University of California, San Francisco

CURRICULUM VITAE

Name: Jonathan H Esensten, MD, PhD

Position: Assistant Professor, Step 2
Laboratory Medicine
School of Medicine

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EDUCATION

2000 - 2004	Harvard University	AB	magna cum laude, biochemical sciences	
2004 - 2012	University of California, San Francisco	MD		
2004 - 2010	University of California, San Francisco	PhD	immunology	Dr. Jeffrey Bluestone
2012 - 2016	University of California, San Francisco	residency	Clinical Pathology	
2014 - 2015	University of California, San Francisco	clinical fellowship	Blood Banking and Transfusion Medicine	
2015 - present	University of California, San Francisco	postdoctoral fellowship		Dr. Wendell Lim

LICENSES, CERTIFICATION

2014	Medical licensure, California (A128404)
2016	Diplomate, American Board of Pathology (Clinical Pathology)
2017	Diplomate, American Board of Pathology (Blood Banking / Transfusion Medicine)

PRINCIPAL POSITIONS HELD

2017 - present	University of California, San Francisco	Adjunct Assistant Professor	Department of Laboratory Medicine

OTHER POSITIONS HELD CONCURRENTLY

2016 - present	University of California, San Francisco	Medical Director, UCSF HICTF and GMP Facility	Diabetes Center
2017 - present	University of California, San Francisco	Co-director, Regulatory T Cell Therapy Group	Diabetes Center
2018 - present	Zuckerberg San Francisco General Hospital	Medical Director, Blood Bank and Transfusion Service	Clinical Laboratory
2018 - present	University of California, San Francisco	cGMP Medical Director	Alpha Stem Cell Clinic

HONORS AND AWARDS

2012	Alpha Omega Alpha Honor Society	University of California, San Francisco
2013	Krevans Award in Laboratory Medicine	San Francisco General Hospital
2016	Leukemia & Lymphoma Society Fellow	Leukemia & Lymphoma Society

KEYWORDS/AREAS OF INTEREST

transfusion medicine, T cell engineering, cellular therapy, synthetic biology

CLINICAL ACTIVITIES

CLINICAL ACTIVITIES SUMMARY

1) I serve as the Medical Director for the UCSF HICTF and GMP Facility, which manufactures T cell therapeutics for 8 clinical trials at UCSF and other centers.

• I am involved in every aspect of laboratory management, including hiring and supervision of personnel
• I personally review and release every T cell product manufactured in the facility
• I provide consultation for clinicians whose patients are receiving products from the facility
• In 2017-2018, I oversaw a $2.7M renovation of the facility to prepare for a major collaborative project with a multinational pharmaceutical company.

2) I serve as the medical director of the blood bank and transfusion service at Zuckerberg San Francisco General Hospital, which is the city's only Level 1 trauma center.

• Assisted/consulted in preparation for a new EMR (Epic) that will roll out in 2019
• Current projects include improving the massive transfusion protocol, improving the blood transfusion consent process, and developing a check specimen (ABO confirmation) policy

• I cover for my colleague Dr. Zane Amenhotep, who is the chief of the laboratory hematology section of the ZSFG clinical lab, when he is on vacation or ill

3) I serve as chair of the transfusion committee at Zuckerberg San Francisco General Hospital.
• I lead quarterly meetings of the committee and I am responsible for reporting to the ZSFG Performance Improvement and Safety Program on behalf of the blood bank

CLINICAL SERVICES

2016 - present	Medical Director, HICTF and GMP Facility	continuous
2018 - present	Medical Director, ZSFG Blood Bank and Transfusion Service	continuous, unless I arrange coverage
2018 - present	Attending physician, Hematology section of the ZSFG Clinical Laboratory	up to 30 days/year (coverage when colleagues are on vacation)

PROFESSIONAL ACTIVITIES

MEMBERSHIPS

2012 - 2015	AABB, member
2017 - present	International Society for Cell Therapy, member

INVITED PRESENTATIONS - NATIONAL

2009	National Institute on Aging (NIA), Baltimore, MD. Host: Dr. Mark Mattson, Senior Investigator and Chief, Laboratory of Neurosciences; Chief, Cellular and Molecular Neurosciences Section, NIA	speaker
2018	Treg Summit 2018: Treg directed therapy for autoimmune disorder	speaker

INVITED PRESENTATIONS - REGIONAL AND OTHER INVITED PRESENTATIONS

2007	UCSF / UC Berkeley Immunology Program Retreat	speaker
2014	59th Annual Meeting of the California Blood Bank Society	speaker
2015	Bio-Rad Sponsored Continuing Education Symposium for laboratory professionals	speaker
2017	Rinat (Pfizer), allogeneic T cell group	speaker
2018	Northern California Society of Toxicoogy	speaker

UNIVERSITY AND PUBLIC SERVICE

SERVICE ACTIVITIES SUMMARY

I am the chair of the Transfusion Committee at Zuckerberg San Francisco General Hospital. I also serve as a lay leader in a local Jewish synagogue.

UCSF CAMPUSWIDE

2018 - present	Transfusion Committee, Zuckerberg San Francisco General Hospital	chair

SCHOOL OF MEDICINE

2012 - 2012	Ad-hoc Disciplinary Committee	member

DEPARTMENTAL SERVICE

2013 - 2014	Resident and Fellow Quality Improvement Incentive Program (Dept. of Laboratory Medicine)	leader

COMMUNITY AND PUBLIC SERVICE

2011 - 2013	Adath Israel Congregation (San Francisco)	member of the board of trustees
2011 - present	Adath Israel Congregation (San Francisco)	fundraiser (gabbai)
2017 - 2018	Oakland Hebrew Day School	member of the board of trustees

TEACHING AND MENTORING

TEACHING SUMMARY

I teach laboratory medicine and transfusion medicine to medical students, laboratory medicine residents, and clinical fellows at Zuckerberg San Francisco General Hospital (ZSFG). I am on site at ZSFG one half day per week, during which I participate in the weekly call conference (teaching conference). When appropriate, I teach about evidence-based transfusion practice, present clinical vignettes, and teach residents about transfusion in the setting of trauma, obstetric hemorrhage, and other clinical situations commonly encountered at ZSFG. I sign out all transfusion cases, so I have regular email and phone contact with residents when I am not on site. I am the preceptor for a student (Theo Roth) in the Medical Scientist Training Program (MD/PhD program). In this capacity, I meet with Theo once per week and go over clinical cases in laboratory medicine and transfusion medicine. I also serve as a mentor for him since he is interested in cellular therapy as a focus of his career.

As described below, I am also the course director of a new cellular therapy elective offered to laboratory medicine residents.

FORMAL TEACHING

	Academic Yr	Course No. & Title	Teaching Contribution	School	Class Size

	Academic Yr	Course No. & Title	Teaching Contribution	School	Class Size
	2018 - 2018	Cellular Therapy and cGMP Manufacturing Elective ZSFGH/UCSF	course head	Medicine	1

INFORMAL TEACHING

2013 - 2017 I tutored students and residents for medical licensing examinations on a private basis.

MENTORING SUMMARY

- I mentored a UC Berkeley undergraduate student during my time in graduate school. He went on to be accepted at the Medical Scientist Training Program at Yale University. I am currently mentoring a graduate student in the laboratory of Dr. Wendell Lim (Joseph Choe), a college student who has worked with me for the past 2 summers (Hannah Brodskaya), and a Staff Research Associate II (Emma Moulton) who joined the Lim lab in 2018. I am mentoring a student in the UCSF Medical Scientist Training Program (MD/PhD program) who is interested in laboratory medicine and cellular therapy (Theo Roth). I am also mentoring Dr. Brian Shy, who is a laboratory medicine resident interested in cellular therapy as a focus of his career. He is actively working on two cellular therapy projects with me and he has completed the elective in cellular therapy that I offered for the first time in 2018.

PREDOCTORAL STUDENTS SUPERVISED OR MENTORED

Dates	Name	Program or School	Mentor Type	Role	Current Position
2007 - 2010	Dimitri de Kouchkovsky	Bluestone Laboratory, UCSF	Research/Scholarly Mentor	undergraduate researcher	Medical Scientists Training Program, Yale University
2015 - present	Joseph Choe	Tetrad graduate program	Research/Scholarly Mentor	graduate student	graduate student
2017 - 2018	Hannah Brodskaya	Wendell Lim Lab summer internship	Research/Scholarly Mentor	intern	undergraduate at Yeshiva University
2018 - present	Theo Roth	UCSF, Medical Scientist Training Program	Research/Scholarly Mentor,Career Mentor	preceptor for Medicine 160.04	student, Medical Scientist Training Program

Dates	Name	Program or School	Mentor Type	Role	Current Position
2018 - present	Emma Moulton	Staff Research Associate, Wendell Lim Lab, UCSF	Research/Scholarly Mentor	Staff Research Associate, UCSF	Staff Research Associate, UCSF

POSTDOCTORAL FELLOWS AND RESIDENTS MENTORED

Dates	Name	Fellow	Mentor Role	Faculty Role	Current Position
2017 - 2018	Dr. Brian Shy	resident, UCSF Department of Laboratory Medicine	Project Mentor,Co-Mentor/Clinical Mentor	faculty mentor	resident, UCSF Department of Laboratory Medicine

RESEARCH AND CREATIVE ACTIVITIES

RESEARCH AND CREATIVE ACTIVITIES SUMMARY

I am currently a postdoctoral fellow in the laboratory of Dr. Wendell Lim. I am working on projects to engineer T lymphocytes for cancer therapy. In particular, I am working to develop synthetic biology control modules for anti-cancer T cells based on chimeric antigen receptor technology. As part of this work with Dr. Lim, I published review article on cell therapy and synthetic biology in 2017:

Esensten JH, Bluestone JA, Lim WA. Engineering Therapeutic T Cells: From Synthetic Biology to Clinical Trials. Annu Rev Pathol. 2016 Dec 05. PMID: 27959633

I am also a co-Director of the clinical Regulatory T Cell program, which involves providing scientific and technical leadership for clinical trials involving regulatory T cell therapy. In that role, I am involved in process development research for new and existing cell therapy products. One example of my recent contributions involved designing experiments and analyzing data for the recent publication of which I am a co-author:

Roth TL et al. Reprogramming human T cell function and specificity with non-viral genome targeting. Nature. 2018 Jul 11. PMID: 29995861

Based on the advances in the above publication, our group is developing a gene edited Treg product for patients with IPEX-like syndrome, a rare autoimmune disease. We are planning to submit a pre-pre-IND to the FDA in the next 1-2 months.

I am also involved with creative activities to develop cord blood based Treg therapies. The goal is to use banked umbilical cord blood as a source for regulatory T cells to treat patients who later develop type 1 diabetes. In this project, I am collaborating with a group at the University of Florida (Dr. Michael Haller and Dr. Todd Brusko) to obtain cord blood, isolate and expand regulatory T cells on clinical scale, and collect data to support an investigational new drug submission to the FDA. I directly supervise a team of 8 staff at UCSF who are involved in this

project. I participate in experimental design and data analysis. I am the main point of contact with the collaborators in Florida.

I am working on the problem of regulatory T cell product failure due to potential EBV reactivation during manufacturing. I directed the work of a postdoctoral fellow (Dr. Karim Lee) who discovered that the EBV testing that we were performing was not appropriate since it was too sensitive and resulted in many false positive results. We have modified our manufacturing protocol for clinical regulatory T cell preps based on this data. I am preparing a manuscript of this work.

I am involved in a major sponsored research project involving Dr. Susan Fisher's group at UCSF (Dept. of Obstetrics and Gynecology) and Novo Nordisk, a major pharmaceutical company. In this collaboration, we are working to develop a method to derive clinical-grade human embryonic stem cells for therapeutic purposes. As director of the UCSF HICTF and GMP Facility, I am providing medical and scientific consultation for this project. I am also overseeing the actual work in the GMP laboratory, which involves review of all processes, procedures, and policies related to this project.

I am the course director of a new cell therapy elective for laboratory medicine residents. The elective was offered for the first time in February 2018. I developed a curriculum for the elective that includes designing and carrying out quality improvement projects for cell therapy manufacturing, reviewing and releasing cell therapy products for infusion, serving as a consultant for clinicians who are running cell therapy clinical trials, and assisting with process development for new cell therapy products. Cell therapy is a major emerging field and this elective is a selling point in recruiting pathology residents to UCSF.

Finally, I am deeply involved in the planning of a new clinical cellular therapy fellowship within the Department of Laboratory Medicine. I hope to take a leadership role in this new fellowship.

RESEARCH AWARDS - CURRENT

1. CA-0088759	PI	100 % effort	Esensten (PI)
Leukemia and Lymphoma Society		07/01/2016	06/30/2019
Local delivery of therapeutic cytokines via engineered T cells in immunocompetent mouse models of cancer		$ 55,000 direct/yr 1	$ 165,000 total

Chimeric antigen receptor (CAR) T cells have been effective in treating B lymphoblastic leukemia and other hematopoetic and non-hematopoetic cancers. However, there is limited control over these cells after they are infused. Therefore, the purpose of this project is to adapt a new type of synthetic antigen receptor based on the Notch receptor to allow mouse and human T cells (with or without CARs) to sense tumor antigen and produce specific anti-tumor proteins independently of T cell activation state. A single synthetic antigen receptor in this system can control the production of multiple specific cytokines, antibodies, or immunomodulatory peptides. Production of these anti-tumor drugs will be controlled by novel small molecule dimerization system that makes use of an FDA-approved drug. Therefore, both the location of therapeutic protein production and the amount of protein produced will be controlled. The specific aims and anticipated results of this proposal are: 1) Develop a transposon-based system to insert anti-hCD19 synthetic Notch receptors stably into primary mouse T cells; 2) Show that hCD19+ target cells induce these gene modified T cells to produce specific cytokines under the control of the synthetic receptor with minimal leakiness, 3) Adoptively transfer the modified cells into immunocompetent mice with human CD19-bearing tumors including hematopoetic-derived and non-hematopoetic derived tumors and show localized tumor production of the cytokine of interest; 4) Adapt a novel small molecular dimerizer system that uses an FDA-approved drug to gate the production of the cytokine of interest to induce maximal anti-tumor effect with minimal systemic toxicity.

PI

PEER REVIEWED PUBLICATIONS

1. Esensten JH, Tsytsykova AV, Lopez-Rodriguez C, Ligeiro FA, Rao A, Goldfeld AE. NFAT5 binds to the TNF promoter distinctly from NFATp, c, 3 and 4, and activates TNF transcription during hypertonic stress alone. Nucleic Acids Res. 2005; 33(12):3845-54. PMID: 16027109.
2. Esensten JH, Lee MR, Glimcher LH, Bluestone JA. T-bet-deficient NOD mice are protected from diabetes due to defects in both T cell and innate immune system function. J Immunol. 2009 Jul 1; 183(1):75-82. PMID: 19535634.
3. Esensten JH, Wofsy D, Bluestone JA. Regulatory T cells as therapeutic targets in rheumatoid arthritis. Nat Rev Rheumatol. 2009 Oct; 5(10):560-5. PMID: 19798031.
4. McClymont SA, Putnam AL, Lee MR, Esensten JH, Liu W, Hulme MA, Hoffmüller U, Baron U, Olek S, Bluestone JA, Brusko TM. Plasticity of human regulatory T cells in healthy subjects and patients with type 1 diabetes. J Immunol. 2011 Apr 1; 186(7):3918-26. PMID: 21368230.
5. Bour-Jordan H, Esensten JH, Martinez-Llordella M, Penaranda C, Stumpf M, Bluestone JA. Intrinsic and extrinsic control of peripheral T-cell tolerance by costimulatory molecules of the CD28/?B7 family. Immunol Rev. 2011 May; 241(1):180-205. PMID: 21488898.
6. de Kouchkovsky D, Esensten JH, Rosenthal WL, Morar MM, Bluestone JA, Jeker LT. microRNA-17-92 regulates IL-10 production by regulatory T cells and control of experimental autoimmune encephalomyelitis. J Immunol. 2013 Aug 15; 191(4):1594-605. PMID: 23858035.
7. Martínez-Llordella M, Esensten JH, Bailey-Bucktrout SL, Lipsky RH, Marini A, Chen J, Mughal M, Mattson MP, Taub DD, Bluestone JA. CD28-inducible transcription factor DEC1

is required for efficient autoreactive CD4+ T cell response. J Exp Med. 2013 Jul 29; 210(8):1603-19. PMID: 23878307.

8. Wiita AP, Hsu GW, Lu CM, Esensten JH, Wells JA. Circulating proteolytic signatures of chemotherapy-induced cell death in humans discovered by N-terminal labeling. Proc Natl Acad Sci U S A. 2014 May 27; 111(21):7594-9. PMID: 24821784.
9. McCleland ML, Soukup TM, Liu SD, Esensten JH, de Sousa E Melo F, Yaylaoglu M, Warming S, Roose-Girma M, Firestein R. Cdk8 deletion in the Apc(Min) murine tumour model represses EZH2 activity and accelerates tumourigenesis. J Pathol. 2015 Dec; 237(4):508-19. PMID: 26235356
10. Esensten JH, Helou YA, Chopra G, Weiss A, Bluestone JA. CD28 Costimulation: From Mechanism to Therapy. Immunity. 2016 May 17; 44(5):973-88. PMID: 27192564.
11. Esensten JH, Bluestone JA, Lim WA. Engineering Therapeutic T Cells: From Synthetic Biology to Clinical Trials. Annu Rev Pathol. 2016 Dec 05. PMID: 27959633
12. Roth TL, Puig-Saus C, Yu R, Shifrut E, Carnevale J, Li PJ, Hiatt J, Saco J, Krystofinski P, Li H, Tobin V, Nguyen DN, Lee MR, Putnam AL, Ferris AL, Chen JW, Schickel JN, Pellerin L, Carmody D, Alkorta-Aranburu G, Del Gaudio D, Matsumoto H, Morell M, Mao Y, Cho M, Quadros RM, Gurumurthy CB, Smith B, Haugwitz M, Hughes SH, Weissman JS, Schumann K, Esensten JH, May AP, Ashworth A, Kupfer GM, Greeley SAW, Bacchetta R, Meffre E, Roncarolo MG, Romberg N, Herold KC, Ribas A, Leonetti MD, Marson A. Reprogramming human T cell function and specificity with non-viral genome targeting. Nature. 2018 Jul 11. PMID: 29995861
13. Esensten JH, Muller YD, Bluestone JA, Tang Q. Regulatory T cell therapy for autoimmune and autoinflammatory diseases: the next frontier. J Allergy Clin Immunol. 2018 Oct 24. PMID: 30367909

REVIEW ARTICLES

1. St. Lezin EM and Esensten JH. To Irradiate or Not to Irradiate: What is the Role of the Transfusion Service in Preventing TA-GVHD? California Blood Bank Society Today. Fall 2013, Vol. 31, No. 2. http://goo.gl/jkRqFb

BOOKS AND CHAPTERS

1. I wrote the following chapters for PATHPrimer (Elsevier online pathology education project):
   Enterobacteraciae
   Serologic Principles of DAT Testing and Adsorption/Elution/> Causes of Positive DAT/> Evidence of In Vivo Hemolysis
   Types of Immune Hemolytic Anemia
   Benefits of Transfusing Packed Red Blood Cells With Plasma and Platelets in Traumatic Hemorrhage
   Effect of Storage on Red Blood Cells

SIGNIFICANT PUBLICATIONS

1. Esensten JH, Lee MR, Glimcher LH, Bluestone JA. T-bet-deficient NOD mice are protected from diabetes due to defects in both T cell and innate immune system function. J Immunol. 2009 Jul 1; 183(1):75-82. PMID: 19535634.

   This was a first author publication from my graduate school work.

2. Martínez-Llordella M, Esensten JH, Bailey-Bucktrout SL, Lipsky RH, Marini A, Chen J, Mughal M, Mattson MP, Taub DD, Bluestone JA. CD28-inducible transcription factor DEC1 is required for efficient autoreactive CD4+ T cell response. J Exp Med. 2013 Jul 29; 210(8):1603-19. PMID: 23878307.

   This was a co-first author publication from my graduate school work.

3. Esensten JH, Bluestone JA, Lim WA. Engineering Therapeutic T Cells: From Synthetic Biology to Clinical Trials. Annu Rev Pathol. 2016 Dec 05. PMID: 27959633

   This was a first author review article from my postdoctoral fellowship in my area of clinical and research focus.