

Ömer Hidir Yilmaz

Curriculum Vitae

Biology Department  
Koch Institute for Integrated Cancer Research  
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Degrees:

Ph.D., Cellular and Molecular Biology, University of Michigan Medical School, Ann Arbor, 2008, Sean J. Morrison Ph.D.

M.D., University of Michigan Medical School, Ann Arbor 2008  
MSTP Program (combined MD PhD program)

B.S. Biochemistry and Physics, University of Michigan, Ann Arbor, 1999

Employment:

Eisen and Chang Career Development Associate Professor of Biology, Massachusetts Institute of Technology, 2019-Present

Attending Pathologist, Assistant Pathologist, Pathology Services, Massachusetts General Hospital, Harvard Medical School, 2014-Present

Lecturer on Pathology, Part-time, Massachusetts General Hospital, Harvard Medical School, 2014-Present

Eisen and Chang Career Development Associate Professor of Biology, Massachusetts Institute of Technology, 2014-2019

Postdoctoral Fellow, Whitehead Institute for Biomedical Research, MIT, David Sabatini MD PhD, 2011-2014

Clinical and Research Fellow in Gastrointestinal Pathology, Department of Pathology, Massachusetts General Hospital, Harvard Medical School, 2008-2014

External Positions Held:

Ad hoc reviewer for CAMP study section, NIH (2016, 2017)

Editorial Board of Current Stem Cell Reports (2017-Present)

External Advisory Board Member, Vanderbilt Gastrointestinal Spore Center (2017-Present)

Ad hoc reviewer for ZRG1 DKUS-N (05) study section (2018)

External Scientific Advisor, NIDDK/NIH Intestinal Stem Cell Consortium (2017-Present)

Licensure and Certification:

USMLE Step 1 (2001)

USMLE Step 2C (2007)

USMLE Step 2 (2008)

USMLE Step 3 (2009)

Full Medical License in the Commonwealth of Massachusetts (valid through 10/28/18)

American Board of Pathology (Anatomic Pathology) (valid through 2022)

Honors:

Kellogg Foundation Scholarship (1995)

University of Michigan Alumni Scholarship (1995)

Branstrom Freshman Prize, University of Michigan (1996)

Gerard Research Fellowship, University of Michigan (1998)

Golden Key (1995 to 1999)

7th Term Angel Scholar, University of Michigan (1998)

Merck Index Award for Chemistry, University of Michigan (1999)

Biomolecular Recognition Fellowship, University of Michigan (1999)

Harold M. Weintraub Award (2007)

Medical Scientist Training Program Award (1999-2008)

Nathan Shock Center Mutant and Transgenic Rodent Core Grant (2002)

Institute of Gerontology Training Grant Pre-doctoral Fellow (2003 to 2006)

Graduation with Distinction in Research Honors (2008)

Dean's Award for Research Excellence (2008)

Warshaw Institute Fellow (Massachusetts General Hospital) (2009-10)

V Foundation Scholar (2014-16)

Sidney Kimmel Scholar (2016-18)

Pew-Stewart Trust Scholar (2016-2020)

AAAS Martin and Rose Wachtel Cancer Research Prize (2018)

Sabri Ulker International Science Award (2018)

Eisen and Chang Career Development Professor (2018)

UROP Students Supervised:

Jung, Cynthia (6/1/2014-4/1/2017)

Sangkhapreecha, Puwanat (09/2014-05/2015)

Wu, Amanda (11/2015-5/1/2017)  
Li, Elizabeth (11/2015-6/1/2017), Current position accepted MD PhD Student at Yale University  
Arias, Erika (01/2015-2017)  
Bauer-Rowe, Khristian E. (09/2011-12/2014), Current position MD student at Stanford Medical School  
Santos, Sebastian (01/2017-to Present), Current position Accepted MD student at UC Davis  
AlDajani, Mohammed (01/2015-to Present)  
Zhang, Daiyao (01/2018-to Present)  
Iqbal, Ameena (01/2018-to Present)  
Poberejsky, David (01/2018-to Present)  
Nguyen, Tam (01/2018-to Present)  
Wesel, Kevin (01/2018-to Present)

#### B.S. Student Thesis Supervised:

Santos, Sebastian 2018. The Role of Oncogenic Kras in the Colon Stem Cell Population.  
Current position: MD student at UC Davis

#### Ph.D. Students Supervised:

Semir Beyaz, The epigenetic regulation of cell fate, 2018 (co-advised with Stuart Orkin, Harvard Medical School), Current position Fellow at Cold Spring Harbor Laboratory

Nuray Gunduz, Molecular analysis of engineered nanomaterials in biomedical and regenerative medicine (co-advised with Caglar Elbuken, Bilkent University), Current position is pending.

#### Postdoctoral Researchers Supervised:

Roper, Jatin MD (03/2014-Present)  
Mana, Miyeko PhD (03/2014-Present)  
Cetinbas, Naniye PhD (10/2014-05/2017), Current position Research Scientist, Agios Pharmaceuticals  
Kedrin, Dmitriy MD PhD (2/1/2015-6/30/2016), Current position Physician Elliot Health System  
Venekar, Amit PhD (2/1/2016-2/1/2018), Current position Assistant Professor  
Cheng, Chia-Wei PhD (4/1/2015-Present)  
Eng, George MD PhD (6/1/16-Present)  
Imada, Shinya MD PhD (6/1/17-Present)  
Braverman, Jonathan PhD (6/1/17-Present)  
Hussey, Amanda PhD (9/1/17-Present)  
Wang, Fang PhD (9/1/17-Present)  
Jessica Shay MD PhD (7/1/19-Present)  
Gizem Calibasi-Kocal PhD (6/18-Present)

Alonso Martinez, Salvador MD (11/2017-6/2019), Current position Heme/Onc fellow at MSKCC

Teaching Experience:

7.95, Cancer Biology, Guest Lecturer, Spring 2015, 2016 MIT

7.02, Introduction to Experimental Biology & Communication, Instructor  
Fall 2015, Spring 2017, Spring 2018 MIT

7.45 The Hallmarks of Cancer, Guest Lecturer, Fall 2018

7.61, Eukaryotic Cell Biology, Guest Lecturer, Fall 2017, Fall 2018 MIT

7.95, Cancer Biology, Instructor, Spring 2017, Spring 2018, Spring 2019 MIT

Service:

Internal service:

Department of Biology

Faculty Search Committee, Whitehead Institute for Biomedical Research and  
Department of Biology, Fall 2014-Spring 2015, MIT

Faculty Search Committee, Broad Institute and Department of Biology, Fall  
2015-Spring 2016, MIT

Faculty Search Committee, Koch Institute for Integrative Cancer Research  
and Department of Biology, Fall 2016-Spring 2017, MIT

Organizer, Koch Institute for Integrative Cancer Research, Annual Retreat  
2015

Undergraduate Advisor and Mentoring

Spencer A. Rust (2015-2018)

Chiara Waingarten (2016-2018)

Juen Lee (2016)

Mohammed AlDajani (2017-2018)

Luis Xavier Ramos Tormo (2017-Present)

Baris Ekim (2017-Present)

Yenthanh Le (2018-Present)

Dallace Francis (2018-Present)

Preliminary Thesis Exam Member

Rachit Neupane, MIT Biology (2015)  
Santiago Naranjo, MIT Biology (2016)  
Nikola Ivica, MIT Biology (2016)  
Azucena Ramos, MIT Biology (2016)  
Christopher Fincher, MIT Biology (2016)  
James Taggart, MIT Biology (2017)  
Albert Magnell, MIT Biology (2018)

Thesis Committee Advisory Member

Rachit Neupane, MIT Biology (2015-2019)  
Santiago Naranjo, MIT Biology (2016-Present)  
Yang Su, MIT Biology (2016-Present)  
Nikola Ivica, MIT Biology (2016-Present)  
Christopher Fincher, MIT Biology (2016-Present)  
Azucena Ramos, MIT Biology (2016-Present)  
Meaghan Flagg, Harvard Medical School, Virology (2016-Present)  
Albert Magnell, MIT Biology (2018-Present)  
Priscilla Cheung, Harvard Medical School, Stem Cell and Regenerative Biology (2018-Present)  
Seth Cassel, Harvard MD PhD, Program in Biological and Biomedical Sciences (September 2018), External Reviewer

External Service:

Professional Societies

International Society for Stem Cell Research (2006-Present)  
American Association for Cancer Research (2018-Present)

Professional Service

International Society for Stem Cell Research, Membership Committee (2018-Present)

Publications:

52. Biton M, Haber AL, Rogel N, Burgin G, Beyaz S, Schnell A, Ashenberg O, Su CW, Smillie C, Shekhar K, Chen Z, Wu C, Ordovas-Montanes J, Alvarez D, Herbst RH, Zhang M, Tirosh I, Dionne D, Nguyen LT, Xifaras ME, Shalek AK, von Andrian UH, Graham DB, Rozenblatt Rosen O, Shi HN, Kuchroo V, Yilmaz ÖH, Regev A, Xavier RJ. T Helper Cell Cytokines Modulate Intestinal Stem Cell Renewal and Differentiation. *Cell*. 2018. Nov. 15;175(5):1307-1320 PMID: 30392957

51. Eng, G., Braverman, J, and Yilmaz, ÖH. CRAD as a cytoskeletal tumor suppressor. *Nature Cell Biology*. 2018. Nov;20(11):1232-33.

50. Yilmaz, ÖH. Dietary regulation of the origins of cancer, *Science Translational Medicine* 2018. Aug 8;19(453). PMID: 30089636 [Cover]

49. Alonso S and Yilmaz ÖH. Nutritional regulation of intestinal stem cells. *Annual Reviews of Nutrition*. 2018. Aug 21;38:273-301. PMID: 29799767

48. Mihaylova M, Cheng CW, Cao AQ, Tripathi S, Mana MD, Bauer-Rowe KE, Abu-Remaih M, Clavin L, Erdemir A, Lewis C, Freinkman E, Huang Y, Bell G, Deshpande V, Carmeliet P, Katajisto P, Sabatini DM, and Yilmaz ÖH. Fasting-Activated Fatty Acid Oxidation Enhances Intestinal Stem Cell Function. *Cell Stem Cell* 2018. May 3:22(5):769-778 PMID: 29727683 [Cover]

- Barisas DAG and Stappenbeck TS. Intestinal stem cells live off the fat of the land. 2018. May 3:22(5):611-612. PMID: 29727673

47. Lannagan TRM, Lee YK, Wang T, Roper J, Bettington ML, Fennell L, Vrbanac L, Jonavicius L, Somashekar R, Gieniec K, Yang M, Ng JQ, Suzuki N, Ichinose M, Wright JA, Kobayashi H, Putoczki TL, Hayakawa Y, Leedham SJ, Abud HE, Yilmaz ÖH, Marker J, Klebe S, Wirapati P, Mukherjee S, Tejpar S, Leggett BA, Whitehall VLJ, Worthley DL, Woods SL. Genetic editing of colonic organoids provides a molecularly distinct and orthotopic preclinical model of serrated carcinogenesis. *Gut* 2018. April 17. PMID: 29666172

46. Braverman J and Yilmaz ÖH. From 3D organoids back to 2D enteroids. *Development Cell*. 2018. Mar 12;44(5):533-534 PMID: 29533766

45. Zhou W, Almeqdadi M, Xifaras ME, Riddell IA, Yilmaz ÖH\*, and Lippard SJ\*. The effect of geometric isomerism on the anticancer activity of the monofunctional platinum complex trans-[Pt(NH<sub>3</sub>)<sup>2</sup>(phenanthridine)Cl]NO<sub>3</sub>. *Chem Commun (Camb)*. 2018 Feb 27. PMID: 29484327. \* co-corresponding senior author

44. Cheng CW and Yilmaz ÖH. FAOund the link: Phospholipid remodeling and intestinal stem cell growth and tumorigenesis. *Cell Stem Cell*. 2018 Feb 1:22(2): 141-3. PMID: 293395049

43. Roper J, Tammela T, Akkad A, Almeqdadi M, Santos, SB, Jacks T, Yilmaz ÖH. Colonoscopy-based colorectal cancer modeling in mice with CRISPR-Cas9 genome editing and organoid transplantation. *Nature Protocols*. 2018 Feb;13(2):217-234. PMID: 29300388

42. Lau AN, Israelsen WJ, Roper J, Sinnamon MJ, Georgeon L, Dayton TL, Hillis AL, Yilmaz ÖH, Di Vizio D, Hung KE, Vander Heiden MG. PKM2 is not required for colon cancer initiated by APC loss. *Cancer Metab*. 2017 Nov 30;5:10. doi: 10.1186/s40170-017-0172-1. PMID: 29214019

41. Haber AL, Biton M, Rogel N, Herbst RH, Shekhar K, Smillie C, Burgin G, Delorey TM, Howitt MR, Katz Y, Tirosh I, Beyaz S, Dionne D, Zhang M, Raychowdhury R, Garrett WS, Rozenblatt-Rosen O, Shi HN, Yilmaz O, Xavier RJ, Regev A. A single-cell survey of the small intestinal epithelium. *Nature*. 2017 Nov 16;551(7680):333-339. PMID: 29144463

40. Roper J, and Yilmaz ÖH. Metabolic Teamwork in the Stem Cell Niche. *Cell Metabolism*. 2017 May 2;25(5):993-994. PMID: 28467944

39. Roper J, Tammela T, Cetinbas NM, Akkad A, Roghanian A, Rickelt S, Almeqdadi M, Wu K, Oberli M, Sánchez-Rivera FJ, Park Y, Liang X, Eng G, Azimi R, Kedrin D, Neupane R, Beyaz S, Sicinska ET, Bass A, Suarez Y, Yoo J, Chen L, Taylor MS, Zukerberg L, Katajisto P, Tschlis PN, Lees J, Deshpande V, Chen J, Hynes RO, Langer R, Bhutkar A, Jacks T, Yilmaz ÖH. Epithelial genome editing and organoid transplantation models of colorectal cancer. *Nature Biotechnology*. 2017 Jun;35(6):569-576. PMID: 28459449
38. Barriga FM, Montagni E, Mana M, Mendez-Lago M, Hernando-Momblona X, Sevillano M, Guillaumet-Adkins A, Rodriguez-Esteban G, Buczacki SJ, Gut M, Heyn H, Winton DJ, Yilmaz OH, Attolini CS, Gut I, Battle E. Mex3a Marks a Slowly Dividing Subpopulation of Lgr5+ Intestinal Stem Cells. *Cell Stem Cell*. 2017 Mar 8. pii: S1934-5909(17)30040-1. PMID: 28285904
37. Cheng CW, Villani V, Buono R, Wei M, Kumar S, Yilmaz OH, Cohen P, Sneddon JB, Perin L, Longo VD. Fasting-Mimicking Diet Promotes Ngn3-Driven  $\beta$ -Cell Regeneration to Reverse Diabetes. *Cell*. 2017 Feb 23;168(5):775-788. PMID: 28235195
36. Cheng CW and Yilmaz ÖH. Starving leukemia to induce differentiation. *Nature Medicine*. 2017 Jan 6; 23(1):14-15. PMID: 28060803
35. Mana, M.D., Kuo, E.YS. & Yilmaz, ÖH. Dietary Regulation of Adult Stem Cells. *Current Stem Cell Reports*. 2017 Mar 3: 1:1-8. PMID: 28966904
34. Beyaz S, Kim JH, Pinello L, Xifaras ME, Hu Y, Huang J, Kerényi MA, Das PP, Barnitz RA, Herculat A, Dogum R, Haining WN, Yilmaz ÖH, Passegue E, Yuan GC, Orkin SH, Winau F. The histone demethylase UTX regulates the lineage-specific epigenetic program of invariant natural killer T cells. *Nature Immunology*. 2017 Feb;18(2):184-195\*
33. Hu B, Jin C, Li HB, Tong J, Ouyang X, Cetinbas NM, Zhu S, Strowig T, Lam FC, Zhao C, Henao-Mejia J, Yilmaz O, Fitzgerald KA, Eisenbarth SC, Elinav E, and Flavell RA. The DNA-sensing AIM2 inflammasome controls radiation-induced cell death and tissue injury. *Science*. 2016 Nov 11; 354(6313): 765-768. PMID:
32. Beyaz S and Yilmaz ÖH. Dietary regulation of stemness and tumor initiation by the PPAR-d pathway. *Clinical Cancer Research*. 2016 Oct 4. PMID: 27702819\*
31. Cetinbas NM, Sudderth J, Harris RC, Cebeci A, Negri GL, Yilmaz ÖH, DeBerardinis RJ, Sorensen PH. Glucose-dependent anaplerosis in cancer cells is required for cellular redox balance in the absence of glutamine. *Sci Rep*. 2016 Sep 8; 6:32606. PMID: 27605385
30. 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, Tworzyanski 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*. 2016 Aug 4;19(2):205-16. doi: 10.1016/j.stem.2016.04.002. PMID: 27184401

29. Cangelosi A and Yilmaz ÖH. (2016) High fat diet and stem cells: Linking diet to intestinal tumor formation. *Cell Cycle*. Jul 2; 15(13): 1657-8. PMID: 27097128

28. Beyaz S, Mana MD, Roper J, Kedrin D, Saadatpour A, Hong SJ, Bauer-Rowe KE, Xifaras ME, Akkad A, Pinello L, Katz Y, Shinagare S, Abu-Remaileh M, Lamming D, Guo G, Selig M, Nielsen GP, Gupta N, Ferrone C, Deshpande V, Yuan GC, Orkin SH, Sabatini DM, and Yilmaz ÖH. (2016) High-fat diet enhances stemness and tumorigenicity of intestinal progenitors. *Nature*. Mar 3; 531(7592):53-8. PMID: 26935695\*

- Preview: Luo C, Puigserver P. Stem cells: Dietary fat promotes intestinal dysregulation. *Nature*. 2016 Mar 3 ; 531(7592):42-43.
- Preview: Haller S and Jasper H. You Are What You Eat: Linking High-Fat Diet to Stem Cell Dysfunction and Tumorigenesis. *Cell Stem Cell*. 2016. May 5; 18(5):564-6.

27. Cheng CW and Yilmaz ÖH. (2015) IGFBP3 and T1D: Systemic Factors in Colonic Stem Cell Function and Diabetic Enteropathy. *Cell Stem Cell*. Oct 1; 17(4): 379-80. PMID: 26431180

26. Golovko D, Kedrin D, Yilmaz ÖH, Roper J. (2015) Colorectal cancer models for novel drug discovery. *Expert Opin Drug Discov*. Aug 21;1-13. [Epub ahead of print] PMID: 26295972

25. Strijbis K, Yilmaz ÖH, Dougan SK, Esteban A, Gröne A, Kumamoto CA, Ploegh HL. (2014) Intestinal Colonization by *Candida albicans* Alters Inflammatory Responses in Bruton's Tyrosine Kinase-Deficient Mice. *PLoS One*. Nov 7;9(11):e112472. PMID: 25387537

24. Lamming DW, Mihaylova MM, Katajisto P, Baar EL, Yilmaz ÖH, Hutchins A, Gultekin Y, Gaiter R, Sabatini DM. (2014) Deletion of Rictor, an essential protein component of mTORC2, decreases male lifespan. *Aging Cell*. Oct; 13(5):911-7. PMID: 25059582

23. Lassen KG, Kuballa P, Conway KL, Patel KK, Becker CE, Peloquin JM, Villablanca EJ, Norman JM, Liu TC, Heath RJ, Becker ML, Fagbami L, Horn H, Mercer J, Yilmaz ÖH, Jaffe JD, Shamji AF, Bhan AK, Carr SA, Daly MJ, Virgin HW, Schreiber SL, Stappenbeck TS, Xavier RJ. (2014) Atg16L1 T300A variant decreases selective autophagy resulting in altered cytokine signaling and decreased antibacterial defense. *PNAS* May 27;111(21):7741-6. PMID: 24821797

22. Mihaylova MM, Sabatini DM, Yilmaz ÖH. (2014) Dietary and Metabolic Control of Stem Cell Function in Physiology and Disease. *Cell Stem Cell*. Mar 6;14(3):292-305. PMID: 24607404

21. Chudnovsky Y, Kim D, Zheng S, Whyte WA, Bansal M, Bray MA, Gopal S, Theisen MA, Bilodeau S, Thiru P, Muffat J, Yilmaz ÖH, Mitalipova M, Woolard K, Lee J, Nishimura R, Sakata N, Fine HA, Carpenter AE, Silver SJ, Verhaak RG, Califano A, Young RA, Ligon KL, Mellingshoff IK, Root DE, Sabatini DM, Hahn WC, Chheda MG. (2014) ZFX4 Interacts with



the NuRD Core Member CHD4 and Regulates the Glioblastoma Tumor-Initiating Cell State. *Cell Rep.* 2014 Jan 30;6(2):313-24. PMID: 24440720

20. Gupta, N.K, Yilmaz, O, Fisher, M., Yajnik, V. (2014) Abatacept: A New Treatment Option for Refractory Adult Autoimmune Enteropathy. *J. Clin. Gastroenterol.* 2014 Jan;48(1):55-8. PMID: 24045285

19. Tse JY, Wu S, Shinagare SA, Lauwers GY, Yilmaz O, Wu CL, Deshpande V. (2013) Peutz-Jeghers syndrome: a critical look at colonic Peutz-Jeghers polyps. *Mod Pathol.* Sep;26(9):1235-40. PMID: 23599156

18. Conway KL, Kuballa P, Song JH, Patel KK, Castoreno AB, Yilmaz ÖH., Jijon HB, Zhang M, Aldrich LN, Villablanca EJ, Peloquin JM, Goel G, Lee IA, Mizoguchi E, Shi HN, Bhan AK, Shaw SY, Schreiber SL, Virgin HW, Shamji AF, Stappenbeck TS, Reinecker HC, Xavier RJ (2013) Atg16l1 is Required for Autophagy in Intestinal Epithelial Cells and Protection of Mice From Salmonella Infection. *Gastroenterology.* Dec;145(6):1347-57. PMID: 23973919

17. Curry NL, Mino-Kenudson M, Oliver TG, Yilmaz ÖH, Yilmaz VO, Moon JY, Jacks T, Sabatini DM, Kalaany, NY. (2013) PTEN-null Tumors Cohabiting the Same Lung Display Differential Akt Activation and Sensitivity to Dietary Restriction. *Cancer Discov.* Aug;3(8):908-21. PMID: 23719831

16. Arnason, T, Pino MS, Yilmaz O., Kirley SD, Rueda BR, Chung DC, Zukerberg LR. (2013) Cables1 is a tumor suppressor gene that regulates intestinal tumor progression in *Apc<sup>min</sup>* mice. *Cancer Biology & Therapy* 14(7), 672-678. PMID: 23792637

15. Wang H, Chen Y, Fernandez-Del Castillo C, Yilmaz O, Deshpande V. (2013) Heterogeneity in signaling pathways of gastroenteropancreatic neuroendocrine tumors: a critical look at notch signaling pathway. *Mod Pathol.* Jan;26(1):139-47. PMID: 22918166

14. Birsoy K, Wang T, Possemato R, Yilmaz ÖH, Koch CE, Chen WW, Hutchins AW, Gultekin Y, Peterson TR, Carette JE, Brummelkamp TR, Clish CB, Sabatini DM. (2012) MCT1-mediated transport of a toxic molecule is an effective strategy for targeting glycolytic tumors. *Nature Genetics* 45(1), 104-108

13. Yilmaz ÖH \*, Katajisto P\*, Lamming DW, Gültekin Y, Bauer-Rowe KE, Sengupta S, Birsoy K, Durun A, Yilmaz VO, Selig M, Nielsen GP, Mino-Kenudson M, Zukerberg LR, Bhan AK, Deshpande V, and Sabatini DM. (2012) mTORC1 in the Paneth cell niche couples intestinal stem-cell function to calorie intake. *Nature* 486, 490-5. PMID: 22722868 \*Equal contributors, co-first authors

- Preview: Clevers H. The Paneth cell, caloric restriction, and intestinal integrity. *N Engl J Med.* 2012 Oct 18;367(16):1560-1
- Preview: Ramos FJ, Kaeberlein M. Ageing: A healthy diet for stem cells. *Nature.* 2012 Jun 27;486(7404):477-8.
- Preview: Harris, TE and Thorner MO. Caloric restriction in mTORC1 control of intestinal homeostasis. *Cell Metab.* 2012 Jul 3;16(1):6-8.

- Preview: Kim TH and Shivdasani RA. Stem cell niches: famished Paneth cells, gluttonous stem cells. *Curr Biol.* 2012 Jul 24;22(14):R579-80.
- Preview: Papatriantafyllou M. Metabolism: WeightWatching for stem cells. *Nat Rev Mol Cell Biol.* 2012 Jun 8;13(7):406.

12. Kelly PJ, Shinagare S, Sainani N, Hong X, Ferrone, C, Yilmaz O, Fernandez-Del Castillo C, Lauwers GY, Deshpande V. (2012) Cystic Papillary Pattern in Pancreatic Ductal Adenocarcinoma: A Heretofore Undescribed Morphologic Pattern That Mimics Intraductal Papillary Mucinous Carcinoma. *Am J Surg Pathol.* 36(5) 696-701. PMID: 22367300

11. Lee JY, Nakada D, Yilmaz ÖH, Tothova Z, Lim MS, Gilliland DG, Morrison SJ. (2010). An mTOR-induced tumor suppressor response contributes to the depletion of hematopoietic stem cells after Pten deletion. *Cell Stem Cell.* 5;7(5):593-605. PMID: 21040901

10. Oravec-Wilson KI\*, Philips ST\*, Yilmaz ÖH\*, Li, L, Lucas PC, Sitwala K, Downing JR, Morrison SJ, Ross TS. 2008. Persistence of Leukemia-initiating Cells in a Novel Mouse Model of Imatinib-Responsive Myeloid Leukemia. *Cancer Cell.* 2009 Aug 4;16(2):137-48. PMID: 19647224 \*Equal contributors, co-first authors

9. Levi B, Yilmaz ÖH, Duester G and Morrison SJ. 2008. Aldehyde dehydrogenase 1a1 is dispensable for murine nervous and hematopoietic stem cell function. *Blood.* 2009 Feb 19;113(8):1670-80. PMID: 18971422

8. Kiel MJ, Yilmaz ÖH, and Morrison SJ. 2008. CD150 negative cells are transiently reconstituting multipotent progenitors with little or no stem cell activity. *Blood.* 2008 Apr 15;111(8):4413-4. PMID: 18398056

7. Yilmaz ÖH and Morrison SJ. 2008. The PI-3kinase pathway in hematopoietic stem cells and leukemia-initiating cells: a mechanistic difference between normal and cancer stem cells. *Blood Cells Mol Dis.* 2008 Jul-Aug;41(1):73-6. PMID: 18387833

6. Kim I, He S, Yilmaz ÖH, Kiel MJ, and Morrison SJ. 2006. Enhanced purification of fetal liver hematopoietic stem cells using SLAM family receptors. *Blood.* 2006 Jul 15;108(2):737-44. PMID: 16569764

5. Yilmaz ÖH, Valdez R, Thiesen BK, Guo W, Ferguson DO, Wu H, and Morrison SJ. 2006. Pten dependence distinguishes haematopoietic stem cells from leukaemia-initiating cells. *Nature.* 2006 May 25;441(7092):475-82. PMID: 16598206. [Cover]

- Preview: Janzen V and Scadden DT. Stem cells: good, bad and reformable. *Nature.* 2006 May 25;441(7092):418-9.
- Preview: Rossi DJ and Weissman IL. Pten, tumorigenesis, and stem cell self-renewal. *Cell.* 2006 Apr 21;125(2):229-31.

4. Yilmaz ÖH, Kiel, MJ and Morrison SJ. 2006. SLAM family markers are conserved among hematopoietic stem cells from old and reconstituted mice and markedly increase their purity. *Blood.* 2006 Feb 1;107(3):924-30. PMID: 16219798

- Previewed Van Zant, G. Stem cell markers: less is more! Blood. 2006 Feb 107(3):855-56

3. Kiel MJ\*, Yilmaz ÖH\*, Iwashita T\*, Terhorst C, and Morrison SJ. 2005. SLAM family receptors distinguish hematopoietic stem and progenitor cells and reveal endothelial niches for stem cells. Cell. 2005 Jul 1;121(7):1109-21. PMID: 15989959 \*Equal contributors, co-first authors

- Preview: Wagers A.J. Stem cell grand SLAM. Cell. 2005 Jul 1;121(7):967-70
- Preview: Lemischka I.R. Nat Med. 2005 Jul 1;11:721-721 (News and Views)

2. Kim I, Yilmaz ÖH, and Morrison SJ. 2005. CD144 (VE-cadherin) is transiently expressed by fetal liver stem cells. Blood. 2005 Aug 1;106(3):903-5. PMID: 15831702

1. Kiel MJ, Iwashita T., Yilmaz ÖH, and Morrison SJ. 2005. Spatial differences in hematopoiesis but not in stem cells indicate a lack of regional patterning in definitive hematopoietic stem cells. Dev Biol. 2005 Jul 1;283(1):29-39. PMID: 15913595

#### Submitted and In Progress Publications:

1. Cheng CW, Biton M, Haber AL, Gunduz N, Eng G, Gaynor L, Tripathi S, Calibasi-Kocal G, Rickelt S, Butty VL, Moreno M, Iqbal AM, Bauer-Rowe KE, Mylonas K, Whary MT, Levine SS, Hynes RO, Mino-Kenudson M, Deshpande V, Boyer LA, Fox JG, Mihaylova MM, Regev A, and Yilmaz ÖH. Endogenous ketones instruct intestinal stem cell fate through Notch signaling. *In Revision at Cell*

2. Beyaz S, Roper J. Bauer-Rowe KE., Xifaras ME. Thaiss CA. Almeqdadi M., Biton M., Shekar, K., Ozata DM., Ergin I., Fox JG., Elinav E., Kucukural A., Regev A., Orkin SH., and Yilmaz ÖH. Dietary suppression of MHC-II expression in intestinal stem cells enhances intestinal tumorigenesis. *Submitted*

#### Book Chapters:

Yilmaz ÖH. and Deshpande V. Pathology and Genetics of Pancreatic Neoplasms. Surgical Pathology Clinics Molecular Oncology; December 2012

Roper J and Yilmaz ÖH. Intestinal Organoids. Encyclopedia of Cancer. 2014

Cetinbas N, Roper J, and Yilmaz ÖH. Cancer Stem Cell Niches. Biology and Engineering of Stem Cell Niches; 2017

#### Patents:

Hematopoietic Stem Cell Identification and Isolation

Ömer H. Yilmaz, Mark J. Kiel, Sean J. Morrison, and Toshide Iwashita, Inventors (Issued 04/05/2011; U.S. Patent No.: 7,919,316 B2)

Hematopoietic Stem Cell Identification and Isolation

Ömer H. Yilmaz, Mark J. Kiel, Sean J. Morrison, and Toshide Iwashita, Inventors (Issued 03/31/2009; U.S. Patent No.: 7,510,877 B2)

Invited Presentations:

“Dietary control of intestinal stem cells in physiology and disease”, Tufts University, Boston, MA April 22, 2019

“Dietary control of intestinal stem cells in physiology and disease”, University of Miami, Miami, FL April 16, 2019

“Dietary control of intestinal stem cells in physiology and disease”, Memorial Sloan Kettering Cancer Center, NY, NY April 8, 2019

“Dietary control of intestinal stem cells in physiology and disease”, Crohn’s and Colitis Annual Meeting, Las Vegas, NV February 6-8, 2019

“Leveraging orthotopic models of colon cancer to uncover disease mechanisms”, Merck Organoid and 3D based platforms for discovery oncology, San Francisco, CA January 28-29, 2019

“Dietary control of intestinal stem cells in physiology and disease”, Microbes within the host in health and disease, Salk Foundation IPSEN SCIENCE 2019, Salk Institute, January 22-24, 2019

“Dietary control of intestinal stem cells in physiology and disease”, NCI/NIH, December 11-12, 2018

“Dietary control of intestinal stem cells in physiology and disease”, Abcam Stem Cells 2.018 October 26-27, 2018

“Dietary control of intestinal stem cells in physiology and disease”, Children’s Research Institute, University of Texas Southwestern; October 17, 2018

“Dietary control of intestinal stem cells in physiology and disease”, Biochemistry Seminar Series, Medical University of South Carolina; October 4, 2018

“Dietary control of intestinal stem cells in physiology and disease”, Experimental Pathology Seminar Series, NYU; September 17, 2018

“Dietary control of intestinal stem cells in physiology and disease”, Department of Biology, MIT; September 14, 2018

“Dietary control of intestinal stem cells in physiology and disease”, Gordon Research Conference, Invited Speaker; Waterville Valley, New Hampshire; August 19-24, 2018

“Dietary control of intestinal stem cells in physiology and disease”, NIH/NCI Wachtel Prize Award Seminar; Bethesda, Maryland; August 10, 2018

“Dietary control of intestinal stem cells in physiology and disease”, Netherlands Cancer Institute (NKI); June 15, 2018

“Dietary control of intestinal stem cells in physiology and disease”, Sabri Ulker Center Symposium, Cambridge, Massachusetts; May 29-30, 2018

“Dietary control of intestinal stem cells in physiology and disease”, Science with/in/sight: Stem Cells and Cancer, Koch Institute, MIT, Cambridge, Massachusetts; May 9, 2018

“Dietary control of intestinal stem cells in physiology and disease”, Cancer Genomics and Epigenomics Symposium, University of Virginia, Charlottesville, Virginia; May 7-8, 2018

“Dietary control of intestinal stem cells in physiology and disease”, 3<sup>rd</sup> Annual IUKOK (Istanbul University Stem Cell Meeting), Istanbul, Turkey; April 28, 2018

“Dietary control of intestinal stem cells in physiology and disease”, American Physiological Society, FASEB Experiment Biology Annual Meeting, San Diego, California; April 23, 2018

“Leveraging orthotopic models of colon cancer to uncover disease mechanisms”, Recent Advances in Diagnostics and Therapeutics Research, American Association for Cancer Research Annual Meeting, Chicago, Illinois; April 17, 2018

“Dietary control of intestinal stem cells in physiology and disease”, Dana-Farber Cancer Institute Cancer Immunology Series, Harvard Medical School, Boston, Massachusetts; February 12, 2018

“Dietary control of intestinal stem cells in physiology and disease”, Baylor College of Medicine, Huffington Center on Aging, Houston, Texas; December 2017

“Dietary control of intestinal stem cells in physiology and disease”, Harvard Science and Technology (HST), Harvard Medical School, Boston, Massachusetts; November 2017

“Dietary control of intestinal stem cells in physiology and disease”, Department of Pathology, MGH, Harvard Medical School, Boston, Massachusetts; November 2017

“Engineering the Cancer Genome”, College of American Pathologists (CAP) Annual Meeting Washington DC; October 2017

“Dietary control of intestinal stem cells in physiology and disease”, Department of Nutrition and Genetics, Case Western Reserve, Cleveland, Ohio; September 21, 2017

“Dietary control of intestinal stem cells in physiology and disease”, Stem Cell and Regenerative Medicine Symposium, University of Wisconsin, Madison, Wisconsin; September 2017

“Dietary control of intestinal stem cells in physiology and disease”, Izmir Biomedicine and Genome Center (IBG-Izmir), Dokuz Eylul University, Izmir, Turkey; August 2017

“Dietary control of intestinal stem cells in aging and cancer”, Center for the Study of Inflammatory Bowel Disease, MGH, Harvard Medical School, Boston, Massachusetts; July 2017

“Dietary control of stem cells and cancer in obesity”, Karolinska Institute, Stockholm, Sweden; June 2017

“Dietary control of stem cells and cancer in obesity”, 27<sup>th</sup> Biennial Sigrid Juselius Symposium Translation of Immunity, Inflammation and Cancer Mechanisms, Helsinki, Finland; June 2017

“Dietary control of stem cells in aging and cancer”, DDW Annual Meeting, Chicago, IL; May 2017

“Dietary control of stem cells and cancer in obesity”, UCLA Medical School, Pathology Research Seminar Series, Los Angeles, CA; April 2017

“Dietary control of stem cells and cancer in obesity”, Annual Pew Foundation Meeting Santa Barbara, CA; March 2017

“Dietary control of stem cells and cancer in obesity”, BI/IMP/IMBA “Advances in modelling development and disease in vitro”, Vienna, Austria; January 2017

“Dietary control of stem cells and cancer in obesity”, Dana Farber Cancer Center Harvard Medical School, Boston, MA; December 2016

“Dietary control of stem cells and cancer in obesity”, University of Utah Medical School, Salt Lake City, Utah; December 2016

“Dietary control of stem cells and cancer in obesity”, University of Utah Medical School Salt Lake City, Utah; December 2016

“Dietary control of stem cells and cancer in obesity”, MGH Department of Surgery/Shriner’s Children Hospital, Harvard Medical School, Boston, MA; October 2016

“Dietary control of stem cells and cancer in obesity”, Harvard Digestive Disease Center Boston Children’s Hospital, Harvard Medical School, Boston, MA; October 2016

“Dietary control of stem cells in physiology and disease”, Joslin Diabetes Center, Harvard Medical School, Boston, MA; October 2016

“Dietary control of stem cells and cancer in obesity”, Pathology Research Series, University of Virginia, Charlottesville, VA; October 2016

“Dietary control of stem cells and cancer in obesity”, Cancer Research Series, University of Mississippi, Jackson, MS; September 2016

“Dietary control stem cells in physiology and aging”, Abcam, Cambridge, MA; September 2016

“Organoid models of intestinal stem cells in obesity and cancer”, Center for the Study of Inflammatory Bowel Disease, MGH, Harvard Medical School, Boston, Massachusetts; July 2016

“Organoids and Beyond-3D Tissue in a Dish” July 2016

<http://view6.workcast.net/register?cpak=9254404560299943&referrer=cell>

“Dietary control of stem cells in obesity and cancer”, 2016 Klarman Cell Observatory Scientific Advisory Board Meeting, Broad Institute, Cambridge, MA; June 2016

“Dietary control of stem cells in obesity and cancer”, Koch Institute 15<sup>th</sup> Annual Symposium Prevention and Early Detection of Cancer, Cambridge, MA; June 2016

“Dietary control of stem cells in obesity and cancer”, Cell Circuits and Epigenomics Seminar Series, Broad Institute, Cambridge, Massachusetts; May 2016

“Dietary control of stem cells in obesity and cancer”, Colloquium of Nanoscience and Nanotechnology, Bilkent University, Ankara, Turkey; April 2016

“Dietary control of stem cells in physiology and disease”, Evergrande Center for Immunologic Diseases, Harvard Medical School, Boston, Massachusetts; March 2016

“Dietary control of stem cells in physiology and disease”, Cell Signaling Technology Beverly, Massachusetts; March 2016

Current Trends in 3D and Organoid Cell Culture for Cancer Research

February, 2016, <http://www.genengnews.com/webinars/current-trends-in-3d-and-organoid-cell-culture-for-cancer-research/272/>

“Dietary control of stem cells in physiology and disease”, Advanced Cell Diagnostics Cambridge, Massachusetts; April 2016

“Dietary control of stem cells in physiology and disease”, National Nanotechnology Research Center (UNAM), Bilkent University, Ankara, Turkey; April 2016

“Dietary control of stem cells in physiology and disease”, IV. International Congress of Molecular Biology Association of Turkey, Ankara, Turkey; November 2015

“Dietary control of stem cells in physiology and disease”, Center for the Study of Inflammatory Bowel Disease Symposium, Massachusetts General Hospital, Boston, Massachusetts; November 2015

“Dietary control of stem cells in physiology and disease”, Hematology/Oncology Grand Rounds Dana Farber Cancer Institute, Boston, Massachusetts; November 2015

“Dietary control of stem cells in physiology and disease”, Abcam Stem Cells 2.015, San Diego, California; November 2015

“Dietary control of stem cells in physiology and disease”, Mechanisms and Models of Cancer Symposium 2015, Salk Institute, San Diego, California; August 2015

“Dietary control of stem cells in physiology and disease”, Calico (Google Cambridge site) Cambridge, Massachusetts; July 2015

“Dietary control of stem cells in physiology and disease”, Mayo Clinic, Rochester, Minnesota; July 2015

“Dietary control of stem cells in physiology and disease”, Merrimack Pharmaceutical Cambridge, Massachusetts; July 2015

“Diet, stem cells, and cancer”, BASF Ideation Event on “Future of Food”, Chicago, Illinois; June 24-25, 2015

“Dietary control of stem cells in physiology and disease”, Third Annual Broad-ISF Cell Circuits Symposium, Jerusalem, Israel; June 2015

“Dietary control of stem cells in physiology and disease”, Sabatini Lab Retreat, Savannah, Georgia; June 2015

“Impact of diet on tissue regeneration and cancer”, MIT Food Innovation, Cambridge, Massachusetts; April 2015

“Diet-induced PPAR-delta links stemness to tumor initiation”, EMBO/EMBL Heidelberg, Germany; March 2015

“Dietary control of stem cells in physiology and disease”, KWS Saat AG, Cambridge, Massachusetts; February 2015

“Diet-induced PPAR-delta links stemness to tumor initiation”, Third Annual Klarman Cell Observatory Retreat, Broad Institute, Cambridge, Massachusetts; January 2015

“Dietary control of intestinal stem cells in physiology and disease”, IAP, Massachusetts Institute of Technology, Cambridge, Massachusetts; January 2015



“Dietary control of intestinal stem cells in physiology and disease”, Molecular Pathology Research Series, Massachusetts General Hospital, Boston, Massachusetts; December 2014

“Dietary control of intestinal stem cells in physiology and disease”, Center for the Study of Inflammatory Bowel Disease Symposium, Massachusetts General Hospital, Boston, Massachusetts; November 2014

“Dietary control of intestinal stem cells in physiology and disease”, Massachusetts Institute of Technology, Department of Biology Faculty Talk, Cambridge, Massachusetts; October 2014

“Dietary control of intestinal stem cells in physiology and disease”, Massachusetts Institute of Technology, Computational and Systems Biology, Cambridge, Massachusetts; October 2014

“Dietary control of intestinal stem cells in physiology and disease”, Albert Einstein School of Medicine, Bronx, New York; September 2014

“Dietary control of intestinal stem cells in physiology and disease”, Massachusetts General Hospital, Boston, Massachusetts; March 2014

“Dietary control of intestinal stem cells in regeneration and cancer”, Washington University Medical School, St. Louis, Missouri; April 2013

“Dietary control of intestinal stem cells in regeneration and cancer”, University of Michigan Medical School, Ann Arbor, Michigan; April 2013

“Dietary control of intestinal stem cells in regeneration and cancer”, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts; April 2013

“Dietary control of intestinal stem cells in regeneration and cancer”, Harvard University Cambridge, Massachusetts; April, 2013

“Dietary control of intestinal stem cells in regeneration and cancer”, University of California San Francisco, San Francisco, California; March 2013

“Dietary control of intestinal stem cells in regeneration and cancer”, Massachusetts Institute of Technology, Cambridge, Massachusetts; March 2013

“Dietary control of intestinal stem cells in regeneration and cancer”, University of Texas Southwestern, Dallas, Texas; March 2013

“Dietary control of intestinal stem cells in regeneration and cancer”, University of Washington Medical School, Seattle, Washington; February 2013

“Physiologic regulation of intestinal stem-cell self-renewal and tumor initiation”, Bursa Uludag University, Prof. Dr. M. Mete Cengiz Conference Center, Bursa, Turkey; December 2012

“Physiologic regulation of intestinal stem-cell self-renewal and tumor initiation”, Harvard University Department of Stem Cell and Regenerative Biology, Cambridge, Massachusetts; October 2012

“Physiologic regulation of intestinal stem-cell self-renewal and tumor initiation”, Whitehead Institute of Biomedical Research/MIT, Cambridge, Massachusetts; October 2012

“Physiologic regulation of intestinal stem-cell self-renewal and tumor initiation”, Cambridge, Massachusetts; September 2012

“mTORC1 in the Paneth cell niche couples intestinal stem-cell function to calorie intake.” Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts; July 2012

“mTORC1 in the Paneth cell niche couples intestinal stem-cell function to calorie intake.” Istanbul University Faculty of Medicine (Çapa), Istanbul, Turkey; May 2012

“Physiologic regulation of intestinal stem cell self-renewal by the Paneth cell niche.” Children’s Hospital Boston, Harvard Medical School, Boston, Massachusetts; April 2012

“mTORC1 in the Paneth cell niche couples intestinal stem-cell function to calorie intake.” Mechanisms of Whole Organ Regeneration Meeting, Breckenridge, Colorado; April 2012

“Physiologic regulation of intestinal stem cell self-renewal by the Paneth cell niche”, Whitehead Institute of Biomedical Research/MIT, Cambridge, Massachusetts; November 2011

“mTORC1 in the Paneth cell niche couples intestinal stem-cell function to calorie intake”, Whitehead Institute of Biomedical Research/MIT, Cambridge, Massachusetts; October 2011

“The role of food deprivation and mTORC1-mediated nutrient signaling on intestinal stem cell maintenance.” Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts; December 2010

“The role of food deprivation and mTORC1-mediated nutrient signaling on intestinal stem cell maintenance.” Whitehead Institute of Biomedical Research/MIT, Cambridge, Massachusetts; October 2010

“Mechanistic Differences between Normal and Cancer Stem Cells”, Ankara, Turkey; October, 2007

“Stem Cell Self-Renewal and Cancer Cell Proliferation.” Fred Hutchinson Cancer Research Center, Seattle, Washington; May 2007

“Hematopoietic Stem Cells: Identity, Regulation, and Leukemogenesis”, University of Michigan Medical School, Ann Arbor, Michigan USA; July 2006

“Stem Cell Self-Renewal and Cancer Cell Proliferation”, Toronto, Canada; June 2006

“Stem Cell Self-Renewal and Cancer Cell Proliferation.”\_Bogazici University,\_Istanbul, Turkey;  
June 2006

“Physiologic regulation of intestinal stem-cell self-renewal and tumor initiation”, Waterville  
Valley Resort, New Hampshire; September 2012

“mTORC1 in the Paneth cell niche couples intestinal stem-cell function to calorie intake”,  
Boston, Massachusetts; May 2012

“mTORC1 in the Paneth cell niche couples intestinal stem-cell function to calorie intake”  
Waterville Valley Resort, New Hampshire; September 2011

“Hematopoietic Stem Cell Identity”, Wayne State University, Detroit, Michigan; April 2005

“Hematopoietic Stem Cell Identity”, Salk Institute, University of California San Diego, San  
Diego, California USA; March 2005

Research Contracts and Grants:

Current Research Support:

NIH/NCI R01, Dietary control of stem cells in physiology and cancer, 9/1/2016-8/31/2021,  
\$267,000

Pew-Stewart Trust Scholar Award, 8/1/2016-7/31/2020, \$240,000

NIH/NCI 4R01CA211184-35, Understanding and improving platinum anticancer agents,  
4/1/2017-3/31/2020, \$438,912

NIH/NCI U54CA224068, An integrated translational approach to overcome drug resistance  
9/30/2017-8/30/2022, \$109,000

MIT RSC grant, Deconstructing the early steps of high fat diet-mediated intestinal tumorigenesis  
6/1/2016-6/30/2018, \$75,000

Koch Institute-Footbridge, Deciphering Obesity-Mediated Immune Evasion Mechanisms in  
Colorectal Tumorigenesis, 4/1/2018-3/30/2109, \$86,000

Koch Institute Frontier Grant, Cetuximab Immunotherapy of Colorectal Cancer in a Genetically  
Engineered Mouse Model, 6/1/2018-5/30/2019, \$100,000

Pending Research Support:

Impact of fasting on intestinal stem cells and cancer, PI, NCI/NIDDK/NIH

Mechanisms of HIV-associated epithelial intestinal stem cell (ISC) dysfunction, co-PI, NIDDK/NIH

Age-related changes in the colorectal cancer cell-of-origin: Implications for aspirin chemoprevention, co-PI, NCI/NIDDK/NIH

Past Research Support:

Bill & Melinda Gates Foundation, Bad water, bad diet, bad stem cells: epigenetic modeling of environmental enteropathy in mice, 7/01/2016-6/30/2018, \$210,000

Sidney Kimmel Scholar Award, Dietary control of stem cells in obesity and cancer, 7/1/2016-10/1/2018, \$200,000

V Foundation Scholar Award, The mammalian stem cell niche in cancer, 10/1/2014-10/1/2016, \$200,000

AFAR Research Grant for Junior Faculty, Dietary and Epigenetic Control of the Intestinal Stem Cell Niche in Aging, 7/1/2015-6/30/2017, \$100,000

NIDDK/NIH DK043351, The mammalian stem cell niche in cancer, 01/2014-12/2015, \$45,000

NIH/NCI T32CA09216, David Louis (PI), Molecular Immunology and Tumor Biology 2012-2013

Cancer Center Support Grant P30-CA14051 NCI/NIH, The mammalian stem cell niche in cancer, 5/1/2014-4/30/2015, \$75,000

Ortho-McNeil-Janssen Pharmaceuticals, Inc., Effects of cMPL inhibition with small molecule antagonists on radiosensitivity, 12/08/2014-11/30/2015, \$105,080

Albert Einstein College Pilot grant as part of the U19 funding at Albert Einstein College of Medicine, Stem cell-based Therapies for Mitigation of Acute Radiation Syndromes (Pilot), 4/1/2015-7/31/2016, \$75,000

Koch Frontier Grant, Effects of cell size on regenerative and tumorigenic properties of stem cells, 7/1/2015-6/30/2016, \$100,000

Koch Frontier Grant, Defining the metabolic dependencies of obesity-mediated tumorigenesis, 7/1/2016-6/30/2017, \$100,000

NIH/NIA R00AG045144, Regulation of the Intestinal Stem Cell Niche in Aging, 9/1/2014-5/31/2018, \$250,000

## Research Summary:

My laboratory studies how adult stem cells and their microenvironment adapt to various diets in the context of tissue regeneration, aging, and cancer initiation. However, the mechanisms through which diet perturbs stem and progenitor cell biology and leads to diseases, such as cancers are poorly understood. Towards this end, we are studying how diverse dietary interventions impact intestinal stem cell (ISC) and progenitor function in the mammalian intestine. Because ISCs, like all adult stem cells, possess the ability to self-renew (i.e. generate daughter stem cells) and the capacity for multipotent differentiation (i.e. generate lineage-committed progenitors and ultimately all mature tissue-specific cell types), they likely play an important role in remodeling the intestine in response to diet-induced physiologies. A majority of ISCs express the leucine-rich repeat-containing G protein-coupled receptor 5 (Lgr5) and reside at the bottom intestinal crypts nestled between Paneth cells in the small intestine and deep secretory cells in the colon; both Paneth cells and deep secretory cells constitute a significant component of the stem cell cellular neighborhood or “niche”. Such niche cells elaborate myriad growth factors and cues necessary for the maintenance of Lgr5+ ISCs. This intercalated positioning of Lgr5+ ISCs and their niche cells make the intestine an elegant system for deciphering the autonomous versus non-autonomous (or niche-mediated) effects of different diets and the gut microbiome on stem cell self-renewal and differentiation and how changes in ISCs contribute to cancer formation and growth. Finally, we have made three major discoveries in the ISC field with respect to how calorie restriction (CR), fasting and a high-fat diet (HFD) regulate ISCs in regeneration and cancer.

In addition, my lab has developed numerous tools and techniques that enable Crispr/Cas9 genetically defined intestinal cancer organoids that can be endoscopically transplanted into the colons of recipient mice. Furthermore, we have devised endoscopic methods for mucosal directed Crispr/Cas9 genome editing to establish intestinal tumors. The development of such tools will enable us to dissect how tumor initiation, growth, aging, metastasis, immunosurveillance and drug resistance are influenced by diverse dietary states and the gut microbiome.