BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
Riddell, Stanley R., MD	Member, Fred Hutchinson Cancer Research Center Professor of Medicine, University of Washington
eRA COMMONS USER NAME (credential, e.g., agency login) SRIDDELL	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
University of Manitoba, Manitoba, Canada	MD	1979	Medicine
University of Manitoba, Manitoba, Canada	Resident	1983	Internal Medicine
University of Manitoba, Manitoba, Canada	Fellow	1985	Hermatology
University of Washington and Fred Hutchinson Cancer Research Center	Fellow	1988	Oncology

A. Personal Statement

My research program has focused on studies of human T cell immunology in an effort to understand the role of T cells in immunity to pathogens and malignant cells, and how antigens are processed and presented to T cells. A major effort has focused on the development and clinical application of adoptive T cell therapy with unmodified and genetically modified antigen-specific T cells for infectious diseases and cancer. These studies required the developing new techniques for isolation, expansion, gene insertion, and re-infusion of T cells, and for monitoring patient safety, cell persistence and function. Many of these methods are now employed broadly in adoptive immunotherapy for cancer. My lab has been engaged in understanding the graft versus leukemia (GVL) effect of allogeneic stem cell transplantation as a model for T cell mediated eradication of cancer, and in defining targets for immunotherapy of solid tumors. We have discovered tumor-associated antigens, including cancer testes antigens that are present on both hematologic malignancies and solid tumors and are candidates for T cell transfer and vaccine development. The lab has recently investigated subsets of memory T cells and how their intrinsic qualities may enable superior persistence and efficacy after adoptive transfer to treat human malignancies.

B. Positions and Honors

Positions and Employment

1988 – 1990 Associate, Division of Clinical Research, FHCRC, Seattle, WA
1990 – 1994 Assistant Member, FHCRC, Seattle, WA
1994 – 1999 Associate Member, FHCRC, Seattle, WA
1994 – 2000 Associate Professor, University of Washington School of Medicine
1999-present Member, Associate Program Head, Program in Immunology, FHCRC, Seattle, WA
2000-present Professor, University of Washington School of Medicine
2008-present Research Affiliate Scientist Washington National Primate Research Center, University of Washington

Honors

1991 Leukemia Society of America Special Fellowship
1992 Cancer Research Institute Partridge Foundation Investigator Award
2008 Fellow of the American College of Physicians (elected)
2009 Hans Fischer Senior Fellow, Institute for Advanced Study, TUM
2010 E Donnall Thomas Lecture, American Society of Blood and Marrow Transplantation
2010 American Association of Physicians (elected)

Other Experience and Professional Memberships (Past 4 years)

NIH CII Study Section Ad hoc member, June, 2009; NIH TTT Study Section Ad hoc member, October 2008; Member, 2010-2012; NCI Intramural Program Review Committee (Surgery Branch) May 2008;

DOD Breast Cancer Research Program Panel Member, 2009; Susan Komen Breast Cancer Grant Review Panel Member, 2009, 2010; Melanoma Research Alliance Grant Review Committee, 2010-date; Board of Scientific Counselors, Memorial Sloan Kettering Cancer Center 2004-date; Scientific Advisory Board Oregon National Primate Research Center 2008 -date. University of Wisconsin Cancer Center External Advisory Board, 2012 – date.

C. Selected Peer-Reviewed Publications (from >185)

1. Walter EA, Greenberg, PD, Gilbert MJ, Finch RJ, Watanabe KS, Thomas ED, Riddell SR. Reconstitution of cellular immunity against cytomegalovirus in recipients of allogeneic bone marrow by transfer of T-cell clones from the donor. N Engl J Med 333:1038-44, 1995.
2. Gilbert MJ, Riddell SR, Plachter B, Greenberg PD. Cytomegalovirus selectively blocks antigen processing and presentation of its immediate-early gene product. Nature 383:720-2, 1996.
3. Riddell S.R., Elliot M., Lewinsohn D., Gilbert M.J., Wilson, L.A., Manley, S.A., Lupton S., Overell, R.W., Corey, L.C., and Greenberg, P.D. T-cell mediated rejection of gene-modified HIV-specific cytotoxic T lymphocytes in HIV-infected patients. Nature Medicine 2(2):216-223, 1996.
4. Ortmann B, Copeman J, Lehner PJ, Sadasivan B, Herberg JA, Grandea AG, Riddell SR, Tampe R, Spies T, Trowsdale J, Cresswell P. A critical role for tapasin in the assembly and function of multimeric MHC Class I-TAP complexes. Science 277:1306-9, 1997.
5. Yee C, Thompson JA, Byrd D, Riddell SR, Roche P, Celis E, Greenberg PD. Adoptive T cell therapy using antigen-specific CD8+ T cell clones for the treatment of patients with metastatic melanoma: In vivo persistence, migration, & antitumor effect of transferred T cells. Proc Natl Acad Sci 99:16168-73, 2002.
6. Wang W, Epler J, Riddell SR. Recognition of breast cancer cells by CD8+ cytotoxic T cell clones specific for NY-BR-1. Cancer Research 66: 6826-6833, 2006.
7. Berger C, Jensen MC, Lansdorp P, Gough M, Elliott C, Riddell SR. Adoptive transfer of effector CD8+ T-cells derived from central memory cells establishes persistent T-cell memory in primates. J Clin Invest 118:294-305, 2008. PMCID: PMC2104476.
8. Nishida T, Hudecek M, Bleakley M, Warren EH, Maloney D, Storb R, Riddell SR. Development of tumor-reactive T cells correlates with efficacy of nonmyeloablative allogeneic hematopoietic stem cell transplant for chronic lymphocytic leukemia Clinical Cancer Research, 15: 4759-4768, 2009.
9. Turtle CJ, Swanson HM, Fujii N, Estey EH, Riddell SR. A distinct subset of self-renewing human memory CD8+ T cells survives cytotoxic chemotherapy Immunity 331: 834-844, 2009. PMCID: PMC2789980.
10. Warren EH, Fujii N, Akatsuka Y, Chaney CN, Mito JK, Loeb KR, Gooley TA, Brown ML, Koo KK, Rosinski KV, Ogawa S, Matsubara A, Appelbaum FR, Riddell SR. Therapy of relapsed leukemia after allogeneic hematopoietic cell transplant with T cells specific for minor histocompatibility antigens. Blood 2010 115:3869-78. PMCID: PMC2869557.
11. Bleakley M, Otterud BE, Richardt JL, Mollerup AD, Hudecek M, Nishida T, Chaney CE, Warren EH, Leppert MF, Riddell SR. Leukemia-associated minor histocompatibility antigen discovery using T cell clones isolated by in vitro stimulation of naïve CD8+ T cells. Blood 115: 4923-4933, 2010. PMCID: PMC2890170.
12. Robins HS, Srivastava SK, Campregher PV, Turtle CJ, Andriesen J, Riddell SR, Carlson CS, Warren EH.Overlap and effective size of the human CD8+ T-cell receptor repertoire. Science Translational Medicine 2:47ra64 2010. PMCID: PMC3212437
13. Terakura S, Yamamoto TN, Gardner RA, Turtle CJ, Jensen MC, Riddell SR. Generation of CD19-chimeric antigen receptor modified CD8+ T cells derived from virus-specific central memory T cells. Blood 119: 72-82, 2012. PMCID: PMC3251238
14. McGoldrick SM, Bleakley ME, Guerrero A, Turtle CJ, Yamamoto T, Pereira SE, Delaney CS, Riddell SR. Cytomegalovirus-specific T cells are primed early after cord blood transplant but fail to control virus in vivo. Blood 121:2796-803, 2013 (PMC in process).
15. Nauerth M, Weisbruch B, Knall R, Franz T, Dossinger G, Bet J, Paszkiewicz PJ, Pfeiffer L, Uckert W, Holtappels R, Reddehase MJ, Riddell SR, Busch DH. TCR-ligand k_{off}-rates identify antigen-specific $CD8^+$ T cells with superior protective capacity for adoptive transfer. Science Translational Medicine, In press.

D. Research Support

R01 AI053193-06A1 (PI: Riddell, S.) 1/1/2009 – 1/31/2014
NIH/NIAID Title: CD8+ T Cell Immunity to Cytomegalovirus
The objectives of this project are to develop and evaluate approaches for rendering macaque and human $CD8^+$ CMV-specific T cells resistant to glucocorticoid signaling through genome editing of the glucocorticoid receptor with zinc finger nucleases. Studies will be performed on both macaque and human cells in vitro and will evaluate the safety and efficacy of adoptively transferring $CD8^+$ CMV-specific T cell clones with an edited glucocorticoid receptor gene in non-human primates.

R01 CA 136551-01A1(PI: Riddell, S.) 7/1/2009 – 5/31/2014
NIH/NCI Title: Targeted therapy of ALL with gene-modified central memory T Cells
The goal of this project is to develop adoptive T cell therapy for patients with acute lymphoblastic leukemia who undergo allogeneic stem cell transplant from an HLA matched related donor. The project will determine the safety and anti-tumor activity of adoptive therapy with donor Tcm-derived bi-specific (CMVxCD19) T_E cells for after HLA matched allogeneic HCT, and will develop and evaluate novel CD19-specific CAR vectors that encode a truncated EGFR that enables rapid selection of transduced T cells, in vivo tracking, and elimination of transferred cells in vivo.

R01 CA 114536-06 (PI: Riddell, S.) 7/1/2010 – 12/31/2014
NIH/NCI Title: Strategies to improve the adoptive transfer of T cells
The goal of this project is to define adoptive transfer regimens that improve the survival of adoptively transferred TE cells and their conversion to memory cells in vivo. Studies are proposed to evaluate the use of IL-15 to promote T cell survival, systemic vaccination for driving the in vivo expansion of adoptively transferred TE cells, and novel strategies for eliminating cells that cause toxicity. The studies will be performed in nonhuman primates to facilitate rapid translation to clinical adoptive therapy.

SPORE TE 4924 (PI: Porter, P.) 7/1/2010 – 6/30/2015
NIH/NCI Title: Seattle Cancer Consortium Breast SPORE
The SPORE is structured to maximally promote dynamic translational breast cancer research by integration of established and new, basic, and clinical breast cancer researchers in a highly interactive and resource-rich environment. The participating institutions support translational science at every stept and there is abundant evidence that the early institution of clinical trials and the translational focus will advance the goal of reducing the impact of breast cancer for all women.
Sub-Project: 2 (Project Leader: Riddell, S.)
Targeted Therapy of Breast Cancer with Central Memory T cells
The objectives of this project are to perform a phase I trial of adoptive T cell therapy with HER-2/neu (HER-2)-specific T cells following in vivo priming with a HER-2 peptide vaccine in patients with advanced HER-2 over-expressing breast cancer; to develop optimized vectors that encode T cell receptor (TCR) genes that redirect specificity to the NY-BR-1 breast differentiation antigen, and to perform a phase I study of adoptive T cell therapy with TCR modified T_{CM} to target NY-BR-1 in patients with advanced NY-BR-1+ breast cancer.

P01 AI033484-14A1 (P.I.: Hansen, J.) 7/21/2009 – 6/30/2014
NIH/NIAID Title: Immunobiology of Tolerance Following Allogeneic Hematopoietic Cell Transplantation
This overall goal is to investigate the pathogenesis of chronic GVHD and the mechanisms underlying establishment of immunologic tolerance after allogeneic HCT
Sub-Project: 1 (Project Leader: Warren, EH., Co-investigator: Riddell, S.)
HY-specific T cell responses in chronic GVHD. The goal of this program project is to dissect the mechanisms that lead to tolerance after allogeneic hematopoietic stem cell transplantation. The work in Project 1 will focus on analysis and regulation of HY-specific T cell responses.

SU2C-AACR-DT10 (Allison J, Ribas T, Co-PIs; Dream Team Principal: Riddell, SR) 3/2013-3/2016
Title: Immunologic Checkpoint Blockade and Adoptive Cell Transfer in Cancer Therapy
The goal of this proposal is to bring together a leading group of tumor immunologists to expand, optimize and explore combinations of two novel immunotherapies, immune checkpoint blockade and adoptive T cell transfer.

E. Completed Research Support (Past 4 years)

RC1 AI086683-01 (P.I.: Riddell, S.) 9/26/2009 – 8/31/2011
NIH Title: Analysis of a Novel Subset of Human CD8+ Memory Cells with Stem Cell Qualities

P01 CA18029 (PI: Appelbaum, F) 12/1/96 – 11/30/2011
NIH/NCI Title: Adult Leukemia Research Center
Project 6 (Riddell – Project Leader)
Targeting Alloreactivity for Leukemia Eradication