AVERY D. POSEY, JR., PH.D.

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EXECUTIVE SUMMARY

I am a classically trained molecular and developmental geneticist that is proficient in the development and pre-clinical characterization of chimeric antigen receptors (CARs) and other engineered T cell strategies for cancer immunotherapy. My current research is focused on the redirection of T cells to target cancer-specific epitopes, especially antigens formed through altered glycosylation in cancer cells, determination of optimal signaling of CAR T cells for effective anti-tumor responses in solid tumors, and gene-editing of checkpoint molecules (PD-1, CTLA-4, etc.) in anti-cancer T cell therapies. The major objective of my research is to increase the efficacy of engineered T cells in solid tumors.

Immuno-Oncology | Chimeric Antigen Receptor Design | T cell Signal Transduction | Molecular Biology | Multicolor Flow Cytometry | Syngeneic & Xenograft Tumor Models | Cell Phenotyping & Subset Analysis | Viral Vector Production

EDUCATION

Doctor of Philosophy (Ph.D.) 2005 – 2011
Genetics
The University of Chicago, Chicago, IL

Bachelors of Science (B.S.) 2001 – 2005
Biochemistry & Molecular Biology
University of Maryland, Baltimore County (UMBC), Baltimore, MD

Bachelors of Science (B.S.) 2001 – 2005
Bioinformatics & Computational Biology
University of Maryland, Baltimore County (UMBC), Baltimore, MD

BIOMEDICAL RESEARCH EXPERIENCE

Instructor
Department of Pathology and Laboratory Medicine April 2016 – Present
University of Pennsylvania, Philadelphia, PA
Research Area: Investigation of glycosylation-specific chimeric antigen receptors for translation into clinical studies in canines and humans.

Postdoctoral Fellow April 2011 – March 2016
Department of Pathology and Laboratory Medicine
University of Pennsylvania, Philadelphia, PA
Advisor: Carl H. June
Research Area: Development and characterization of chimeric antigen receptors for *in vivo* detection and elimination of tumor cells

- Designed a chimeric antigen receptor against the Tn-antigen of MUC1, a glycoepitope only exposed in malignant cells, using the scFv of the 5E5 mAb and evaluated *in vitro* and *in vivo* function of redirected 5E5CAR T cells against multiple tumor targets. This CAR will be tested clinically in 2016.
- Designed a novel scFv and chimeric antigen receptor against SSEA-4, an embryonic antigen also found in multiple cancers, and evaluated the function of the SSEA4CAR T cells *in vitro* and *in vivo*. I found that this CAR is detrimental clinically as it targets vascular endothelial cells.
- Constructed chimeric antigen receptors using the intracellular signaling domain of CD2 and compared the cytotoxicity, signaling, and *in vivo* persistence of CD2-based receptors to CD28- and CD137-based receptors.
- Performed mutagenesis of the CD28 and ICOS signaling domains within chimeric antigen receptors and evaluated the signaling, cytokine secretion, anti-tumor efficacy of these CAR cells *in vitro*, as well as identified the signaling mutants that perform better and persisted longer *in vivo* than native signaling CAR constructs.
- Studied the dynamics of CAR aggregation through the creation of monomer CAR molecules, and evaluated the function of monomer CAR T cells *in vitro*. The monomer CAR T cells demonstrated improved safety *in vitro*.

- Characterized the calcium flux, proximal and distal signaling, and differential gene expression of T cells redirected with chimeric antigen receptors containing the 4-1BB or CD28 costimulation domains via lentiviral transduction or RNA electroporation.
- Managed graduate and undergraduate student scientific development and supervised project progress.

Graduate Student/Research Assistant June 2006 – March 2011
Department of Medicine, Section of Cardiology
The University of Chicago, Chicago, IL
Advisor: Elizabeth M. McNally
Research Area: Identification of the molecular function and interacting partners of fer-1-like-5 (Fer1L5) to improve our understanding of skeletal and cardiac muscle development. Fer1L5 is a previously uncharacterized homolog of dysferlin, myoferlin, and otoferlin, molecules implicated in vesicular trafficking. Dysferlin mutations cause limb-girdle muscular dystrophy type 2B.

- Determined that Fer1L5 has a role in myoblast fusion through siRNA reduction of Fer1L5 and quantification of myoblast fusion.
- Cloned the Fer1L5 cDNA through RT-PCR and quantified the fusion indexes of C2C12 myoblasts overexpressing the Fer1L5 cDNA in an effort to develop a therapeutic approach to improve loss-of-function dysferlin mutations.
- Identified protein-protein interactions between Fer1L5 and members of the endocytic recycling pathway, EHD1 and EHD2.
- Quantified the fusion indexes of myoblasts from a C2C12 muscle cell line after siRNA reduction of EHD1 and EHD2 and after overexpression of mutant forms of EHD2 that disrupt the ATPase activity of EHD2.
- Analyzed histological sections of skeletal muscle from EHD1 null mice for indications of developmental and regenerative muscle defects.
- Managed the scientific development of undergraduate and visiting high school students.

Research Technician August 2004 – May 2005
The Institute of Human Virology
University of Maryland School of Medicine, Baltimore, MD
Advisor: George K. Lewis
Research Area: To identify monoclonal antibodies useful for the creation of a HIV vaccine.

- Cultured hybridoma cell lines and performed ELISAs to identify monoclonal antibodies with specificity for gp120, a glycoprotein exposed on the surface of the HIV envelope.

Research Technician June 2003 – August 2003
Department of Molecular Genetics and Microbiology
Duke University, Durham, NC
Research Area: To investigate molecules that influence inborn immunity against pathogenic hosts.
Advisor: Alejandro Aballay

- Performed an RNAi screen of the *C. elegans* genome to identify genes involved in innate immunity.
- Created GFP-fusion proteins of identified genes and microinjected *C. elegans* to establish transgenic lines.

U. S. PATENTS

"CD28 Compositions and Methods for Chimeric Antigen Receptor Therapy." U.S. Provisional Patent Application. Filed 01/26/17. Co-inventors: Sonia Guedan & Carl H. June.

"Subset-optimized Chimeric Antigen Receptor-containing Cells." U. S. Patent. 15/327,794. Filed 01/20/17. Co-inventors: Sonia Guedan & Carl H. June.

"Regulating Transgene Expression Level Using Variants of the PGK Promoter." U. S. Patent. PCT/US2016/013637. Co-inventors: Jihyun Lee & Carl H. June.

"Use of the CD2 Signaling Domain in Second-Generation Chimeric Antigen Receptors." U. S. Patent. WO2013126729 A1. Published August 29, 2013. Co-inventors: Carl H. June & John Scholler.

PUBLICATIONS

Posey, A. D. Jr., June, C. H., Levine, B. L. (2017) Cancer Killers. *Scientific American* 316:38-43.

Posey, A. D. Jr., Clausen, H., June, C. H. (2016) Distinguishing Truncated and Normal MUC1 Glycoform Targeting from Tn-MUC1-Specific CAR T Cells: Specificity Is the Key to Safety. *Immunity* 45:947-948.

Posey, A. D. Jr., Schwab, R. D., Boestaneau, A. C., Steentoft, C., Mandel, U., Engels, B., Stone, J. D., Madsen, T. D., Schreiber, K., Haines, K. M., Cogdill, A. P., Chen, T. J., Song, D., Scholler, J., Kranz, D. M., Feldman, M. D., Young, R., Keith, B., Schreiber, H., Clausen, H., Johnson, L. A., June, C. H. (2016) Engineered CAR T Cells Targeting the Cancer-Associated Tn-Glycoform of the Membrane Mucin MUC1 Control Adenocarcinoma. *Immunity* 44:1444-54.

Kawalekar, O. U., O'Connor, R. S., Fraietta, J. A., Guo, L., McGettigan, S. E., **Posey, A. D. Jr.**, Patel, P., Guedan, S., Scholler, J., Keith, B., Snyder, N., Blair, I., Milone, M. C., June, C. H. (2016) Distinct Signaling of Coreceptors Regulates Specific Metabolism Pathways and Impacts Memory Development in CAR T Cells. *Immunity* 44:380-90.

Posey, A. D. Jr., Kawalekar, O. U., June, C. H. (2015). Measurement of intracellular ions by flow cytometry. *Curr Prot Cytometry.* 72:9.8.1-9.8.21.

Johnson, L. A., Scholler, J., Ohkuri, T., Kosaka, A., Patel, P. R., McGettigan, S. E., Nace, A. K., Dentchev, T., Thekkat, P., Loew, A., Boestaneau, A. C., Cogdill, A. P., Chen, T., Fraietta, J. A., Kloss, C. C., **Posey, A. D. Jr.**, Engels, B., Singh, R., Ezell, T., Idamakanti, N., Ramones, M. H., Li, N., Zhou, L., Plesa, G., Seykora, J. T., Okada, H., June, C. H., Brogdon, J. L., Maus, M. V. (2015). Rational development and characterization of humanized anti-EGFR variant III chimeric antigen receptor T cells for glioblastoma. *Sci Transl Med* 7:275ra22.

Frigault, M. J.*, Lee, J.*, Basil, M. C., Carpenito, C., Shinichiro, M., Scholler, J., Kawalekar, O. U., Guedan, S., McGettigen, S. E., **Posey, A. D. Jr.**, Ang, S., Cooper, L. J. N., Platt, J., Johnson, F. B., Paulos, C. M., Zhao, Y., Kalos, M., Milone, M. C., June, C. H. (2015). Identification of chimeric antigen receptors that mediate constitutive or inducible proliferation of T cells. *Cancer Immunology Research* 3:356-67.

Guedan, S., Chen, X., Madar, A., Carpenito, C., McGettigan, S. E., Frigault, M. J., Lee, J., **Posey, A. D. Jr.**, Scholler, J., Scholler, N., Bonneau, R., June, C. H. (2014). ICOS-based chimeric antigen receptors program bipolar TH17/TH1 cells. *Blood* 124:1070-80.

Posey, A. D. Jr., Swanson K. E., Alvarez, M. G., Krishnan, S., Earley, J, Band, H., Pytel, P. McNally, E. M., Demonbreun, A. R. (2014). EHD1 mediates vesicle trafficking required for normal muscle growth and tubule development. *Dev. Biol.* 387:179-90.

Posey, A. D. Jr., Demonbreun, A. R., McNally, E. M. (2011). Ferlin family members in myogenesis. *Curr Top Dev Biol* 96:203-30. *Review.*

Posey, A. D. Jr., Pytel, P., Heretis, K., Demonbreun, A. R., Rainey, M., George, M., Band, H., McNally, E. M. (2010). Endocytic recycling proteins EHD1 and EHD2 interact with Fer-1-like-5 (Fer1L5) and mediate myoblast fusion. *J. Biol Chem.* 286:7379-88.

Demonbreun, A. R., **Posey, A. D.**, Heretis, K., Swaggart, K. A., Earley, J. U., Pytel, P., McNally, E. M. (2010). Myoferlin is required for insulin-like growth factor response and muscle growth. *FASEB J.* 24, 1284-95.

Doherty, K. R., Demonbreun, A., Wallace, G. Q., Cave, A., **Posey, A. D.**, Heretis, K., Pytel, P. and

McNally, E. M. (2008). The Endocytic Recycling Protein EHD2 Interacts with Myoferlin to Regulate Myoblast Fusion. *J Biol Chem* 283:20252-60.

Doherty, K. R., Cave, A., Davis, D. B., Delmonte, A. J., **Posey, A.**, Earley, J. U., Hadhazy, M. and McNally, E. M. (2005). Normal myoblast fusion requires myoferlin. *Development* 132, 5565-75.

INVITED SEMINARS

Early Stage Professional Presentation, International Society for Cellular Therapy 2017 Annual Meeting, May 3-6, 2017, London, UK.

Keynote Seminar, 10th Annual Pan-Pacific Symposium on Stem Cells and Cancer Research, April 15-17, 2017, Hualien, Taiwan.

Basic and Translational Studies, World ADOPT Summit, March 7-9, 2017, London, UK.

Cancer Glycoimmunology, Danish Conference on Glycobiology and Carbohydrate Biotechnology, May 26-27, 2016, Vejle, Denmark.

PROFESSIONAL TRAINING AND DEVELOPMENT

American Association of Immunologists 2011 Introductory Course in Immunology University of Pennsylvania, Philadelphia, PA	July 9-14, 2011

PROFESSIONAL MEMBERSHIPS

Parker Institute for Cancer Immunotherapy Scientific Advisory Board	2016 – Present
Journal of Immunology Research and Therapy, Editorial Board	2016 – Present
American Association of Gene and Cell Therapy, Educational Committee	2016 – Present
Keystone Symposia Scientific Advisory Board	2015 – 2016
American Association of Immunologists	2011 – Present
American Association for Cancer Research	2011 – Present
American Society for Hematology	2011 – Present

SELECTED HONORS & AWARDS

Immuno Oncology Young Investigators' Forum Junior Faculty Clinical/Translational Grand Prize	April 2017
2016 Keystone Symposia Fellow	2015-2016
American Society of Gene & Cell Therapy Meritorious Abstract Travel Award	2015
Gordon Research Conference Carl Storm Underrepresented Minority Fellowship	2015
American Society of Hematology Abstract Achievement Award	2014
UNCF*Merck Postdoctoral Science Research Fellowship	2014 – Present
University of Pennsylvania Immunology Training Grant, T32CA009140	2011 – 2014
2010 Biotechnology Institute Minority Fellow	2010
FASEB MARC Poster/Presentation Travel Award	2010
University of Chicago Cardiovascular Research Training Grant, T32HL007381	2008 – 2010
University of Chicago Genetics & Regulation Training Grant, T32GM007197	2005 – 2008
University of Chicago McNair Scholar	June – August 2004
UMBC MARC U*STAR Trainee	2003 – 2005
UMBC Meyerhoff Scholar	2003 – 2005
UMBC University Scholar	2001 – 2003

TEACHING EXPERIENCE

Teaching Assistant, The University of Chicago, Chicago, IL January – March 2007; January – March 2010
Biological Systems

- Led discussion sessions for advanced first-year undergraduates on groundbreaking research articles in the fields of molecular biology and genetics.
- Met with students outside of class to provide assistance to answer questions regarding homework assignments.

Teaching Assistant, The University of Chicago, Chicago, IL September – December 2009
Cell and Molecular Biology Laboratory

- Experiments consisted of using immunofluorescence and live cell microscopy to identify organelles, DNA mapping through restriction analysis, western blotting to determine abnormal cell signaling, and mitochondrial respiration.
- Prepared weekly laboratory introduction presentation.
- Graded lab reports and homework assignments.
- Managed class during lab and guided students through experiments.

Teaching Assistant, The University of Chicago, Chicago, IL April – June 2009
Developmental Biology Laboratory

- Experiments consisted of studying sea urchin fertilization, Drosophila and *C. elegans* anterior-posterior patterning, hindbrain development and sensitivity to retinoic acid in zebrafish, as well as somitogenesis and neurulation in chicks.

Teaching Assistant, The University of Chicago, Chicago, IL January – March 2006; January – March 2008
Genetics Laboratory

- Experiments consisted of DNA fingerprinting, yeast mutation and complementation, DNA cloning and transformation, and mapping recombination in Drosophila.

* Denotes equal contribution