BIOGRAPHICAL SKETCH

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NAME: Parveen Shiraz, MD

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POSITION TITLE: Instructor

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)*	Start and Completion Dates MM/YYYY	FIELD OF STUDY
Kilpauk Medical College, India	MBBS	08/1989 to 01/1995	Bachelor of Medicine, Bachelor of Surgery
Cedars-Sinai Med Center/UCLA, Los Angeles, CA	Internship	06/1997 to 06/1998	Internal Medicine
St. Mary's Medical Center, San Francisco, CA	Residency	07/1998 to 06/2000	Internal Medicine
Loma Linda University, Loma Linda, CA	Fellowship	06/2012 to 06/2015	Hematology/Medical Oncology
Stanford University, Stanford, CA	Fellowship	07/2015 to 06/2016	Blood and Marrow Transplantation
Stanford University, Stanford, CA	Instructor	08/2021 - present	Blood and Marrow Transplantation

A. Personal Statement

I am a physician-scientist in the Division of Blood and Marrow Transplantation/Cell Therapy (BMT/CT) at Stanford University. The dearth of effective therapies for refractory leukemias and the curative potential of hematopoietic stem cell transplant (HCT) prompted me to pursue a career in HCT. As a BMT clinician, caring for patients suffering from the toxicities of HCT and post-HCT leukemia relapse motivated me to pursue laboratory and translational research in search of less toxic and more effective HCT conditioning strategies. In 2021, I became an instructor in the laboratory of Dr. Judith Shizuru who specializes in CD117 antibody based non-toxic HCT conditioning. We have produced anti-CD117 multi-antigen targeting and NK, macrophage or T cell engaging antibodies to eradicate residual leukemic clones and permit engraftment of normal donor HSCs. Our *invitro* studies are already showing superiority of the multiantigen targeting NK engaging antibodies and *invivo* studies of these antibodies in xenograft models of myelodysplastic syndrome and acute myeloid leukemia are in progress.

B. Positions, Scientific Appointments and Honors

Professional Experience

04/1996-05/1997 - Research Assistant, Endocrinology and Metabolism, Stanford University, Stanford, CA
06/1997-06/1998 - Intern, Dept of Internal Medicine, Cedars-Sinai Medical Center, Los Angeles, CA
07/1998-06/2000 - Resident, Dept of Internal Medicine, St. Mary's Medical Center, San Francisco, CA
09/2000-06/2012 - Hospitalist, Kaiser Permanente Medical Center, San Jose, CA

06/2012-06/2015 - Fellow, Hematology/Medical Oncology, Loma Linda University, Loma Linda, CA
07/2015-06/2016 - Fellow, Blood and Marrow Transplantation/Cell Therapy, Stanford University, CA
08/2016-01/2019 - Hematologist, Leukemia/Lymphoma Centers of Excellence, NCAL Kaiser Permanente, CA
02/2019-07/2021 - Assistant Clinical Professor, Division of BMT/CT, Stanford University, Stanford, CA
08/2021-present - Instructor, Division of BMT/CT, Shizuru Lab, Stanford University, CA

Professional Memberships
07/2012 – current American Society of Hematology
07/2015 – current American Society of Transplant and Cell Therapy

C. Current Research Support

Sponsor: California Institute of Regenerative Medicine (DISC2-13400) (09/2022 – 08/2024)

Role: Chief Scientist
Title: Targeted Immunotherapy-based Blood Stem Cell Transplantation

Sponsor: EvansMDS Discovery Research Grant 2022 (09/2022 – 08/2025)

Role: Chief Scientist
Title: Blood Stem Cell Transplantation with Targeted Eradication of MDS Clones

Sponsor: TRAM Scholar Program, Stanford University (08/2022 – 08/2024)

Role: Principal Investigator
Title: Evaluating Thymic Stromal Lymphopoietin (TSLP) as a Biomarker for Acute Graft Versus Host Disease.

TSLP isoforms play a key role in mucosal homeostasis and inflammation, and our preliminary data demonstrate elevated plasma levels of TSLP isoforms in fatal acute GI-GVHD (aGVHD). We are collaborating with the MAGIC consortium to evaluate TSLP as a prognostic biomarker in acute GI GVHD.

D. Contributions to Science

My clinical and research interest in acute leukemia led me to author the following review articles and book chapter.

a. Gowda C, Olivia L. Francis, Yali Ding, **Shiraz P**, Dovat S, and Payne KJ. Pediatric High-Risk Leukemia – Molecular Insights. In, Leukemia – Various Types. Published Nov11, 2015. ISBN 978- 953-51-2202-9. Eds Margarita Guenova and Gueorgui Balatzenko. Intech Open Access.

b. Lee CJ, **Shiraz P**, Muffly L. Pharmacological Maintenance Strategies Following Allogeneic Hematopoietic Cell Transplantation for Acute Myeloid Leukemia. Leuk Lymphoma. 2017 Mar;58(3):516-527. doi: 10/1080/10428194.2016.1205744. Epub 2016 Aug 11. PMID: 27685315

c. **Shiraz P**, Payne KJ, Muffly L. The Current Genomic and Molecular Landscape of Philadelphia-like Acute Lymphoblastic Leukemia. Int J Mol Sci. 2020 Mar 22;21(6):2193. doi: 10.3390/ijms21062193 PMID: 32235787

d. **Shiraz P**, Jehangir W, Agrawal V. T-Cell Acute Lymphoblastic Leukemia – Current Concepts in Molecular Biology and Management. Biomedicines 2021, 9(11), 1621

My lab research training during hematology fellowship focused on describing the molecular landscape and identifying potential targets in CRLF2 B-ALL which is a high-risk B-ALL subtype. As a leukemia and transplant clinician, I have collaborated with other investigators in clinical trials to study the utilization of pediatric regimens in young adults, measurable residual disease (MRD) assessment and CAR-T cell therapy for B-ALL and the use of engineered grafts to reduce toxicity from HCT.

1. CRLF2 overexpressing B-ALL is a high-risk leukemia characterized by poor outcomes. It is five times more common among Hispanics and is therefore a major contributor to health care disparity in leukemia outcomes. There is no FDA approved therapy targeting this subgroup of ALL. During lab research training at Loma Linda University, we studied CRLF2-TSLP ligand-receptor interaction and

the downstream signaling pathways to identify potential targeted therapies.

a. **Shiraz P**, Francis O, Baez I, Conception K, Mayagoitia K, Ginelli E, Martinez S, Coats J, Fisher R, Morris C, Zhang X, Ruijun S, Dovat S, Payne K. TSLP-induced alterations of multiple signaling pathways in primary CRLF2 B-ALL xenografts. ASH Annual Meeting, San Francisco,2014.
b. **Shiraz P**, Francis O, Baez I, Salcedo-Conception K, Mayagoitia K, Ginelli E, Milford TA, Coats J, Fisher R, Morris C, Zhang X, Ruijun S, Payne K. Therapies for CRLF2 B-cell Acute Lymphoblastic Leukemia. Western Regional Meeting of the American Federation for Medical Research, Carmel 2015.
c. Francis OL, Martinez SR, Milford TM, Baez I, Coats JS, Mayagoitia K, Conception KR, Ginelli E, Benitez A, Weldon AJ, Arogyaswamy K, **Shiraz P**, Fisher R, Morris CL, Zhang XB, Filippov V, Van Handel B, Zheng Ge, Song C, Dovat S, Su RJ, and Payne KJ. A novel xenograft model to study the role of TSLP-induced CRLF2 signals in normal and malignant human B lymphopoiesis. Haematologica. 2016 Apr;101(4):417-26. PMCID: PMC5004401.
d. **Shiraz P**, Francis O, Baez I, Salcedo-Conception K, Mayagoitia K, Ginelli E, Milford TA, Coats J, Fisher R, Morris C, Zhang X, Ruijun S, Payne K. Therapies for CRLF2 B-cell Acute Lymphoblastic Leukemia. Western Regional Meeting of the American Federation for Medical Research, Carmel 2015.
e. Francis OL, Martinez SR, Milford TM, Baez I, Coats JS, Mayagoitia K, Conception KR, Ginelli E, Benitez A, Weldon AJ, Arogyaswamy K, **Shiraz P**, Fisher R, Morris CL, Zhang XB, Filippov V, Van Handel B, Zheng Ge, Song C, Dovat S, Su RJ, and Payne KJ. A novel xenograft model to study the role of TSLP-induced CRLF2 signals in normal and malignant human B lymphopoiesis. Haematologica. 2016 Apr;101(4):417-26. PMCID: PMC5004401.

2. Despite several publications in the early 2000's demonstrating superior outcomes with pediatric regimens in adolescents and young adults (AYA) with ALL, only a minority of AYAs with ALL received pediatric regimens in adult cancer centers until 2010. We were one of the first to demonstrate that high volume centers were more likely to administer pediatric regimens.
    a. Muffly L, Lichtensztajn D, **Shiraz P**, Abrahao R, McNeer J, Stock W, Keegan T, Gomez SL. Adoption of Pediatric-Inspired Acute Lymphoblastic Leukemia Regimens by Adult Oncologists Treating Adolescents and Young Adults: A Population-Based Study. Cancer. 2017 Jan 1;123(1):122-130. doi: 10/1002/cncr.30322. Epub 2016 Sep 13. PMID: 27622953

3. Measurable residual disease (MRD) monitoring is an essential part of ALL management with a well-established prognostic value. MRD is traditionally measured in samples obtained from bone marrow biopsy which is an invasive procedure. We have demonstrated a strong correlation between MRD monitoring in the bone marrow and blood, thereby showing that NGS based monitoring from peripheral is an adequate alternative to frequent invasive bone marrow aspirations.
    a. Muffly L, Sundaram V, Chen C, Yurkiewicz I, Kuo E, Burnash S, Spiegel JY, **Shiraz P**, […], Liedtke M, Vempaty HT, Miklos DB. Concordance of peripheral blood and bone marrow measurable residual disease in adult acute lymphoblastic leukemia. Blood Adv. 2021 Aug 24;5(16):3147-3151. doi: 10.1182/bloodadvances.2021004234. PMID: 34424318

4. To overcome antigen loss associated with CD19 targeting CAR-T cells, our group tested a bispecific CAR targeting CD19 and 22 in a phase 1 clinical trial of adults with relapsed/refractory B-ALL and large B cell lymphoma. Manufacturing feasibility and safety were demonstrated. Although response rates were high, relapses were significant and were associated with CD19 loss, implicating antigen loss as a major cause of CAR-T cell resistance and highlighting the challenge of engineering multi-specific CAR-T cells.
    a. Spiegel JY, Patel S, Muffly L, Frank MJ, Oak J, **Shiraz P**, […], Feldman S, Mackall C, 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. doi: 10.1038/s41591-021- 01436-0. PMID: 34312556
5. Graft versus host disease (GVHD) is a frequent and serious complication of HCT despite pharmacological prophylaxis. We conducted a phase 1b/2 multicenter trial using a CD34 selected,

T-reg engineered graft, and demonstrated a doubling of GVHD and relapse free survival (GRFS) compared to a contemporaneous standard of care arm. In another phase 1 study, we demonstrated that type 1 regulatory T cells are inducible, interleukin10+FOXP3- and can suppress GvHD after HCT.

a. Meyer EH, Hoeg R, Moroz A, Miklos DB, **Shiraz P**, Muffly L, […], McClellan SS, Negrin RS. Orca-T, a Precision Treg-Engineered Donor Product, Prevents acute GvHD with less immunosuppression in an early multicenter experience with myeloablative HLA-matched transplants. ASH Annual Meeting Oral presentation, Virtual, Dec 2020
b. Chen PP, Agarwal-Hashmi R, Saini G, […], **Shiraz P**, Bertaina A, Bacchetta R, Roncarolo MG. Alloantigen-specific type 1 regulatory T cells suppress through CTLA-4 and PD-1 pathways and persist long-term in patients. Sci Transl Med. 2021 Oct 27;13(617):eabf5264. doi: 10.1126/scitranslmed.abf5264. Epub 2021 Oct 27. PMID: 34705520
c. Bader CS, Pavlova A, Lowsky R, Muffly LS, **Shiraz P**, […], Negrin RS, Meyer EH. Single- center randomized trial of T-reg graft alone vs T-reg graft plus tacrolimus for the prevention of acute GVHD. Blood Adv. 2024 Mar 12;8(5):1105-1115. Doi: 1182/bloodadvances.2023011625

Publications not listed above:

a. Bankova A, Caveney J, […], **Shiraz P**, […], Shizuru JA, Arai S. Real-World Experience of Cryopreserved Allogeneic Hematopoietic Grafts during the COVID-19 Pandemic: A Single-Center Report. Transplant Cell Ther. 2022 Apr;28(4):215.e1-215.e10. PMID 35042013
b. Liang EC, Craig J, […], **Shiraz P**, […], Bharadwaj S, Muffly L. Allogeneic Hematopoietic Cell Transplantation for Adult Acute Lymphoblastic Leukemia in the Modern Era. Transplant Cell ther. 2022 Aug;28(8):490-495. PMID: 35584783
c. Spinner MA, Sica RA, […], **Shiraz P**, […], Advani R, Arai S. Improved outcomes for relapsed/refractory Hodgkin Lymphoma after autologous transplantation in the era of novel agents.
Blood. 2023 Jun 1;141(22):2727-2737. PMID: 36857637
d. Liang EC, Dekker SE, […], **Shiraz P**, […], Muffly L. Next-generation sequencing-based MRD in adults with ALL undergoing hematopoietic cell transplantation. Blood Adv. 2023 Jul 25;7(14):3395-3402.
PMID: 37196642
e. Schultz LM, Jeyakumar N, […], **Shiraz P**, […], Muffly L. CD22 CAR T cells demonstrate high response rates and safety in pediatric and adult B-ALL: Phase 1b results. Leukemia. 2024 May;38(5):963-968. PMID: 38491306
f. Hamilton MP, Craig E, […], **Shiraz P**, […], Miklos DB. CAR19 monitoring by peripheral blood immunophenotyping reveals histology-specific expansion and toxicity. Blood Adv. 2024 Mar 18:bloodadvances.2024012637. PMID: 38498731
g. Veilleux O, Socola F, […], **Shiraz P**, […], Weng WK. Management of post-autologous transplant relapse in patients with T-cell lymphomas. Am J Hematol. 2024 Apr 25. PMID: 38661220

Complete list of published work in MyBibliography:

https://pubmed.ncbi.nlm.nih.gov/?term=Shiraz%2C%2BParveen%5BAuthor%5D&sort=date