

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 Sean J. Morrison	POSITION TITLE Professor		
eRA COMMONS USER NAME (credential, e.g., agency login) gandym			
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
Dalhousie University, Halifax, Canada	BSc	1986-1991	Biology and Chemistry
Stanford University, Palo Alto, CA	Ph.D	1991-1996	Immunology
California Institute of Technology, Pasadena, CA	Fellow	1996-1999	Neurobiology

A. Research and Professional Experience

1986 - 1990 President and Director of Endogro Systems Inc.
 1991 - 1996 Graduate student in the laboratory of Dr. Irving L. Weissman, Stanford University
 1996 - 1999 Postdoctoral scholar in the lab of Dr. David J. Anderson, California Inst. of Technology.
 1999 - 2004 Assistant Professor, Department of Internal Medicine, University of Michigan
 2000 - present Investigator, Howard Hughes Medical Institute
 2004 - 2008 Associate Professor, Department of Internal Medicine, University of Michigan
 2005 - 2008 Research Associate Professor, Life Sciences Institute, University of Michigan
 2005 - present Director, University of Michigan Center for Stem Cell Biology
 2005 - present Henry Sewall Professor of Medicine
 2008 - present Professor, Department of Internal Medicine, University of Michigan
 2008 - present Research Professor, Life Sciences Institute, University of Michigan

Honors and Awards

1986 Young Canadians Award for Excellence in Science.
 1991 Dalhousie University Medal in Biology
 1991 Natural Sciences and Engineering Research Council 1967 Scholarship (declined).
 1991-1996 Howard Hughes Institute Predoctoral Fellowship in Biological Sciences.
 1996-1998 Natural Sciences and Engineering Research Council Postdoctoral Fellowship.
 1997-1998 American Cancer Society, California Division Junior Postdoctoral Fellowship.
 1999 American Cancer Society, California Division Senior Postdoctoral Fellowship.
 2000-2003 Searle Scholar
 2002 Named to TR100 list: MIT Technology Review Magazine's list of 100 young innovators
 2003 Wired Magazine Rave Award for Science
 2003 Presidential Early Career Award for Scientists and Engineers, White House
 2004 Dean's Award for Basic Science, University of Michigan Medical School
 2006 Detroit News Michiganiaan of the Year
 2007 Pfizer Young Michigan Biomedical Investigator of the Year Award
 2007 McCulloch and Till Award, International Society for Hematology and Stem Cells
 2008 American Association of Anatomists Harland Winfield Mossman Award
 2009 MERIT Award, National Institute on Aging, National Institutes of Health

B. Selected Peer-Reviewed Publications (Partial Listing – 42 of 71 publications):

1. Morrison, S.J., and I.L. Weissman. 1994 The long term repopulating subset of hematopoietic stem cells is deterministic and isolatable by phenotype. *Immunity* 1:661-673.

2. **Morrison, S.J.**, H.D. Hemmati, A.M. Wandycz, and I.L. Weissman. 1995. The purification and characterization of fetal liver hematopoietic stem cells. Proc. Natl. Acad. Sci. USA 92:10302-10306.
3. **Morrison, S.J.**, K.R. Prowse, P. Ho, and I.L. Weissman. 1996. Telomerase activity in hematopoietic cells is associated with self-renewal potential. Immunity 5:207-216.
4. **Morrison, S.J.**, A.M. Wandycz, K. Akashi, A. Globerson, and I.L. Weissman. 1996. The aging of hematopoietic stem cells. Nature Medicine 2:1011-1016.
5. **Morrison, S.J.**, N.M. Shah, and D.J. Anderson. 1997. Regulatory mechanisms in stem cell biology. Cell 88:287-298.
6. **Morrison, S.J.**, P.M. White, C. Zock, and D.J. Anderson. 1999. Prospective identification, isolation by flow cytometry and in vivo self-renewal of multipotent mammalian neural stem cells. Cell 96:737-749.
7. **Morrison, S.J.**, S.E. Perez, J.M. Verdi, C. Hicks, G. Weinmaster, D.J. Anderson. 2000. Notch activation instructs rapid glial differentiation by multipotent neural crest stem cells. Cell 101:499-510
8. Reya, T.,* **Morrison, S.J.**,* Clarke, M.F. and Weissman, I.L. 2001. Stem cells, cancer, and cancer stem cells. Nature 414:105-111. * These two authors contributed equally
9. **Morrison, S.J.** and S.H. Orkin. 2002. Stem-cell competition. Nature 418:25-27.
10. Bixby, S., G.M.. Kruger, J.T. Mosher, N. Joseph, and **S.J. Morrison**. 2002. Cell-intrinsic differences between neural stem cells from different regions of the peripheral nervous system regulate the generation of neural diversity. Neuron 35:643-656.
11. Kruger, G.M., J. Mosher, S. Bixby, N. Joseph, T. Iwashita, and **S.J. Morrison**. 2002. Neural crest stem cells persist in the adult gut but undergo perinatal changes in self-renewal potential, neuronal subtype potential, and responsiveness to lineage determination factors. Neuron 35:657-669.
12. Kruger, G.M. and **S.J. Morrison**. 2002 Brain repair by endogenous progenitors. Cell 110:399-402.
13. Al-Hajj, M., M.S. Wicha, A. Benito-Hernandez, **S.J. Morrison**, and M.F. Clarke. 2003. Prospective identification of tumorigenic breast cancer cells. Proc. Natl. Acad. Sci. USA 100:3983-3988.
14. Park, I-K, Q. Dalong, M. Kiel, M.W. Becker, M. Pihalja, I.L. Weissman, **S.J. Morrison**, and M.F. Clarke. 2003. Bmi-1 is required for maintenance of adult self-renewing haematopoietic stem cells. Nature 423:302-305.
15. Iwashita, T., G.M. Kruger, R. Pardal, M.J. Kiel, and **S.J. Morrison**. 2003. Hirschsprung disease is linked to defects in neural crest stem cell function. Science 301:972-976.
16. Molofsky, A.V., R. Pardal, T. Iwashita, I-K. Park, M.F. Clarke, and **S.J. Morrison**. 2003. *Bmi-1* dependence distinguishes stem cell self-renewal from restricted progenitor proliferation. Nature 425:962-967.
17. Alvarez-Dolado, M., R. Pardal, J.M. Garcia-Verdugo, J.R. Fike, H.O. Lee, K. Pfeffer, C. Lois, **S.J. Morrison** and A. Alvarez-Buylla. 2003. Fusion of bone-marrow-derived cells with Purkinje neurons, cardiomyocytes and hepatocytes. Nature 425:968-973.
18. Pardal, R., M.F. Clarke, and **S. J. Morrison**. 2003. Applying the principles of stem cell biology to cancer. Nature Reviews Cancer 3:895-902.
19. Kruger G.M., Mosher, J.T., Y.H. Tsai, K.J. Yeater, T. Iwashita, C. E. Gariepy and **S.J. Morrison**. 2003. Temporally distinct requirements for endothelin receptor B in the generation and migration of gut neural crest stem cells. Neuron 40:917-929.
20. Joseph, N.M., Y. Mukoyama, J.T. Mosher, M. Jaegle, S.A. Crone, E-L. Dormand, K-F. Lee, D. Meijer, D.J. Anderson and **S.J. Morrison**. 2004. Neural crest stem cells undergo multilineage differentiation in developing peripheral nerves to generate endoneurial fibroblasts in addition to Schwann cells. Development 131:5599-5612.
21. Kim, I., O.H. Yilmaz, and **S.J. Morrison**. 2005. CD144 (VE-cadherin) is transiently expressed by fetal liver hematopoietic stem cells. Blood 106:903-905.
22. Molofsky, A.V., S. He, M. Bydon, **S.J. Morrison**, and R. Pardal. 2005. Bmi-1 promotes neural stem cell self-renewal and neural development but not mouse growth and survival by repressing the p16^{Ink4a} and p19^{Af} senescence pathways. Genes and Development 19:1432-1437.
23. Kiel, M.J., O.H. Yilmaz, T. Iwashita, O.H. Yilmaz, C. Terhorst, and **S.J. Morrison**. 2005. SLAM family receptors distinguish hematopoietic stem and progenitor cells and reveal endothelial niches for stem cells. Cell 121:1109-1121.

24. Joseph, N.M. and **S.J. Morrison**. 2005. Toward an understanding of the physiological function of mammalian stem cells. Developmental Cell 9:173-183.
25. Yilmaz, O.H., M.J. Kiel, and **S.J. Morrison**. 2006. SLAM family markers are conserved among hematopoietic stem cells from old and reconstituted mice and markedly increase stem cell purity. Blood 107:924-930.
26. Kim, I., S. He, O. Yilmaz, M.J. Kiel, and **S. J. Morrison**. 2006. Enhanced purification of fetal liver hematopoietic stem cells using SLAM family receptors. Blood108:737-744.
27. Yilmaz, O.H., R. Valdez, B. Theisen, W. Guo, D. Ferguson, H. Wu, **S.J. Morrison**. 2006. Pten dependence distinguishes haematopoietic stem cells from leukaemia-initiating cells. Nature 441:475-482.
28. **Morrison, S. J.**, J. Kimble. 2006. Asymmetric and symmetric stem-cell divisions in development and cancer. Nature 441:1068-1074.
29. Molofsky, A.V., S.G. Slutsky, N.M. Joseph, S. He, R. Pardal, J. Krishnamurthy, N. Sharpless and **S.J. Morrison**. 2006. Increasing *Ink4a* expression decreases forebrain progenitor function and neurogenesis during ageing. Nature 443:448-452.
30. Taylor, M.K., K. Yeager and **S.J. Morrison**. 2007. Physiological Notch signaling promotes gliogenesis in the peripheral and central nervous systems. Development 134:2435-2447. PMID: PMC2653864
31. Kim, I., T.L. Saunders, and **S.J. Morrison**. 2007. Sox17 dependence distinguishes the transcriptional regulation of fetal from adult hematopoietic stem cells. Cell 130:470-483.
32. Kiel, M., G.L. Radice and **S.J. Morrison**. 2007. Lack of evidence that hematopoietic stem cells depend on N-cadherin-mediated adhesion to osteoblasts for their maintenance. Cell Stem Cells 1:204-217.
33. Kiel, M., S. He, R. Ashkenazi, S.N. Gentry, M. Teta, J.A. Kushner, T.L. Jackson and **S. J. Morrison**. 2007. Hematopoietic stem cells do not asymmetrically segregate chromosomes or retain bromodeoxyuridine. Nature 449:238-242. PMID: 17728714.
34. Joseph, N.M., J.T. Mosher, J. Buchstaller, P. Snider, P.E. McKeever, M. Lim, S. J. Conway, L.F. Parada, Y. Zhu, and **S. J. Morrison**. 2008. The loss of Nf1 transiently promotes self-renewal but not tumorigenesis by neural crest stem cells. Cancer Cell 13: 129-140. PMID: 18242513.
35. **Morrison, S.J.** and A. Spradling. 2008. Stem Cells and Niches: Mechanisms that promote stem cell maintenance throughout life. Cell 132: 598-611. PMID: 18295578.
36. Kiel, M.J. and **S.J. Morrison**. 2008. Uncertainty in the niches that maintain haematopoietic stem cells. Nature Reviews Immunology 8: 290-301. PMID: 18323850.
37. Kiel M.J., O.H. Yilmaz, and **S.J. Morrison**. 2008. CD150- cells are transiently reconstituting multipotent progenitors with little or no stem cell activity. Blood 111: 4413-4. PMID: 18398056.
38. Nishino, J., I. Kim, K. Chada, and **S.J. Morrison**. 2008. Hmga2 promotes neural stem cell self-renewal in young, but not old, mice by reducing p16^{Ink4a} and p19^{Arf} expression. Cell 135: 227-239. PMID: 18957199.
39. Levi, B.P., O.H. Yilmaz, G. Duyster, and **S.J. Morrison**. 2008. Aldehyde dehydrogenase 1a1 is dispensable for stem cell function in the mouse hematopoietic and nervous systems. Blood 113: **1670-1680**. PMID: 18971422.
40. Quintana, E., M. Shackleton, M. Sabel, D. Fullen, T.M. Johnson and **S.J. Morrison**. 2008. Efficient tumor formation by single human melanoma cells. Nature 456: 593-598. PMID: PMC2597380
41. Kiel M.J., M. Acar, G.L. Radice and **S.J. Morrison**. 2009. Hematopoietic stem cells do not depend on N-cadherin to regulate their maintenance. Cell Stem Cell 4: 170-179. PMID: 19119091.
42. Shackleton, M., E. Quintana, E.R. Fearon, and **S.J. Morrison**. 2009. Heterogeneity in cancer: cancer stem cells versus clonal evolution. Cell In Press.

C. Ongoing Research Support

001823 (PI, Morrison) Howard Hughes Medical Institute Funding is not associated with a specific project	6/1/05-6/30/12
2 R37 AG024945 06 (PI, Morrison) NIH/NIA (MERIT Award) "The Regulation of Stem Cell Aging"	9/01/09-7/31/14 Direct Costs: \$205,000/year

The goals of this project are to test whether let-7 microRNAs, the JunB transcription factor, and the p19Arf tumor suppressor regulate the decline in neural stem cell function and neurogenesis during aging.

R01 NS40750-02 (PI, Morrison) 2/1/01-8/31/09

NIH/NINDS

“Stem Cells in Peripheral Nervous System Development”

The goals of this project are to study the types of cells that arise in peripheral nerves from neural crest stem cells (NCSCs), whether NCSCs persist into late gestation in other regions of the fetal PNS, whether there are differences in the neuronal subtype potentials of NCSCs from different regions of the PNS, and whether NCSCs persist in the postnatal gut.

1 R01 HL097760 01 (PI, Morrison) 8/24/09-7/31/13

NIH/NHLBI

“Genetic analysis of stem cell maintenance in vivo”

The goals of this project are to determine whether osteoblasts, megakaryocytes, and/or endothelial cells are the physiologically important sources of Stem Cell Factor (SCF) or Angiopoietin-1 for hematopoietic stem cell maintenance in vivo.

1 R01 DK083288 01 (PI, Morrison) 9/10/09-7/31/11

NIH/NIDDK

“The derivation of enteric neural crest stem cells from human embryonic stem cells”

The goals of this project are to derive enteric neural crest stem cells from human embryonic stem cells, and to test whether these cells can give rise to enteric neurons and glia upon transplantation into a rodent model of Hirschsprung disease.

The Ellison Medical Research Foundation 9/01/07 – 8/31/11

Principal Investigator: Sean Morrison

“The physiological role of stem cells in the maintenance and function of the aging brain”

The goal of this project is to test whether ongoing stem cell activity and neurogenesis in the adult brain is required for adult brain maintenance, learning, or memory.

Goldhirsch Foundation (PI, Morrison) 07/01/2009-06/30/2010

Research Grant

“Do glioblastomas follow a cancer stem cell model?”

The goal of this project is to perform limit dilution assays to determine the frequency of cells with tumorigenic potential among glioblastoma specimens obtained from 10 patients.

Recently Completed Research Support

Department of Defense 6/23/03 -6/22/08

“Engineering Hybrid Bony Organs”

Principal Investigator: David Mooney (Sean Morrison co-investigator)

Type: Multidisciplinary Research Program of the University Research Initiative (MURI)

The goal of this multidisciplinary project is for laboratories in the areas of tissue engineering, mathematical modeling, signal transduction, and stem cell research to collaborate on the creation of an artificial organ in culture composed of bone and bone marrow. The Morrison laboratory’s component will be to introduce purified hematopoietic stem cells into the engineered bony organ and then analyze their ability to give rise to normal hematopoiesis.

J.S. McDonnell Foundation Morrison, P.I. 11/01/04 – 11/01/06

JSMF #220020050.01

“The role of *bmi-1* in neural stem cell self-renewal and neoplastic proliferation”

The goal of this project was to determine whether the overexpression of *bmi-1* leads to CNS cancers and whether *bmi-1* is overexpressed in human glioblastomas.