BIOGRAPHICAL SKETCH

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NAME: Kevin Joseph Curran, MD

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

POSITION TITLE: Assistant Attending (MSKCC/NYPH); Assistant Professor (Weil Cornell Medical College)

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
Villanova University, Villanova PA	BS	May 2000	Biology
Georgetown University School of Medicine, Washington, D.C.	MD	May 2004	Medicine
Tuft New England Medical Center, Boston, MA		June 2007	Pediatrics
Memorial Sloan-Kettering Cancer Center, New York, NY		June 2010	Ped. Heme/Oncology Chief Fellow (2010)
Certified, American Board of Pediatrics		2009 2011	General Pediatrics Ped. Heme/Oncology

A. Personal Statement

My research focus is on the translation of novel cellular therapies into new treatment strategies for children with cancer. Specifically, T cells can be genetically modified to target tumor antigens through the expression of a chimeric antigen receptor (CAR). My position (Assistant Attending, Transplant and Cellular Therapy Service - MSK Kids (Department of Pediatrics, MSK) has allowed me to conduct clinical trials using CAR T cells in patients with relapsed/refractory malignancies.

Ongoing and recently completed projects that I would like to highlight include:

William Lawrence and Blanche Hughes Foundation Grant
Title: Adoptive Therapy with CD19 Targeted T cells in Pediatric Patients with Relapsed B-ALL.
Duration: 8/01/18 – 7/31/2021
Role: Protocol Investigator

BMT PO1 - 2P01CA023766-39A1
Title: Off the Shelf CAR T cells for Hematologic Malignancies
Duration: 09/3/97 – 6/30/2024
Role: Protocol Investigator (Project 6 – Clinical Trials)

Comedy vs Cancer
Title: Off the Shelf CAR T cells – Production/Cell Bank Costs
Duration 9/1/2019 – 12/31/2021
Role: PI

B. Positions, Scientific Appointments, and Honors

Positions and Scientific appointments

2004-2007 Tuft-New England Medical Center, Boston, MA.
Pediatric Resident, Department of Pediatrics

2007-2010 New York Presbyterian (Cornell)/Memorial Sloan Kettering Cancer Center, New York, N.Y.
Fellow, Hematology/Oncology, Department of Pediatrics

2009-2010 Memorial Sloan Kettering Cancer Center, New York, N.Y.
Chief Fellow, Department of Pediatrics

2008-2011 Memorial Sloan Kettering Cancer Center, New York, N.Y.
Research Fellow, Laboratory of Renier J. Brentjens MD, PhD

2011-2015. Memorial Sloan Kettering Cancer Center, New York, N.Y.
Instructor, Bone Marrow Transplant Service, Department of Pediatrics

2014-Pres. Memorial Sloan Kettering Cancer Center, New York, N.Y.
Member, Cellular Therapeutic Center (CTC)

2015-Pres. Memorial Sloan Kettering Cancer Center, New York, N.Y.
Assistant Attending, Bone Marrow Transplant Service, Department of Pediatrics

2015-2016. Weil Cornell Medical College, New York, N.Y.
Instructor in Pediatrics, Department of Pediatrics

2015-Pres. New York Presbyterian Hospital, New York, N.Y.
Assistant Attending, Department of Pediatrics

2015-Pres. Memorial Sloan Kettering Cancer Center New York N.Y
Member, Center for Cell Engineering (CCE)

2016-Pres. Weil Cornell Medical College, New York, N.Y.
Assistant Professor in Pediatrics, Department of Pediatrics

2018-2021 Memorial Sloan Kettering Cancer Center, New York, N.Y.
Pediatric Director, Cellular Therapeutic Center

2018-Pres. Memorial Sloan Kettering Cancer Center, New York, N.Y.
Director, MSKCC FACT IEC Program

Honors

2006 Tufts School of Medicine, Distinguished Teaching Award
2009 St. Baldrick's Foundation Post Doctoral Fellowship for Childhood Cancer Research
2009 Laura Rosenberg Foundation Fellowship in Pediatric Leukemia
2010 St. Baldrick's Foundation Research Continuation Grant for Childhood Cancer Research
2010 New York Presbyterian Hospital (Cornell) Department of Pediatrics Fellowship Research Award
2010 American Society of Hematology Travel Award (ASH Annual Meeting 2010)
2011 National Institutes of Health Loan Repayment Program (NIH-LRP) Award
2012 American Society of Hematology Clinical Research Training Institute (ASH-CRTI)
2012 St. Baldrick's Foundation Scholar (Career Development Award)
2012 Young Investigator Award (2nd Int'l Workshop on the Biology, Prevention, and Treatment of Relapse After HSCT Hematopoietic Stem Cell Transplantation
2014 American Society of Hematology Advocacy Leadership Institute (ASH-ALI)
2014 Young Investigator Award (American Society of Pediatric Hematology/Oncology – ASPHO)
2015 Society of Hematologic Oncology (SOHO) Young Investigator Travel Award (Annual Meeting)

C. Contributions to Science

1. Clinical application of CD19-specific chimeric antigen receptor (CAR) T cells

T cells can be genetically modified to target tumor antigens through the expression of a chimeric antigen receptor (CAR). The basic design of CARs consists of two domains – the antigen binding portion (commonly composed of a single chain variable fragment (scFv) derived from a monoclonal antibody) joined to one or more intracellular signaling domains. Our group and others have demonstrated promising clinical responses using T cells targeting the CD19 antigen through the expression of a chimeric antigen receptor (CAR) in patients with relapsed or

refractory (R/R) B-ALL. The focus of my research is the clinical application and extension of this novel immunotherapy (CD19-specific CAR T cells) to children with R/R B-ALL.

a. **Curran KJ**, Brentjens RJ. Chimeric Antigen Receptor T cells for Cancer Immunotherapy. *Journal of Clinical Oncology.* 2015 May 20;33(15):1703-6*.*
b. **Curran KJ**, Margossian SP, Kernan NA, Silverman LB, Williams DA, Shukla N, Kobos R, Forlenza CJ, Steinherz P, Prockop S, Boulad F, Spitzer B, Cancio MI, Boelens JJ, Kung AL, Szenes V, Park JH, Sauter CS, Heller G, Wang X, Senechal B, O'Reilly RJ, Riviere I, Sadelain M, Brentjens RJ. Toxicity and response after CD19-specific CAR T-cell therapy in pediatric/young adult relapsed/refractory B-ALL. *Blood*. 2019 Dec 26;134(26):2361-2368
c. Fabrizio, V. A., Boelens, J. J., Mauguen, A., Baggott, C., Prabhu, S., Egeler, E., Mavroukakis, S., Pacenta, H., Phillips, C. L., Rossoff, J., Stefanski, H. E., Talano, J. A., Moskop, A., Margossian, S. P., Verneris, M. R., Myers, G. D., Karras, N. A., Brown, P. A., Qayed, M., Hermiston, M., Satwani, P., Krupski, C., Keating, A. K., Wilcox, R., Rabik, C. A., Chinnabhandar, V., Kunicki, M., Goksenin, A. Y., Mackall, C. L., Laetsch, T. W., Schultz, L. M., **Curran, KJ**. Optimal fludarabine lymphodepletion is associated with improved outcomes after CAR T-cell therapy. *Blood Advances* (2022) 6(7): 1961-1968
d. Shahid, S., Ramaswamy, K., Flynn, J., Mauguen, A., Perica, K., Park, J. H., Forlenza, C. J., Shukla, N. N., Steinherz, P. G., Margossian, S. P., Boelens, J. J., Kernan, N. A., **Curran, K**J. Impact of bridging chemotherapy on clinical outcomes of CD19-specific CAR T cell therapy in children/young adults with relapsed/refractory B cell acute lymphoblastic leukemia. *Transplantation and Cellular Therapy* (2022) 28(2): 72.e1-72.e8

2. Pre-clinical development of next generation CAR T cells termed "armored CAR" T cells

To be effective following infusion, CAR T cells must expand, persist, exhibit enduring anti-tumor cytotoxicity, overcome targeted tumor antigen escape, and importantly counteract the immunosuppressive tumor microenvironment. This hostile tumor microenvironment allows for tumor evasion through the recruitment of inhibitory immune cells including regulatory CD4 T cells (Tregs), myeloid derived suppressor cells (MDSCs), tumor associated macrophages (TAMs), and the expression of immune suppressive ligands (PD-L1, PD-L2), and/or cytokines (TGFb, IL-10). Current CAR T cell technology is unlikely to overcome this hostile microenvironment which may explain the poor clinical efficacy CAR T cells have thus far demonstrated in solid malignancies. To overcome this limitation we have focused on additional genetic modification of CAR T cells (constitutive expression of CD40L or IL-12) designed to generate "armored" CAR T cells endowed the abilities to be effective within any microenvironment.

a. Pegram HJ, Purdon TJ, van Leeuwen DG, **Curran KJ**, Giralt SA, Barker JN, Brentjens RJ. IL-12-secreting CD19-targeted cord Blood-derived T cells for the Immunotherapy of B-cell Acute Lymphoblastic Leukemia. *Leukemia.* 2015 Feb;29(2):415-22
b. **Curran K**J, Seinstra BA, Nikhamin Y, Yeh R, Usachenko Y, van Leeuwen DG, Purdon T, Pegram HJ, Brentjens RJ. Enhancing Antitumor Efficacy of Chimeric Antigen Receptor T Cells Through Constitutive CD40L Expression*. Mol Ther*. 2015 Jan 13.
c. Kuhn NF, Purdon TJ, van Leeuwen DG, Lopez AV, **Curran KJ**, Daniyan AF, Brentjens RJ. CD40 Ligand-Modified Chimeric Antigen Receptor T cells Enhance Antitumor Function by Eliciting an Endogenous Antitumor Response. *Cancer Cell*. 2019 March 18;35(3): 473-488

3. Clinical application of allo-HSCT for pediatric patients with malignant and non-malignant disorders.

My clinical practice is within the pediatric bone marrow transplant service at MSKCC. Our service expertise is use of T-cell depleted/$CD34^+$ enriched allo-HSCT for malignant and non-malignant disorders of childhood. We also have a robust cellular therapy program which includes adoptive transfer of viral specific and tumor specific immune effectors.

a. **Curran KJ**, Kernan NA, Prockop S, Scaradavou A, Small T, Kobos R, Castro-Malaspina H, Araten D, DiMichele D, O'Reilly RJ, Boulad F. Paroxysmal Nocturnal Hemoglobinuria in Pediatric Patients. *Pediatric Blood and Cancer*. 2011 September; 59 (3): 525-9.
b. Fabrizio V, Kernan N, Boulad F, Cancio M, Allen J, Higman M, Margossian SP, Mauguen A, Prockop S, Scaradavou A, Shah N, Spitzer B, Stieglitz E, Yeager N, O'Reilly RJ, Brentjens RJ. , Boelens JJ, **Curran KJ.** Low Toxicity and Favorable Overall Survival in Relapsed/Refractory B-ALL Following CAR T Cells and CD34-selected T-cell Depleted Allogeneic Hematopoietic Cell Transplant *Bone Marrow Transplant*. 2020 May 10