BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
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NAME	POSITION TITLE
FEARON, ERIC R.	Professor of Internal Medicine, Human Genetics, and Pathology
eRA COMMONS USER NAME (credential, e.g., agency login) fearon	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Johns Hopkins University (Baltimore, MD)	B.A.	1983	Biophysics
Johns Hopkins University (Baltimore, MD)	M.D.	1990	Medicine
Johns Hopkins University (Baltimore, MD)	Ph.D.	1990	Biology (Hum Genetics)

A. Positions and Honors

Positions and Employment

1990-1992 Post-doctoral fellowship, The Johns Hopkins University. School of Med., The Oncology Center and Division of Hematology, Dept. of Medicine
1992-1995 Assistant Professor of Pathology and Biology, Yale University School of Medicine
1995-2001 Associate Professor of Internal Medicine, Division of Molecular Medicine and Genetics, Human Genetics, & Pathology, University of Michigan School of Medicine
1995- Associate Director for Basic Science and Maisel Professor, Univ. of Michigan Cancer Center
1999- Co-Director, Cancer Genetics Program, Univ. of Michigan Comprehensive Cancer Center
2001- Professor, Depts of Internal Medicine (Molecular Medicine & Genetics), Human Genetics, Pathology, University of Michigan School of Medicine
2005- Deputy Director, University of Michigan Comprehensive Cancer Center

Other Experience and Memberships on Federal Advisory Groups

1991,1994,1996-2000 Pathology B Study Section (Ad hoc member)
1992-1995 Board of Scientific Counselors, Division of Cancer Prevention and Control, NCI
1995 Panel to Review the NIH Investment in Gene Therapy Research
1996-1999 Board of Scientific Advisors, National Cancer Institute, National Institutes of Health
1996-1998 Member, NCI Developmental Diagnostics Working Group
1996-1997 Member, NCI Prevention Review Group
1997-1998 Member, National Human Genome Research Institute Scientific Planning Subcommittee
2000-2003 Member and Chair, Pathology B Study Section (Chair 2001-2003)
2003-2004 Chair and Member, Cancer Genetics Study Section

Honors

1983 Phi Beta Kappa
1983 Martin G. Larrabee Prize for research in biophysics, Johns Hopkins University
1990 David Israel Macht Prize, Johns Hopkins University School of Medicine
1990 Alpha Omega Alpha Medical Honor Society
1990 Wilson S. Stone Award, University of Texas-M.D. Anderson Cancer Center
1992-1995 McDonnell Fellow in Molecular Medicine in Cancer Research
1998 American Society for Clinical Investigation (Vice-Pres 2003-4; Pres-Elect 2004-5; President 2005-6)
2003 Association of American Physicians
2007 Johns Hopkins University Society of Fellows

B. Selected Publications (from 106 peer-reviewed research papers; 29 reviews/editorials; 23 book chapters)

Fearon ER, Burke PJ, Schiffer CA, Zehnbauer BA, Vogelstein B. Differentiation of leukemia cells to polymorphonuclear leukocytes in patients with acute nonlymphocytic leukemia. *N Engl J Med* 1986, 315:15-24. PMID: 3086723

Fearon ER, Hamilton SR, Vogelstein B. Clonal analysis of human colorectal tumors. *Science* 1987, 238:193-7. PMID: 2889267

Fearon ER, Cho KR, Nigro, Kern SE, Simons JW, Ruppert JM, Hamilton SR, Preisinger AC, Thomas G, Kinzler KW, Vogelstein B. Identification of a chromosome 18q gene which is altered in colorectal cancers. *Science* 1990, 247:49-56. PMID: 2294591

Fearon ER, Pardoll DM, Itaya T, Golumbek P, Levitsky HI, Simons JW, Karasuyama H, Vogelstein B, Frost P. Interleukin-2 production by tumor cells bypasses T helper function in the generation of an anti-tumor response. *Cell* 1990, 60:397-403. PMID: 2137372

Fearon ER, Vogelstein B. A genetic model for colorectal tumorigenesis. *Cell* 1990, 61:759-767. PMID: 2188735

Hu G, Zhang S, Vidal, M, La Baer J, Xu T, **Fearon ER**. Mammalian homologs of *sina* (*seven in absentia*) regulate DCC via the ubiquitin-proteasome pathway. *Genes & Development* 1997, 11:2701-14. PMID: 9334332

Fearon ER. Human cancer syndromes: clues to the origin and nature of cancer. *Science* 1997, 278:1043-50. PMID: 9353177.

Kolligs FT, Kolligs B, Hajra KM, Hu G, **Fearon ER**. γ-catenin is regulated by the APC tumor suppressor and its oncogenic activity is distinct from that of β-catenin. *Genes & Development*, 2000, 14:1319-31. PMID: 10837025

Kolligs FT, Nieman MT, Winer I, Hu G, Van Mater D, Feng Y, Smith IM, Wu R, Zhai Y, Cho KR, **Fearon ER**. *ITF-2* a downstream target of the Wnt pathway, is activated in human cancers with β-catenin defects and promotes neoplastic transformation. *Cancer Cell* 2002, 1:145-55. PMID: 12086873

Van Mater D, Kolligs FT, Dlugosz A, **Fearon ER**. Transient activation of ш-catenin signaling in cutaneous keratinocytes is sufficient to trigger the active growth phase of the hair cycle in mice. *Genes Dev* 2003, 17:1219-24. PMID: 12756226

Feng Y, Bommer GT, Winer I, Zhai Y, Lin HV, Cadigan KM, Cho KR, **Fearon ER**. *Drosophila split ends* homologue *SHARP* functions in a positive feedback loop to enhance Wnt/β-catenin/TCF signaling and neoplastic transformation. *Cancer Res* 2007, 67:482-91. PMID: 17234755

Wu R, Hendrix-Lucas N, Kuick R, Zhai Y, Schwartz DR, Aytekin Akyol, Hanash S, Misek DE, Katabuchi H, Wiliams BO, **Fearon ER**, Cho KR. Mouse model of human ovarian endometrioid adenocarcinoma based on somatic defects in the Wnt/ш-catenin and PI3K/Pten signaling pathways. *Cancer Cell* 2007, 11:321-33. PMID: 17418409

Bommer GT, Gerin I, Feng Y, Kaczorowski AJ, Kuick R, Love RE, Zhai Y, Giordano TJ, Qin ZS, Moore BB, MacDougald OA, Cho KR, **Fearon ER**. p53-mediated activation of miRNA34 candidate tumor suppressor genes. *Current Biol* 2007, 17:1-10. PMID: 17656095

Hinoi T, Akyol A, Theisen BK, Ferguson DO, Greenson JK, Williams BO, Cho KR, **Fearon ER**. Mouse model of colonic adenoma-carcinoma progression based on somatic *Apc* inactivation. *Cancer Res* 2007,67:9721-30. PMID: 17942902

Zhai Y, Kuick R, Nan B, Ota I, Weiss SJ, Trimble CL, **Fearon ER**, Cho KR. Gene expression analysis of preinvasive and invasive cervical squamous cell carcinomas identifies HOXC10 as a key mediator of invasion. *Cancer Res* 2007, 67:10163-72. PMID: 17974957

Burstein E, **Fearon ER**. Colitis and cancer: a tale of inflammatory cells and their cytokines. *J Clin Invest* 2008, 118:464-7. PMID 18219390

Akyol A, Hinoi T, Feng Y, Bommer GT, Glaser TM, **Fearon ER**. Use of a long mononucleotide sequence tract to generate somatic mosaicism in transgenic mice. *Nature Methods* 2008, 5:231-3. PMID: 18246119.

Whiteman EL, Liu CJ, **Fearon ER**, Margolis B. The transcription factor snail represses Crumbs3 expression and disrupts apico-basal polarity complexes. *Oncogene* 2008 27:3875-9. PMID: 18264107.

Sangha N, Wu R, Kuick R, Powers S, Mu D, Fiander D, Yuen K, Katabuchi H, Tashiro H, **Fearon ER**, Cho KR. Neurofibromin 1 (NF1) defects are common in human ovarian serous carcinomas and co-occur with TP53 mutations. *Neoplasia* 2008 10:1362-72. PMID: 19048115

Rowe RG, Li XY, Hu Y, Saunders TL, Virtanen I, de Herreros AG, Becker KF, Ingvarsen S, Engelholm LH, Bommer GT, **Fearon ER,** Weiss SJ. Mesenchymal cells reactivate Snail1 expression to drive 3-dimensional invasion programs. *J Cell Biol* 2009, 184:399-408. PMID: 1914891

Wang L, Heidt DG, Lee CJ, Yang H, Logsdon CD, Zhang L, **Fearon ER**, Ljungman M, Simeone DM. Oncogenic function of ATDC in pancreatic cancer through Wnt pathway activation and β-catenin stabilization. *Cancer Cell* 2009 15:207-19. PMID: 1924967

Vilar E, Mukherjee B, Kuick R, Raskin L, Misek DE, Taylor JM, Giordano TJ, Hanash SM, **Fearon ER**, Rennert G, Gruber SB. Gene expression patterns in mismatch repair-deficient colorectal cancers highlight the potential therapeutic role of inhibitors of the phosphatidylinositol 3-kinase-AKT-mammalian target of rapamycin pathway. *Clin Cancer Res* 2009, 15:2829-39. PMID: 19351759

Ji Q, Hao X, Zhang M, Tang W, Yang M, Li L, Xiang D, Desano JT, Bommer GT, Fan D, **Fearon ER**, Lawrence TS, Xu L. MicroRNA miR-34 inhibits human pancreatic cancer tumor-initiating cells. PLoS One. 2009 Aug 28;4(8):e6816. PMID: 19714243

C. RESEARCH SUPPORT

ACTIVE

2 R01 CA82223-10 Fearon (PI) 08/15/99 - 05/31/10
NIH/NCI
"CDX-2 Tumor Suppressor Pathway Defects in Colon Cancer"
Major goals of the project are to better understand the contribution of CDX2 defects to the pathogenesis of gastrointestinal tumors. The specific aims are: I) Define specific cellular genes that are directly regulated by CDX2. II) Assess the role of selected CDX2-regulated genes in proliferation, differentiation, and tumorigenic growth of gastrointestinal cancer cells. III) Explore the role of *Cdx2* and a limited number of high interest CDX2-regulated genes in the pathogenesis of colon tumors, using mouse cancer models.

2 R01 CA85463-09 Fearon (PI) 06/01/00 - 05/31/10
NIH/NCI
"The Role of β-catenin/Tcf Pathway Defects in Cancer"
Specific aims are: I) To identify downstream genes whose expression is specifically regulated by β-catenin/TCF in colon and other cancer cells where β-catenin is constitutively activated. II) To utilize robust model systems to assess the role of selected β-catenin/TCF target genes and their protein products in the altered phenotype of colon and other cancer cells. III) To assess the role of selected β-catenin/TCF target genes in intestinal and colonic tumorigenesis, using mouse transgenic and knockout models.

2R01 CA094172-06A1 Cho (PI) 08/01/07 - 05/31/12
NIH/NCI (Fearon – co-investigator)
"Molecular Pathogenesis of Ovarian Endometrioid Adenocarcinomas"
Aims are: 1) To continue efforts to identify and characterize β-cat/Tcf regulated genes important in OEA pathogenesis; 2) To complete a comprehensive mutational analysis of genes encoding proteins known to regulate PI3K/Akt/Pten signaling in OEAs, and to define a gene expression signature associated with defects in this signaling pathway; 3) To define and characterize key downstream transcriptional target genes linked to deregulated PI3K/Akt/Pten signaling in OEA pathogenesis; and 4) To continue efforts to develop and characterize mouse models of OEA, and to use gene expression profiling as a means to determine how well murine tumors arising in the setting of specific genetic alterations recapitulate human OEAs..

2 P30 CA46592-21; Wicha (PI) 6/1/06 - 5/31/11
NIH/NCI (Fearon – Associate Director for Basic Science and Deputy Director)
University of Michigan Comprehensive Cancer Center Core Grant; Fearon - Basic Science Director.
Aims of the University of Michigan Cancer Center Core Grant are: To provide support for Cancer Center research programs, core facilities, leadership, and development activities. Dr. Fearon serves as the director of research in the Basic Science Division in the University of Michigan Comprehensive Cancer Center.

2 P30 CA46592-21; Wicha (PI) 6/1/06 - 5/31/11
NIH/NCI (Fearon – Program Co-leader)
University of Michigan Comprehensive Cancer Center Core Grant; Fearon - Program Co-Leader.
Aims of the University of Michigan Cancer Center core grant are: To provide support for Cancer Center research programs, core facilities, leadership, and development activities. Dr. Fearon serves as co-leader of the Cancer Genetics Program

1R01 C116516-01A1; Weiss (PI) 09/20/06 – 07/31/11
NIH/NCI (Fearon – co-investigator)
"Snail-Dependent Regulation of EMT in Cancer"
Aims are: I) Characterize the Wnt-1-initiated regulation of carcinoma cell EMT by the Snail/ш-catenin/TCF axis; II) Define the Snail-dependent regulation of ш-catenin/TCF-induced EMT by Axin2; III) Define the structure-function relationships underlying Axin2 nuclear-cytoplasmic trafficking and Snail-dependent EMT; IV) Characterize the Axin2-dependent control of GSK3ш nuclear-cytoplasmic trafficking and its impact on Snail-dependent EMT.

2 P50 CA093990-07A1; Ross (PI) 09/22/2008 – 03/31/2013
NIH/NCI (Fearon – co-investigator)
In Vivo Imaging of Neoplasia
Goal: The studies proposed here will result in the identification of novel therapies as well as imaging biomarkers that report on key molecular events and therapeutic response will be identified. These studies will enable individualization of cancer therapy.
Overlap – None.

U54 CA136429-01; Wang (PI) 10/01/08 – 09/30/13
NIH/NCI (Fearon – co-investigator, project #1)
In Vivo Detection of Neoplasia in the Digestive Tract
The goal is to develop novel optical imaging probes and instruments that can be evaluated in pre-clinical models, as well as translated to the clinic as a practical screening tool for the early detection of cancer in hollow organs. (Project 1)
Overlap – None.

W81XWH-09-2-0014; Wicha (PI) 03/25/09-04/24/10
Department of Defense (Fearon- project leader, project #1)
National Functional Genomics Center
Goal: I) Generate new mouse models of colon cancer via use of CDX2 transgenic elements to over-express potential oncogenes and CDX2-Cre transgenes to inactivate potential tumor suppressor genes; II) Generate new mouse models of ovarian cancer via the use of adenoviral Cre recombinase injection into the ovarian bursal to activate candidate oncogenes and inactivate tumor suppressor genes.
Overlap – None.

COMPLETED

1 RO1 CAS1488-10 Gruber (PI) 01/01/99 - 03/31/09
NIH/NCI (Fearon – co-investigator)
"Molecular Epidemiology of Colorectal Cancer"
Major goals of the project are to measure risks of developing cancer associated with the APC I1307K allele; to identify and measure potential effect modification of genetic and environmental risks in colorectal cancer pathogenesis in those carrying the APC I1307K allele; to define the somatic mutational spectrum in the APC gene in colorectal cancers arising in those who carry the APC I1307K allele; and to establish a resource for further epidemiologic studies and genome screening to map novel, low penetrance colorectal cancer genes.

OC030117; Wu (PI) 02/01/04 - 01/31/07
Dept. of Defense OCRP (Fearon – co-investigator)
Development and Characterization of a Murine Model of Endometrioid Adenocarcinoma Induced by Tissue Specific Expression of β-Catenin.
The goals of the project are: I) To create and characterize transgenic mice with constitutive ovarian surface epithelium (OSE)-selective expression of mutant β-catenin; II) To generate and characterize transgenic mice with inducible expression of Cre-recombinase (Cre) in murine OSE; and III) To breed and characterize transgenic animals with MOSE-selective inactivation of PTEN, alone and in combination with mutant β-catenin