BIOGRAPHICAL SKETCH

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NAME: Deepta Bhattacharya

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

POSITION TITLE: Associate Professor of Immunobiology

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
Indiana University, Bloomington, IN	BS	1996	Biochemistry
University of California, Berkeley, CA	PhD	2002	Molecular & Cell Biology
Stanford University, Palo Alto, CA	N/A	2008	Hematopoiesis

A. Personal Statement

My laboratory merges the fields of stem cell biology and immunology, both to understand basic aspects of lymphocyte development and to develop novel translational strategies to combat infectious disease. Using functional genomics approaches, my lab studies the metabolic and extrinsic control of hematopoietic stem cell and progenitor fate decisions, the molecular basis of the long-lived plasma vs. memory B cell fate decision, the molecular program of memory B cell self-renewal, and the differences in specificities between memory B cells and long-lived plasma cells. We strive to be early adopters of the latest technology to study functional genomics and metabolomics in the immune system, with an emphasis on *in vivo* biology and single cell resolution. My work established the metabolic basis of plasma cell longevity in two papers published in Immunity in 2016, and in Cell Reports in 2018. In these papers, we established the concept of metabolic buffering against glucose, amino acid, and energy shortages as the primary mechanism controlling the duration of immunity. These studies merged the latest technologies in bioenergetic profiling, stable isotope tracing, and genetic model systems. Using the latest methods in population and single cell RNA-sequencing, we further demonstrated remarkably similar transcriptomes between short- and long-lived plasma cell. We have an ongoing interest in protective and pathogenic antibody responses to flaviviruses, which we will merge with our interest in metabolism in this proposal. We have applied these skills, expertise, and track record, to help in the current pandemic, evidenced by a manuscript recently published in Immunity.

B. Positions and Honors

Positions

1996-2001 Graduate Student, University of California, Berkeley; Laboratory of William C. Sha, M.D., Ph.D
2002 Postdoctoral Fellow, University of California, Berkeley; Laboratory of William C. Sha, M.D., Ph.D
2003-2008 Postdoctoral Fellow, Stanford University; Laboratory of Irving L. Weissman, M.D.
2008-2016 Assistant Professor, Washington University, Department of Pathology and Immunology
2017 Associate Professor with tenure, Washington University, Dept. of Pathology and Immunology
2017- Associate Professor with tenure, University of Arizona, Department of Immunobiology

Honors

1992 Indiana University Honors Division Scholarship
1995 Indiana University Undergraduate Research Scholarship
1996 Phi Beta Kappa
1999 University Outstanding Graduate Student Instructor
2004 Cancer Research Institute Postdoctoral Fellowship

2007 National Institutes of Health K01 Career Development award
2012 New York Stem Cell Foundation-Robertson Investigator
2013 American Cancer Society Research Scholar
2020 Allen Distinguished Scholar nomination

C. Contribution to Science

1) We have published several studies that focus on viral immunology and antibody responses. These studies defined the different functional roles and developmental pathways between memory B cells and long-lived plasma cells. These papers demonstrated that the most important role for memory B cells is to respond to pathogens such as flaviviruses that have changed since the first exposure and evade pre-existing antibodies. We have also defined molecular pathways that restrain responses to chronic infections such as CMV. Ongoing work focuses on responses to SARS-CoV-2 in the human population.

   a) Ripperger TJ[*], Uhrlaub JL[*], Watanabe M[*], Wong R[*], Castaneda Y, Pizzato HA, Thompson MR, Bradshaw C, Erickson HL, Weinkauf C, Bime C, Knox K, Bixbie B, Dake MD, Parthasarathy S, Capaldi AP, Spier CM, Kaplan ME, Harris DT, Lafleur BJ, Sprissler R, Nikolich-Zugich J[**], **Bhattacharya D**[**]. (2020). Orthogonal SARS-CoV-2 serological assays enable surveillance of low prevalence communities and reveal durable humoral immunity. Immunity, 53(5): 925-933. PMCID: PMC7554472

   b) Wong, R., Belk, J.A., Govero. J., Uhrlaub, J.L., Reinartz, D., Zhao, H., Errico, J.M., D'Souza, L., Ripperger, T.J., Nikolich-Zugich, J., Shlomchik, M.J., Satpathy, A.T., Fremont, D.H., Diamond, M.S., **Bhattacharya, D.** (2020). Affinity-restricted memory B cells dominate recall responses to heterologous flavivirus challenges. Immunity, 53(5):1078-1094. PMCID: PMC7677180

   c) Jash, A., Zhou, Y.W., Gerardo, D.K., Ripperger, T.J., Parikh, B.A., Piersma, S., Jamwal, D.R., Kiela, P.R., Boon, A.C.M., Yokoyama, W.M., Hsieh, C.S., & **Bhattacharya, D.** (2019). ZBTB32 restrains antibody responses to murine cytomegalovirus infections, but not other repetitive challenges. Scientific Reports, 9(1): 15257. PMCID: PMC6813321

   d) Purtha, W.E., Tedder, T.F., Johnson, S., **Bhattacharya, D.***, & Diamond, M.S.* (2011). Memory B cells, but not long-lived plasma cells possess antigen specificities for viral escape mutants. Journal of Experimental Medicine, 208(13), 2599-2606. PMCID: PMC3244041

2) My lab has identified several new metabolic and transcriptional regulators of B cell differentiation and immunity. We reported that specific metabolic pathways are different between and functionally distinguish short- from long-lived plasma cells—these were the first studies of their kind. We also reported two new BTB-POZ transcription factors that exert opposing effects on plasma cell lifespan. These studies defined the principal that plasma cell lifespan is imprinted early during B cell activation.

   a) Lam WY, Jash A, Yao C, D'Souza L, Wong R, Nunley RM, Meares GP, Patti GJ, & **Bhattacharya D.** (2018). Metabolic and Transcriptional Modules Independently Diversify Plasma Cell Lifespan and Function. Cell Reports, 24(9), 2479-2492. PMCID: PMC6172041

   b) Lam WY*, Becker AM*, Kennerly KM*, Wong R, Curtis JD, Payne EM, McCommis KS, Fahrmann J, Pizzato, HA, Nunley RM, Lee J, Wolfgang MJ, Patti GJ, Finck BN, Pearce EL, & **Bhattacharya D.** (2016). Mitochondrial pyruvate import promotes the long-term survival of antibody-secreting plasma cells. Immunity, 45(1), 60-73. PMCID: PMC4956536

   c) Jash, A., Wang, Y, Weisel, F.J., Scharer, C.D., Boss, J.M., Shlomchik, M.J., & **Bhattacharya, D.** (2016). Zbtb32 restricts the duration of memory B cell recall responses. Journal of Immunology, 197(4), 1159-1168. PMCID: PMC4975986

   d) Wang, Y. & **Bhattacharya, D.** (2014). Adjuvant-specific regulation of long-term antibody responses by ZBTB20. Journal of Experimental Medicine, 211(5), 841-856. PMCID: PMC4010912

3) Our work has also led to the identification of important cellular and molecular stages of early B cell and lymphoid development. Using a novel computational approach, we identified a marker that identifies the first B cell-committed precursor. Using these cellular stages we have described global transcriptional profiles during lymphoid commitment. Using these data, my lab demonstrated that IRF8 extinguishes neutrophil potential in both the myeloid and lymphoid arms of hematopoiesis. The latter work came from my independent lab, while the earlier work came from my experimental work as a postdoctoral fellow.

    a) Becker, A.M., Callahan, D.J., Richner, J.M., Choi, J., DiPersio, J.F., Diamond, M.S., and **Bhattacharya, D.** (2015). GPR18 controls reconstitution of mouse small intestine intraepithelial lymhocytes following bone marrow transplantation. PLoS One, 10(7), e0133854. PMCID: PMC4510063

    b) Becker, A.M., Walcheck, B., & **Bhattacharya, D.** (2015). ADAM17 limits the expression of CSF1R on murine hematopoietic progenitors. Experimental Hematology, 43(1), 44-52. PMCID: PMC4268392

    c) Becker, A.M., Michael, D.G., Satpathy, A., Sciammas, R., Singh, H., & **Bhattacharya, D.** (2012). IRF-8 extinguishes neutrophil potential and promotes dendritic cell lineage commitment in both myeloid and lymphoid mouse progenitors. Blood, 119(9), 2003-2012. PMCID: PMC3311244

    d) Inlay, M.A.*, **Bhattacharya, D.***, Sahoo, D., Serwold, T., Seita, J., Karsunky, H., Plevritis, S.K., Dill, D.L., & Weissman, I.L. (2009). Ly6d marks the earliest stage of B cell specification and identifies the branchpoint between B and T cell development. Genes & Development, 23(20), 2376-2381. PMCID: PMC2764492

4) My earlier work demonstrated dynamic interactions between hematopoietic stem cells and their bone marrow niches. This work established that hematopoietic stem cell transplantation is inefficient due to host niche occupancy, but that engraftment can be enhanced through antibody-mediated clearance of niches and by timed administration of donor cells to capitalize on constitutive host cell egress. I performed most of the experiments for this work during my postdoctoral period.

    a) **Bhattacharya, D.***, Czechowicz, A.*, Ooi, A.G., Rossi, D.J., Bryder, D., & Weissman, I.L. (2009). Niche recycling through division-independent egress of hematopoietic stem cells. Journal of Experimental Medicine, 206(12), 2837-2850. PMCID: PMC2806613

    b) Czechowicz, A., Kraft, D., Weissman, I.L.*, & **Bhattacharya, D.*** (2007). Efficient transplantation via antibody-based clearance of hematopoietic stem cell niches. Science, 318(5854), 1296-1299. PMCID: PMC2527021

    c) **Bhattacharya, D.***, Bryder, D.*, Rossi, D.J., & Weissman, I.L. (2006). Rapid lymphocyte reconstitution of unconditioned immunodeficient mice with non-self-renewing multipotent hematopoietic progenitors. Cell Cycle 2006, 5(11), 1135-1139. NIHMSID 705947

    d) **Bhattacharya, D.**, Rossi, D.J., Bryder, D., & Weissman, I.L. (2006). Purified hematopoietic stem cell engraftment of rare niches corrects severe lymphoid deficiencies in unconditioned hosts. Journal of Experimental Medicine, 203(1), 73-85. PMCID: PMC2118067

5) I performed a substantial amount of early work on optimization of retroviral vectors and delivery as a graduate student, leading to the first version of MSCV IRES GFP, a now ubiquitously used vector. This vector was used to optimize delivery to primary lymphocytes, and later to hematopoietic stem cells.

    a) Ranganath S, Ouyang W, **Bhattarcharya (sic) D**, Sha WC, Grupe A, Peltz G, Murphy KM. GATA-3-dependent enhancer activity in IL-4 gene regulation. (1998). Journal of Immunology, 161(8), 3822-3826. PMID: 9780146

    b) Ouyang W, Ranganath SH, Weindel K, **Bhattacharya D**, Murphy TL, Sha WC, Murphy KM. (1998). Inhibition of Th1 development mediated by GATA-3 through an IL-4-independent mechanism. Immunity, 9(5), 745-755. PMID: 9846495

c) **Bhattacharya D**, Logue EC, Bakkour S, Degregori J, Sha WC. (2002). Identification of gene function by cyclical packaging rescue of retroviral cDNA libraries. Proceedings of the National Academy of Sciences USA. 99(13), 8838-8843. PMCID: PMC124385

d) **Bhattacharya D**, Lee DU, Sha WC. (2002). NF-κB-mediated regulation of isotype switching: Retroviral expression of RelB specifically inhibits class switch recombination to IgG1, but not to IgE. International Immunology. 14(9), 983-991. PMID: 12202396

*equal contribution/co-corresponding author

Complete list of published work in MyBibliography
http://www.ncbi.nlm.nih.gov/sites/myncbi/deepta.bhattacharya.1/bibliography/40869667/public/?sort=date&direction=ascending

D. Research Support

ACTIVE

NIH/R01AI099108 09/24/12 – 11/30/22
Transcriptional regulation of antibody responses and immunity
The goal of this proposal is to identify and manipulate the molecular mechanisms that regulate both the duration and cross-reactivity of antibody responses after vaccination.
Role: PI

NIH/R01AI129945 12/13/17 – 11/30/22
Glucose and amino acid catabolism in plasma cell biology
The major goal of this project is to define how nutrient uptake controls antibody production and plasma cell lifespan.
Role: PI

44418/OPP1206188 11/15/18 – 05/14/23
Bill and Melinda Gates Foundation
Plasma cell therapies for infectious disease
The long-term goals of this research are 1) to generate minimally immunogenic pluripotent stem cells from which mature cell types can be provided to recipients without risk of rejection; and 2) to use these scalable and minimally immunogenic pluripotent stem cells to generate pathogen-specific plasma cells which confer protection against infectious disease.
Role: PI

JDRF/3-SRA-2020-895-S-B 02/01/20 – 01/31/22
Juvenile Diabetes Research Foundation
Overcoming Immune Barriers to Stem Cell-Derived Beta Cell Transplantation
The goal of this research is to define and eliminate immune barriers to pluripotent stem cell-derived beta cell transplantation for type 1 diabetes.
Role: co-I

COMPLETED

NIH/R21AI132910-01 12/22/17 – 11/30/20
Pluripotent stem cell-based immunotherapies
The major goal of this project is to differentiate human pluripotent stem cells into universally transplantable long-lived plasma cells.
Role: PI