BIOGRAPHICAL SKETCH

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NAME: Robert Korngold, Ph.D.

eRA COMMONS USER NAME (credential, e.g., agency login): rxk112

POSITION TITLE: Chairman, Department of Biomedical Research & Senior Scientist

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
Rutgers College, Rutgers U., New Brunswick, NJ	B.A.	May, 1973	Biological Science
Rutgers Graduate School, New Brunswick, NJ	M.S.	May, 1974	Zoology
University of Pennsylvania, Philadelphia, PA	Ph.D.	Dec, 1979	Immunology

A. Personal Statement

My training and experience over the last 39 years has been in the field of Immunology, with a focus on T cell immunobiology related to allogeneic hematopoietic cell transplantation (HCT), including graft-versus-host disease (GVHD), graft-versus-tumor (GVT) responses, immune reconstitution, and immunotherapeutic approaches. We developed several important murine models for GVHD directed to minor histocompatibility antigens (miHA), models for studying GVT responses, particularly to novel murine myeloid leukemia lines generated by c-myc retrovirus induction. In collaboration with Dr. Feinman, we are determining whether the correlation between specific intestinal microbiota and improved response in high-risk multiple myeloma patients treated with targeted and immunotherapies in the post-autologous stem cell transplantation consolidative setting is associated with an activated T cell phenotype.

Some noteworthy manuscripts from 156 published over my career establishing my expertise in murine models for GVHD and GVT:

Korngold R, Sprent J: Lethal graft-versus-host disease following bone marrow transplantation across minor histocompatibility barriers in mice. Prevention by removing mature T cells from marrow. J. Exp. Med. 148: 1687-1698, 1978.

Korngold R, Sprent J: Variable capacity of L3T4^{+} cells to cause lethal graft-versus-host disease across minor histocompatibility barriers. J. Exp. Med. 165: 1552-1564, 1987.

Korngold R, Leighton C, Manser T: Graft-versus-myeloid leukemia responses following syngeneic and allogeneic bone marrow transplantation. Transplantation 58:278-287, 1994.

Fanning SL, Zilberberg J, Stein J, Vazzana K, Berger SA, **Korngold R**, Friedman TM: Unraveling graft-versushost disease and graft-versus-leukemia responses using TCR Vβ spectratype analysis in a murine bone marrow transplantation model. J Immunol, 190:447-457, 2013.

B. Positions and Honors

12/79 Doctoral Thesis entitled: "T Cell Responses to Minor Histocompatibility Antigens In Vivo." Advisor: Jonathan Sprent, M.D., Ph.D.
12/79-05/80 Postdoctoral Fellow, University of Pennsylvania Medical School, Philadelphia, PA. Mentor: Jonathan Sprent, M.D., Ph.D.
06/80-09/81 Postdoctoral Fellow, The Wistar Institute, Philadelphia, PA. Mentor: Peter C. Doherty, Ph.D.
10/81-07/87 Assistant Professor, The Wistar Institute, Philadelphia, PA
07/85-07/87 Adjunct Assistant Professor, Dept. of Pathology and Laboratory Medicine, Univ. of Pennsylvania School of Medicine, Philadelphia, PA
08/87-06/94 Associate Professor, Dept. of Microbiology and Immunology, Jefferson Medical College, Thomas Jefferson University, Philadelphia, PA
07/91-06/94 Associate Professor, Jefferson Cancer Institute
07/91-10/04 Director, Ph.D. Program in Immunology, Dept. of Microbiology and Immunology, Jefferson Medical College, Thomas Jefferson University
07/94-10/04 Professor, Dept. of Microbiology and Immunology; Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA
03/04-10/04 Associate Director for Basic Research in the Blood and Marrow transplant Program, TJU
11/04-Pres Chief, Basic Research Division, The Cancer Center, Hackensack University Medical Center
11/04-Pres Senior Scientist, The David & Alice Jurist Institute for Research, Hackensack University Medical Center
08/05-Pres Adjunct Professor, Department of Medicine, University of Medicine & Dentistry of New Jersey
07/07-06/09 Associate Dean of Research and Professor, Touro University College of Medicine, Hackensack, NJ (a new medical school venture)
07/07-Pres Chairman, Department of Biomedical Research, Hackensack University Medical Center
07/15-Pres Adjunct Professor, Department of Oncology, Georgetown University School of Medicine
07/15-Pres Member, Lombardi Comprehensive Cancer Center, Georgetown University
08/17-Pres Professor, Department of Medical Sciences, Seton Hall University/Hackensack-Meridian School of Medicine

Honors and Professional Service
1988-99 NCI/NIH Special Emphasis Panel Reviewer - Program Project Site Visits (Total of 16)
1999-02 Ad Hoc Member of Experimental Therapeutics-2 Study Section, NIH
1999-02 Ad Hoc Member of NCI Manpower Review Committee
2002-03 Member of Experimental Therapeutics-2 Study Section, NIH
2003-04 Member of Cancer Immunopathology and Immunotherapy Study Section, NIH
2002-04 Clinical Immunology Sub-Committee, American Association of Immunologists 2002-10 Scientific Advisory Board, CD4 BioSciences, Inc.
1994-99 Editorial Board Member, Transplantation
1997-01 Associate Editor, Journal of Immunology
1995-00 Associate Editor, Biology of Blood and Marrow Transplantation
2001-Pres Editor-in-Chief, Biology of Blood and Marrow Transplantation
2001-Pres Executive Committee and Board Member, American Society Blood and Marrow Transplantation
2004 Alumni Association Education Award, Jefferson College of Graduate Studies, TJU
2005, 06 Co-Organizer of the Inaugural Joint American-Israeli Conference on Cancer, Jerusalem, Israel, March 16-18, 2005; and the Second JAICC, Jerusalem, Israel, June 28-30, 2006.
2007-10 Advisory Review Panel member for Negrin PPG grant, Stanford University.
Advisory Board member for the Experimental Transplantation and Immunology Branch of the National Cancer Institute, Bethesda, MD, March 14.
Chairman, Scientific Review Panel for Blood Cancer, Dept. of Defense, Peer-Reviewed Medical Research Program, Sept. 14-16.
Special Emphasis Panel Reviewer for NCI Loan Repayment Program, May 18
Special Emphasis Review Panel – Chairman – NIAID Ancillary Grants, Nov 17
Ad Hoc Member, Transplantation, Tolerance, & Tumor Immunology Study Section, NIH, Feb 4-5.
2010 Special Emphasis Panel Reviewer for NCI Loan Repayment Program, May 17
American Society of Hematology – Abstract Reviewer and Co-Chair of Oral Session for Annual Meeting

Grant Reviewer for Amy Strelzer Menasevit Award Program, Be the Match Foundation, Jan 15
2014 NIH NIAID Sponsored Meeting – Graft vs. Host Responses in HIV Eradication – Speaker and Invited Participant, Feb 10-11.
2014 Scientific Advisory Board member for J. Ferrara P01 grant on Cellular and Molecular Studies of Bone Marrow Transplant, University of Michigan, Feb.
2014 Special Emphasis Panel Reviewer for NCI Loan Repayment Program, May.
American Society of Hematology – Committee Chairman and Abstract Reviewer for Experimental Transplantation GVHD and GVL Grouping and Co-Chair of Oral Session for Annual Meeting
Ad Hoc Member of Cancer Immunopathology and Immunotherapy Study Section, NIH, Feb 2324
2015-Pres Member of the Lombardi Comprehensive Cancer Center Developmental Review Committee
2015-Pres Member of the Lombardi Comprehensive Cancer Center Clinical Research Committee
2015-Pres Member of the Lombardi Comprehensive Cancer Center Immunology/Transplant Working Group
Lifetime Achievement Award from the American Society of Blood and Marrow Transplantation – Honolulu, HI, Feb 20.
2016 Edward J. Ill Excellence in Medicine Award for Outstanding Scientist - Lawrenceville, NJ, May 4. 2017
Grant Reviewer for Amy Strelzer Menasevit Award Program, Be the Match Foundation, Jan

C. Contribution to Science

My thesis work with Dr. Jonathan Sprent and in continued collaboration afterwards focused on the role of allogeneic donor T cells in the etiology of graft-versus-host disease (GVHD) across minor histocompatibility barriers. In the late 1970's, it was unclear what caused this disease in MHC-matched sibling transplants and and our initial work in a series of novel murine models basically provided the evidence needed to support the use of T-cell depletion to prevent GVHD in the clinical situation. The 1978 J Exp Med article was recognized in 2008 as a "classic" paper and one of the top ten most cited articles in J Exp Med for the previous 30-year period. The "Korngold/Sprent B10.BR<->CBA model for GVHD became a mainstay of numerous future studies in the field. Unfortunately, although T-cell depletion in the clinical transplant situation proved successful over the next decade in preventing GVHD, it did not adequately address the problem of tumor relapse, and the development of optimum approaches to separate out GVHD responses from graft-versus-tumor (GVT) effects is still under study.

Korngold R, Sprent J: Lethal graft-versus-host disease following bone marrow transplantation across minor histocompatibility barriers in mice. Prevention by removing mature T cells from marrow. J. Exp. Med. 148: 1687-1698, 1978.

Korngold R, Sprent J: Selection of cytotoxic T-cell precursors specific for minor histocompatibility determinants. I. Negative selection across H-2 barriers induced with disrupted cells but not with glutaraldehyde-treated cells: Evidence for antigen-processing. J. Exp. Med. 151: 314-327, 1980.

Korngold R, Sprent J: Negative selection of T cells causing graft-versus-host disease across minor histocompatibility barriers: Role of the H-2 complex. J. Exp. Med. 151: 1114-1124, 1980.

Korngold R, Sprent J: Features of T cells causing H-2 restricted lethal graft-vs-host disease across minor histocompatibility barriers. J. Exp. Med. 155: 872-883, 1982.

My postdoctoral work with Dr. Peter C. Doherty at the Wistar Institute focused on thymic education in radiation chimeras and MHC-restricted recognition of viral antigens. These studies helped our understanding of how host elements in the thymus could control how T cells developed their T cell receptors in terms of what they could recognize.

Korngold R, Bennink JR, Doherty PC: Early dominance of irradiated host cells in the responder profiles of thymus from P->F1 radiation chimeras. J. Immunol. 127: 124-129, 1981.

Doherty PC, **Korngold R**: Effects of cyclophosphamide and cortisone on the virus-immune response characteristics of thymocytes and the early reconstitution profiles of P-> F1 chimeras. Cell. Immunol. 65: 33-

39, 1981.

Korngold R, Doherty PC: Sequential analysis of the virus-immune responder characteristics of thymocytes from F1->parent radiation chimeras. Thymus 4: 119-133, 1982.

With my own laboratory established in 1982 at the Wistar Institute, I proceeded to focus on studies supported by an NIH grant on the etiology of GVHD, which I continuously held for 29 years. Our major contribution in the 1980's was in defining the biological roles of CD4 and CD8 T cell subsets in causing GVHD. These observations helped serve as the basis for selective T cell subset removal in clinical trials conducted at several institutions.

Korngold R, Sprent J: Surface markers of T cells causing lethal graft-versus-host disease to class I versus class II H-2 differences. J. Immunol. 135:3004-3010, 1985.

Sprent J, Schaefer M, Lo D, **Korngold R**: Properties of purified T cell subsets. II. In vivo responses to class I vs. class II H-2 differences. J. Exp. Med. 163: 998-1011, 1986.

Korngold R, Sprent J: Variable capacity of $L3T4^+$ cells to cause lethal graft-versus-host disease across minor histocompatibility barriers. J. Exp. Med. 165: 1552-1564, 1987.

Sprent J, Schaefer M, Gao E-K, **Korngold R**: Role of T cell subsets in lethal graft-vs.-host disease directed to class I vs. class II H-2 differences. I. L3T4+ cells can either augment or retard GVHD elicited by $Lyt\text{-}2^+$ cells in class I-different hosts. J. Exp. Med. 167:556-569, 1988.

Studies were conducted in the 1990's in initial collaboration with Dr. Peter Wettstein, who previously examined immunodominance in the CTL response in vitro of C57Bl/6 T cells to BALB.B minor histocompatibility antigens distributed throughout several recombinant inbred strains. The question was whether this immunodominance also operated and controlled anti-miHA directed GVHD and we established and investigated the B6 anti-BALB.B model system for GVHD. These studies concluded that immunodominance did not operate in vivo, but then led to a series of discoveries about how severe and lethal GVHD was dependent upon a limited number of select T cell specificities, amongst a larger milieu of responsive T cells.

Korngold R, Wettstein PJ: Immunodominance in the graft-versus-host disease T cell response to minor histocompatibility antigens. J. Immunol. 145: 4079-4088, 1990.

Wettstein PJ, **Korngold R**: T cell subsets required for the generation of in vitro CTL activity directed to single and multiple histocompatibility antigens. Transplant. 54:296-307, 1992.

Berger M, Wettstein PJ, **Korngold R**: T cell subsets involved in lethal graft-vs-host disease directed to immunodominant minor histocompatibility antigens. Transplant. 57:1095-1102, 1994.

Korngold R, Leighton C, Mobraaten LE, Berger MA: Inter-strain graft-versus-host disease T cell responses to immunodominant minor histocompatibility antigens. Biol. Blood Mar. Transplant. 3:57-4, 1997.

For the last seventeen years, we have been using T cell repertoire analysis to define GVHD T cell responses and those with GVT potential as a means of separating the effects to improve BMT outcomes. Much of our early work in this arena utilized Vb CDR3 size spectratyping which was on the cutting edge of the field at the time, and more recently we have been utilizing the newer techniques of next generation TCR sequencing, which is our current effort. In collaboration with my colleague, Dr. Thea Friedman, we were able to dissect both CD4 and CD8 responses responsible for GVHD in the B6->BALB.B model as well as others, and utilized spectratyping as a GVHD predictor of what would develop in BMT patients. Analysis of potential GVT responses in murine models also allowed us to manipulate selective donor T cell populations in the graft to achieve GVT responses with minimization of GVHD.

Friedman TM, Gilbert M, Briggs C, **Korngold R**: Repertoire analysis of $CD8^+$ T cell responses to minor histocompatibility antigens involved in graft-versus-host disease J. Immunol. 161:41-48, 1998.

Friedman TM, Statton D, Jones SC, Berger MA, Murphy GF, Korngold R: Vb repertoire analysis of $CD4^+$ T cell responses to minor histocompatibility antigens involved in graft-versus-host disease. Biol. Blood Marrow Transplant. 7: 2-13, 2001.

Patterson AE, **Korngold R**: Infusion of select leukemia-reactive TCR Vb^+ T cells provides graft-versusleukemia responses with minimization of graft-versus-host disease following murine hematopoietic stem cell transplantation. Biol. Blood Marrow Transplant. 7: 187-196, 2001.

Jones SC, Friedman TM, Murphy GF, **Korngold R**: Specific donor Vb-associated $CD4^+$ T cell responses correlate with severe acute graft-versus-host disease directed to multiple minor histocompatibility antigens. Biol. Blood Marrow Transplant. 10:91-105, 2004.

Fanning SL, Zilberberg J, Stein J, Vazzana K, Berger SA, **Korngold R**, Friedman TM: Unraveling graftversus-host disease and graft-versus-leukemia responses using TCR Vβ spectratype analysis in a murine bone marrow transplantation model. J Immunol, 190:447-457, 2013.

Complete List of Published Work in MyBibliography: http://www.ncbi.nlm.nih.gov/pubmed/?term=Korngold+R

D. Research Support Ongoing Research Support

Breast Cancer Research Foundation 04/01/17-9/30/18
Co-PIs: Montgomery and Feinman; Korngold, Co-Invest
"Gut Microbiome Effect on Neoadjuvant Chemotherapy-induced Immunosurveillance in Triple Negative Breast Cancer"
Main Goal: Determine whether distinct gut microbial communities increase the efficacy of neoadjuvant chemotherapy by reestablishing tumor immunosurveillance in patients with triple negative breast cancer.

NIH R03 CA216136-01 (Sabatino, PI; Korngold, Co-PI) 06/22/17-05/31/19
"NK Cell-Dependent Cancer Immunotherapy with Semi-Synthetic Peptide-Protein Bio-Conjugates"
Main Goals: To develop new Pep42-B7-H6 conjugates that provide effective NK cell targeting and killing of GRP78 overexpressing tumors that lack cell surface B7-H6.

Completed Research (Past 3 years)

NIH R21 HL102886-03 (J. Zilberberg, P.I.; R. Korngold, Co-Invest) 07/01/10-06/30/13 Stable
shRNA-mediated gene silencing of the b7 integrin to ameliorate graft-versus-host disease Main Goals: To investigate ex vivo gene silencing as a means of controlling GVHD development.
NIH R21 AI092501-02 (S. Iyengar, P.I.; R. Korngold, Co-Invest) 12/01/11-8/31/13
ROCK inhibitor suppression of GVHD with retention of GVL response
Main Goals: To investigate whether inhibition of Rho associated coiled coil kinases can interfere with donor T cell alloreactivity and mobility involved in graft-versus-host disease development.
Onyx Pharmaceuticals (Korngold, PI) 02/01/12- 7/31/14
Effect of an Immunoproteosone Inhibitor on Development of GVHD in Murine Models
NIH R01 CA-154244-08 (Korngold, PI) 06/01/10-03/31/16
T Cell Repertoire in Graft-vs-Host Disease and Graft-vs-Leukemia Responses
Main Goals: TCR Vb spectratype analysis to selectively delete GVHD-reactive donor T cells to allow reconstitution and potential leukemia-specific responses in the allogeneic bone marrow transplantation setting. Involves murine models and human in vitro studies.