BIOGRAPHICAL SKETCH

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NAME: Hinrichs, Christian S.

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POSITION TITLE: Chief, Section of Cancer Immunotherapy and Co-Director, Cancer Immunology and Metabolism Center of Excellence

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
University of Missouri – Kansas City, Kansas City, MO	BA/MD	06/1996	Biology/Medicine
University of Missouri – Kansas City, Kansas City, MO	Resident	06/2001	General Surgery
Roswell Park Cancer Institute, Buffalo, NY	Fellow	06/2003	Surgical Oncology
National Cancer Institute – Surgery Branch, Bethesda, MD	Fellow	06/2009	Surgical Oncology and Tumor Immunology
George Washington Hospital, Washington, DC	Resident	06/2010	Internal Medicine
National Cancer Institute – Medical Oncology Branch, Washington, DC	Fellow	06/2014	Medical Oncology

A. Personal Statement

I am a medical oncologist and immunologist with a research focus on cell therapy for HPV-associated cancers and other epithelial malignancies. My initial medical training was in general surgery and surgical oncology. Recognizing the limitations of existing cancer treatments, I began laboratory research under the mentorship of Nicholas P. Restifo, M.D. through a fellowship at the National Cancer Institute (NCI). While conducting cancer research, I lost an eye to ocular melanoma and decided to retrain in internal medicine and medical oncology. As a medical oncology fellow, I researched cell therapy for HPV-associated cancers, initially working in the laboratory of Steven A. Rosenberg, M.D., Ph.D. at the NCI. Following fellowship, I was selected for a position as an Assistant Clinical Investigator in the NCI Center for Cancer Research Clinical Investigator Development Program and then as a tenure-track Investigator in the NIH Lasker Clinical Research Scholar program (Si2 grant). The short-term goal of my research is to investigate principles of cellular therapy in epithelial cancers using HPV-associated carcinomas as a disease model. The long-term goal is to discover and develop cellular therapy for HPV-associated cancers and other malignancies. Research by my group includes the discovery of tumor-infiltrating T cell therapy for HPV-associated cancers, gene-engineered T cell receptor (TCR)-T cell therapy for HPV-associated cancers, and new TCR and other technologies for a range of malignancies. It also includes translational research to elucidate mechanisms of tumor response and resistance to cell therapy and immunotherapy. I received tenure at the NIH in 2020 and began as Chief of the Cancer Immunotherapy Section and Co-director of the Cancer Immunology and Metabolism Center of Excellence at Rutgers Cancer Institute of New Jersey in 2021. My role on the Cancer Center Support Grant is Program Co-Leader of the Cancer Metabolism and Immunology Program and Senior Faculty Director of the Immune Monitoring and Flow Cytometry Shared Resource.

Citations:

1. Nagarsheth NB, Norberg SM, Sinkoe AL, Adhikary S, Meyer TJ, Lack JB, Warner AC, Schweitzer C, Doran SL, Korrapati S, Stevanović S, Trimble CL, Kanakry JA, Bagheri MH, Ferraro E, Astrow SH, Bot A, Faquin WC, Stroncek D, Gkitsas N, Highfill S, **Hinrichs CS**. TCR-engineered T cells targeting E7 for patients with metastatic HPV-associated epithelial cancers. Nat Med. 2021 Mar;27(3):419-425. PubMed Central PMCID: PMC9620481.

2. Doran SL, Stevanović S, Adhikary S, Gartner JJ, Jia L, Kwong MLM, Faquin WC, Hewitt SM, Sherry RM, Yang JC, Rosenberg SA, **Hinrichs CS**. T-Cell Receptor Gene Therapy for Human Papillomavirus-Associated Epithelial Cancers: A First-in-Human, Phase I/II Study. J Clin Oncol. 2019 Oct 20;37(30):2759-2768. PubMed Central PMCID: PMC6800280.
3. Stevanović S, Pasetto A, Helman SR, Gartner JJ, Prickett TD, Howie B, Robins HS, Robbins PF, Klebanoff CA, Rosenberg SA, **Hinrichs CS**. Landscape of immunogenic tumor antigens in successful immunotherapy of virally induced epithelial cancer. Science. 2017 Apr 14;356(6334):200-205. PubMed Central PMCID: PMC6295311.
4. Stevanović S, Draper LM, Langhan MM, Campbell TE, Kwong ML, Wunderlich JR, Dudley ME, Yang JC, Sherry RM, Kammula US, Restifo NP, Rosenberg SA, **Hinrichs CS**. Complete regression of metastatic cervical cancer after treatment with human papillomavirus-targeted tumor-infiltrating T cells. J Clin Oncol. 2015 May 10;33(14):1543-50. PubMed Central PMCID: PMC4417725.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2021 -	Chief, Section of Cancer Immunotherapy and Co-Director, Cancer Immunology and Metabolism Center of Excellence, The Rutgers Cancer Institute of New Jersey
2021 -	Professor, Department of Medicine, Rutgers-Robert Wood Johnson Medical School
2020 - 2021	Senior Investigator, National Cancer Institute – Genitourinary Malignancies Branch
2015 - 2020	Investigator, Lasker Clinical Research Scholar, National Cancer Institute – Experimental Transplantation and Immunology Branch
2012 - 2015	Assistant Clinical Investigator, National Cancer Institute – Surgery Branch

Honors

2015 - 2020	Lasker Clinical Research Scholar, NIH
2018 - 2019	Associate Scientific Advisor, Science Translational Medicine
2012 - 2015	Clinical Investigator Development Program, NCI
2020	Visiting Professor Lecture (Head & Neck Core Curriculum), MD Anderson Cancer Center
2020	Technology Transfer Award, NCI
2020	Performance Award, NIH
2020	Technology Transfer Award, Federal Laboratory Consortium (FLC)
2019	Technology Transfer Award, NCI
2019	Immunology Interest Group Speaker, NIH
2019	Center for Excellence in Immunology Speaker, NCI
2019	Performance Award, NIH
2019	Oncology Center of Excellence Mini-symposium Speaker, FDA
2018	Technology Transfer Mid-Atlantic Award, Federal Laboratory Consortium
2018	Technology Transfer Award, NCI
2018	Keynote Speaker, The San Diego Center for Precision Immunotherapy (SDCPI) Inaugural Scientific Retreat
2018	Speaker, NCI Workshop on Cell-based Immunotherapy for Solid Tumors
2018	Performance Award, NIH
2017	Performance Award, NCI
2017	Speaker, NCI Center for Cancer Research Grand Rounds
2017	Idea Blast Speaker, FDA
2016	Technology Transfer Award, NCI
2016	Performance Award, NIH
2016	Clinical Center Grand Rounds, NIH
2016	Oncology Center of Excellence Mini-symposium Speaker, FDA
2015	Mentor, NCI Director's Career Development Award
2015	Performance Award, NIH
2015	Technology Transfer Award, NCI

2015 Research Highlights Award, NCI
2015 Member, Alpha Omega Alpha Honor Medical Society
2014 Performance Award, NIH
2014 Merit Award, American Society of Clinical Oncology
2014 Annual Meeting Press Program, American Society of Clinical Oncology
2014 Mentor, NIH FARE Award
2013 Time-off Award, NIH
2013 Abstract Travel Award, Society for Immunotherapy of Cancer
1999 Outstanding Resident Performance Award, University of Missouri, Kansas City, Dept. of Surgery
1996 Department of Surgery Award, University of Missouri - Kansas City
1996 Harry S. Jonas Ambassador's Award, Western Friends of UMKC School of Medicine

C. Contribution to Science

1. *Clinical activity of gene-engineered TCR-T cell therapy in HPV-associated epithelial cancers and identification of mechanisms of treatment resistance.* Engineered T cell therapy has shown clinical activity in certain solid tumors such as melanoma and synovial cell sarcoma, but proof of principle in epithelial cancers has been difficult to achieve. Our research showed that gene-engineered TCR-T cell therapy targeting an HPV oncoprotein could mediate robust tumor responses in metastatic HPV-associated cancers including tumors resistant to immune checkpoint blockade. It further identified tumor intrinsic gene defects in antigen processing and interferon response as mechanisms of treatment resistance. These findings reveal the potential for TCR-T cell therapy in epithelial cancers and define the challenges to be overcome by next generation approaches.
    a. Nagarsheth NB, Norberg SM, Sinkoe AL, Adhikary S, Meyer TJ, Lack JB, Warner AC, Schweitzer C, Doran SL, Korrapati S, Stevanović S, Trimble CL, Kanakry JA, Bagheri MH, Ferraro E, Astrow SH, Bot A, Faquin WC, Stroncek D, Gkitsas N, Highfill S, **Hinrichs CS**. TCR-engineered T cells targeting E7 for patients with metastatic HPV-associated epithelial cancers. Nat Med. 2021 Mar;27(3):419-425. PubMed Central PMCID: PMC9620481.
    b. Doran SL, Stevanović S, Adhikary S, Gartner JJ, Jia L, Kwong MLM, Faquin WC, Hewitt SM, Sherry RM, Yang JC, Rosenberg SA, **Hinrichs CS**. T-Cell Receptor Gene Therapy for Human Papillomavirus-Associated Epithelial Cancers: A First-in-Human, Phase I/II Study. J Clin Oncol. 2019 Oct 20;37(30):2759-2768. PubMed Central PMCID: PMC6800280.

2. *Durable, complete responses to tumor-infiltrating T cell therapy in HPV-associated epithelial cancers.* Adoptive transfer of tumor-infiltrating T cells can mediate regression of metastatic melanoma inducing durable, complete responses in some patients. Efforts to extend this approach to epithelial cancers had not been successful. We showed that adoptive transfer of tumor infiltrating T cells could induce regression of HPV-associated cancers, including durable, complete regression (i.e., cure) in some patients. We further elucidated the antigen-targeting landscape and the importance of both viral and non-viral antigens in successful treatments.
    a. Stevanović S, Helman SR, Wunderlich JR, Langhan MM, Doran SL, Kwong MLM, Somerville RPT, Klebanoff CA, Kammula US, Sherry RM, Yang JC, Rosenberg SA, **Hinrichs CS**. A Phase II Study of Tumor-infiltrating Lymphocyte Therapy for Human Papillomavirus-associated Epithelial Cancers. Clin Cancer Res. 2019 Mar 1;25(5):1486-1493. PubMed Central PMCID: PMC6397671.
    b. Stevanović S, Pasetto A, Helman SR, Gartner JJ, Prickett TD, Howie B, Robins HS, Robbins PF, Klebanoff CA, Rosenberg SA, **Hinrichs CS**. Landscape of immunogenic tumor antigens in successful immunotherapy of virally induced epithelial cancer. Science. 2017 Apr 14;356(6334):200-205. PubMed Central PMCID: PMC6295311.
    c. Stevanović S, Draper LM, Langhan MM, Campbell TE, Kwong ML, Wunderlich JR, Dudley ME, Yang JC, Sherry RM, Kammula US, Restifo NP, Rosenberg SA, **Hinrichs CS**. Complete regression of metastatic cervical cancer after treatment with human papillomavirus-targeted tumor-infiltrating T cells. J Clin Oncol. 2015 May 10;33(14):1543-50. PubMed Central PMCID: PMC4417725.

3. *Discovery of TCR technology targeting a wide range of cancers.* In contrast to chimeric antigen receptors (CARs), which can target only cell surface antigens, TCRs can target antigens from any cellular

compartment. Development of new TCR-T cell therapies requires the discovery high affinity TCRs that target high-value cancer antigens. We have discovered TCRs directed against a range of therapeutic targets including HPV E6, HPV E7, KK-LC-1, and EBV LMP2.

a. **Hinrichs CS**, Xiang L., inventors. HLA class I-restricted T cell receptors against LMP2. USA 63/008,949. 2020 April 13.
b. Marcinkowski B, Stevanović S, Helman SR, Norberg SM, Serna C, Jin B, Gkitsas N, Kadakia T, Warner A, Davis JL, Rooper L, **Hinrichs CS**. Cancer targeting by TCR gene-engineered T cells directed against Kita-Kyushu Lung Cancer Antigen-1. J Immunother Cancer. 2019 Aug 28;7(1):229. PubMed Central PMCID: PMC6712783.
c. Jin BY, Campbell TE, Draper LM, Stevanović S, Weissbrich B, Yu Z, Restifo NP, Rosenberg SA, Trimble CL, **Hinrichs CS**. Engineered T cells targeting E7 mediate regression of human papillomavirus cancers in a murine model. JCI Insight. 2018 Apr 19;3(8) PubMed Central PMCID: PMC5931134.
d. Draper LM, Kwong ML, Gros A, Stevanović S, Tran E, Kerkar S, Raffeld M, Rosenberg SA, **Hinrichs CS**. Targeting of HPV-16+ Epithelial Cancer Cells by TCR Gene Engineered T Cells Directed against E6. Clin Cancer Res. 2015 Oct 1;21(19):4431-9. PubMed Central PMCID: PMC4603283.

4. *Discovery of cytokine technologies for enhanced efficacy of gene-engineered T cells for cell therapy of cancer.* New technologies are needed to improve the efficacy of cell therapy in epithelial cancers and to reduce or eliminate the requirement for host conditioning and for adjuvant cytokine support. We have identified new strategies and technologies based on T cell expression of membrane-restricted cytokines to enhance the anti-tumor activity of cell therapy.

   a. Zhang L, Davies JS, Serna C, Yu Z, Restifo NP, Rosenberg SA, Morgan RA, **Hinrichs CS**. Enhanced efficacy and limited systemic cytokine exposure with membrane-anchored interleukin-12 T-cell therapy in murine tumor models. J Immunother Cancer. 2020 Jan;8(1) PubMed Central PMCID: PMC7057422.
   b. **Hinrichs CS**, Jin BY., inventors. Tethered interleukin-15 and interleukin-21. USA 19/016,975. 2019 February 07.

5. *Elucidation of the impact of cytokine programming and T cell subset ontogeny on the efficacy of therapeutic T cells.* This research demonstrated that the efficacy of T cells for cell therapy could be enhanced by in vitro programming with cytokine signals including type 17 polarization and IL-21-mediated constraint of terminal differentiation. In addition, it defined the importance of memory subset ontogeny on the efficacy of therapeutic T cells.

   a. **Hinrichs CS**, Borman ZA, Gattinoni L, Yu Z, Burns WR, Huang J, Klebanoff CA, Johnson LA, Kerkar SP, Yang S, Muranski P, Palmer DC, Scott CD, Morgan RA, Robbins PF, Rosenberg SA, Restifo NP. Human effector CD8+ T cells derived from naive rather than memory subsets possess superior traits for adoptive immunotherapy. Blood. 2011 Jan 20;117(3):808-14. PubMed Central PMCID: PMC3035075.
   b. **Hinrichs CS**, Borman ZA, Cassard L, Gattinoni L, Spolski R, Yu Z, Sanchez-Perez L, Muranski P, Kern SJ, Logun C, Palmer DC, Ji Y, Reger RN, Leonard WJ, Danner RL, Rosenberg SA, Restifo NP. Adoptively transferred effector cells derived from naive rather than central memory CD8+ T cells mediate superior antitumor immunity. Proc Natl Acad Sci U S A. 2009 Oct 13;106(41):17469-74. PubMed Central PMCID: PMC2762661.
   c. **Hinrichs CS**, Kaiser A, Paulos CM, Cassard L, Sanchez-Perez L, Heemskerk B, Wrzesinski C, Borman ZA, Muranski P, Restifo NP. Type 17 CD8+ T cells display enhanced antitumor immunity. Blood. 2009 Jul 16;114(3):596-9. PubMed Central PMCID: PMC2713473.
   d. **Hinrichs CS**, Spolski R, Paulos CM, Gattinoni L, Kerstann KW, Palmer DC, Klebanoff CA, Rosenberg SA, Leonard WJ, Restifo NP. IL-2 and IL-21 confer opposing differentiation programs to CD8+ T cells for adoptive immunotherapy. Blood. 2008 Jun 1;111(11):5326-33. PubMed Central PMCID: PMC2396726.

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/myncbi/christian.hinrichs.1/bibliography/public/