OMB No. 3145-0279 (Expiration Date 10/31/2026)

NIH BIOGRAPHICAL SKETCH COMMON FORM

Name: Engleman, Edgar

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0002-2096-9279

Position Title: Professor of Pathology and Medicine

Organization and Location: Stanford University School of Medicine, Palo Alto, California, United States

PROFESSIONAL PREPARATION

INSTITUTION AND LOCATION	DEGREE	Start Date	Completion Date	FIELD OF STUDY
Stanford University School of Medicine, Stanford, California, United States	Postdoctoral Fellow	09/1976	09/1978	Immunology and Rheumatology
National Institutes of Health, Bethesda, Maryland, United States	Postdoctoral Fellow	09/1973	09/1976	Biochemistry
Univeristy of California, San Francisco, San Francisco, California, United States	Resident	07/1971	07/1973	Internal Medicine
Columbia University College of Physicians and Surgeons, New York, New York, United States	Doctor of Medicine (MD)	09/1967	06/1971	Medicine
Harvard University, Cambridge, Massachusetts, United States	Bachelor of Arts (BA)	09/1963	06/1967	Psychology

Appointments and Positions

1990 - present	Professor of Pathology and Medicine, Stanford University School of Medicine, Palo Alto, California, United States
2005 - present	Co-Leader, Research Program in Cancer Immunotherapy, Stanford Cancer Institute, Stanford, California, United States
1984 - 1990	Associate Professor of Pathology and Medicine, Stanford University School of Medicine, Stanford, California, United States
1978 - present	Founding Director, Stanford Blood Center, Stanford University School of Medicine, Stanford, California, United States
1978 - 2004	Attending Physician in Immunology and Rheumatology, Stanford University Medical Center, Stanford, California, United States
1978 - 1984	Assistant Professor of Pathology and Medicine, Stanford University School of Medicine, Stanford, California, United States

Products

Products Closely Related to the Proposed Project

1. Carmi Y, Spitzer MH, Linde IL, Burt BM, Prestwood TR, Perlman N, Davidson MG, Kenkel JA, Segal E, Pusapati GV, Bhattacharya N, Engleman EG. Allogeneic IgG combined with dendritic cell stimuli induce antitumour T-cell immunity. Nature. 2015 May 7;521(7550):99-104. PubMed Central PMCID: PMC4877172.
2. Ackerman SE, Pearson CI, Gregorio JD, Gonzalez JC, Kenkel JA, Hartmann FJ, Luo A, Ho PY, LeBlanc H, Blum LK, Kimmey SC, Luo A, Nguyen ML, Paik JC, Sheu LY, Ackerman B, Lee A, Li H, Melrose J, Laura RP, Ramani VC, Henning KA, Jackson DY, Safina BS, Yonehiro G, Devens BH, Carmi Y, Chapin SJ, Bendall SC, Kowanetz M, Dornan D, Engleman EG, Alonso MN. Immune-stimulating antibody conjugates elicit robust myeloid activation and durable antitumor immunity. Nat Cancer. 2021 Jan;2(1):18-33. PubMed Central PMCID: PMC9012298.
3. Linde IL, Prestwood TR, Qiu J, Pilarowski G, Linde MH, Zhang X, Shen L, Reticker-Flynn NE, Chiu DK, Sheu LY, Van Deursen S, Tolentino LL, Song WC, Engleman EG. Neutrophil-activating therapy for the treatment of cancer. Cancer Cell. 2023 Feb 13;41(2):356-372.e10. PubMed Central PMCID: PMC9968410.

4. Bagchi S, Yuan R, Huang HL, Zhang W, Chiu DK, Kim H, Cha SL, Tolentino L, Lowitz J, Liu Y, Moshnikova A, Andreev O, Plevritis S, Engleman EG. The acid-sensing receptor GPR65 on tumor macrophages drives tumor growth in obesity. Sci Immunol. 2024 Oct 18;9(100):eadg6453. PubMed Central PMCID: PMC12104511.
5. Chiu DK, Zhang X, Cheng BY, Liu Q, Hayashi K, Yu B, Lee R, Zhang C, An X, Rajadas J, Reticker-Flynn NE, Rankin EB, Engleman EG. Tumor-derived erythropoietin acts as an immunosuppressive switch in cancer immunity. Science. 2025 Apr 25;388(6745):eadr3026. PubMed Central PMCID: PMC12110762.

Other Significant Products Highlighting Contributions to Science

1. Engleman EG, Benike CJ, Grumet FC, Evans RL. Activation of human T lymphocyte subsets: helper and suppressor/cytotoxic T cells recognize and respond to distinct histocompatibility antigens. J Immunol. 1981 Nov;127(5):2124-9. PubMed PMID: 6457863.
2. Hsu FJ, Benike C, Fagnoni F, Liles TM, Czerwinski D, Taidi B, Engleman EG, Levy R. Vaccination of patients with B-cell lymphoma using autologous antigen-pulsed dendritic cells. Nat Med. 1996 Jan;2(1):52-8. PubMed PMID: 8564842.
3. Spitzer MH, Carmi Y, Reticker-Flynn NE, Kwek SS, Madhireddy D, Martins MM, Gherardini PF, Prestwood TR, Chabon J, Bendall SC, Fong L, Nolan GP, Engleman EG. Systemic Immunity Is Required for Effective Cancer Immunotherapy. Cell. 2017 Jan 26;168(3):487-502.e15. PubMed Central PMCID: PMC5312823.
4. Reticker-Flynn NE, Zhang W, Belk JA, Basto PA, Escalante NK, Pilarowski GOW, Bejnood A, Martins MM, Kenkel JA, Linde IL, Bagchi S, Yuan R, Chang S, Spitzer MH, Carmi Y, Cheng J, Tolentino LL, Choi O, Wu N, Kong CS, Gentles AJ, Sunwoo JB, Satpathy AT, Plevritis SK, Engleman EG. Lymph node colonization induces tumor-immune tolerance to promote distant metastasis. Cell. 2022 May 26;185(11):1924-1942.e23. PubMed Central PMCID: PMC9149144.
5. Zhang X, McGinnis CS, Yu G, Chen S, Zheng P, Schürch CM, Hiam-Galvez KJ, Reticker-Flynn NE, Guo W, Yao W, Qiu J, Muselman A, Linde IL, Hickey JW, Yan H, Tran VM, Qiu W, Brichart-Vernos D, Hirai T, Yu B, An X, Xiao Y, Paidassi H, Scharschmidt TC, Angelo M, Sheppard D, Chi H, Satpathy AT, Way SS, Malissen B, Strober S, Engleman EG. Erythropoietin receptor on cDC1s dictates immune tolerance. Nature. 2026 Feb;650(8101):470-480. PubMed Central PMCID: PMC12929016.

Certification:

I certify that the information provided is current, accurate, and complete. This includes but is not limited to information related to domestic and foreign appointments and positions.

I also certify that, at the time of submission, I am not a party to a malign foreign talent recruitment program.

Misrepresentations and/or omissions may be subject to prosecution and liability pursuant to, but not limited to, 18 U.S.C. §§ 287, 1001, 1031 and 31 U.S.C. §§ 3729-3733 and 3802.

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NIH BIOGRAPHICAL SKETCH SUPPLEMENT

Name: Engleman, Edgar

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0002-2096-9279

Position Title: Professor of Pathology and Medicine

Organization and Location: Stanford University School of Medicine, Palo Alto, California, United States

Personal Statement

For the past 40 years my research has been directed at discovering ways to manipulate the immune system for the treatment and prevention of life-threatening diseases. At the start of my career, I generated the first monoclonal antibodies to human T lymphocytes, including anti-CD4 and anti-CD8, enabling me and others to isolate these cells and analyze their functions. In addition to these fundamental studies, I used the antibodies to develop a screening test for blood donors prior to the discovery of HIV, and later I used them to study the role of CD4 in HIV infection. Thereafter, I began a decades-long investigation into myeloid cell biology, focusing initially on dendritic cells (DCs). My group was the first to develop a method for isolating and arming human dendritic cells and evaluate their ability to induce anti-tumor immunity in cancer patients. Our work led to the development of the first immune cell therapy, Sipuleucel-T (Provenge), which was approved by the FDA in 2010 for the treatment of advanced prostate cancer. This accomplishment paved the way to a new era in which immune cell therapies have become standard treatments for several cancers. In the past decade, my research has been aimed at understanding the cellular and molecular basis of peripheral immune tolerance in health and disease. This effort led to the discovery that tumor cells that invade lymph nodes (LNs) alter LN-resident immune cells, resulting in the generation of tumor-specific Tregs that disseminate throughout the host and promote distant metastasis. Recently, we discovered that erythropoietin (Epo)-mediated activation of its receptor (EpoR) on macrophages and Type 1 DCs causes these cells to become tolerogenic and suppress anti-cancer immunity through their induction of antigen-specific Tregs and inhibition of CD8 cytotoxic T cells. This discovery was enabled by methods we developed for analyzing the immune response systemwide and our generation of novel mouse models of cancer that mimic their human counterparts in their driver mutations, growth characteristics and immune profiles. Beyond my research contributions, I am proud of having trained more than 100 graduate and postdoctoral students, many of whom have gone on to distinguished academic careers. Examples include Miriam Merad (Mount Sinai School of Medicine), Lawrence Fong (Fred Hutchinson Cancer Center), Matthew Spitzer (University of California, San Francisco) and Nathan Reticker-Flynn (Stanford University).

Ongoing projects that I would like to highlight include:

P30 CA124435
Artandi (PI)
Role: Co-director, Tumor Immunotherapy Research Program
06/01/16-05/31/27
Stanford University Cancer Institute

U54 CA274511
Engleman (Co-PI)
07/01/23-08/31/28
Systems Biology of Tumor-Immune-Stromal Interactions in Metastatic Progression

Honors

2026	Landsteiner-Alter Prize for Biomedical Research, Association for the Advancement of Blood & Biotherapies
2022	Gold Medal for Outstanding Achievements in Medical Research, Columbia University
2017	K. Fong Prize in Life Sciences, Chinese American Biopharmaceutical Society
2004	Outstanding Inventor Award, Stanford University
1998	Membership, Association of American Physicians
1990	Benjamin Franklin Literary and Medical Society Award for AIDS Research, Benjamin Franklin Literary and Medical Society
1984	Membership, Pluto Club, Association of University Pathologists

1982	Membership, American Society for Clinical Investigation
1967	Magna cum laude, Harvard University
1967	Nominee, Rhodes Scholarship, Rhodes Trust

Contributions to Science

1. DEFINING HUMAN T CELL SUBSETS AND SURFACE MARKERS AND THE ROLE OF CD4 IN HIV INFECTION.
When my career began, there was little knowledge of the cellular components of the human immune system. To begin to address this fundamental question, working collaboratively with Robert Evans, I generated a series of mouse monoclonal anti-human leukocyte antibodies and used them to identify and characterize the CD4 and CD8 subsets of human T cells (Engleman et al J Immunol 1981). These antibodies enabled us to develop the first screening test for the AIDS carrier state in blood donors and probe the mechanism by which HIV enters and kills susceptible cells after binding to its cell surface receptor, CD4. Our findings were published in papers in Science, Nature and Cell, and our monoclonal antibodies, which were licensed to Becton-Dickinson in 1981, remain widely used standards in the field.

2. IDENTIFYING AND REVERSING MYELOID CELL MEDIATED IMMUNE SUPPRESSION IN CANCER.
Beginning in 1990 I became interested in the biology and functions of dendritic cells (DCs). After developing a method for isolating human DCs from blood, I led the first clinical trials to evaluate the utility of antigen-loaded DCs for tumor immunotherapy (Hsu et al Nat Med 1996). Our methods for isolating and arming human DCs with tumor antigens provided the basis for the Sipuleucel-T (Provenge) vaccine for the treatment of metastatic prostate cancer, the first cell therapy to be approved by the FDA (in 2010). By demonstrating that immune cells activated ex vivo could induce clinically meaningful anti-tumor immunity, Provenge helped pave the way to a new era in which cell-based immunotherapies have become a standard component of cancer treatment. To assess the mechanisms and impact of our immunotherapeutic strategies, we developed new methods to analyze the immune landscape both systemwide and in tumors (Spitzer et al Cell 2017). These methods enabled our discovery (published in Nature) of a novel mechanism that enables arming and activation of tumor associated DCs in situ in tumor bearing hosts based on the simultaneous delivery of tumor-binding antibodies and DC stimulating molecules. By directly linking the stimulatory molecules to the tumor-binding antibodies, these immune stimulating antibody conjugates can be delivered to tumors via systemic administration (published in Nature Cancer). This approach is currently being evaluated in a multicenter clinical trial. More recently, we reported in Cancer Cell a strategy that induces host neutrophils to become potent tumor-killing cells able to eradicate primary tumors and reduce distant metastases.

3. PROBING THE ROLE OF THE IMMUNE SYSTEM IN OBESITY ASSOCIATED DISEASES.
For the past fifteen years, my lab has been investigating the role of the immune system in obesity-associated diseases. As reported in Nature Medicine, we showed that T lymphocytes infiltrating the visceral fat of diet induced obese (DIO) mice can both induce and protect against the development of diabetes. This study was followed by our discovery, also reported in Nature Medicine, that B cells and autoantibodies play a key role in the development of obesity-associated diabetes. Subsequently, we showed that the pro-inflammatory effects of B cells in obesity-associated diabetes are mediated by B-2 cells, while a small population of IL-10-secreting regulatory B cells, that normally helps maintain a state of insulin sensitivity, is deficient in obese insulin resistant mice. We expanded on these findings by performing deep sequencing of the immunoglobulin repertoire from DIO mice and found that their antibody repertoire is significantly altered in the intestine and visceral adipose tissue relative to control mice on a regular diet. Most recently, we have begun to study the role of innate immune cells in adipose tissue inflammation and the development of obesity-associated diabetes. Separately, we are studying the mechanisms responsible for obesity-associated cancers, and our initial investigations (reported in Science Immunology) identified GPR65 on tumor associated macrophages as a key contributor.

4. APPLYING TOTAL LYMPHOID IRRADIATION TO INDUCE LIFELONG TOLERANCE TO ORGAN ALLOGRAFTS.
This research, performed in collaboration with Samuel Strober's group at Stanford, showed that treating recipients of allogeneic organ transplants with total lymphoid irradiation (TLI) and small numbers of donor bone marrow cells enables complete withdrawal of immunosuppressive drugs without organ rejection. More than 40 patients treated with this tolerance-induction strategy have retained their transplanted kidneys over a median follow-up period of 10 years with no serious toxicity. Using mouse models, we discovered that tolerance induction from TLI and donor BM results from a cascade of cellular interactions starting with host type 1 dendritic cells (cDC1s) and including Gr-1+CD11b+ myeloid cells, NKT cells and Tregs, each of which is required for the development of immune cell chimerism and sustained immune tolerance. Further studies in these mice enabled us to discover the critical role of erythropoietin and its receptor on cDC1s in this process (Zhang et al Nature 2025).

5. DISCOVERY OF THE ROLE OF ERYTHROPOIETIN AND ITS RECEPTOR IN IMMUNE TOLERANCE IN CANCER.
For the past decade, my research has been aimed at understanding the mechanistic basis of immune tolerance in cancer. This effort led initially to our discovery that tumor cells invading lymph nodes (LNs) alter LN-resident immune cells, leading to the

generation of tumor-specific Tregs that disseminate throughout the host and promote distant metastasis (Reticker-Flynn et al Cell 2022). Subsequently, in studies of mouse models of hepatocellular carcinoma (HCC) we discovered that erythropoietin (Epo) activation of its receptor (EpoR) on tumor associated macrophages and cDC1s causes these cells to become tolerogenic and suppress antitumor immunity through their induction of antigen-specific Tregs and suppression of CD8 cytotoxic T cells. This discovery, which was reported in Science in 2025, was enabled by our development of mouse models of HCC that mimic their human counterparts in their driver mutations, immune landscapes and response to immune checkpoint blockade (ICB). Moreover, removal or blockade of EpoR on these myeloid cells results not only in the loss of tolerance but in the generation of a powerful anti-tumor CD8 T cell response as well as sensitization of the tumor to ICB. Since additional findings indicate this mechanism also induces immune tolerance in non-cancer settings (Zhang et al Nature 2025), blocking or agonizing it can potentially be used to treat a wide range of diseases.

Certification:

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I also certify that, at the time of submission, I am not a party to a malign foreign talent recruitment program.

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