus of Zona Occludens-3 binds and recruits a mammalian homologue of discs lost to tight junctions. *J Biol Chem.* 277:27501-9, 2002.
16. Patrie KM, Drescher AJ, Welihinda A, Mundel P and **Margolis B.** Interaction of two actin-binding proteins, synaptopodin and a-actinin-4, with the tight junction protein MAGI-1. *J Biol Chem.* 277:30183-90, 2002.
17. Hurd TW, Gao L, Roh MH, Macara IG, and. Direct interaction of two polarity complexes implicated in epithelial tight junction assembly. *Nat Cell Biol.* 5:137-42 **Margolis B.** 2003.
18. Roh M.H., Fan S., Liu, C-J. and **Margolis, B.** The Crumbs3/Pals1 Complex Participates in the Establishment of Polarity in Mammalian Epithelial Cells. *J. Cell Sci.*, 116:2895-906, 2003.
19. Hurd, T.W., Fan, S., Liu, C-J., Kweon, HY, Hakansson, K., and **Margolis B.** Phosphorylation-dependent binding of 14-3-3 to the polarity protein Par3 regulates cell polarity in mammalian epithelia. *Current Biology*, 13:2082-90, 2003.
20. Straight, S.W., Shin K., Fogg V.C., Fan S., Liu C.J., Roh M., and **Margolis B.** Loss of PALS1 expression leads to tight junction and polarity defects. *Mol Biol Cell.* 15:1981-90, 2004.
21. Wang Q, Hurd TW, **Margolis B.** Tight junction protein Par6 interacts with an evolutionarily conserved region in the amino-terminus of PALS1/stardust. *J Biol Chem.* 279:30715–30721, 2004
22. Li Y, Karnak D, Demeler B, **Margolis B** and Lavie A. Structural basis for L27 domain-mediated assembly of signaling and cell polarity complexes. *EMBO J.* 23:2723-33, 2004
23. Fan S., Hurd T.W., Liu C.J., Straight S.W., Weimbs T., Hurd E.A., Domino S.E., and **B. Margolis.** Polarity proteins control ciliogenesis via kinesin motor interactions. *Current Biology*, 14:1451-61, 2004.
24. Shin, K, Straight S. and **Margolis, B.** PATJ Regulates Tight Junction Formation and Polarity in Mammalian Epithelial Cells. *J. Cell Biol*, 168:705-11, 2005
25. Fogg, VC, Liu, CJ, and **Margolis, B.** Multiple regions of Crumbs3 are required for tight junction formation in MCF10A cells. *J. Cell. Sci.* 118:2859-69, 2005.
26. Khanna H, Hurd TW, Lillo C, Shu X, Parapuram SK, He S, Akimoto M, Wright AF, **Margolis B**, Williams DS, Swaroop A., RPGR-ORF15, which is mutated in retinitis pigmentosa, associates with SMC1, SMC3, and microtubule transport proteins. *J Biol Chem.* 280:33580-7, 2005
27. Straight SW, Pieczynski JN, Whiteman EL, Liu CJ, **Margolis B.** Lin-7 stabilizes polarity protein complexes. *J Biol Chem.* 281:37738-47, 2006.
28. Jenkins PM, Hurd TW, Zhang L, McEwen DP, Brown RL, **Margolis B**, Verhey KJ, Martens JR., Ciliary targeting of olfactory CNG channels requires the CNGB1b subunit and the kinesin-2 motor protein, KIF17. *Curr Biol.* 16:1211-6, 2006.
29. Wang Q, Chen XW, **Margolis B.** PALS1 Regulates E-Cadherin Trafficking in Mammalian Epithelial Cells. *Mol Biol Cell.* 18:874-85, 2007.
30. Shin K, Wang Q, **Margolis B.** PATJ regulates directional migration of mammalian epithelial cells. *EMBO Rep.* 8:158-64, 2007.
31. Fan S, Fogg V, Wang Q, Chen XW, Liu CJ, **Margolis B.** A novel Crumbs3 isoform regulates cell division and ciliogenesis via importin β interactions. *J. Cell. Biol*, 178:387-98, 2007
32. Whiteman E.L., Liu C.J., Fearon E.R. and **Margolis B.** The transcription factor snail represses Crumbs3 expression and disrupts apico-basal polarity complexes. *Oncogene*, 27:3875-9, 2008.
33. Schlüter M.A., Pfarr, C.S., Pieczynski J., Whiteman E.L., Hurd T.W., Fan S., Liu C.J., and Margolis B. Trafficking Of Crumbs3 During Cytokinesis Is Crucial For Lumen Formation. *Molecular Biology of the Cell*, in press

C. Research Support.

Ongoing Research Support

NIH 2R01DK058208-05 (Margolis)
NIH 07/01/05-06/30/10
Tight Junction Proteins and Epithelial Polarity

This is the funded renewal for the RO1 grant "Targeting By mLin-7 Binding Partners In Renal Epithelia". It has three specific aims: to understand the mechanism of PATJ targeting in nonpolarized and polarized epithelial cells; to identify the domains of PATJ that are crucial for protein trafficking, tight junction formation and apico-basal polarization and to better understand the role of the PALS1 protein-protein interaction domains in PALS1 trafficking and function. Role: PI

NIH 1R01DK069605-01 (Margolis)
NIH 2/15/05-1/30/10
Title: Crumbs3 in epithelial polarity and ciliogenesis

This proposal aims to study the role of the apical transmembrane protein Crumbs3 in cell polarity and ciliogenesis. The specific aims will exam the residues that target Crumbs3 to the apical membrane and the effects of reducing Crumbs3 expression by siRNA. It will also study Crumbs3 targeting to cilia and the proteins that interact with Crumbs3 in cilia. Role: PI

NIH 1R01DK DK084725 (Margolis)
NIH 9/28/2009 to 7/31/2011
Title: Novel Cilia Trafficking Mechanisms

This proposal aims to study the role of the Ran GTPase and its Importin binding partners in the trafficking of cilia proteins
Role: PI

PKD Foundation Research Grant in Aid 3/1/08-2/30/10
Title: Regulation of Ciliary Trafficking by RP2

This application proposes to examine the role of the Retinitis Pigmentosa 2 protein in the cilia trafficking of polycystin2.
Role: PI

2T35HL007690-26A2
NIH 05/01/1980-03/31/13
Title: Short Term Biomedical Research Training Program for Medical Students

This grant supports summer research experiences for medical students. I have assumed the role of PI from Dr. Robert Todd.

Completed Research Support

5 P30 CA46592 Cancer Center Support Grant (Wicha)
NIH 6/01/06 – 12/1/08

The core grant supports the senior leadership, programs and shared facilities of the Cancer Center. The Center provides the organizational framework to promote interdisciplinary research through the development of defined clinical, basic science and prevention programs in cancer research, and the development and support of shared resources. Role: Co-Director Cancer Cell Biology Program

2P50DK39255-16A (Wiggins)

NIH

9/01/03-2/28/09 (no cost extension)

Biology of the Glomerular Podocyte

Project Title: Junctional Proteins of the Slit Diaphragm

To examine the role of Pals1 and associated proteins in the junctional complex at the podocyte slit diaphragm. This proposal will also examine another PDZ protein Magi-1 that is found in the glomerulus. Role: PI Subproject.