

## BIOGRAPHICAL SKETCH

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NAME Deborah L. Gumucio	POSITION TITLE Professor, Dept of Cell & Developmental Biology, Director, Center for Organogenesis		
eRA COMMONS USER NAME (credential, e.g., agency login) dgumucio			
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 Michigan	B.A.	1971	Medical Technology
University of Michigan	M.P.H.	1975	Epidemiology
University of Michigan	Ph.D.	1986	Cell & Molec Biol

### A. Positions and Honors.

#### Positions and Employment

8/86 - 8/88 Postdoctoral Fellow: University of Michigan, Internal Medicine (Mentor: Francis S. Collins)  
 8/88 - 8/91 Assistant Research Scientist: University of Michigan, Department of Internal Medicine  
 8/91 - 8/96 Assistant Professor: University of Michigan, Department of Anatomy & Cell Biology  
 8/96 - 8/02 Associate Professor: University of Michigan, Department of Anatomy and Cell Biology  
 8/02 - Professor: University of Michigan, Department of Cell and Developmental Biology

#### Other Experience and Professional Memberships

1995 - 2006 Co-Director, Center for Organogenesis, University of Michigan  
 1989-96 Member, American Society for Microbiology  
 1990- Member, American Association for the Advancement of Science  
 1996- Member, Society for Developmental Biology  
 Member, Society for Gene Therapy  
 2001- External Scientific Advisory Board, University of California at Davis, Primate Center  
 2002, 2005 International Organizing Board, Third and Fourth International Conferences on Familial Mediterranean Fever and hereditary inflammatory disorders (France)  
 2004- Associate Editor, Molecular and Cellular Biology  
 2001-2004 National Science Foundation Advisory Committee for the Establishment of a Non-human Primate Biomaterials and Informatics Resource (IPBIR)  
 2006- Director, Center for Organogenesis, University of Michigan

#### Honors

1986 Distinguished Dissertation Award, Rackham School of Graduate Studies, University of Michigan  
 1994, 1997 Dean's Faculty Recognition Award,  
 2001 Faculty Career Development Award, Office of the Provost, University of Michigan  
 2005 Sheldon Wolff Award in Translational Research from the International Congress on Systemic Autoinflammatory Diseases  
 2007 NIH-NICHD Mentor Award for Excellence in Research Training

### **B. Selected peer-reviewed publications (in chronological order).** (From 64 peer-reviewed publications)

1. The International FMF consortium (Group 4: Richards, N., Shelton, D.A., and Gumucio, D.): Ancient missense mutations in a new member of the RoRet gene family are likely to cause familial Mediterranean fever. *Cell*. 90:797-807, 1997. PMID: 9288758

2. Pinson, K., Dunbar, L., Samuelson, L.C. and Gumucio, D.L.: Targeted disruption of the mouse villin gene does not impair the morphogenesis of microvilli. *Dev. Dyn.*, 211:109-121, 1998. PMID: 9438428
3. Zhu, W., TomHon C., Mason M., Campbell, T., Shelden, E., Richards, N., Goodman, M. and Gumucio, D.L.: Analysis of linked human  $\omega$  and  $\omega$  transgenes: effect of Locus Control Region hypersensitive sites 2 and 3 or a distal YY1 mutation on stage-specific expression patterns. *Blood*, 93:3540-3549, 1999. PMID: 10233907
4. Schaner, P., Richards, N., Wadhwa, A., Aksentijevich, I., Kastner, D., Tucker, P. and Gumucio, D.: Episodic evolution of pyrin in primates: human mutations recapitulate ancestral amino acid states. *Nature Genetics* 27:318-321, 2001. PMID: 11242116
5. Richards, N., Schaner, P., Diaz, A., Stuckey, J., Shelden, E., Wadhwa, A., and Gumucio, D.L.: Interaction between pyrin and the Apoptotic Speck Protein (ASC) modulates ASC-induced apoptosis. *J. Biol. Chem.* 276:39320-39329, 2001. PMID: 11498534
6. Braunstein, E.M., Qiao, T., Madison, B., Pinson, K. Dunbar, L., and Gumucio, D.L. Villin: a marker for development of the epithelial pyloric border. *Dev. Dyn.* 224:90-102, 2002. PMID: 11984877
7. Madison, B., Qiao, T., Braunstein, E., Dunbar, L., and Gumucio, D.L. "Cis elements of the villin gene control expression in restricted domains of the vertical (crypt) and horizontal (duodenum, cecum) axes of the intestine" *J Biol Chem.* 277:33275-33283, 2002. PMID: 12065599
8. Yu, T., Thomas, D. Zhu, W., Goodman, M. and Gumucio, D.L. Regulation of fetal vs. Embryonic gamma globin genes: appropriate developmental stage expression patterns in the presence of HS2 of the locus control region. *Blood*, 99:1082-1084, 2002. PMID: 11807017
9. Diaz, A., Hu, C., Kastner, D.L., Schaner, P., Reginato, A.M., Richards, N., and Gumucio, D.L.: Expression of multiple alternatively spliced MEFV transcripts in human synovial fibroblasts induced by lipopolysaccharide. *Arthritis Rheum*, 50:3679-89. 2004. PMID: 15529356 [
10. Madison, B., Braunstein, K., Qiao, X., Kuizon, E., and Gumucio, D.: Epithelial Hedgehog signals pattern the intestinal crypt-villus axis. *Development*, 132:279-89, 2005. PMID: 15590741
11. Schaner, P. and Gumucio, D.L.: Familial Mediterranean fever in the post-genomic era (How an ancient disease is providing new insights into inflammatory pathways). *Curr Drug Targets Inflamm Allergy*, 4:67-76, 2005. PMID: 15720238
12. Rieder, G., Tessier, A.J., Qiao, X.T., Madison, B., Gumucio, D. and Merchant, J.L.: Helicobacter-induced intestinal metaplasia in the stomach correlates with Elk-1 and serum response factor induction of villin. *J. Biol. Chem.*, 280:4906-12, 2005. PMID: 15576363
13. Adachi, M., Kurotani, R., Morimura, K., Shah, Y., Sanford, M., Madison, B.B., Gumucio, D.L., Martin, H.E., Peters, J.M. Young, H.A., and Gonzalez, F.J.: PPAR $\omega$  in colonic epithelial cells protects against experimental inflammatory bowel disease. *Gut*, 55:1104-13,2006. PMID: 16547072
14. Jones, R.G., Li, X., Gray, P.D., Kuang, J., Clayton, F., Samowitz, W.S., Madison, B.B., Gumucio, D.L. and Kuwada, S. K.: Conditional deletion of beta1 integrins in the intestinal epithelium causes a loss of Hedgehog expression, intestinal hyperplasia and early postnatal lethality. *J. Cell Biol.* 175:505-14, 2006. PMID: 17088430
15. Li, X., Madison, B.B., Zachanrias, W., Kolterud, Å, States, D. and Gumucio, D.L.: Deconvoluting the intestine: molecular evidence for a major role of the mesenchyme in the modulation of signaling crosstalk. *Physiol Genomics.* 29(3):290-301, 2007. PMID: 17299133
16. Nenci, A., Becker, C., van Loo, G., Danese, S., Huth, M., Nikolaev, A., Gumucio, D., Neurath, M.G. and Pasparakis, M.: Epithelial NEMO/IKKg links innate immunity to chronic intestinal inflammation. *Nature.* 446(7135):557-61, 2007. PMID: 17361131
17. Lopez-Diaz, L., Jain, R.N., Keeley, T.M., VanDussen, K.L., Brunkan, C.S., Gumucio, D.L. and Samuelson, L.C. Intestinal neurogenin 3 directs differentiation of a bipotential secretory progenitor to endocrine cell rather than goblet cell fate. *Dev. Biol.* 309:298-305, 2007. PMID: 17706959
18. Zavros, Y., Waghray, M., Tessier, A., Bai, L., Todisco, A., Gumucio, D., Samuelson, L.C., Dlugosz, A., and Merchant, J.L.: Reduced pepsin a processing of sonic hedgehog in parietal cells precedes gastric atrophy and transformation. *J Biol Chem.* 282:33265-74, 2007. PMID: 17872943
19. Qiao, X.T., Ziel, J.W., McKimpson, W., Madison, B.B., Todisco, A., Merchant, J.L., Samuelson, L.C., and Gumucio, D.L.: Prospective identification of a multi-lineage progenitor in stomach epithelium. *Gastroenterology.* 133:1989-98, 2007. PMID: 18054570

20. Gumucio, D.L., Fagoonee, S., Qiao, X.T., Liebert, M., Merchant, J.L., Altruda, F., Rizzetto, M., and Pellicano, R.: Tissue stem cells and cancer stem cells: potential implications for gastric cancer. *Panminerva Med.* 50:65-71, 2008. PMID: 18427389
21. Yang, H., Madison, B., Gumucio, D.L. and Teitelbaum, D.H.: Specific overexpression of IL-7 in the intestinal mucosa: the role in intestinal intraepithelial lymphocyte development. *Am J Physiol Gastrointest Liver Physiol.* 294:G1421-30. 2008. PMID: 18403617
22. Balci-Peynircioglu, B., Waite, A.L., Hu, C., Richards, N., Staubach-Grosse, A., Yilmaz, E. and Gumucio, D.L.: Pyn, product of the MEFV locus, interacts with the proapoptotic protein, Siva. *J Cell Physiol.* 216:595-602, 2008. PMID: 18330885
23. Yang, H., Gumucio, D.L. and Teitelbaum, D.H.: Intestinal specific overexpression of interleukin-7 attenuates the alternation of intestinal intraepithelial lymphocytes after total parenteral nutrition administration. *Ann Surg.* 248:849-56. 2008. PMID: 18948814
24. Balci-Peynircioglu, B.L., Waite, A.L., Schaner, P., Ekim Taskiran, Z., Richards, N., Orhan, D., Gucer, S., Ozen, S., Gumucio\*, D.L., and Yilmaz\*, E. (\*co-senior authors): Expression of ASC in renal tissues of FMF patients with amyloidosis; postulating a role for ASC in AA type amyloid deposition. *Exp. Biol. Med.* 233:1324-33 2008. PMID: 18791131
25. Lees, C.W., Zacharias, W., Tremelling, M., Noble, C.L., Nimmo, E.R., Tenesa, A., Cornelius, J., Ho, G-T., Torkvist, L., Lofberg, R., Farrington, S., Fitch, P., Drummond, H.E., Arnott, I.D.R., Appelman, H.D., Loane, J., Diehl, L., Campbell, H., Dunlop, M.G., Parkes, M., Howie, S.E.M., Gumucio, D.L. and Satsangi, J.: Identification of GLI1 as an IBD2 susceptibility gene in ulcerative colitis provides novel evidence for the role of hedgehog signaling in regulating colonic inflammatory pathways. *PLOS Medicine*, 5(12):e239, 2008. PMID: 19071955.
26. Waite, A.L., Schaner, P., Richards, N., Balci-Peynircioglu, B., Masters, S.L., Brydges, S.D, Fox, M., Hong, A., Yilmaz, E., Kastner, D.L., Reinherz, E.L. and Gumucio, D.L.: Pyn modulates the intercellular distribution of PSTPIP1. Accepted, PLoS ONE, 2009. (PMID pending).
27. Kolterud, Å, Grosse, A.S., Zacharias, W.J., Walton, K.D., Kretovich, E.K., Madison, B.B., Waghray, M., Ferris, J.E., Hu, C., Merchant, J.L., Dlugosz, A. Kottmann, A.H. and Gumucio, D.: Paracrine hedgehog signaling in stomach and intestine: new roles for hedgehog in gastrointestinal patterning. *Gastroenterology*, May 12, [epub], 2009. PMID: 19445942.

### C. Research Support

#### Ongoing Research Support

**P01 DK62041** MERCHANT (PI); GUMUCIO (SUBPROJECT #1 PI) 8/1/08-7/31/13  
 NIH/NIDDK "Regulation of Intestinal Cell Identity" 2.4 calendar months

Major Goals: This is part of a recently renewed Program Project Grant, and constitutes Project #1. This project will be devoted to the characterization of progenitor cells that we previously identified in the epithelium of antral glands. We will determine if Hh and/or Bmps regulate cell division or quiescence and will lineage trace gastric tumors using Cre drivers that are expressed in the progenitor cells.

Role: PI on Project #1 (No overlap)

**P01 DK62041-01** MERCHANT (PI); GUMUCIO (CELL BIOLOGY CORE, PI) 8/1/08-7/31/13  
 NIH/NIDDK "Cell Biology Core A" 0.6 calendar months

Major goals: This Core provides services for three investigators involved in the PPG. Core services include microscopy, image analysis, specimen processing, staining, immunohistochemistry, quantitative RT-PCR.

Role: Project Director of Core (No overlap)

**R01 DK065850** GUMUCIO (PI) 4/1/05-3/31/010  
 NIH/NIDDK "Cell:Cell interactions in Intestinal Development" 2.4 calendar months

Major Goals: This grant is focused on the role of hedgehog signals during late intestinal development. A combination of mouse models and bioinformatics techniques are used to define the molecular targets of hedgehog signals and to establish the role of hedgehog targets in mesenchymal patterning.

Role: PI (*this project*)

**K18 DK075843** LIEBERT (PI)/ Gumucio (mentor) 9/1/07-8/31/09  
NIH/NIDDK "Senior Investigator Training in Stem Cell Biology" 0 calendar months  
This is a mentored K18 award designed to provide Dr. Monica Liebert, a senior investigator in the field of molecular urology, with expertise in working with adult stem/progenitor cells that are derived from endoderm.  
Role: Mentor (No overlap)

**T32-HD007505** GUMUCIO (PD) 5/1/07-4/30/12  
NIH/NICHD "Training Program in Organogenesis" 0.6 calendar months  
Major Goals: This grant supports a pre-and post-doctoral Training Program in organogenesis, emphasizing a two-mentor structure to facilitate cross-disciplinary training in basic, clinical and applied aspects of organ formation and maintenance, especially as these processes intersect with organ disease and the generation of artificial organ systems.  
Role: Project Director (No overlap)

**University of Michigan CTSA Pilot Study** 12/1/08-11/31/09 0.36 calendar months  
"Role of Hedgehog signaling in inflammatory bowel disease"  
Major goals are to use mouse and human cells to determine whether and how hedgehog signals might impact the innate immune system in the colon.  
Collaborative research grant with John Kao, MD (PI) and Deborah Gumucio, Ph.D. (Co-PI) (No overlap)

**Recently Completed Support:**

**P01 DK62041** MERCHANT (PI); GUMUCIO (SUBPROJECT #1 PI) 7/01/02-06/30/08  
NIH/NIDDK "Regulation of Intestinal Cell Identity" 1.92 calendar months  
Major Goals: This project examines the regulation of villin both in ontogeny and during the development of intestinal metaplasias. Aims are: 1) To identify cis and trans regulators of villin in specific domains of the intestine (crypt-specific and duodenum-specific expression; LCR activity) 2) To examine factors involved in epithelial compartmentalization at the pyloric border; 3) To identify the cis and trans factors that regulate villin induction in intestinal metaplasias.  
Role: PI on Project #1

**P01 DK62041-01** MERCHANT (PI); GUMUCIO (CELL BIOLOGY CORE, PI) 7/01/02-06/30/08  
NIH/NIDDK "Cell Biology Core A" 0.6 calendar months  
Major goals: This Core provides services for four investigators involved in the PPG. Core services include microscopy, image analysis, specimen processing, staining, immunohistochemistry, quantitative RT-PCR. Currently under bridging support, renewal pending.  
Role: Project Director of Core

**RO1 AI53262** GUMUCIO (PI) 12/1/02-11/30/08 1.92 calendar months  
NIH-NIAIMS "Molecular etiology of familial Mediterranean fever"  
Major Goals: This project examines the role of pyrin, protein product of MEFV, in apoptosis, cytoskeletal signaling and cytokine secretion. Aims are to study the functional consequences of pyrin's interaction with ASC (apoptosis speck-associated protein with CARD domain) and PSTPIP1 (proline serine threonine phosphatase interacting protein 1).  
Role: PI

**R21-CA124589** GUMUCIO (PI) 1/1/07-12/31/08 12% EFFORT  
NIH-NCI "A cellular key to the inflammation-metaplasia-carcinoma sequence?"  
Major goals: Characterize the life cycle of putative gastric stem cells. Determine the effects of inflammatory challenge on cell proliferation, and trace whether these cells give rise to tumors in the gastrin null mouse model.  
Role: PI