BIOGRAPHICAL SKETCH

NAME: Ali Ellebedy

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

POSITION TITLE: Professor

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
Cairo University, Egypt	B.Sc.	05/2004	Pharmaceutical Sciences
University of Tennessee Health Science Center	Ph.D.	05/2011	Virology/Immunology
Emory University	Postdoctoral fellow	06/2017	Immunology

A. Personal Statement

I am a viral immunologist with 16 years of experience studying murine and human B cell responses to viral infections and vaccination. Over the past ten years, I have been directly involved in the design and execution of over 20 vaccination studies in humans. I was the study PI of half of these studies. The focus of my research has been on viral pathogens, including seasonal and avian influenza, Ebola, Lassa, Chikungunya, and SARS-CoV-2. I have unique expertise in the evaluation of B cell and antibody responses to vaccination that will guarantee the successful completion of the goals of this application.

The ability of B cells to expand and differentiate into memory B and long-lived plasma cells in response to antigenic stimulation underlies the success of most vaccines currently in use. We still do not have a thorough understanding of what controls the generation, heterogeneity, and longevity of vaccine-induced B cell responses. Such understanding will be key in our quest to develop vaccines that elicit broadly protective and durable immune responses against rapidly evolving pathogens, such as influenza and SARS-CoV-2 viruses. Our laboratory uses a combination of genetic, biochemical, and computational approaches to track B cell differentiation longitudinally in humans. More recently, we started complementing these analyses with the functional interrogation of the transcriptional determinants of vaccine-induced B cell differentiation and persistence in mouse models.

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2023-Pres Leo Loeb Professor, Dept. of Pathology and Immunology, Washington University School of Medicine, St. Louis, MO USA

2021-2023 Associate Professor, Dept. of Pathology and Immunology, Washington University School of Medicine, St. Louis, MO USA

2018-2020 Mucosal Immunology Studies Team (MIST) Young Scholar

2017-2021 Assistant Professor, Dept. of Pathology and Immunology, Washington University School of Medicine, St. Louis, MO USA

2016-2017 Senior Research Associate, Emory University, Atlanta, GA, USA

2014-2017 Edward Jenner Vaccine Society Young Investigator

2011-2016 Post-doctoral Research Fellow, Emory University, Atlanta, GA, USA

2006-2011 Research Assistant, University of Tennessee Health Science Center, Memphis, TN, USA

2004-2006 Teaching and Research Assistant, Department of Microbiology and Immunology, Cairo University, Egypt

C. Contributions to Science (* Co-corresponding authors) (Investigators participating in this proposal are identified in blue):

1) Defining the specificity, phenotype and transcriptional program of human B cell responses after viral infections and vaccination:

I defined the phenotype and transcriptional program of an antigen-specific B cell subset that I termed activated B cells (ABCs). I showed that these cells are distinct from the terminally differentiated plasmablasts (PBs) and are committed to the memory B cell lineage. I showed that ABCs were detected in humans after infection with either Ebola or influenza viruses and after seasonal and avian influenza virus vaccination. Simultaneously analyzing antigen-specific PBs (effector) and ABCs (memory) allowed us to address some of the fundamental questions regarding the differentiation, maturation, and longevity of B cell responses.

a) Ellebedy AH, Jackson KJ, Kissick HT, Nakaya HI, Davis CW, Roskin KM, McElroy AK, Oshansky CM, Elbein R, Thomas S, Lyon GM, Spiropoulou CF, Mehta AK, Thomas PG, Boyd SD, Ahmed R.. "Defining antigen specific plasmablast and memory B cell subsets in blood following viral infection and vaccination of humans." **Nat Immunol**. 2016;17(10):1226-34. PMCID:PMC5054979

b) Ellebedy AH, Nachbagauer R, Jackson KJL, Dai YN, Han J, Alsoussi WB, Davis CW, Stadlbauer D, Rouphael N, Chromikova V, McCausland M, Chang CY, Cortese M, Bower M, Chennareddy C, Schmitz AJ, Zarnitsyna VI, Lai L, Rajabhathor A, Kazemian C, Antia R, Mulligan MJ, Ward AB, Fremont DH, Boyd SD, Pulendran B, Krammer F, Ahmed R.. "Adjuvanted H5N1 influenza vaccine enhances both cross-reactive memory B cell and strain-specific naive B cell responses in humans." **Proc Natl Acad Sci U S A**. 2020;117(30):17957-17964. PMCID: PMC7395544

c) Amanat F, Thapa M, Lei T, Ahmed SMS, Adelsberg DC, Carreno JM, Strohmeier S, Schmitz AJ, Zafar S, Zhou JQ, Rijnink W, Alshammary H, Borcherding N, Reiche AG, Srivastava K, Sordillo EM, van Bakel H; Personalized Virology Initiative, Turner JS, Bajic G*, Simon V*, Ellebedy AH*, Krammer F*. "SARS-CoV-2 mRNA vaccination induces functionally diverse antibodies to NTD, RBD, and S2." **Cell**. 2021;184(15):3936-3948.e10. PMCID: PMC8185186

2) Defining the dynamics of germinal center and long-lived bone marrow plasma cells responses in humans:

Our laboratory has pioneered the use of fine needle aspiration (FNA) of draining lymph nodes to study germinal center (GC) B cell responses in humans. We defined the dynamics and specificity of GC B cell responses after intramuscular injection of seasonal influenza virus split vaccines and SARS-CoV-2 mRNA vaccines in humans. We demonstrated that both vaccinations could elicit a GC reaction that recruits pre-existing, cross-reactive memory B cells as well as novel B cell clones that can target new epitopes, thereby broadening the spectrum of vaccine-induced protective antibodies. We have also tracked the fate of these GC B cell clones as they terminally differentiated into long-lived bone marrow plasma cells.

a) Turner JS, Zhou JQ, Han J, Schmitz AJ, Rizk AA, Alsoussi WB, Lei T, Amor M, McIntire KM, Meade P, Strohmeier S, Brent RI, Richey ST, Haile A, Yang YR, Klebert MK, Suessen T, Teefey S, Presti RM, Krammer F, Kleinstein SH, Ward AB, Ellebedy AH. Human germinal centres engage memory and naive B cells after influenza vaccination. **Nature** 2020 Oct;586(7827):127-132. PMCID: PMC7566073

b) Turner JS, Kim W, Kalaidina E, Goss C, Rauseo A, Schmitz A, Hansen L, Haile A, Klebert M, Pusic I, O'Halloran J, Presti R, Ellebedy AH. SARS-CoV-2 infection induces long-lived bone marrow plasma cells in humans. **Nature.** Jul;595(7867):421-425. PMID: 34030176

c) Turner JS, O'Halloran JA, Kalaidina E, Kim W, Schmitz AJ, Zhou JQ, Lei T, Thapa M, Chen RE, Case JB, Amanat F, Rauseo AM, Haile A, Xie X, Klebert MK, Suessen T, Middleton WD, Shi PY, Krammer F, Teefey SA, Diamond MS, Presti RM*, Ellebedy AH. SARS-CoV-2 mRNA vaccines induce persistent human germinal centre responses. **Nature**. 2021 Aug;596(7870):109-113. PMCID: PMC8935394

d) Kim W, Zhou JQ, Horvath SC, Schmitz AJ, Sturtz AJ, Lei T, Liu Z, Kalaidina E, Thapa M, Alsoussi WB, Haile A, Klebert MK, Suessen T, Parra-Rodriguez L, Mudd PA, Whelan SPJ, Middleton WD, Teefey

SA, Pusic I, O'Halloran JA, Presti RM, Turner JS, Ellebedy AH. Germinal centre-driven maturation of B cell response to mRNA vaccination. **Nature**. 2022 Apr;604(7904):141-145. PMCID: PMC9204750

3) Developing broadly cross-reactive monoclonal antibodies against seasonal, pre-pandemic, and pandemic viral infections:

In a series of studies, our laboratory has generated and fully characterized murine and human recombinant monoclonal antibodies against the H1 HA of the 2009 pandemic H1N1 influenza virus, the NA of all seasonal influenza viruses, and the spike protein of SARS-CoV-2. These antibodies are being developed as potent therapeutics and have also informed the design of better vaccines against these pathogens.

a) Nachbagauer R, Shore D, Yang H, Johnson SK, Gabbard JD, Tompkins SM, Wrammert J, Wilson PC, Stevens J, Ahmed R, Krammer F, Ellebedy AH. Broadly Reactive Human Monoclonal Antibodies Elicited following Pandemic H1N1 Influenza Virus Exposure Protect Mice against Highly Pathogenic H5N1 Challenge. **J Virol**. 2018;92(16):e00949-18. PMCID: PMC6069173

b) Stadlbauer D, Zhu X, McMahon M, Turner JS, Wohlbold TJ, Schmitz AJ, Strohmeier S, Yu W, Nachbagauer R, Mudd PA, Wilson IA*, Ellebedy AH*, Krammer F*. Broadly protective human antibodies that target the active site of influenza virus neuraminidase. **Science**. 2019;366(6464):499-504. PMCID: PMC7105897

c) Alsoussi WB, Turner JS, Case JB, Zhao H, Schmitz AJ, Zhou JQ, Chen RE, Lei T, Rizk AA, McIntire KM, Winkler ES, Fox JM, Kafai NM, Thackray LB, Hassan AO, Amanat F, Krammer F, Watson CT, Kleinstein SH, Fremont DH, Diamond MS, Ellebedy AH. A Potently Neutralizing Antibody Protects Mice against SARS-CoV-2 Infection. **J Immunol**. 2020 Aug 15;205(4):915-922. PMCID: PMC7566074

d) Schmitz AJ, Turner JS, Liu Z, Zhou JQ, Aziati ID, Chen RE, Joshi A, Bricker TL, Darling TL, Adelsberg DC, Altomare CG, Alsoussi WB, Case JB, VanBlargan LA, Lei T, Thapa M, Amanat F, Jeevan T, Fabrizio T, O'Halloran JA, Shi PY, Presti RM, Webby RJ, Krammer F, Whelan SPJ, Bajic G, Diamond MS, Boon ACM*****, Ellebedy AH*. A vaccine-induced public antibody protects against SARS-CoV-2 and emerging variants. **Immunity**. 2021 Sep 14;54(9):2159-2166.e6. PMCID: PMC8010723

Complete List of Published Work can be found in MyBibliography (>60 peer-reviewed publications plus several pre-prints on different aspects of SARS-CoV-2 biology and immunology at the time of submission of this proposal): https://www.ncbi.nlm.nih.gov/pubmed/?term=Ellebedy+A