BIOGRAPHICAL SKETCH

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NAME: June, Carl H.

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

POSITION TITLE: Richard W. Vague Professor in Immunotherapy

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
United States Naval Academy, Annapolis, MD	B.S.	1975	Biology
Baylor College of Medicine, Houston, TX	M.D.	1979	Medicine

A. Personal Statement

I am a physician-scientist, with board certifications in internal medicine and medical oncology. My laboratory has been dedicated to develop new forms of T cell based therapies for more than two decades. We have discovered several principles of lymphocyte costimulation, including CD28, 4-1BB and ICOS as examples. We translated these basic findings by developing a robust T cell culture system. Using this culture system, we conducted the first clinical evaluation of lentiviruses as a vector to modify T cells, initially in HIV and then in cancer patients with advanced leukemia. We conducted the first-in-human evaluation of chimeric antigen receptors (CAR) in T cells. We have since conducted many clinical trials with CAR T cells in patients with HIV infection and diverse forms of cancer. The impact of this work has become widely recognized as a major turning point that is delivering on the long-held promise of cancer gene therapy. The CAR T cells invented in the June laboratory were awarded "Breakthrough Therapy" status by the FDA for acute leukemia in children and adults in 2014 and lymphoma for adults in 2018. The June laboratory has been highly productive with >400 peer reviewed publications (Google Scholar h-index: 117 and 49,000 citations). The technology invented in the June laboratory is now being developed for widespread use by Novartis, with FDA approval anticipated in 2017. These accomplishments have been recognized by the White House on several occasions.

1. Thompson, C. B., T. Lindsten, J. A. Ledbetter, S. L. Kunkel, H. A. Young, S. G. Emerson, J. M. Leiden and **C.H. June**. CD28 activation pathway regulates the production of multiple T-cell-derived lymphokines/cytokines. Proc.Natl.Acad.Sci. 1989; 86: 1333-1337. PMCID: PMC286684 **(Cited 721 times**)
2. Rapoport AP, Stadtmauer EA…27 authors… Levine BL, Cross A, **C.H.June.** Restoration of immunity in lymphopenic individuals with cancer by vaccination and adoptive T-cell transfer. Nature Med. 2005; 11(11):1230-7. (**Cited 267 times**)
3. Tebas P, Stein D, Tang WW, Frank I, Wang SQ, Lee G, Spratt SK, Surosky RT, Giedlin MA, Nichol G, Holmes MC, Gregory PD, Ando DG, Kalos M, Collman RG, Binder-Scholl G, Plesa G, Hwang W-T, Levine BL, **C.H. June**. Gene editing of CCR5 in autologous CD4 T cells of persons infected with HIV. N Engl J Med. 2014; 370:901-910. PMCID: PMC4084652 **(Cited 595 times and featured in accompanying editorial**)
4. Porter DL, Levine BL, Kalos M, Bagg A, **June CH**. Chimeric antigen receptor-modified T cells in chronic lymphoid leukemia. N Engl J Med. 2011; 365(8):725-33. PMCID: PMC3387277 (**Cited 1743 times**)

B. Positions and Honors

Positions and Employment

1978-1979 Research Fellow, World Health Organization Immunology Research and Training Center, Geneva, Switzerland
1979-1980 Internship: Basic Medicine, National Naval Medical Center, Bethesda, Maryland

1980-1982 Teaching Fellow, Department of Medicine, Uniformed Services, University of the Health Sciences, Bethesda, MD
1980-1982 Residency: Internal Medicine, National Naval Medical Center, Bethesda, Maryland
1982-1983 Instructor, Department of Medicine, Uniformed Services University
1982-1983 Chief Resident: Internal Medicine, National Naval Medical Center, Bethesda, Maryland
1983-1985 Fellow in Oncology, University of Washington and Fred Hutchinson Cancer Research Center, Seattle, Washington
1986-1990 Assistant Professor, Department of Medicine, Uniformed Services
1990-1995 Associate Professor, Department of Medicine, Uniformed Services
1995-1999 Professor, Department of Medicine, Uniformed Services University of
1999-2001 Professor of Molecular and Cellular Engineering, University of Pennsylvania School of Medicine
2001-present Professor of Pathology and Laboratory Medicine, University of Pennsylvania School of Medicine
2004-present Professor of Medicine, University of Pennsylvania School of Medicine
2015-present Director, Center for Cellular Immunotherapies at the University of Pennsylvania
2016-present Director, Parker Institute for Cancer Immunotherapy at the University of Pennsylvania

Other Experience and Professional Memberships

1999-present American Society of Gene Therapy
Chair, Genetic Vaccines Committee (2005-2007)
1986-present American Society Hematology
Chair, Scientific Committee on Lymphocyte Biology (2002-2005)
2007-present International Society for Biologic Therapies
Elected, Board of Directors, 2008
1995-present Clinical Immunology Society
President, 2009-2010
1994-1998 NIAID, Member, Allergy and Immunology Transplantation Study Section
2005-2007 NCI, Subcommittee D (Clinical Studies)
2009-2014 NCI Board of Scientific Counselors, Clinical Sciences and Epidemiology, member

Honors

1996 Legion of Merit, US Navy
1996 Dexter Conrad Award, Office of Naval Research, Navy's highest award for Scientific Achievement
1997 Frank Brown Berry Prize in Federal Medicine
2001 Burroughs Wellcome Fund Award: visiting professor in the basic medical sciences
2002 Lifetime Achievement Award, Leukemia and Lymphoma Society of America
2002 William Osler Award, University of Pennsylvania School of Medicine
2005 Federal Laboratory Award for Excellence in Technology Transfer
2005 Bristol-Myers Squibb Freedom to Discover Award
2005 Federal Laboratory Award for Excellence in Technology Transfer, Federal Laboratory Consortium for Technology Transfer
2006 American Association of Physicians
2012 William B Coley Award in Tumor Immunology
2012 Ernest Beutler Lecture and Prize, American Society of Hematology
2012 Institute of Medicine
2013 Philadelphia Award
2013 Richard V Smalley Award, Society for Immunotherapy of Cancer
2014 Steinman Award for Human Immunology Research, American Assn Immunologists
2014 Taubman Prize for Excellence in Translational Medical Science
2014 Karl Landsteiner Memorial Award, AABB
2014 American Academy of Arts & Sciences
2015 AACR-Cancer Research Institute Lloyd J. Old Award in Cancer Immunology
2015 Debrecen Award for Molecular Medicine
2015 Paul Ehrlich and Ludwig Darmstaedter Prize (shared with J. Allison)
2016 Novartis Prize for Immunology, (shared with S. Rosenberg and Z. Eshhar),

International Congress of Immunology
2017 Karnofsky Prize, ASCO
2018 Passano Award (shared with M. Sadelain)
2018 Albany Medical Prize (shared with J. Allison and S. Rosenberg)

C. Contribution to Science

1. Costimulation and CAR T cell therapy.

In the 1980s, the June laboratory first identified the major growth control switch for T cells, and showed that it was controlled by the CD28 molecule. This work was assigned to the Office of Naval Research and patented by the US Government (USPTO 08/435,816 and others). In the last fifteen years, June and his team developed chimeric antigen receptor (CAR) T cells. He initially tested this approach in patients with acute and chronic lymphocytic leukemia. The initial patients were treated in 2010 and two of the first three remain disease free more than 4 years since infusion. They have since treated more than 100 patients with advanced leukemia in adults and children with similar success. Based on the clinical results, the FDA awarded breakthrough designation status for the treatment of pediatric and adult lymphocytic leukemia. This is the first therapy ever developed entirely in an academic setting to receive FDA "breakthrough" status, awarded by FDA in July 2014.

a. Kalos M, Levine BL, Porter DL, Katz S, Grupp SA, Bagg A, and **C.H. June**. T cells with chimeric antigen receptors have potent antitumor effects and can establish memory in patients with advanced leukemia. Sci Transl Med. 2011 Aug 10; 3(95):95ra73. PMCID: PMC3393096.
b. Grupp SA, Kalos M, Barrett D, Aplenc R, Porter DL, Rheingold SR, Teachey DT, Chew A, Hauck B, Wright JF, Milone MC, Levine BL, **June CH**. Chimeric antigen receptor-modified T cells for acute lymphoid leukemia. N Engl J Med. 2013 Apr 18; 368(16):1509-18. PMCID: PMC4058440.
c. Rapoport AP, Stadtmauer EA...31 authors…Kalos M, **June CH**. NY-ESO-1-specific TCR-engineered T cells mediate sustained antigen-specific antitumor effects in myeloma. Nature Med. 2015 Aug; 21(8):914-21. PMCID: PMC4529359.
d. Kawalekar OU, O'Connor R, Fraietta JA, Guo L, McGettigan S, Posey AD, Jr., Patel P, Guedan S, Scholler J, Keith B, Snyder N, Blair I, Milone M, **June CH**. Distinct signaling of coreceptors regulates specific metabolism pathways and impacts memory development in CAR T cells. Immunity. 2016; Feb 16; 44(2):380-90.
e. Posey AD, Jr., Schwab RD, Boesteanu AC, Steentoft C, Mandel U, Engels B, Stone JD, Madsen TD, Schreiber K, Haines KM, Cogdill AP, Chen TJ, Song D, Scholler J, Kranz DM, Feldman MD, Young R, Keith B, Schreiber H, Clausen H, Johnson LA, **June CH**. Engineered CAR T Cells Targeting the Cancer-Associated Tn-Glycoform of the Membrane Mucin MUC1 Control Adenocarcinoma. Immunity. 2016;44(6):1444-54.

2. HIV immunopathology and immunotherapy.

In preclinical studies, June's laboratory along with scientists at Sangamo Biosciences designed Zinc Finger Nuclease (ZFN) pairs consisting of two 4-finger proteins that bind to a target site within the human chemokine receptor 5 gene (CCR5). ZFNs are artificial restriction enzymes that can be designed to cleave DNA at specific sites. In preclinical tests, CCR5-modified CD4 T cells were protected from human immunodeficiency virus (HIV) infection, and reduced HIV RNA levels in a humanized mouse model involving xenotransplantation of HIV infection (Perez EE,...June CH. Establishment of HIV-1 resistance in CD4+ T cells by genome editing using zinc-finger nucleases. Nat Biotechnol. 26:808-16, 2008). Therapies based on the CCR5 have gained interest after a man known as the "Berlin Patient" was "functionally" cured after a stem cell transplant from a donor who had CCR5 mutation in both alleles. June's team is attempting to replicate this phenomenon using autologous cells because a bone marrow transplant is not a practical solution for HIV patients who do not have blood cancers. In the current study, to knock-out CCR5 in autologous CD4 T cells, June's team used an adenoviral vector constructed to express ZFNs. Since mutations are commonly induced during the natural repair of these breaks, it becomes possible to disrupt the ability of the targeted allele to make a functional protein, in this case CCR5. 12 patients were infused and CD4 T cell counts increased in all participants. After 36 weeks of follow up, the median increase was 615 cells. The genetically modified cells persist in vivo with a half-life of nearly a year; they also appear to be protected from HIV infection, because when antiretroviral therapy is stopped, they are depleted at a slower

rate than are unmodified cells. In summary, this is the first example in humans that targeted gene modification can be used to knock-in a disease resistance gene. An accompanying editorial in the New England Journal of Medicine (PMID 24597871) had the following concluding paragraph: "This proof-of-principle study is an important first step, not just in the treatment of those infected with HIV but also for genome editing in a broader sense…The potential future of gene knockout by ZFNs and other techniques is not restricted to HIV infection."

a. Levine BL, Humeau LM, Boyer J, MacGregor RR, Rebello T, Lu X, Binder GK, Slepushkin V, Lemiale F, Mascola JR, Bushman FD, Dropulic B, **June CH**. Gene transfer in humans using a conditionally replicating lentiviral vector. Proc Natl Acad Sci U S A. 2006 Nov 14; 103(46):17372-7. PMCID: PMC1635018.
b. Perez EE, Wang J, Miller JC, Jouvenot Y, Kim KA, Liu O, Wang N, Lee G, Bartsevich VV, Lee YL, Guschin DY, Rupniewski I, Waite AJ, Carpenito C, Carroll RG, Orange JS, Urnov FD, Rebar EJ, Ando D, Gregory PD, Riley JL, Holmes MC, **June CH**. Establishment of HIV-1 resistance in CD4+ T cells by genome editing using zinc-finger nucleases. Nat Biotechnol. 2008 Jul; 26(7):808-16. PMCID: PMC3422503.
c. Scholler J, Brady TL, Binder-Scholl G, Hwang WT, Plesa G, Hege KM, Vogel AN, Kalos M, Riley JL, Deeks SG, Mitsuyasu RT, Bernstein WB, Aronson NE, Levine BL, Bushman FD, **June CH**. Decade-long safety and function of retroviral-modified chimeric antigen receptor T cells. Sci Transl Med. 2012 May 2; 4(132):132ra53. PMCID: PMC4368443.
d. Tebas P, Stein D, Tang WW, Frank I, Wang SQ, Lee G, Spratt SK, Surosky RT, Giedlin MA, Nichol G, Holmes MC, Gregory PD, Ando DG, Kalos M, Collman RG, Binder-Scholl G, Plesa G, Hwang WT, Levine BL, **June CH**. Gene editing of CCR5 in autologous CD4 T cells of persons infected with HIV. N Engl J Med. 2014 Mar 6; 370(10):901-10. PMCID: PMC4084652.

Complete List of Published Work in My Bibliography:
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Sort descending:
http://www.ncbi.nlm.nih.gov/pubmed/?term=June+c

D. Research Support
Ongoing Research Support

ACTIVE
1P01CA214278-01 June (PI) 08/15/17-7/31/22
NIH/ NCI
Enhancing Chimeric Antigen Receptor T Cell Therapies for Hemotologic Malignancies: Beyond CART 19
Our goal is to develop next generation immunotherapy for hematologic malignancies which strike more than 200,000 people every year in the United States. Our approach involves the development of next generation therapies with chimeric antigen receptor (CAR) T cells, involving innovative combinations of CAR T Cells and generic editing with CRISPR/Cas9 technology to be tested in four clinical trials
Role: Program Leader

UL1-TR-001878-01 FitzGerald (PI) 07/01/16-05/31/21
NIH/ NCRR
Institutional Clinical and Translational Science Award: "Program in Novel Biotherapeutics" (PINB)
This is a program directed by Dr. June as part of the CTSA for University of Pennsylvania. The primary goal of the PINB is to stimulate synergistic interactions between clinical and laboratory-based investigators to accelerate the testing of novel biotherapeutics.

Novartis (June) June (PI) 10/02/12- 12/31/18
Novartis Research Alliance
The purpose of this research is to develop non-CD19 Cart T cells in oncology

Role: Program Leader

Prostate Cancer Foundation June (PI) 06/18/14-06/18/19
Phase 1 Study of PSMA-TGFBR DN CAR Modified T Cells in Patients with Advanced Castrate Resistant Prostate Cancer
Role: PI

U19 AI117950-02 Riley (PI) 04/10/15-03/31/20
NIH/ NIAID
Role: Clinical Trial Sponsor
Engineering T Cells to Provide Durable Control of HIV-1 Replication
Role: Clinical Trial Sponsor

5P0 CA174523 Herlyn (PI) 04/01/14-03/31/19
National Institute of Health
SPORE in Skin Cancer
Role: Co-Project leader “Engineered T Cell therapy for melanoma”

UM1 AI126620-01 Riley (PI) 08/01/16-6/30/2021
NIH/ NIAID
BEAT HIV: Delaney Collaborative to Cure HIV-1 Infection by Combination Immunotherapy
Role: Sponsor

SU2C/ Lustgarten June (PI) 04/01/2017 – 03/31/2019
Stand up to Cancer
Chimeric Antigen Receptor T Cell Therapy for Pancreatic Cancer
Role: Program Leader

1-R01-CA-226983 June (PI) 03/01/2018-2/28/23
NIH
Directing the metabolic fate of CAR T cells
Role : PI

Yale University/Stand up to Cancer June (sub-PI) 01/01/2011-2/31/202001
Single-Cell Functional Proteomics to Characterize and Monitor CAR-T Therapy
Role: Sub PI

Tmunity Therapeutics & Parker Institute June (PI) 11/1/17-1/31/20
Autologous T cells transduced with a lentiviral vector to express NY-ESO-1 and electroporated with CRISPR guide RNA to disrupt expression of endogenous TCR and PD-1 (UPCC# 25416)