CURRICULUM VITAE

Anna Lois Means, PhD

PERSONAL DATA

Work address: Anna L. Means
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Place of birth: Gainesville, FL
Citizenship: U.S.A.

EDUCATION

Ohio University, 8/1980-6/1984. B.S., Honors Tutorial College, major in Zoology, received 6/1984.

University of Wisconsin--Madison, 1984-1986. Graduate studies in the Cell and Molecular Biology Program with Dr. Janet E. Mertz in the Department of Oncology.

University of Wisconsin--Madison, 1987-1991. Graduate studies in the Cell and Molecular Biology Program with Dr. Peggy J. Farnham in the Department of Oncology. Ph.D. received 5/1991.

Thesis title: Identification, Purification, and Characterization of HIP1: A Protein That Positions Transcription Initiation Of The Dihydrofolate Reductase Gene.

Cornell University Medical College, Department of Pharmacology, 1991-1999. Postdoctoral associate with Dr. Lorraine J. Gudas, Department of Pharmacology.

Vanderbilt University Medical Center, 1999-2000. Research Associate, Division of Surgical Oncology.

ACADEMIC APPOINTMENTS

Vanderbilt University Medical Center, 2000-2004. Research Assistant Professor, Division of Surgical Oncology.

Vanderbilt University Medical Center, 2004-present. Assistant Professor, Division of Surgical Oncology and Department of Cell and Developmental Biology.

PROFESSIONAL ASSOCIATIONS

American Association for Cancer Research
Society for Developmental Biology
American Society for Cell Biology
American Pancreatic Association

Vanderbilt-Ingram Cancer Center
Vanderbilt Digestive Disease Research Center
Vanderbilt Diabetes Research and Training Center
Vanderbilt Program in Developmental Biology

PROFESSIONAL ACTIVITIES

TEACHING

Molecular Developmental Biology (CDB 341)
Introductory module
Endodermal development, lecture and discussion, 2004-2007
Ectodermal development, lecture and discussion, 2005-2007
Branching morphogenesis module
Branching morphogenesis in the pancreas, lecture and discussion, 2007
Tissue morphogenesis module, 2008
Organized 4 week module (8 classes)
Invited and hosted outside speaker
Led four lectures and discussion sessions
Worked with other investigators to present remaining four sessions
Size regulation via Hippo/Warts pathway, 2012
Organized 4 week module (8 classes)
Invited and hosted outside speaker
Led five lecture and discussion sections
Supervised senior graduate student leading one lecture/discussion

Cancer and Embryonic Development (CDB 320/CANB 320)
Epithelial-mesenchymal interactions, lecture and discussion, 2007, 2009

Epithelial Pathobiology (CDB 324)
Tubulogenesis lecture and discussion, 2008

RESEARCH SUPERVISION

Undergraduate students:
Leah McMillan, 2004, 2006
Katherine Guess, 2008
Kayla Bell, 2010
Elizabeth Moss, 2011
Katherine Lee, 2011-present

Graduate summer programs:
Kevin Branch, 2005. Incoming IGP student.
Susan Anthony, 2005. Incoming IGP student.

Ben Adebayo, 2008. Vanderbilt Diabetes Research Training Program for medical students
Khaisha Johnson, 2010. Vanderbilt Diabetes Research Training Program for medical students

Graduate student trainee:
Billy J. Carver, IGP student, 2006-2008.

Postdoctoral Trainee:
Stacy A. Blaine, 2006-2009.

Other training:
Isolation and culture of primary pancreatic acinar cells:
Howard Crawford (Lynne Matrisian lab), 2001
Yiannis Drosos (Beatriz Sosa-Pineda lab), 2010
Jackie Ellis (Joseph Kissil lab), 2010

Dissection and culture of embryonic pancreas:
Ben Rhoades (Anil Rustgi lab), 2004
Elizabeth Tweedie Ables (Maureen Gannon lab), 2005
Michelle Guney (Maureen Gannon lab), 2007

OTHER PROFESSIONAL ACTIVITIES

Vanderbilt Pancreatic Cancer Researchers (VPCR), Founder and organizer, 2010-present
I brought together all those at Vanderbilt studying pancreatic cancer both at bench and at bedside for a monthly research conference.

Beta Cell Interest Group, 2004-present
Organizer, 2009-present, seminar series for internal investigators to report and get feedback on studies related to pancreas development and function.

Beta Cell Biology Histology Core, Supervisor, 2002-2004
Supervised histology services for members of the Beta Cell Biology Consortium.
Worked with investigators to plan and interpret data from this core.

Pilot & Feasibility Grant Review Panel, Vanderbilt Digestive Disease Research Center, 2007-2009.

NIH CIGP study section, ad hoc reviewer, 2006.

Pancreatic Cancer Action Network, Nashville Chapter
Volunteer, 2010-present.

PENDING RESEARCH SUPPORT

NIH/NCI R21 application
"Kras and HB-EGF synergy in the regulation of pancreatic cancer induction"
The objective of this work is to understand the role of HB-EGF signaling in Kras-initiated pancreatic cancer.

NIH/NCI R21 application

"Regulation of pancreatic cancer by the tumor microenvironment"

The work proposed here develops and uses novel 3-dimensional co-culture systems and mouse models to understand how inflammatory cells and fibrotic cells regulate promotion and progression of pancreatic cancer.

COMPLETED RESEARCH SUPPORT

P50CA095103 (Robert J. Coffey, PI) NIH/NCI

06/01/2008 – 05/31/2010

SPORE in GI Cancer

Pilot & Feasibility Award (Means, PI)

The roles of Kras and EGFR signaling in pancreatic and intestinal tumorigenesis

This pilot grant has enabled us to determine whether activation of a condition $Kras^{G12D}$ allele via the CK19-CreERT gene would allow us to investigate tumorigenesis in the pancreas or whether tumors would more quickly develop in other organs expressing CK19.

1 R01 CA98322 (Anna L. Means, PI) NIH/NCI 3/1/04 - 2/28/10

"Heparin-binding EGF in pancreatic disease"

The goal of this project is to elucidate the roles of the epidermal growth factor receptor and its ligand, HB-EGF, in establishment of the pancreatic fibrosis that is associated with both chronic pancreatitis and pancreatic cancer.

R21CA123061-01 (Anna L. Means, PI), NIH/NCI, 7/1/06 – 6/30/09

"The role of EGFR signaling in progression of Kras-induced pancreatic tumors"

The goal of this grant is to determine the role that signaling through the epidermal growth factor receptor plays in pancreatic tumors that result from activation of Kras. These experiments use genetically engineered mice to express mutated Kras in combination with either increased or decreased EGFR signaling.

JDRF 1-2006-759 (Anna L. Means, PI), Juvenile Diabetes Research Foundation 07/01/06-06/30/09

"Generating New Islets In Vivo And In Vitro"

The goal of this project is define the cell of origin for the duct-associated endocrine cells that arise in association with activation of the EGF receptor.

UO1 CA84239 (Robert J. Coffey, PI) NIH/NCI, 4/1/04 - 3/31/09

"Prevention and metastasis: Final frontiers in colon cancer"

The goals of this grant are to understand the genetic and environmental influences on establishment and metastasis of colon cancer using mouse models. Dr. Means's role in this project is to establish mouse tumor models that have conditional deletion of tumor suppressor genes specifically in the intestinal tract and pancreas.

5P30 DK58404 (D. Brent Polk, PI) NIH/NIDDK, 6/1/02 – 5/31/07

"Molecular and Cellular Basis for Digestive Diseases"

Pilot& Feasibility Study (Means, Anna L., PI), 6/1/05 – 5/31/07

"Regulation of differentiation in the embryonic pancreas"

The goal of this project is to elucidate the role of EGFR signaling in early branching and differentiation of the embryonic pancreas.

P01 DK42502 (Mark Magnuson, PI) NIH/NIDDK, 7/01/00 - 06/30/05

"Pancreatic Morphology Core, Core D, Genes of Pancreatic Function and Development"

The goal of this project is to provide histological support to members of this program project grant. Dr. Means is responsible for overseeing a technician who embeds, sections, and performs immunohistochemistry. Dr. Means also provides training for members of the program project grant, and aids in planning and interpretation of histological experiments.

UO1 CA84239-05 (Robert J. Coffey, PI) NIH/NCI 9/30/99 – 3/31/04

"Mouse Cancer Models via TGF-β RII Loss"

The goals of this project were to develop mouse models of cancer via loss of the TGFβ RII receptor. Dr. Means's responsibility was to assist in the establishment and analyses of genetically altered mice that model stages of colon and pancreatic cancer.

PEER-REVIEWED PUBLICATIONS

1. Farnham, P.J., and **Means, A.L**. 1990. Sequences downstream of the transcription initiation site modulate the activity of the murine dihydrofolate reductase promoter. Mol. Cell. Biol. 10: 1390-1398.

2. **Means, A.L**., and Farnham, P.J. 1990. Transcription initiation from the DHFR promoter is positioned by HIP1 protein binding at the initiation site. Mol. Cell. Biol. 10: 653-661.

3. **Means, A.L**., Slansky, J.E., McMahon, S.L., Knuth, M.W., and Farnham, P.J. 1992. The HIP1 binding site is required for growth regulation of the DHFR promoter. Mol. Cell. Biol. 12: 1054-1063.

4. **Means, A.L**. and Gudas, L.J. 1996. FGF-2, BMP-2, and BMP-4 regulate retinoid binding proteins and receptors in 3T3 cells. Cell Growth and Differentiation 7: 989-996.

5. **Means, A.L**. and Gudas, L.J. 1997. The CRABP I gene contains two separable, redundant regulatory regions active in neural tissues in transgenic mouse embryos. Developmental Dynamics 209: 59-69.

6. **Means, A.L**., Thompson, J.R., and Gudas, L.J. 2000. Transcriptional regulation of the cellular retinoic acid binding protein I gene in F9 teratocarcinoma cells. Cell Growth and Differentiation 11: 71-82.

7. Scoggins CR, Meszoely IM, Wada M, **Means AL**, Yang L, Leach SD. 2000. p53-dependent acinar cell apoptosis triggers epithelial proliferation in duct-ligated murine pancreas. Am J Physiol Gastrointest Liver Physiol. (5):G827-36.

8. Meszoely, I.M., **Means, A.L**., Scoggins, C.R., Leach, S.D. 2001. Developmental aspects of early pancreatic cancer. Cancer Journal 7: 242-250.

9. **Means, A.L**. and Leach, S.D. 2001. Lineage commitment and cellular differentiation in exocrine pancreas. Pancreatology 1: 587-596.

10. **Means, A.L**., Ray, K.C., Singh, A.B., Washington, M.K., Whitehead, R.H., Harris, R.C., Wright, C.V.E., Coffey, R.J., and Leach, S.D. 2003. Overexpression of heparin-binding EGF-like growth factor in mouse pancreas results in fibrosis and epithelial metaplasia. Gastroenterology 124: 1020-1036.

11. Samaras, S.E., Zhao, L., **Means, A**., Henderson, E., Matsuoka, T., and Stein, R. 2003. The islet b cell-enriched RIPE3b1/Maf transcription factor regulates *pdx*-1 expression. J. Biol. Chem. 278: 12263-70.

12. Matsuoka, T., Zhao, L. Jarrett, H.W., Friedman, D., **Means, A**., Stein, R. 2003. Members of the large Maf transcription family regulate insulin gene transcription in islet beta-cells. Mol Cell Biol.: 23:6049-62.

13. Nomura, S., Settle, S.H., Leys, C., **Means, A.L**., Peek, R., Leach, S.D. Wright, C.V., Coffey, R.J., and Goldenring, J.R. 2005. Evidence for repatterning of the gastric fundic epithelium associated with Ménétrier's disease and TGFa overexpression. Gastroenterology 128: 1292-1305.

14. **Means, A.L**., Chytil, A., Moses, H.L., Coffey, R.J., Wright, C.V.E., Taketo, M.M., Grady, W.M. 2005. The keratin 19 gene drives Cre recombinase expression throughout the early post-implantation mouse embryo. Genesis 42: 23-27.

15. **Means, A.L**., Meszoely, I.M., Suzuki, K., Miyamoto, Y., Rustgi, A.K., Coffey, R.J., Wright, C.V., Stoffers, D.A., and Leach, S.D. 2005. Pancreatic epithelial plasticity mediated by acinar cell transdifferentiation and generation of nestin-positive intermediates. Development 132: 3767-3776.

16. **Means, A.L**., Xu, Y., Zhao, A., Ray, K.C., and Gu, G. 2008. A CK19-CreER^{T} knockin mouse line allows for conditional DNA recombination in epithelial cells in multiple endodermal organs. Genesis 46: 318-323.

17. Ray, KC, Blaine, SA, Washington, MK, Braun, A.H., Singh, A.B., Harris, R.C., Harding, P.A., Coffey, R.J. and **Means, A.L**. 2009 Transmembrane and soluble isoforms of heparin-binding EGF-like growth factor regulate distinct processes in the pancreas. Gastroenterology 137: 1785-1794. PMC2767440

18. Blaine, S.A., Ray, K.C., Branch, K.M., Robinson, P.S., Whitehead, R.H., and **Means, A.L**. 2009. The epidermal growth factor receptor regulates pancreatic fibrosis. Am J Physiol, Gastrointest Liver Physiol 297: 434-441. PMC2739824

19. Zhang H, Ables ET, Pope CF, Washington MK, Hipkens S, **Means AL**, Path G, Seufert J, Costa RH, Leiter AB, Magnuson MA, Gannon M. (2009). Multiple, temporal roles for HNF6 in pancreatic endocrine and ductal differentiation. Mech Dev 126: 958-973. PMC2783291

20. Wescott MP, Rovira M, Reichert M, von Burstin J, **Means A**, Leach SD, Rustgi AK. (2009) Pancreatic Ductal Morphogenesis and the Pdx-1 Homeodomain Transcription Factor. Mol Biol Cell 20: 4838-4844. PMC2777112

21 Blaine, SA, Ray, KC, Anunobi, R, Gannon MA, Washington, MK, **Means, AL**. 2010. Adult pancreatic acinar cells give rise to ducts but not endocrine cells in response to growth factor signaling. Development 137:2289-2296. PMC2889602

22. Ray, KC, Bell, KM, Yan, J, Gu, G, Chung, CH, Washington, MK, **Means, AL**. 2011. Epithelial tissues have varying degrees of susceptibility to KrasG12D-initiated tumorigenesis in a mouse model. PlosOne 6: e16786. PMC3032792

23. Guney, MA, Petersen, CP, Boustani, A, Duncan, MR, Gunasekaran, U, Menon, R, Warfield, C, Grotendorst, GR, **Means, AL**, Economides, AN, Gannon, M. 2011. Connective tissue growth factor acts within both endothelial cells and beta cells to promote proliferation of developing beta cells. PNAS 108:15242-15247. PMC3174622

24. Vanderpool, C, Sparks, EE, Huppert, KA, Gannon, M, **Means, AL**, Huppert, SS. 2011. Genetic interactions between hepatocyte nuclear factor-6 and notch signaling regulate mouse intrahepatic bile duct development in vivo. Hepatology 55: 233-243. PMC3235248

25. Freeman, TJ, Smith, JJ, Chen, X., Washington MK, Roland, JT, **Means, AL**, Eschrich, SA, Yeatman, TJ, Deane, NG, and Beauchamp, RD. 2012. Smad4-mediated signaling inhibits intestinal neoplasia by inhibiting expression of beta-catenin. Gastroenterology 142: 562-571.

26. Westmoreland JJ, Drosos Y, Kelly J, Ye J, **Means AL**, Washington MK, Sosa-Pineda, B. 2012. Dynamic distribution of claudin proteins in pancreatic epithelia undergoing morphogenesis and neoplastic transformation. Dev. Dyn. 241: 583-594. PMC3288608

27. Powell, AE, Yi, L, Franklin, JL, Wang, Y, Higginbotham, JN, Meador, CB, Poulin, E, **Means AL**, Washington, MK, Haigis, KM, Coffey, RJ. 2012. Lrig1, a pan-ErbB negative regulator, marks quiescent intestinal stem cells and acts as a tumor suppressor. Cell, 149(1):146-158. PMID:22464327

28. Ray, KC, Revetta, FL, Blaine, SA, Bridges, LR, Guess, KE, Washington, MK Crawford, HC, **Means, AL**. Heparin-Binding Epidermal Growth Factor-like Growth Factor eliminates constraints on activated Kras for the rapid promotion of pancreatic neoplasia. *In review*.

REVIEWS AND BOOK CHAPTERS

1. Means, Anna L. and Gudas, Lorraine J. 1995. The roles of retinoids in vertebrate development. Annu. Rev. Biochem. 64: 201-233.

2. Means, Anna L. 1997. Transgenic Mice in Cancer Research. In Encyclopedia of Cancer, Vol. III. J. R. Bertino, Editor-in-Chief. Academic Press: San Diego. Pp. 1777-1784.

3. Meszoely, I.M., Means, A.L., Scoggins, C.R., Leach, S.D. 2002. Epithelial stem cell in pancreatic regeneration and neoplasia. In Pancreatic Cancer. Springer-Verlag, New York. Pp. 63-72.