BIOGRAPHICAL SKETCH

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NAME: **Beauchamp, Robert Daniel**

eRA COMMONS USER NAME (credential, e.g., agency login): **BEAUCHRD**

TITLE: Professor of Surgery; Professor of Cellular and Developmental Biology; Professor of Cancer Biology

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable*	Completion Date MM/YYYY	FIELD OF STUDY
Texas Tech University, Lubbock, TX	B.S.	05/1978	Microbiology
University of Texas Medical Branch, Galveston, TX	M.D.	05/1982	Medicine
University of Texas Medical Branch, Galveston, TX	Internship	06/1987	General Surgery
Vanderbilt University Medical Center, Nashville, TN	Fellowship	06/1989	Cell Biology

A. Personal Statement.

I serve as the John Clinton Foshee Distinguished Professor of Surgery served as Chairman of the Section of Surgical Sciences and Surgeon-in-Chief of Vanderbilt University Hospital for 17 years, from July 2001 through June 2018. As of July 1, 2018, I have a role as Vice President for Vanderbilt-Ingram Cancer Center Network Affairs, planning strategic growth of our cancer center. I hold a joint appointment as Professor in the Department of Cell and Developmental Biology. My service also includes functioning as Deputy Director of the Vanderbilt-Ingram Cancer Center and as co-leader of the GI Cancer Program for the Cancer Center. Our research efforts have largely involved colorectal carcinogenesis, the biology of GI cancer cell invasion and metastasis, and in the identification of novel molecular biomarkers and therapeutic targets in colorectal and other alimentary tract malignancies. I also have a longstanding interest and experience in the field of TGF-beta superfamily signaling and its roles in the GI tract and in GI carcinogenesis, particularly in the colon. My laboratory uses molecular genetics and 3-D cell culture and organoid culture of small intestinal epithelium and colon as approaches to examine mechanistic questions in epithelial cell biology. Our laboratory uses a variety of mouse models, including xenografts and genetically modified mouse models. We also use de-identified human intestinal tissues and tumor tissues in our research under approved protocols. Extending from a post-doctoral fellowship in the laboratory of Dr. Hal Moses, my research focus has included understanding the roles of transforming growth factors in the GI tract and in GI malignancies, along with epithelial to mesenchymal transition. Our work identified unexpected tumor promoting roles of TGFβ by cancer cells that was significantly different than effects on normal/non-cancer cell types. Over the past 25 years, I have trained and mentored 26 postdoctoral fellows, served as primary mentor for 6 graduate students who have completed their Ph.D. work in my laboratory and co-mentor for at least 6 other doctoral students, mentored at least eight junior faculty members in their research career development, and have supervised and mentored numerous college undergraduate students and medical students for summer research rotations or year-long medical scholars projects or honors thesis work.

a. Smith JJ, Deane NG, Wu F, Merchant NB , Zhang B, Jiang A, Lu P, Johnson JC, Schmidt C, Bailey CE, Eschrich S, Kis C, Levy S, Washington MK, Heslin MJ, Coffey RJ, Yeatman TJ, Shyr Y, **Beauchamp RD**. Experimentally Derived Metastasis Gene Expression Profile Predicts Recurrence and Death in Patients with Colon Cancer. *Gastroenterology.* 2010 Mar, 138(3):958-68. Epub 2009 Nov 13. PMID: 19914252. PMCID: PMC3388775
b. Freeman TJ, Smith JJ, Chen X, Washington MK, Roland JT, Means AL, Eschrich SA, Yeatman TJ, Deane NG, **Beauchamp RD**. Smad4-Mediated Signaling Inhibits Intestinal Neoplasia by Inhibiting Expression of β-Catenin. *Gastroenterology.* 2012 Mar;142(3):562-571.e2. Epub 2011 Nov 22. PMID: 22115830. PMCID: PMC3343368

c. Hanson AJ, Wallace HA, Freeman TJ, **Beauchamp RD**, Lee LA, Lee E. XIAP monoubiquitylates Groucho/TLE to promote canonical Wnt signaling. *Mol Cell.* 2012 Mar 9:45(5):619-628. Epub 2012 Feb 1. PMID: 22304967. PMCID: PMC3299836
d. Sato-Diaz K, Benchabane H, Tiwari A, Tien A, Li B, Thompson JJ, Hyde AS, Sawyer LM, Jodoin JN, Santos E, Lee LA, Coffey RJ, **Beauchamp RD**, Williams CS, Kenworthy AK, Robbins DJ, Ahmed Y, Lee E. APC inhibits ligand-independent Wnt signaling by the clathrin endocytic pathway. Dev Cell 2018 Mar 12; 44:566-581, e8, PMID:29537782; PMC5884143

B. Positions and Honors

Positions and Employment

1987-1988 Research Instructor of Cell Biology, Vanderbilt University, Nashville, TN
1988-1989 Research Assistant Professor of Cell Biology and Assistant Professor of Surgery (non-tenure track), Vanderbilt University, Nashville, TN
1989-1993 Assistant Professor, Departments of Surgery and Human Biological Chemistry & Genetics (tenure track), UTMB, Galveston, TX
1993-1994 Associate Professor with tenure, Departments of Surgery and Human Biological Chemistry and Genetics, UTMB, Galveston, TX
1994-1997 Associate Professor with tenure, Departments of Surgery (Division of Surgical Oncology) and Cell and Developmental Biology, Vanderbilt University School of Medicine, Nashville, TN
1995-1999 Deputy Associate Director for Clinical Programs, The Vanderbilt Cancer Center
1997-2001 Professor of Surgery, The John Sawyers Professor of Surgery, Director, Division of Surgical Oncology, Vanderbilt University
1997-present Professor, Department of Cell and Developmental Biology, Vanderbilt University
1999-2011 Associate Director for Clinical Programs, Vanderbilt-Ingram Cancer Center
2001-present Professor, Department of Cancer Biology, Vanderbilt University
2001-present J.C. Foshee Distinguished Professor and Chairman, Section of Surgical Sciences, Vanderbilt University, Surgeon-in-Chief, Vanderbilt University Hospital
2011-present Deputy Director, Vanderbilt-Ingram Cancer Center, Nashville, TN
2014-present Co-Director, GI Oncology Program, Vanderbilt-Ingram Cancer Center

Other Experience and Professional Memberships

1990-present Member, American Gastroenterological Association
1990-present Fellow: American College of Surgeons
1991-present Member: American Association for Cancer Research
1992-present Member: Society of University Surgeons, past Councilman at large, past President.
1993-present Member: American Society for Cell Biology
1993-present Member: Society for Surgery of the Alimentary Tract
1994-present Member: American Society of Clinical Oncology
1994-present Member: Society of Surgical Oncology
1995-present Member: Eastern Cooperative Oncology Group
1996-2003 Editorial Board Member: *Journal of Surgical Research*
1997-1012 Fellow: American Surgical Association, program committee member, Chair 2012
1997-2005 Editorial Board Member: *Surgery*
1998-present Associate Editor: *Sabiston Textbook of Surgery*, Editions 16-20
1999-2003 Editorial Board Member: *Annals of Surgical Oncology*
2001-2006 Member: Surgical Research and Education Committee, American College of Surgeons
2001-present Member: American Society for Clinical Investigation
2003 NIH SPORES in Pancreatic Cancer Peer Review Study Section
2003-2007 NIH Gastrointestinal Cell and Molecular Biology (GCMB) Study Section, regular member
2003-present Editorial Board Member: *Journal of the American College of Surgeons*
2007-2010 American Gastroenterology Association Institute, Research Awards Panel
2007-present Editorial Board Member: *American Journal of Surgery*
2010-2011 Member: Pancreatic Cancer Action Network-AACR Innovative Grants Scientific Review Committee
2010-2012 NIH College of CSR Reviewer
2016-present *Gastroenterology*, Advisory Board member

Honors

1981 Elected to Alpha Omega Alpha
1982 The Herman R. Barnett Memorial Award for Academic Achievement in Surgery and Anesthesiology- UTMB Galveston
1982 Gold Headed Cane Award, Honorable Mention-UTMB Galveston
1982 UTMB Medical School, Graduated Highest Honors
1983 Outstanding Surgical PGY-1 House Officer
1987 Physician Scientist Award, NCI, K11
1997 First recipient of the John Sawyers Endowed Professorship, Vanderbilt University
2001 Elected to the American Society for Clinical Investigation
2009 The Frank Boehm Award for Excellence in Teaching Continuing Medical Education
2009-2012 Vanderbilt University Faculty Senate, elected
2012 Elected to the National Academy of Medicine (previously IOM), inducted October 2013
2013 Elected Fellow of the American Association for the Advancement of Science, inducted Feb 2014
2015 The Flance-Karl Award for Scientific Achievement from the American Surgical Association
2015 Ashbel Smith Distinguished Alumnus Award, UTMB Galveston
2016 The Rodman E. Sheen and Thomas G. Sheen Award

C. Contributions to Science (selected from 153 peer-reviewed publications)

1. We identified inhibition of cyclin D1 expression and G1 cell cycle arrest as an important effect of TGFβ on intestinal epithelial cells. We further showed that intestinal adenomas from Min/+ mice expressed decreased levels of TGFβ type II receptor, along with increased levels of cyclin D1 and Cdk4. Human adenomas from FAP patients also exhibited increased levels of cyclin D1 and Cdk4. We subsequently demonstrated that forced expression of cyclin D1 in the liver caused hepatic adenomas and hepatocellular carcinoma in transgenic mice.

a. Ko TC, Sheng H-M, Reisman D, Thompson EA, **Beauchamp RD**. Transforming growth factor- β 1 inhibits cyclin D1 expression of intestinal epithelial cells. *Oncogene* 1995, 10:177-184.
b. Ko TC, Yu W, Sakai T, Sheng H, Shao J, **Beauchamp RD**, Thompson EA. TGF-β1 effects on proliferation of rat intestinal epithelial cells are due to inhibition of cyclin D1 expression. *Oncogene* 1998, 16:3445-3454.
c. Zhang T, Nanney LB, Peeler MO, Williams CS, Lamps L, Heppner KJ, DuBois RN, **Beauchamp RD**. Decreased TGF- β Type II receptor expression in intestinal adenomas from Min/+ Mice is associated with increased cyclin D1 and Cdk4 expression. *Cancer Research* 1997, 57:1638-1643.
d. Deane NG, Parker MA, Aramandla R, Diehl L, Lee WJ, Washington MK, Nanney LB, Shyr,Y., and **Beauchamp RD**. Hepatocellular Carcinoma Results from Chronic Cyclin D1 Overexpression in Transgenic Mice. *Cancer Research* 2001, 61 (14):5389-5395.

2. Our work elucidated the role of COX2 and its regulation, in part by TGFβ, in intestinal neoplasia, particularly in cells with activated RAS. COX-2 was shown to be an important potential therapeutic target for both chemoprevention of colorectal cancers and possibly therapeutic for established cancers. Our laboratory helped to identify important mechanisms involved in upregulation of COX-2 expression in colorectal cancer.

a. Sheng H, Shao J, Kirkland SC, Isakson P, Coffey RJ, Morrow J, **Beauchamp RD**, DuBois RN. Inhibition of human colon cancer cell growth by selective inhibition of cyclooxygenase-2. *The Journal of Clinical Investigation* 1997, 99:2254-2259.
b. Sheng H, Williams CS, Shao J, Liang P, DuBois RN, **Beauchamp RD**. Induction of cyclooxygenase-2 by activated Ha-ras oncogene in Rat-1 fibroblasts and the role of mitogen-activated protein kinase pathway. *The Journal of Biological Chemistry* 1998, 273:22120-22127.
c. Sheng H, Shao J, Dixon DA, Williams CS, Prescott SM, DuBois RN, **Beauchamp RD**. TGF-β1 enhances Ha-Ras-induced expression of cyclooxygenase-2 in intestinal epithelial cells via stabilization of mRNA. *Journal of Biological Chemistry* 2000, 275 (9):6628-6635.
d. Dixon D, Balch G, Kedersha N, Anderson P, Zimmerman G, **Beauchamp RD**, Prescott SM. Regulation of Cyclooxygenase-2 Expression by the translational Silencer TIA-1. *Journal of Experimental Medicine* 2003, Vol 198 (3):475-81. PMID: 12885872

3. In collaboration with colleagues in the departments of Biostatistics and Biomedical Informatics, we have conducted studies to identify molecular subtypes of primary human colorectal cancers in order to identify

prognostic, and eventually predictive, molecular biomarkers to guide therapeutic decisions. This work also has the goal improving our understanding of the complex biology underpinning the genomic alterations in colorectal cancers.

a. Smith JJ, Deane NG, Wu F, Merchant NB , Zhang B, Jiang A, Lu P, Johnson JC, Schmidt C, Bailey CE, Eschrich S, Kis C, Levy S, Washington MK, Heslin MJ, Coffey RJ, Yeatman TJ, Shyr Y, **Beauchamp RD**. Experimentally Derived Metastasis Gene Expression Profile Predicts Recurrence and Death in Patients with Colon Cancer. *Gastroenterology.* 2010 Mar, 138(3):958-68. Epub 2009 Nov 13. PMID: 19914252. PMCID: PMC3388775
b. Oh SC, Park YY, Park ES, Lim JY, Kim SM, Kim SB, Kim J, Kim SC, Chu IS, Smith JJ, **Beauchamp RD**, Yeatman TJ, Kopetz S, Lee JS. Prognostic Gene Expression Signature Associated with Two Molecularly distinct subtypes of Colorectal Cancer. *Gut.* 2012 Sep; 61(9):1291-8. Epub 2011 Oct 13. PMID: 21997556. PMCID: PMC3419333.
c. Tripathi MK, Deane NG, Zhu J, An H, Mima S, Wang X, Padmanabhan S, Shi Z, Prodduturi N, Ciombor KK, Chen X, Washington MK, Zhang B, **Beauchamp RD**. Nuclear Factor of Activated T-cell Activity is Associated with Metastatic Capacity in Colon Cancer. *Cancer Res.* 2014 Dec1;74(23):6947-57. doi: 10.1158/0008-5472. CAN-14-1592. Epub: 2014 Oct 15. PMID: 25320007. PMCID: PMC4252979
d. Zhu J, Deane NG, Lewis KB, Padmanabhan C, Washington MK, Ciombor KK, Timmers C, Goldberg RM, **Beauchamp RD**, Chen X. Evaluation of frozen tissue-derived prognostic gene expression signatures in FFPE colorectal cancer samples. *Sci Rep.* 2016 Sep 14;6:33273. doi: 10.1038/srep33273. PMID: 27623752

4. Much of our work over the past decade has been focused on understanding EMT and its roles in cancer cell invasion and metastasis. As part of that investigation, we have explored the dysregulation of epithelial cell junctional proteins such as E-cadherin and adherens junction components such as β-catenin in colorectal cancers. This work has also led to improved understanding of Wnt signaling in colorectal cancer.

a. Dhawan P, Singh AB, Deane NG, No Y, Shiou SR, Schmidt C, Neff JG, Washington MK, **Beauchamp RD**. Claudin-1 regulates cellular transformation and metastatic behavior in colon cancer. *J Clinical Investigation* 2005, 115:1765-1176. PMID: 15965503
b. Singh AB, Sharma A, Smith JJ, Krishnan M, Chen X, Eschrich S, Washington MK, Yeatman TJ, **Beauchamp RD**, Dhawan P. Claudin-1 Up-regulates the Repressor ZEB-1 to Inhibit E-Cadherin Expression in Colon Cancer Cells. *Gastroenterology.* 2011 Dec;141(6): 2140-53. Epub 2011 Aug 28. PMID: 21878201. PMCID: PMC3395068
c. Williams CS, Zhang B, Smith JJ, Jayagopal A, Barrett CW, Pino C, Russ P, Presley SH, Peng D, Rosenblatt DO, Haselton FR, Yang JL, Washington MK, Chen X, Eschrich S, Yeatman TJ, El-Rifai W, **Beauchamp RD**, Chang MS. BVES regulates EMT in human corneal and colon cancer cells and is silenced via promoter methylation in human colorectal carcinoma. *J Clin Invest.* 2011 Oct; 121(10):4056-4069. Epub 2011 Sep 12. PMID: 21911938. PMCID: PMC3195453
d. Hanson AJ, Wallace HA, Freeman TJ, **Beauchamp RD**, Lee LA, Lee E. XIAP monoubiquitylates Groucho/TLE to promote canonical Wnt signaling. *Mol Cell.* 2012 Mar 9:45(5):619-628. Epub 2012 Feb 1. PMID: 22304967. PMCID: PMC3299836

5. Our work has contributed to a better understanding of the complex roles of TGFβ family signaling, particularly via the canonical SMAD4 pathway, in normal intestinal epithelial homeostasis and how this signaling is altered in colorectal carcinomas and other cancers. We demonstrated that RAS oncogene activation markedly alters responses to TGFβ signaling from tumor suppression to tumor promoting effects. Our work has also elucidated the importance of TGFβ signaling in tumor immunosurveillance.

a. Torre-Amione G, **Beauchamp RD**, Koeppen H, Park BH, Schreiber H, Moses HL, Rowley DA. A highly immunogenic tumor transfected with a murine transforming growth factor type β_1 cDNA escapes immune surveillance. *Proc Natl Acad of Sci USA*, 1990 Feb; 87(4):1486-1490.
b. Shiou SR, Singh AB, Moorthy K, Datta PK, Washington MK, **Beauchamp RD**, Dhawan P. Smad4 Regulates Claudin-1 Expression in a Transforming Growth Factor-β – Independent Manner in Colon Cancer Cells. *Cancer Res.* 2007 Feb 15, 67(4):1571-1579. PMID: 17308096.
c. Freeman TJ, Smith JJ, Chen X, Washington MK, Roland JT, Means AL, Eschrich SA, Yeatman TJ, Deane NG, **Beauchamp RD**. Smad4-Mediated Signaling Inhibits Intestinal Neoplasia by Inhibiting Expression of β-Catenin. *Gastroenterology.* 2012 Mar;142(3):562-571.e2. Epub 2011 Nov 22. PMID: 22115830. PMCID: PMC3343368

d. Means AL, Freeman TJ, Zhu J, Woodbury LG, Marincola-Smith P, Wu C, Meyer AR, Weaver CJ, Padmanabhan C, An H, Zi J, Wessinger BC, Chaturvedi R, Brown TD, Deane NG, Coffey RJ, Wilson KT, Smith JJ, Sawyers CL, Goldenring JR, Novitskiy SV, Washington MK, Shi C, Beauchamp RD. Epithelial Smad4 deletion upregulates inflammation and promotes inflammation-associated cancer. Cellular and Molecular Gastroenterology and Hepatology 2018. Published online **2018** May 24. doi: 10.1016/j.jcmgh.**2018**.05.006. PMCID: PMC6083016

Complete List of Published Work in MyBibliography: http://www.ncbi.nlm.nih.gov/sites/myncbi/1RQ-hyyYj505g/bibliography/47914453/public/?sort=date&direction=ascending

Ongoing Research Support:

VUMC59318(R01CA158472) **PI: Beauchamp** **06/01/2016-05/31/2019**
NIH/NCI
Integrative prediction models for metastasis risk in colon cancer
The long-term goal for this proposal is to develop a clinically useful metastasis score from diverse type of data that can be applied to stage II and III colon cancer patients for the purpose of reducing mortality, morbidity, and the cost associated with colon cancer and colon cancer treatment.

5P30CA068485-21 **PI: Pietenpol** **04/30/2016 – 08/31/2020**
NCI
Cancer Center Support Grant
To coordinate and integrate the cancer-related activities of Vanderbilt, conduct support and enhance cancer research and integrate cancer-related research throughout the university and to coordinate and integrate the care of cancer patients at VUMC and VA.

Completed Research Support

5R01GM088822-04 **PI: Zhang/Beauchamp** **08/20/2009-06/30/2014**
NIH/NIGMS
Systems approach to the biological basis of colon cancer metastases
The proposed studies will provide important information on the network mechanisms of CRC metastasis and use this information to improve patient prognosis and discover novel therapeutic targets.

5R01CA158472-04 **PI: Chen/Beauchamp** **08/01/2012-06/30/2015**
NIH/NCI
Integrative prediction models for metastasis risk in colon cancer
The long-term goal for this proposal is to develop a clinically useful metastasis score from diverse type of data that can be applied to stage II and III colon cancer patients for the purpose of reducing mortality, morbidity, and the cost associated with colon cancer and colon cancer treatment.

6R01 CA069457-20 **PI: Beauchamp** **06/01/2016 -05/31/2017**
NIH/NCI (CA)
EMT Regulation in Gastrointestinal Epithelial Cells
This application seeks to explore the mechanisms underlying the transition of tumor cells from a benign to a malignant phenotype.

3R01 CA069457-20S1 **PI: Beauchamp** **06/01/2016 -05/31/2017**
NIH/NCI (CA)
EMT Regulation in Gastrointestinal Epithelial Cells
This application seeks to explore the mechanisms underlying the transition of tumor cells from a benign to a malignant phenotype.

6P50 CA95103-15 **PI: Coffey** **05/01/2016 -04/30/2017**
NIH/NCI (CA)
Spore in GI cancer
Molecular Markers for CRC Recurrence
The major goals of this project are to 1) Develop our 34-gene nucleic acid-based colon cancer prognostic classifier for use in FFPE tissue samples and refine through a competitive evaluation of selected and published signature elements, using the novel nCounter multiplex expression analysis approach. 2) Develop our 34-gene nucleic acid-based colon cancer prognostic classifier for use in FFPE tissue samples and refine through a

competitive evaluation of selected and published signature elements, using the novel nCounter multiplex expression analysis approach.