NIH Biographical Sketch Common Form

Name:

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0003-0359-9023

Position Title: Ernest and Amelia Gallo Family Professor and Professor of Pediatrics and Medicine

Organization and Location:Stanford University, Stanford, California, United States

PROFESSIONAL PREPARATION

INSTITUTION AND LOCATION	DEGREE	Start Date	Completion Date	FIELD OF STUDY
Experimental Immunology Branch, National Cancer Institute, Bethesda, Maryland, United States	Postdoctoral Fellow	07/1989	06/1996	Immunology
Pediatric Oncology Branch, National Cancer Institute, Bethesda, Maryland, United States	Fellow	07/1989	06/1992	Pediatric Oncology
Akron General Medical Center/Children's Hospital of Akron, Akron, Ohio, United States	Resident	07/1984	12/1988	Internal Medicine/Pediatrics
Northeastern Ohio Universities College of Medicine, Rootstown, Ohio, United States	Doctor of Medicine (MD)	06/1980	06/1984	Medicine
University of Akron, Akron, Ohio, United States	Bachelor of Science (BS)	06/1978	06/1980	Natural Sciences

Appointments and Positions

2016 - present	Ernest and Amelia Gallo Family Professor and Professor of Pediatrics and Medicine, Stanford University, Stanford, California, United States
2024 - present	President, ACCESSforKIDS, Stanford, California, United States
2021 - present	Co-Founder, Link Cell Therapies, South San Francisco, California, United States
2017 - present	Co-Founder, Lyell Immunopharma, South San Francisco, California, United States
2017 - present	Founding Director, Stanford Center for Cancer Cell Therapy, Stanford University, Stanford, California, United States
2016 - present	Director, Parker Institute for Cancer Immunotherapy @ Stanford, Stanford, California, United States
2016 - present	Associate Director Stanford Cancer Institute, Stanford University, Stanford, California, United States
2020 - 2025	Co-Founder, CARGO Therapeutics, San Carlos, California, United States
2008 - 2015	Chief Pediatric Oncology Branch, National Cancer Institute, Bethesda, Maryland, United States
2005 - 2008	Acting Chief, Pediatric Oncology Branch, National Cancer Institute, Bethesda, Maryland, United States
2003 - 2015	Tenure Principal Investigator and Head Immunology Section, Pediatric Oncology Branch, National Cancer Institute, Bethesda, Maryland, United States
1998 - 2003	Principal Investigator, Tenure Track, Pediatric Oncology Branch, National Cancer Institute, Bethesda, Maryland, United States

Products

Products Closely Related to the Proposed Project

1. Yamada-Hunter SA, Theruvath J, McIntosh BJ, Freitas KA, Lin F, Radosevich MT, Leruste A, Dhingra S, Martinez-Velez N, Xu P, Huang J, Delaidelli A, Desai MH, Good Z, Polak R, May A, Labanieh L, Bjelajac J, Murty T, Ehlinger Z, Mount CW, Chen Y, Heitzeneder S, Marjon KD, Banuelos A, Khan O, Wasserman SL, Spiegel JY, Fernandez-Pol S, Kuo CJ, Sorensen PH, Monje M, Majzner RG, Weissman IL, Sahaf B, Sotillo E, Cochran JR, Mackall CL. Engineered CD47 protects T cells for enhanced antitumour immunity. Nature. 2024 Jun;630(8016):457-465. PubMed Central PMCID: PMC11168929.
2. Good Z, Spiegel JY, Sahaf B, Malipatlolla MB, Ehlinger ZJ, Kurra S, Desai MH, Reynolds WD, Wong Lin A, Vandris P, Wu F, Prabhu S, Hamilton MP, Tamaresis JS, Hanson PJ, Patel S, Feldman SA, Frank MJ, Baird JH, Muffly L, Claire GK, Craig J,

Kong KA, Wagh D, Coller J, Bendall SC, Tibshirani RJ, Plevritis SK, Miklos DB, Mackall CL. Post-infusion CAR T(Reg) cells identify patients resistant to CD19-CAR therapy. Nat Med. 2022 Sep;28(9):1860-1871. PubMed Central PMCID: PMC10917089.

3. Spiegel JY, Patel S, Muffly L, Hossain NM, Oak J, Baird JH, Frank MJ, Shiraz P, Sahaf B, Craig J, Iglesias M, Younes S, Natkunam Y, Ozawa MG, Yang E, Tamaresis J, Chinnasamy H, Ehlinger Z, Reynolds W, Lynn R, Rotiroti MC, Gkitsas N, Arai S, Johnston L, Lowsky R, Majzner RG, Meyer E, Negrin RS, Rezvani AR, Sidana S, Shizuru J, Weng WK, Mullins C, Jacob A, Kirsch I, Bazzano M, Zhou J, Mackay S, Bornheimer SJ, Schultz L, Ramakrishna S, Davis KL, Kong KA, Shah NN, Qin H, Fry T, Feldman S, Mackall CL, Miklos DB. CAR T cells with dual targeting of CD19 and CD22 in adult patients with recurrent or refractory B cell malignancies: a phase 1 trial. Nat Med. 2021 Aug;27(8):1419-1431. PubMed Central PMCID: PMC8363505.
4. Monje M, Mahdi J, Majzner R, Yeom KW, Schultz LM, Richards RM, Barsan V, Song KW, Kamens J, Baggott C, Kunicki M, Rietberg SP, Lim AS, Reschke A, Mavroukakis S, Egeler E, Moon J, Patel S, Chinnasamy H, Erickson C, Jacobs A, Duh AK, Tunuguntla R, Klysz DD, Fowler C, Green S, Beebe B, Carr C, Fujimoto M, Brown AK, Petersen AG, McIntyre C, Siddiqui A, Lepori-Bui N, Villar K, Pham K, Bove R, Musa E, Reynolds WD, Kuo A, Prabhu S, Rasmussen L, Cornell TT, Partap S, Fisher PG, Campen CJ, Grant G, Prolo L, Ye X, Sahaf B, Davis KL, Feldman SA, Ramakrishna S, Mackall C. Author Correction: Intravenous and intracranial GD2-CAR T cells for H3K27M(+) diffuse midline gliomas. Nature. 2024 Dec;636(8043):E6. PubMed Central PMCID: PMC11655351.
5. Freitas KA, Belk JA, Sotillo E, Quinn PJ, Ramello MC, Malipatlolla M, Daniel B, Sandor K, Klysz D, Bjelajac J, Xu P, Burdsall KA, Tieu V, Duong VT, Donovan MG, Weber EW, Chang HY, Majzner RG, Espinosa JM, Satpathy AT, Mackall CL. Enhanced T cell effector activity by targeting the Mediator kinase module. Science. 2022 Nov 11;378(6620):eabn5647. PubMed Central PMCID: PMC10335827.

Other Significant Products, Whether or Not Related to the Proposed Project

1. Lee DW, Kochenderfer JN, Stetler-Stevenson M, Cui YK, Delbrook C, Feldman SA, Fry TJ, Orentas R, Sabatino M, Shah NN, Steinberg SM, Stroncek D, Tschernia N, Yuan C, Zhang H, Zhang L, Rosenberg SA, Wayne AS, Mackall CL. T cells expressing CD19 chimeric antigen receptors for acute lymphoblastic leukaemia in children and young adults: a phase 1 dose-escalation trial. Lancet. 2015 Feb 7;385(9967):517-528. PubMed Central PMCID: PMC7065359.
2. Long AH, Haso WM, Shern JF, Wanhainen KM, Murgai M, Ingaramo M, Smith JP, Walker AJ, Kohler ME, Venkateshwara VR, Kaplan RN, Patterson GH, Fry TJ, Orentas RJ, Mackall CL. 4-1BB costimulation ameliorates T cell exhaustion induced by tonic signaling of chimeric antigen receptors. Nat Med. 2015 Jun;21(6):581-90. PubMed Central PMCID: PMC4458184.
3. Fry TJ, Shah NN, Orentas RJ, Stetler-Stevenson M, Yuan CM, Ramakrishna S, Wolters P, Martin S, Delbrook C, Yates B, Shalabi H, Fountaine TJ, Shern JF, Majzner RG, Stroncek DF, Sabatino M, Feng Y, Dimitrov DS, Zhang L, Nguyen S, Qin H, Dropulic B, Lee DW, Mackall CL. CD22-targeted CAR T cells induce remission in B-ALL that is naive or resistant to CD19-targeted CAR immunotherapy. Nat Med. 2018 Jan;24(1):20-28. PubMed Central PMCID: PMC5774642.
4. Lynn RC, Weber EW, Sotillo E, Gennert D, Xu P, Good Z, Anbunathan H, Lattin J, Jones R, Tieu V, Nagaraja S, Granja J, de Bourcy CFA, Majzner R, Satpathy AT, Quake SR, Monje M, Chang HY, Mackall CL. c-Jun overexpression in CAR T cells induces exhaustion resistance. Nature. 2019 Dec;576(7786):293-300. PubMed Central PMCID: PMC6944329.
5. Weber EW, Parker KR, Sotillo E, Lynn RC, Anbunathan H, Lattin J, Good Z, Belk JA, Daniel B, Klysz D, Malipatlolla M, Xu P, Bashti M, Heitzeneder S, Labanieh L, Vandris P, Majzner RG, Qi Y, Sandor K, Chen LC, Prabhu S, Gentles AJ, Wandless TJ, Satpathy AT, Chang HY, Mackall CL. Transient rest restores functionality in exhausted CAR-T cells through epigenetic remodeling. Science. 2021 Apr 2;372(6537) PubMed Central PMCID: PMC8049103.

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.

I also certify that, as senior/key personnel listed within this application, I have taken the required research security training consistent and in compliance with Section 10634 of the CHIPS and Science Act of 2022.

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:

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0003-0359-9023

Position Title: Ernest and Amelia Gallo Family Professor and Professor of Pediatrics and Medicine

Organization and Location: Stanford University, Stanford, California, United States

Personal Statement

I am the Ernest and Amelia Gallo Family Professor of Pediatrics and Medicine at Stanford University, the Founding Director of the Stanford Center for Cancer Cell Therapy, Director of the Parker Institute for Cancer Immunotherapy @ Stanford, and Co-Leader of the Cancer Immunotherapy Program. During a 27-year tenure at NCI culminating as Chief of the Pediatric Oncology Branch and Head of the Immunology Section and since 2016 at Stanford, I've led an internationally recognized translational research program focused on immune-oncology. My work has advanced understanding of fundamental immunology and translated this understanding for the treatment of human disease with a major focus on children's cancers. I've led numerous first-in-human and first-in-child clinical trials spanning dendritic cell vaccines, cytokines, and adoptive immunotherapy using NK cells and genetically modified T cells. My work identified an essential role for the thymus in human T cell regeneration (NEJM 1995) and discovered IL-7 as the master regulator of T cell homeostasis (Blood 2001, J Exp Med 2008). My group was among the first to demonstrate impressive activity of CD19-CAR in pediatric leukemia (Lancet 2015), developed a CD22-CAR that is the only active salvage therapy for CAR19 resistant B cell malignancies (Nat Med 2018, J Clin Onc 2020, Blood 2021, Lancet 2024), demonstrated superiority of regional CNS delivery of CAR T cells for brain tumors (Nat Med 2020) and activity of GD2 targeting CARs for pediatric diffuse intrinsic pontine glioma (NCT04196413), results that are among the first to demonstrate significant and consistent activity of CAR T cells in solid cancers (Nature 2022, Nature 2024). My group was the first to identify T cell exhaustion as a major barrier to success of CAR T cell therapies (Nat Med 2015) and we have used these insights to create exhaustion-resistance/reversal platforms (Nature 2019, Science 2021, Nature 2024) and potency enhanced immune cells (Science 2022). We apply novel synthetic biology approaches to augment immune cell therapies CAR T cell platform (Cell, 2022; Cell 2024) and are translating these discoveries to the clinic. My group has played a leading role in defining mechanisms of resistance to adoptive cell therapies, implicating antigen loss, inadequate antigen density and CAR Tregs as barriers to efficacy of CAR T cells (Nature Med 2022). Our work was the first to demonstrate reproducible activity of CAR T cells in brain tumors and has informed toxicity management across cell therapeutics. I am a member of the National Academy of Medicine, American Association of Physicians and the American Society of Clinical Investigation a Fellow of the AACR Academy, a Fellow of the Academy of Immuno-oncology. I received the Smalley Award for outstanding contributions to cancer immunotherapy from the Society for the Immunotherapy of Cancer, the AACR-St.Baldrick's Distinguished Achievement Award for Pediatric Cancer Research, and the Pediatric Oncology Award from the American Society of Clinical Oncology. I have co-founded 3 biotech companies (Lyell Immunopharma, CARGO Therapeutics, Link Cell Therapies), and ACCESSforKIDS a non-profit dedicated to developed advanced medicines for pediatric cancer. I have published over 300 manuscripts, my work has been cited more than 60,000 times and my h-index in January 2026 according to google scholar is 120.

Honors

2025	Lloyd Old Award in Cancer Immunology, AACR-Cancer Research Institute
2025	Prize for Excellence in Medicine the Clinical Sciences, Italian-American Cancer Foundation
2023	Top 20 Most Influential Women in Biopharma, Endpoints News
2023	George Stamanopoulos Lecture Award, American Society of Gene and Cell Therapy
2023	Fellow, Academy of Immunooncology, Society for the Immunotherapy of Cancer
2023	Edward Netter Leadership Award, Alliance for Cancer Gene Therapy
2022	Fellow, American Association for Cancer Research
2022	Elected Member, National Academy of Medicine
2022	Nobility in Science Award, Sarcoma Foundation of America
2021	Outstanding Achievement in Pediatric Cancer Research, American Association for Cancer Research-St. Baldrick's Foundation
2021	Richard Smalley Award and Lectureship, Society for the Immunotherapy of Cancer
2015	Elected Member, Assocation of American Physicians
2005	Elected Member, American Society of Clinical Investigation

1984	Elected member, Alpha Omega Alpha Honorary Medical Society
2025 - 2029	Board of Directors, American Association for Cancer Research

Contribution to Science

1. Development of Chimeric Antigen Receptor Therapies for B cell malignancies and Leading Efforts to Understand and Manage Toxicities in this setting. My group was among the first to demonstrate the potency of CD19-CAR in pediatric B-ALL (Lee, Lancet 2015) and based upon significant morbidity and risk associated with cytokine release syndrome, I led effort to generate a consensus grading system and treatment algorithm for management of CRS (Lee, Blood, 2014). Noting relapse with antigen negative leukemia, my group developed a novel CAR targeting CD22, another pan-B cell marker, and conducted first-in-human and first-in-child trials of the CD22-CAR for B-ALL, which demonstrated complete response rates of 70% (Fry, Nature Med 2018). This agent has been awarded Breakthrough Therapy designation from the FDA. I led work at Stanford demonstrating a significant rate of antigen loss and downmodulation following CD19-CAR therapy for diffuse large B cell lymphoma (Spiegel Nat Med 2021) and demonstrated that the CD22-CAR mediates potent activity in CAR19 refractory large B cell lymphoma refractory to CAR19 therapy (Baird, Blood, 2021 and Frank, Lancet, 2024). Our recent studies are showing promising results with sequential CAR T cell therapies to overcome relapse associated with high disease burden in diffuse large B cell lymphoma and in pediatric B-acute lymphoblastic leukemia. In response to concerns regarding risk of secondary malignancies in CAR T cell recipients, my group led work demonstrating a low risk of insertional mutagenesis (Hamilton, NEJM, 2024) but significant issues related to prolonged cytopenia and myeloid malignancies related to clonal hematopoiesis.
2. Defining Mechanisms of Resistance to CAR Based Therapies. We were the first to demonstrate an outsized role for intrinsic T cell dysfunction as a result of T cell exhaustion in limiting the efficacy of CAR T cells (Long, Nat Med 2015). This work changed the paradigm for considering the basis for limited activity in solid tumors, highlighting the need for new approaches to augment endogenous T cell potency. We were among the first to identify a role of CAR expression regulatory T cells in progression following CAR19 therapy for diffuse large B cell lymphoma (Good, Nature Med 2022). This work identified a novel axis for therapeutic manipulation but also provided proof-of-concept that regulatory T cells can be engineered to express receptors modulating targeting specificity, thereby opening the field for use of these therapeutics in the setting of autoimmunity. Our group has provided extensive evidence implicated heterogeneous antigen expression, antigen loss and inadequate antigen expression in resistance to CAR T cell therapies (Majzner, Cancer Discovery 2020, Spiegel Nat Med 2021).
3. Engineering Next Generation Platforms to Augment T cell Potency. My groups has used insights into the mechanisms of resistance described in contribution #2 as well as advanced synthetic biology to create potency enhanced products suitable for clinical testing. We demonstrated that overexpression of c-JUN endows exhaustion resistance thereby enhancing the activity of CAR T cells that are prone to tonic signaling or cells exposed to high tumor burdens (Lynn, Nature, 2019). We demonstrated that transient cessation of T cell receptor signaling can prevent and reverse T cell exhaustion, including reversal of the epigenetic footprint of exhaustion (Weber, Science, 2021) and that overexpression of FOXO1 endows a stemness program which augments persistence and functionality (Doan, Nature 2024). Using CRISPR based screening we identified a role of MED12 in preventing full T cell effector differentation (Freitas, Science, 2022), Using a Cas13d platform, we demonstrated impressive efficacy of Cas13d based multiplexed RNA knockdown in identifying combinatorial regulators of T cell function (Tieu, Cell, 2024). We demonstrated that incorporation of NS3 proteases and NS3 proteas cutsights in trans in synthetic receptors endowed the capacity for remote control, providing a safety switch to reverse toxicity but also augmenting efficacy (Labanieh, Cell 2022). We discovered a high rate of macrophage mediated phagocytosis of CAR T cells exascerbated by CD47 blockage and developed a mutant CD47 that could protect T cells while augmenting macrophage mediated phagocytosis of tumors (Yamada-Hunter, Nature, 2024).
4. Developing and Testing CAR T cell Therapies for Pediatric Brain and Solid Tumors. We developed GD2-CAR T cells targeting H3K27M diffuse midline gliomas, showed activity in preclinical models (Mount, Nat Med 2018) with enhanced potency following intracerebroventricular (ICV) administration compared to intravenous (IV) (Theruvath, Nat Med 2020). We launched a Phase I clinical trial testing IV and ICV administration which demonstrated impressive activity and durable disease control in some patients (Majzner, Nature 2022, Monje Nature 2024). We also developed a b7H3-CAR with significant preclinical activity in models of pediatric solid tumors (Majzner, Clin Cancer Res 2019) and are testing this in pediatric patients with refractory solid tumors. We further developed a CAR targeting glypican-2, demonstrating that limiting antigen density is a risk factor for relapse (Heitzeneder, Cancer Cell, 2022) and have credentialed this target for medulloblastoma and other embryonal pediatric brain tumors. We are leading a first -in-child trial testing this therapeutic.
5. My work demonstrated that thymic insufficiency is the fundamental factor that limits T cell regeneration in humans (Mackall, NEJM, 1995; Hakim J Clin Invest 2005) and discovered that IL-7 is the master regulator of T cell homeostasis (Fry, Blood 2001) and that administration of IL-7 mediate potent immunorestorative properties (Sportes, J Exp Med 2008). This work served as the foundational science supporting the incorporating of lymphodepleting regimens into current adoptive cell therapy strategies.

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