



# nAb scientific summit: Thursday, August 20, 2020

**12:30** Introductions and learnings from plasma by Dr. Collins and Dr. Woodcock

**1:00** **Topic presentation and discussion: Safety - Antibody-dependent enhancement**

- Discuss lessons learned on ADE based enhanced respiratory disease from previous therapeutics
- Review potential implications for COVID-19 nAbs
- Review ADE screening and monitoring process for COVID-19 nAb development (for neutralizing and non-neutralizing antibodies that might contribute to ADE)

**1:35** **Coffee break**

**1:45** **Topic presentation and discussion: Safety – Epitope binding and viral resistance**

- Discuss whether epitope binding sites or combinations of site predict therapeutic efficacy
- Discuss range of epitopes being targeted by nAbs and likelihood of viral resistance based on epitope conservation and use of cocktail vs. single nAb

**2:20** **Topic presentation and discussion: Efficacy – Effector function & antibody optimization**

- Review mutations being explored to increase half-life or effector function (e.g. YTE, LS) and any initial efficacy/safety data from animal studies
- Discuss potential impact of mutations on Fc-mediated antibody effector functions and use of Fc region to specify and optimize immune response
- Discuss optimization of antibodies to support manufacturability

**2:55** **Topic presentation and discussion: Efficacy – Learnings form other fields**

- Discuss lessons learned from nAb development and efficacy results from flu, Ebola and HIV
- Discuss lessons learned and implications for prevention and vaccine development

**3:20** **Coffee break**

**3:30** **Topic presentation and discussion: Assay development – assay standardization**

- Discuss in vitro and in vivo screening characteristics that predict efficacy and safety
- Discuss process for screening for combinatorial nAb candidates and indicators of optimal nAb combinations

**4:05** **Closing remarks**

# Antibody-dependent enhancement

## WHITE PAPER AUTHOR



### Barney Graham

M.D., Ph.D., Deputy Director of the Vaccine Research Center and the Chief of the Viral Pathogenesis Laboratory (NIAID/VRC)

- Dr. Graham's primary interests are vaccine development for viral diseases, viral pathogenesis, mechanisms of immunity and pandemic preparedness
- His laboratory has developed novel vaccines for RSV, influenza, Zika, and coronaviruses including the first Covid-19 vaccine and monoclonal antibody products to enter clinical testing

## MODERATOR



### Ann M. Arvin

M.D., Professor of Pediatrics and Microbiology & Immunology, Stanford University and Chief of Infectious Diseases at the Packard Children's Hospital

- Research focuses on the molecular virology of varicella-zoster virus, immune responses of children to viral infections and vaccines and herpes viruses in pregnancy
- Committee service includes National Vaccine Advisory Committee; chair, WHO Committee on Measles Vaccine Research; NIAID and PCAST Influenza Working Groups; member, National Academy of Medicine; American Academy of Arts & Sciences

## PANELISTS



### Mark Esser

Ph.D, Vice President of Microbial Sciences at AstraZeneca

- Leads drug discovery, translational research and clinical dev't of innovative medicines targeting microbiome and in vivo expressed biologics
- Immunologist with experience in clinical development for Vx, T cell therapy, biomarkers and diagnostics



### Amanda Peppercorn

M.D., Medicine Development Leader, R&D at GlaxoSmithKline

- Dr. Peppercorn has worked in all phases of development and infectious diseases strategy at GSK
- Leader in development of biomedical countermeasures following dev't of IV zanamivir for pandemic/severe flu, raxibacumab for anthrax, & antibiotics for multi-drug resistant bacteria
- Significant experience in development and execution of Phase 2/3 trials



### Jeffrey Ravetch

M.D., Ph.D., Professor at Rockefeller University

- Head of Leonard Wagner Lab of Molecular Genetics and Immunology
- Acting as scientific advisor to Vir
- Studies at his lab, The Ravetch Lab, focus on the interactions between antibodies and immune cells' Fc receptors to better understand and treat disease



### Takashi Komatsu

Ph.D, Senior Clinical Virology Reviewer at FDA CDER

- Reviews nonclinical and clinical virology data and clinical trial protocols for antiviral drugs
- Actively involved in the establishment of FDA policies and guidance on antiviral drug development

# Epitope binding and viral resistance

## WHITE PAPER AUTHOR



### Paul Bieniasz

Ph.D., Professor and Head of the Laboratory of Retrovirology at Rockefeller University and Howard Hughes Medical Institute Investigator

- His research explores virus-host interactions in a variety of viral systems, but with a major focus on HIV-1 replication in individual cells and animal models
- His lab works on both innate and adaptive antiviral immunity and has discovered a number of novel mechanisms by which hosts defend themselves against viruses
- Acted as Chair of the NIH AIDS Molecular and Cellular Biology study section from 2004 to 2009 and served on the NCI Board of Scientific Counselors from 2010 to 2014, Currently serves on the NIAID AIDS Research Advisory Committee

## MODERATOR



### David Ho

M.D., Director of Aaron Diamond AIDS Research Center and Clyde and Helen Wu Professor of Medicine at Columbia University

- HIV/AIDS researcher who has made many scientific contributions to the understanding and treatment of HIV infection
- Dr. Ho's group has engineered potent antibodies that neutralize divergent strains of HIV. The most promising neutralizing agent is a bispecific monoclonal antibody that entered a first-in-human clinical trial in 2019
- Isolated and characterized a large panel of potent and diverse monoclonal antibodies that neutralize SARS-CoV-2

## PANELISTS



### Alina Baum

Ph.D., Senior Staff Scientist at Regeneron

- Leads the COVID-19 spike antibody program currently in clinical trials.
- Leads a virology research group developing novel Tx for viral infections including influenza and hepatitis B, emerging pathogens such as Ebola and SARS-CoV-2, as well as the development of oncolytic viruses and Vx for cancer immunotherapy



### Katharine J. Bar

M.D., Assistant Professor of Medicine and Director of the CFAR Virus and Reservoirs Core at UPenn

- Research focuses on studying the basic mechanisms of transmission, pathogenesis and persistence in HIV and other chronic viral infections
- Serves as PI, co-PI or Investigator on HIV broadly nAb clinical trials for HIV therapy, cure and prevention
- Serves as co



### Ed Scolnick

M.D., Core Member of Broad Institute, Chief Scientist Emeritus at Stanley Center and Professor of Biology at MIT

- Previously served as President of Merck Research Laboratories, where he helped develop 28 drugs and Vx, with 7 safe and effective Vx approved
- Current research focus is on mental illness, e.g., bipolar disorder
- Also holds an academic appointment at MIT as a Professor in the Department of Biology



### MAJ Jeff Kugelman

Ph.D, Head of the Center for Genome Sciences at the U.S. Army Medical Research Institute of Infectious Diseases

- Biodefense viral geneticist and computational biologist
- Interests include outbreak response, viral population genetics, and epitope mapping
- Set up genomics lab at Liberian Institute for Biomedical Research to characterize Ebola viral genomes, assess for diagnostic and Tx targets and characterize sexual transmission of Ebola

# Antibody optimization and effector function

## WHITE PAPER AUTHOR



### Galit Alter

Ph.D., Professor of Medicine at Harvard Medical School, Group Leader at the Ragon Institute of MGH, MIT and Harvard and Co-Director of the Harvard University Center for AIDS Research (CFAR)

- Dr. Alter's work focuses on the development of systems biology tools to define the correlates of immunity against infectious diseases. She seeks to define the role of innate immune recruiting antibodies in providing specificity to the innate immune system to kill virally infected cells
- Has developed a suite of antibody profiling assays, deemed Systems Serology, that aims at gaining a deeper appreciation of the correlates of humoral immune activity against HIV, tuberculosis, malaria and beyond

## MODERATOR



### Michel Nussenzweig

M.D., Ph.D., Zanvil A. Cohn and Ralph M. Steinman Professor and a senior physician at the Rockefeller University.

- Studies molecular aspects of the immune system's adaptive and innate responses, using a combination of biochemistry, molecular biology, and genetics
- Focus of the Nussenzweig laboratory is to understand the development of effective antibody responses with the ultimate goal of learning how to elicit vaccine responses against complex pathogens such as HIV-1
- Member of US National Academy of Medicine and US National Academy of Sciences

## PANELISTS



### Dan Barouch

M.D., Ph.D., Professor of Medicine and Immunology at Harvard

- Also Director of the Center for Virology and Vaccine Research at Beth Israel Deaconess Medical Center and member of the Ragon Institute
- Lab focuses on studying immunology and virology of HIV-1 infection and developing novel vaccine strategies
- Group has also applied their Vx expertise to preclinical and clinical studies of other infectious diseases



### Christos Kyratsous

Ph.D., VP of Research - Infectious Diseases and Viral Vector Technologies at Regeneron

- Oversees preclinical research into a diverse portfolio of anti-pathogen fully-human monoclonal antibodies and novel gene and cell therapies
- Focuses on designing drugs for viral pathogens, used to develop REGN-EB3 for Ebola, and now has informed Regeneron's efforts to develop novel antibodies against Covid-19



### Randal Ketchem

Ph.D., Vice President of Molecular Design at Just Biotherapeutics

- Extensive experience in Tx design with particular experience in antibody design, analysis, and optimization for efficacy, half life and developability
- Has directed and completed projects in Tx development pipelines at Immunex, Amgen, and Just Biotherapeutics and Just - Evotec Biologics



### Danilo Casimiro

Ph.D., Vice President & Head of Global Research and External Innovation at Sanofi Pasteur

- Responsible for vaccine research and search-and-evaluation function for Vx opportunities, with 20+ years of experience in R&D of Vx and biologics
- Contributed to development and licensure of Merck's HPV vaccine, and selection of numerous Vx candidates and monoclonal antibodies for clinical development

# Lessons from other fields

## WHITE PAPER AUTHOR



### Dennis Burton

Chair of the Department of Immunology and Microbiology at Scripps Research and Steering Committee Member of the Ragon Institute

- Also acts as Director of the NIH Consortium for HIV Vaccine Development (CHAVD) and Scientific Director of the IAVI Neutralizing Antibody Center (NAZ)
- Pioneered the discovery and characterization of human neutralizing antibodies to viruses, particularly broadly neutralizing antibodies to HIV and HCV, but also to RSV and Ebola virus, and the use of such antibodies to facilitate rational HIV vaccine design

## MODERATOR



### Jorge Tavel

M.D., Senior Group Medical Director in Early Clinical Development at Genentech

- Has led the development and execution of first in human and proof of concept clinical trials for multiple antimicrobial programs
- Prior to joining Genentech, served as Deputy Director, Division of Clinical Research at the National Institutes of Health
- Previously responsible for strategy and protocol designs for studies in patient populations who failed standard-of-care HCV therapy and for HIV/HCV co-infected patient

## PANELISTS



### Shelly Krebs

Chief of B cell Biology, Military HIV Research Program, WRAIR

- Antibody research focuses on learning how HIV-positive individuals develop potent antibody responses, using those insights to inform HIV Vx strategies
- Recently has focused on effects of Zika Vx in flavivirus-endemic populations to elicit cross-reactive ab responses
- Lab section has pivoted to developing ab products for SARS-Cov-2 virus to help detect, prevent and treat coronavirus



### James Crowe

Director of Vanderbilt Vaccine Center and Professor of Pediatrics and Pathology

- His laboratory has a broad portfolio of work in the area of viral immunology and antibody sciences, with the goal to discover mechanisms of immunity important to developing new therapeutics and vaccines
- Founder of IDBiologics, an early stage biotech company, developing human mAbs for infectious diseases



### Jonathan Abraham

M.D., Ph.D., Assistant Professor, Department of Microbiology at Harvard Medical School

- Work focuses on developing ab-based Tx to treat emerging viral infections
- Co-leads the Therapeutics Working Group of the Massachusetts Consortium on Pathogen Readiness which conducts research that involves isolating abs from convalescing individuals to determine how these abs work against SARS-CoV-2's spike protein



### Yunda Huang

Ph.D., Principal Staff Scientist at Fred Hutchinson and Affiliate Associate Professor, University of Washington

- Research focuses on:
- Statistical design and analysis of Vx and mAb clinical trials related to the prevention and/or treatment of HIV and other infectious diseases
- Development of statistical methods for analyses of Vx-induced immune responses, and HIV mAb PK/PD
- Design and analysis of assay qualification/validation

# Assay standardization

## WHITE PAPER AUTHOR



**Erica Ollmann Saphire**

Ph.D., Professor of the La Jolla Institute for Immunology

- Research focuses on explaining at the molecular level, how and why viruses are pathogenic and providing the 3D roadmap for medical defense
- Dr. Saphire's team has conducted extensive research and solved the structures of the Ebola, Sudan, Marburg, Bundibugyo and Lassa virus glycoproteins, explaining where human abs can defeat these viruses, and what ab features correlate with protection
- Currently leads a Bill & Melinda Gates Foundation- and NIAID-supported consortium to evaluate antibody therapeutics against SARS-CoV-2 to prevent and treat COVID-19

## MODERATOR



**John Dye**

Ph.D., Chief of Viral Immunology at U.S. Army Medical Research Institute of Infectious Diseases

- Oversees the execution of research programs to develop medical countermeasures against highly pathogenic viruses of military importance that are studied in Biosafety Level 3 and Level 4 containment laboratories
- Research focuses on filovirus vaccines and therapeutics, with the ultimate aim of counteracting the Ebola virus and other related viruses
- Has led teams to track immune response in hundreds of survivors of high-risk pathogens, determining an "immune profile" to drive Vx and Tx development

## PANELISTS



**Holly Soares**

Ph.D., Vice President and Head of Precision Medicine at Pfizer

- Her group supports biomarker strategies for proof of mechanism, early signs of efficacy and patient stratification
- Previously has led translational medicine groups at Pfizer, BMS and Abbvie
- Has chaired fNIH public private scientific boards and has authored 100+ publications



**Bette Korber**

Ph.d., Laboratory Fellow and Scientist Level 6 at the Los Alamos National Laboratory

- Heads the HIV sequence and immunology database project ([www.hiv.lanl.gov](http://www.hiv.lanl.gov)) and the new Covid-19 analysis pipeline project ([www.cov.lanl.gov](http://www.cov.lanl.gov))
- Leads an interdisciplinary team that provides bioinformatics, theoretical, and statistical support, focusing on viral diversity and the human immune response to infection



**Steven Kozlowski**

M.D., Director of Office of Biotechnology Products (OBP) in OBQ at CDER/FDA

- His office is responsible for the quality review of monoclonal antibodies and most therapeutic proteins at CDER
- Has been involved in all phases of the regulatory process from pre-IND product development through licensing and post-approval supplements
- Has a background in immunology and has been involved in manufacturing initiatives to advance quality



**Hendrik Neubert**

Ph.D, Senior Director of Biomedicine Design at Pfizer

- Leads a translational biometrics and protein biomarkers group across several disease areas
- Has developed biomarker assays based on mass spectrometry and flow cytometry to enable mechanistic PK/PD and PBPK modeling