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BIOGRAPHICAL SKETCH

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NAME: Miklos, David B.

eRA COMMONS USER NAME : MIKLOS.DAVID

POSITION TITLE: Associate Professor of Medicine

| EDUCATION/TRAINING INSTITUTION AND LOCATION | DEGREE | Completion Date | FIELD OF STUDY |
| --- | --- | --- | --- |
| University of Notre Dame, South Bend, IN | B.S. | 06/1987 |  |
| Yale University School of Medicine, New Haven, CT | M.D./Ph.D | 06/1995 | Medicine |
| Yale University, New Haven, CT | Ph.D. | 06/1995 | Genetics |
| Brigham and Women’s Hospital, Boston, MA |  | 06/1998 | Internal Medicine |
| Dana Farber Cancer Institute, Boston, MA |  | 06/2001 | Hematology/Oncology |

# A. Personal Statement

I am a physician-scientist focusing on human translational immunology research, and I have a strong track record mentoring and promoting laboratory immunologists and clinical-translational researchers. My laboratory research focuses on 1) B cell reconstitution after allogeneic hematopoietic cell transplantation (alloHCT), 2) lymphoid neoplasia minimal residual disease (MRD) quantification using Immune receptor high throughput sequencing technology, 3) prevention and treatment of chronic Graft versus host disease (cGVHD), and 4) CAR-T Cancer Cell Therapies (CAR-T). With my promotion to Associate Professor spring 2016, I became Clinical Director of Stanford’s Cancer Cell Therapy (CCT) Program. Stanford performs 125 CAR-T therapies annually characterized by comprehensive clinical databases with linked biorepositories for both industry sponsored and investigator initiated clinical trials.

Over the past 15 years I have successfully mentored 11 Heme-BMT-CCT fellows including: George Chen MD (Roswell Park Research Institute), Aaron Logan MD/PhD (Univ. Cal. San Francisco), Everett Meyer MD/PhD (Stanford Univ.), and Hideki Nakasone MD (Jichi Medical University, Japan), Saurabh Dahiya (Univ. of Maryland), Nash Hossain (Loyola University) Lori Muffly (Stanford Univ), Surbhi Sidana (Stanford), Matthew Frank (Stanford), Jay Spiegel (Stanford fellow), and John Baird (Stanford fellow). Starting January 2021, I will become Division Chief of Stanford BMT and Cell Therapy and continuing our BMT fellowship successes advancing clinical translational and physician scientists careers will remain my highest priority.

**B. Positions and Honors**

1989-1993 Howard Hughes Medical Institute Predoctoral Fellowship

1993-1995 Medical Scientist Training Program Fellowship

1995-1998 Intern and Resident in Medicine, Brigham and Women’s Hospital, Boston, Massachusetts

1998-2001 Clinical Fellow, Adult Hematology and Oncology, Dana-Farber/Partners Cancer Care, Boston, MA

2001-2003 Harvard-MIT Clinical Investigator Training Program Fellowship

Academic Appointments

* 1. Instructor of Introduction to Clinical Medicine, Harvard Medical School

2000-2004 Hematology Tutorial Instructor, Harvard Medical School

2001 2004 Instructor in Medicine, Harvard Medical School

2004-2015 Assistant Professor, Laboratory Principle Investigator, Stanford University, Department of Medicine, Division of Blood and Marrow Transplantation

2016- Associate Professor, Laboratory Principle Investigator, Stanford University, Department of Medicine, Division of Blood and Marrow Transplantation

Awards and Honors

1987 Summa Cum Laude, University of Notre Dame

1987 Phi Beta Kappa, Alpha Epsilon Delta, Notre Dame Scholar

1988 March of Dimes Summer Research Scholarship

1995 Alpha Omega Alpha Medical Honor Society

# C. Contributions to Science

**1) Dr. Miklos is an experienced CAR-T clinician and Clinical Director of Stanford’s Cancer Cell Therapy**

Dr. Miklos served as prior Medical director of Stanford’s Cancer Cell Therapy Correlative Science Unit (CCSU). Dr. Miklos combined his basic science knowledge, clinical trial experience, and cell therapy management experience to institute and direct Stanford’s Cancer Cell Therapy Clinical Research Group June 2016. He is the Stanford PI for 9 CAR-T studies. Dr Miklos’ clinical study teams have undergone two successful FDA inspections for indications in 2017 (KTE-c19 for rel/ref DLCL Zuma1 and Ibrutinib for cGVHD).

1. NeelapuSS, LockeFL BartlettNL, LekakisLJ, **MiklosDB**, JacobsonCA, Braunschweig I, OluwoleO, SiddiqiT, Lin Y, TimmermanJ, Stiff PJ, Friedberg JW, Flinn I, Goy, HillBT, Smith MR, Deol A, Farooq U, McSweeney P, Munoz J, Avivi I, Castro JE, Westin JR, Chavez JC, Ghobadi A, Komanduri, K, Levy R, JacobsenED, Witzig TE, Reagan P,Bot A, Rossi J, Navale L, ianh Y, Jeff Aycock J, Elias M, Chang D, Wiezorek J, Go WY. Axicabtagene Ciloleucel (CD19 CAR T) in Refractory Large B-Cell Lymphoma. N Engl J Med. 2017 Dec 28;377(26):2531-2544. doi: 10.1056/NEJMoa1707447. Epub 2017 Dec 10. PMID: 29226797.
2. HossainNM, DahiyaS, LeR, AbramianAM, Kong KA, Muffly, LS, and **Miklos DB**. Circulating tumor DNA assessment in patients with Diffuse Large B-Cell Lymphoma following CAR T-cell therapy. Leuk Lymphoma. 2018 Jul 3:1-4. doi: 10.1080/10428194.2018.1474463. PMID:29966461
3. Nastoupil LJ\*, Jain MD\*, FengL, Spiegel, JY, GhobadiA, LinY, DahiyaS, Lunning M, Lekakis L, ReaganP, Oluwole O, McGuirk J, Deol A, Sehgal AR, Goy A, Hill BT, Vu K, Andreadis C, Munoz J, Westin J, ChavezJ, Cashen A, Bennani NN, Rapoport AP, Vose JM, **Miklos DB\*\*,** Neelapu SS\*\*, Locke FL\*\*; Standard of Care Axicabtagene Ciloleucel for Relapsed or Refractory Large B-cell Lymphoma: Results from the US Lymphoma CAR T Consortium. Journal of Clinical Oncology; Accepted for Publication 3/10/2020 \*\* Co Senior Author
4. **Dr. Miklos’ group discovered that allogeneic antibodies target minor histocompatibility antigens (mHA) develop after allogeneic HCT in association with cGVHD.**

As a BMT fellow working in the lab of Dr. Jerome Ritz, we discovered males with female donors develop allogeneic antibodies against H\_Y antigens in association with chronic GVHD. As an independent investigator at Stanford we developed HY microarrays to multiplex and more accurately detect HY antibodies. Testing prospective blood sample collections following alloHCT demonstrated HY-Ab develop 3 months following F🡪M HCT and strongly predict cGVHD and non-relapse mortality. Dr. Miklos’ group developed flow cytometry method for H-Y antigen specific B cell characterization.

1. **Miklos DB**, Kim HT, Miller KH, Guo L, Zorn E, Lee SJ, Hochberg EP, Wu CJ, Alyea EP, Cutler C, Ho V, Soiffer RJ, Antin JH, Ritz J. Antibody Responses to H-Y Minor Histocompatibility Antigens Correlate with Chronic Graft versus Host Disease and Disease Remission. Blood 2005; 105(7):2973-8. PMCID: PMC1350982.
2. Nakasone H, Tian L, Sahaf B, Kawase T, Schoenrock K, Perloff S, Ryan CE, Paul J, Popli R, Wu F, Otani JM, Coller J, Warren EH , and **Miklos DB**. Allogeneic H-Y antibodies detected 3 months after female to male sex-mismatched HCT predict chronic GVHD and non-relapse mortality. Blood. 2015 May 14;125(20):3193-201. PMCID: PMC4432013.
3. Sahaf B, Yang Y, Arai S, Herzenberg L, Herzenberg LA, **Miklos DB**. H-Y antigen binding B cells develop in male recipients of female hematopoietic cells and associate with chronic graft vs host disease. Proc Natl Acad Sci USA, 2013 Feb 19;110(8): 3005-10. PMCID: PMC3581974.
4. **Dr. Miklos’ group demonstrated that depletion of allogeneic B cells prevents and effectively treats chronic graft versus host disease (cGVHD) and led phase II clinical trial supporting FDA approval of Ibrutinib for chronic GVHD treatment failure.**

We have completed four phase II clinical trials depleting alloreactive donor B cells targeting CD20 with rituximab therapy confirming cGVHD therapeutic and prevention benefits. We have developed our novel HY microarray to facilitate multiplexed accurate HY-Ab testing. HY-Ab correlative science testing has shown rituximab prophylaxis two months following alloHCT prevents alloreactive B cell development. Most recently, my research group has lead a multi-site phase I/II clinical trial testing the safety and tolerability of Ibrutinib for the treatment of 42 steroid refractory /dependent cGVHD patients reporting 67% overall response. Based on this study, The FDA approved ibrutinib for the treatment of adult patients with chronic graft versus host disease (cGVHD) after failure of one or more lines of systemic therapy August 2nd 2017. This is the first FDA-approved therapy for the treatment of cGVHD.

1. Cutler C\*, **Miklos D\***, Kim HT, Treister N, Woo SB, Bienfang D, Klickstein LB, Levin J, Miller K, Reynolds C, Macdonell R, Pasek M, Lee SJ, Ho V, Soiffer R, Antin JH, Ritz J, Alyea E. Rituximab for steroid-refractory chronic graft-vs.-host disease. Blood 2006; 108:756-62. \*both authors contributed equally. PMCID: PMC1895490.
2. Arai S, Sahaf B, Narasimhan B, Chen G, Jones C, Lowsky R, Shizuru J, Johnston L, Laport G, Weng WK, Benjamin J, Schaenman J, Brown J, Ramirez J, Zehnder JL, Negrin, RS, **Miklos, DB**. Prophylactic Rituximab after Allogeneic Transplantation Decreases B cell Alloimmunity with Low Chronic GVHD Incidence. Blood. 2012 Jun 21;119(25):6145-54. PMCID: PMC3383022.

3. **Miklos D,** Cutler CS, Arora M, Waller EK, Jagasia M, Pusic, Flowers ME, Logan AC, Nakamura R, Blazar BR, Li Y, Chang S, Lal I, Dubovsky J, James DF, Styles L, Jaglowski S. Ibrutinib for chronic graft-versus-host disease after failure of prior therapy. [Blood.](https://www.ncbi.nlm.nih.gov/pubmed/?term=Ibrutinib+for+chronic+graft-versus-host+disease+after+failure+of+prior+therapy) 2017 Nov 23;130(21):2243-2250. PMCID: [PMC6033048](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6033048/).

**4) Dr. Miklos’ group developed ultrasensitive lymphoid neoplasia quantification methods using high-throughput sequencing (HTS) of immune receptors and demonstrated clinical utility for a variety of hematologic malignancies.**

1. Boyd SD, Marshall EL, Merker JD, Maniar JM, Zhang LN, Sahaf B, Jones CD, Simen BB, Hanczaruk B, Nguyen KD, Nadeau KC, Egholm M, **Miklos DB**, Zehnder JJ, Fire AZ, Measurement and clinical monitoring of human lymphocyte clonality by massively parallel V-D-J pyrosequencing. Sci. Transl. Med. 1, 12ra23 (2009). PMCID: PMC2819115.
2. Logan AC, Gao H, Wang C, Sahaf B, Jones CD, Marshall EL, Buño I, Armstrong R, Fire AZ, Weinberg KI, Mindrinos M, Zehnder JL, Boyd SD, Xiao W, Davis RW, **Miklos DB**.High-throughput VDJ sequencing for quantification of minimal residual disease in chronic lymphocytic leukemia and immune reconstitution assessment. Proc Natl Acad Sci USA, 2011 Dec 27; 108(52):21194-9. PMCID: PMC3248502.
3. Logan AC, Zhang B, Narasimhan B, Carlton V, Zheng J, Moorhead M, Krampf MR, Jones CD, Waqar AN, Faham M, Zehnder JL, **Miklos DB**. Minimal Residual Disease Quantification Using Consensus Primers and High-Throughput IGH Sequencing Predicts Post-Transplant Relapse in Chronic Lymphocytic Leukemia. [Leukemia.](http://www.ncbi.nlm.nih.gov/pubmed/?term=Logan+AC%2C+Zhang+B%2C+Narasimhan+B%2C+Carlton+V%2C) 2013 Aug;27(8):1659-65. PMCID: PMC3740398.

## Complete List of 85 peer-review Miklos publications:

<http://www.ncbi.nlm.nih.gov/pubmed/?term=Miklos%2C+David+B>

D. Research Support

**Ongoing Research Support**

P01 CA049605 (Negrin PI) 4/15/1989 – 8/31/2024

National Institutes of Health - NCI

Bone Marrow Grafting and Cellular Therapy for Leukemia and Lymphoma

Project: Project 4 (Mackall project leader)

Goals: Enhance the Efficacy of Chimeric Antigen Receptor Therapy for B-ALL and DLBCL

Role: Co-PI project 4

Kite Pharmaceuticals Miklos (PI) 5/1/2020 – 4/30/2022

Kite Pharmaceuticals

Identification of Axi-Cel Expressing T cells in Lymph node and Blood Samples

Role: PI

PCYC-1140IM Miklos (PI) 12/01/16-11/30/22

Pharmacyclics, Inc

Work Order number 19578, Ibrutinib trial

A Randomized, Double-Blind Phase 3 Study of Ibrutinib in

Combination With Corticosteroids versus Placebo in Combination With Corticosteroids in Subjects with New Onset Chronic Graft Versus Host Disease (cGVHD)

Role: PI

Kite Pharmaceuticals Miklos (PI) 08/19/15-07/31/25

Kite Pharmaceuticals

ZUMA1 Phase 1b/II study of anti-CD19 chimeric antigen receptor T cell therapy for refractory diffuse large cell lymphoma (DLCL)

Role: PI

Kite Pharmaceuticals Miklos (PI) 10/20/16 -09/30/21

Kite Pharmaceuticals

ZUMA6 Phase 1b/II study of anti-CD19 chimeric antigen receptor T cell therapy and Atezolizumab for refractory diffuse large cell lymphoma (DLCL)

Role: PI

Kite Pharmaceuticals Miklos (PI) 02/28/17-02/28/22

Kite Pharmaceuticals

Goals: ZUMA2: A Phase 2 Multicenter Study Evaluating the Efficacy of KTE-C19 in Subjects with Relapsed/Refractory Mantle Cell Lymphoma (r/r MCL)

Role: PI

Kite Pharmaceuticals Miklos (PI) 03/30/18-03/31/22

Kite Pharmaceuticals

Goals: ZUMA7: To determine if axicabtagene ciloleucel is superior to standard of care (SOC) as measured by event-free survival (EFS), as determined by blinded central review.

Role: PI

Kite Pharmaceuticals Miklos (PI) 07/20/17-07/31/21

Kite Pharmaceuticals

Goals: ZUMA9: To provide access to axicabtagene ciloleucel (also known by the company code KTE-C19) for subjects with relapsed/refractory transplant ineligible aggressive NHL until axicabtagene ciloleucel is commercially available in each respective participating country.

Role: PI

1153413 Project 1 Miklos (PI: Cutler) 09/01/15-08/31/22

Dana-Farber Cancer Institute/NIH

Mechanisms, Prevention and Treatment of Chronic Graft-vs.-Host Disease - Project 1

Goals: Stanford Site PI enrolling patients onto RCT of Obintuzumab-v-placebo preventing cGVHD

Role: Site PI

1272413 Project 3 Miklos (PI: Ritz) 09/01/15-08/31/22

Dana-Farber Cancer Institute/NIH

Mechanisms, Prevention and Treatment of Chronic GVHD - Project 3

Goals: Performing correlative measurements of allogeneic B cells and other cGVHD assays

Role: Co PI

CLIN2-10846 Miklos (PI: Mackall) 06/01/18-05/31/22

California Institute of Regenerative Medicine (CIRM)

Phase 1 Study of CD19/CD22 Chimeric Antigen Receptor (CAR) T Cells in Adults with Recurrent or Refractory B Cell Malignancies

Project: Cell Therapy for Leukemia and Lymphoma

Co-Investigator: (PI: Crystal Mackall)

Goals: Determine feasibility, safety, and efficacy of bi-specific CAR targeting CD19 and CD22 in patients with refractory/relapsed Diffuse large B cell lymphoma (DLBCL) or Acute Lymphoblastic Leukemia (ALL)

Role: Clinical Trial PI: Phase 1b Clinical Trial of Bi-specific CAR19-22

## Completed Research Support

0261-01STAN (Miklos, David - Project 111206) 9/1/2014-8/31/2017
Prime Sponsor: National Institutes of Health

NIH/NIAMS Small Grant Program For New Investigators (R03)

Oklahoma Medical Research Foundation

Antibody Mediated Spontaneous Abortion in Lupus Pregnancies

Role: Miklos Co PI - responsible for measuring 1800 sera for HY and HX Ab and assisting with analysis

Correlative studies for PCYC-1129 Miklos (PI) 01/20/16-01/31/20

Pharmacyclics, Inc.

Goals: Development and optimization of a simultaneous analysis of 28 phenotypic markers for cell identity in combination with 1 to 4 regulatory phosphorylation markers as sentinels of ibrutinib activity, and indicators of DNA content and cell viability.

Role: PI

P0 1CA049605 Negrin (PI) 04/15/89-03/31/19

NIH/National Cancer Institute

Bone Marrow Grafting for Leukemia and Lymphoma

Role: Project 4 leader - Improving Graft-vs.-Leukemia Alloimmunity against CLL

Goals: 1. To validate immunoglobulin heavy chain (IGH) high throughput sequence (HTS) methods to quantify CLL minimal residual disease (MRD) as a predictor of relapse.

2. To evaluate B and T cell repertoire diversity and tempo of development following alloHCT in relation to CLL MRD response and GVHD.

3. Phase II clinical trial to determine if alloCIK cell infusion in CLL patients with mixed donor chimerism will improve immune reconstitution, GVL, and prevent CLL relapse.

R01 HL114591 (Negrin PI) 09/01/12-05/31/18

NIH/National Heart, Lung and Blood Institute

Regulatory T cells in allo HCT

Goals: To utilize highly purified CD4+CD25+CD127-FoxP3+ regulatory T cells in allogeneic hematopoietic cell transplantation clinical trials and assess their efficacy in preventing and treating graft vs host disease in the clinic.

54179060LYM2008-BMT1651 Jagasia (PI) 06/30/17-06/30/20

Vanderbilt University (Janssen Scientific Affairs LLC)

Optimizing Post-Allogeneic Hematopoietic Cell Transplant Outcomes for Lymphoma Using Ibrutinib

Goals: Determine If Post alloHCT Ibrutinib decreases cGVHD and relapse

Role: Clinical Site PI and overall correlative science Co-PI

BMT CTN PROTOCOL 1202(Miklos – 114379) 6/1/13 – 6/30/19

NIH BMT Clinical Trials Network

National Marrow Donor Program

Prospective Multi-Center Cohort for the Evaluation of Biomarkers Predicting Risk of Complications and Mortality Following Allogeneic HCT.

Role: Site PI: Miklos