BIOGRAPHICAL SKETCH

NAME: **James E. Crowe, Jr., M.D.**

eRA COMMONS USER NAME: **croweje**

TITLE: **Ann Scott Carell Chair; Prof. of Peds, Path/Micro/Immunol; Director, Vanderbilt Vaccine Center**

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Davidson College, Davidson, NC	B.S.	05/1983	Premedicine
University of NC School of Medicine, Chapel Hill, NC	M.D.	05/1987	Medicine
University of NC School of Medicine, Chapel Hill, NC	Residency	06/1990	Pediatrics
National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD	Postdoc	10/1995	Virology, Vaccines
Vanderbilt University Medical Center, Nashville, TN	Fellowship	10/1996	Ped. Infectious Dis.

A. Personal Statement. I have 26 years of experience in basic research of virology and immunology, especially antiviral antibodies. Most of the current work in my laboratory is focused on virus neutralization by antibodies. My laboratory has made seminal contributions in the area of development of human neutralizing antibodies to microbial pathogens. We have been one of the leading groups in development of innovative technologies for isolation and study of human monoclonal antibodies. Our group has isolated human monoclonal antibodies that neutralize Zika virus, HIV, chikungunya virus, dengue virus, human metapneumovirus, influenza virus, Marburg and Ebola viruses, norovirus, respiratory syncytial virus, Rift Valley fever virus, rotavirus, and others. I have a wealth of experience directing and working in multi-investigator groups to study human immune responses to virus infection or vaccines. My laboratory has continually conducted experiments to further develop new methods for antibody engineering and molecular recognition studies. Five of our antibody portfolios have been licensed out to commercial partners for ongoing clinical development. My group is expert in nextgen immune repertoire deep sequencing analysis. For example, we are executing the **HUMAN IMMUNOME PROJECT**, the largest human genetic sequencing effort to date, in which we are determining the complete sequences of BCRs/TCRs in 40 billion PBMCs for each of 1,000 subjects. I have directed successfully a large number of multi-investigator programs.

B. Positions and Honors

Positions and Employment

1993-1995	Senior Research Investigator, RVS, LID, NIAID, NIH, Bethesda, MD
1995-1996	Instructor in Pediatrics, Div. of Pediatric Inf. Dis., Vanderbilt Univ. Med. Ctr. (VUMC)
1996-2001	Assistant Professor, Pediatrics, Microbiology and Immunology, Vanderbilt
2001-2004	Associate Professor, Pediatrics, Microbiology and Immunology, Vanderbilt
2001-present	Scientific Director, Flow Cytometry Core Laboratory, Vanderbilt
2003-present	Scientific Director, Human Immunology Core Laboratory, Vanderbilt
2004-present	Director, Vanderbilt Alliance for Nanomedicine (VUMC and Oak Ridge National Laboratory)
2004-present	Professor, Pediatrics, Pediatrics, Pathology, Microbiology and Immunology, Vanderbilt
2005-present	Director, Vanderbilt Vaccine Center
2012-present	Director, Vanderbilt Technologies for Advanced Genomics
2005-2013	Ingram Professor of Research, Vanderbilt (endowed chair)
2013-present	Ann Scott Carell Chair, Vanderbilt (endowed chair)

Honors

1996	Pfizer New Faculty Award
1998	Basil O'Connor Research Scholar, March of Dimes Foundation
1999	Dade Microscan Young Investigator Award, American Society of Microbiology
2000	Young Investigator Award, Pediatric Infectious Diseases Society
2001	Young Investigator Award, Society of Pediatric Research

2002 Judson Daland Prize, American Philosophical Society
2004 American Society for Clinical Investigation
2005 Oswald Avery Award, Infectious Diseases Society of America
2006 E. Mead Johnson Award, Society for Pediatric Research
2007 Outstanding Investigator Award, American Federation for Medical Research
2007 F. Peter Guengerich Award for Mentoring Postdoctoral Fellows, Vanderbilt University
2007 Ernest W. Goodpasture Faculty Research Award, Vanderbilt University
2007 Chancellor's Faculty Research Award, Vanderbilt University
2007 Fellow, Infectious Diseases Society of America
2009 American Association of Physicians
2010 Norman Siegel New Member Outstanding Sci. Award, American Pediatric Society
2010 Fellow, American Association for the Advancement of Science
2010 Fellow, American Academy of Microbiology
2012 Mentor of the Year, Vanderbilt Postdoctoral Association
2014 National Academy of Medicine, Elected Member
2016 John H. Exton Award for Research Leading to Innovative Biological Concepts, Vanderbilt
2017 Samuel Rosenthal Prize for Excellence in Academic Pediatrics, Samuel Rosenthal Fdn.
2017 Stanley J. Korsmeyer Award, American Society for Clinical Investigation

NIH Study sections: *Ad hoc* 29 separate NIH study sections, chair of three; MIDRC member 2004-2008.

C. Contributions to Science

Immunity to emerging viruses. In the last several years, we have studied antibody-mediated immunity to a wide variety of agents of bioterror and emerging infectious diseases, including chikungunya virus, dengue viruses, filoviruses (Ebola and Marburg), poxviruses (vaccinia, cowpox, monkeypox, variola), Rift Valley fever virus and others. The goal of these studies is to define the major molecular mechanisms of inhibition of these microbes by naturally-occurring antibodies from human survivors. This work is significant because of the variety of types of structural determinants and mechanisms of inhibition that we have discovered. A central theme of this work has been the recurring finding that neutralizing antibodies often recognize very complex and sometimes dynamic quaternary structures on the surface of viral particles that are challenging to recapitulate in any subunit or recombinant vaccine strategy. Thus, this work has informed vaccine design and testing. For example, many of the antibodies we have described have been licensed by major vaccine companies to characterize their vaccine candidates or release lots, to confirm that the vaccines retain the critical neutralizing determinants. I am listed as inventor or co-inventor on a large number of patents describing antibodies for emerging infectious diseases.

- Flyak, AI, Ilinykh PA, Murin CD, Garron T, Shen X, Fusco ML, Hashiguchi T, Bornholdht ZA, Slaughter JC, Sapparapu G, Ksiazek TG, Ward AB, Ollmann Saphire E, Bukreyev A, **Crowe JE Jr.** Mechanism of human antibody-mediated neutralization of Marburg virus. ***Cell*** 2015; 160: 893 – 903. PMC ID 4344968. *Journal cover*. Also: ***Cell*** 2015; 160: 904 – 912. PMC ID 4344967.
- Fibriansah G, Ibarra KD, Ng T-S, Smith SA, Tan JL, Lim X-N, Ooi JSG, Kostyuchenko VA, Wang J, de Silva AM, Harris E, **Crowe JE Jr***, Lok S-M*. CryoEM structure shows antibody neutralizes dengue virus serotype 2 by locking E protein dimers. ***Science*** 2015; 349: 88-91. PMC ID 26138979.
- Flyak AI, Shen X, Murin CD, Turner HL, David JA, Fusco ML, Lampley R, Kose N, Ilinykh PA, Kuzmina N, Branchizio A, King H, Brown L, Bryan C, Davidson E, Doranz BJ, Slaughter JC, Sapparapu G, Klages C, Ksiazek TG, Saphire EO, Ward AB, Bukreyev A, **Crowe JE Jr.** Cross-reactive and potent neutralizing antibody responses in human survivors of natural Ebolavirus infection. ***Cell*** 2016***;*** 164:392-405. PMC ID 4733404.
- Gilchuk I, Gilchuk P, Sapparapu G, Lampley R, Singh V, Kose N, Blum DL, Hughes-Baker LJ, Panayampalli SS, Townsend M, Kondas A, Reed Z, Weiner Z OlsonV, Hammarlund E, Raue H-P, Slifka MK, Slaughter JC, Graham BS, Edwards KM, Eisenberg RJ, Cohen GH, Joyce S, **Crowe JE Jr.** Cross-neutralizing and protective antibody specificities of the human B cell response to poxvirus infections. ***Cell*** 2016; 167:684-694. PMC ID 5093772.

- Sapparapu G, Fernandez E, Kose N, Cao B, Fox JM, Bombardi RG, Zhao H, Nelson CA, Bryan AL, Trevor Barnes, Davidson E, Mysorekar IU, Fremont DH, Doran BJ, Diamond MS, **Crowe JE Jr.** Neutralizing human antibodies prevent Zika virus replication and fetal disease in mice. ***Nature*** 2016; 540:443-447. PMID 27819683. PMC in Process.

Immunity to respiratory viruses (influenza, RSV, MPV). We have elucidated the genetic and structural basis for antibody-mediated neutralization of the major human respiratory viruses. Our work on the isolation and characterization of human monoclonal antibodies to influenza HA and RSV and MPV fusion proteins has defined canonical modes of recognition of these major antigenic targets. We also performed some of the critical epidemiology studies in the field (for ex. MPV, ***NEJM*** 2004; 350: 443-50, cited 825 times). I have generated a large number of live attenuated RSV vaccine candidates, five of which have been tested in Phase I or II clinical trials in humans. I am listed as inventor or co-inventor on over a dozen families of patents on respiratory virus vaccines and antibodies.

- Yu X, Tsibane T, McGraw PA, House F, Keefer CJ, Tumpey T, Pappas C, Perrone, Martinez O, Stevens J, Wilson I, Aguilar, Altschuler E, Basler C, **Crowe JE Jr.** Neutralizing antibodies derived from the B cells of 1918 influenza pandemic survivors, ***Nature*** 2008; 455:532-536. PMC ID: 2848880.
- Xu R, Ekiert DC, Krause JC, Palese P, **Crowe JE Jr**, Wilson IA. Structural basis of pre-existing immunity to the 2009 H1N1 pandemic influenza virus. ***Science*** 2010; 328:357-60. PMC ID: 2897825.
- Thornburg NJ, Zhang H, Bangaru S, Sapparapu G, Kose N, Lampley RM, Bombardi RG, Yu Y, Graham S, Branchizio A, Yoder SM, Rock MT, Creech CB, Edwards KM, Lee D, Li S, Wilson IA, García-Sastre A, Albrecht RA, Crowe JE Jr. H7N9 influenza virus neutralizing antibodies that possess few somatic mutations. ***Journal of Clinical Investigation*** 2016; 126:1482-94. PMC ID: 4811156.
- Thornburg NJ, Blum DL, Belser JA, Tumpey TM, Desphande S, Fritz GA, Krause JC, Winarski KL, Spiller BW, Nannemann DP, Meiler J, **Crowe JE Jr**. Human antibodies that neutralize respiratory droplet transmissible H5N1 influenza viruses. ***Journal of Clinical Investigation*** 2013; 123:4405-9. PMC ID: 3784541.
- Mousa JJ, Sauer MF, SevyAM, Finn JA, Bates JT, Alvarado G, King HG, Loerinc LB. Fong RH, Doranz BJ, Correia B, Kalyuzhniy O, Wen X, Jardetzky TS, Schief WR, Ohi MD, Meiler J, **Crowe JE Jr.** Structural basis for human antibody neutralization of respiratory syncytial virus at antigenic site II. ***Proceedings of the National Academy of Sciences USA*** 2016;113: E6849-E6858. PMC ID: 5098655.

Computational immunology. One of the long-term goals of the work focused on discovering the structural basis of virus neutralization is to move the vaccine design field away from empiricism and toward a new paradigm of rational vaccine development based on structure-based design ("reverse vaccinology"). We have made great strides in recent years to integrate our structural and functional information into predictive models using computational platforms. This work, mostly in collaboration with computational scientists in the ROSETTA community, has led to the first real success in reverse vaccinology with an RSV F vaccine candidate. We also have learned how to design optimal antibody structures, for example our recent redesign of HIV neutralizing antibodies with long antibody HCDR3 loops to achieve increased breadth and potency of neutralization based on enhancing antibody thermodynamic stability.

- Correia BE, John T. Bates JT, Loomis RJ, Baneyx G, Jardine JG, Rupert P, Carrico C, Correnti C, Kalyuzhniy O, Vittal V, Connell MJ, Stevens E, Schroeter A, Chen M, Skye MacPherson S, AM, Yumiko Adachi Y, Holme MA, Li Y, Klevit RE, Graham BS, Wyatt RT, Baker D, Strong RK, **Crowe JE Jr**, Johnson PR, Schief WR. Epitope scaffolds elicit neutralizing antibodies to a major human pathogen. ***Nature*** 2014; 507:201-6. PMC ID: 4260937.
- Willis JR, Briney BS, DeLuca SL, **Crowe JE Jr**, Meiler J. Human germline antibody gene segments encode polyspecific antibodies. ***PLoS Computational Biology*** 2013; 9(4): e1003045. PMC ID: 3636087.
- Sevy AM, Jacobs TM, **Crowe JE Jr**, Meiler J. Design of protein multi-specificity using an independent sequence search reduces the barrier to low energy sequences. ***PLoS Computational Biology*** 2015; 11:e1004300. PMC ID 4493036.

Immunity to HIV. We have studied the human antibody response to HIV-1 infection, focusing on development of laboratory tools for isolating quaternary epitope-specific human monoclonal antibodies, next-generation

sequencing methods for deep antibody variable gene repertoire analysis, and computational tools for exploring the structure/function features underlying virus neutralization.

- Willis JR, Finn JA, Briney BS, Sapparapu G, Singh V, King HG, LaBranche CC, Montefiori DC, Meiler J, **Crowe JE Jr**. Long antibody HCDR3s from HIV-naïve donors mediate HIV neutralization. ***Proceedings of the National Academy of Sciences USA*** 2016*;* 113:4446-51. PMC ID: 4843476.
- Willis JR, Sapparapu G, Moola S, Julien J-P, Singh V, King HG, Xia Y, Pickens JA, Labranche CC, Finn JS, Briney BS, Montefiori DC, Wilson IA, Meiler J, **Crowe JE Jr.** Redesigned PG9 variant monoclonal antibodies that exhibit enhanced HIV neutralizing potency and breadth. ***Journal of Clinical Investigation*** 2015; 125:2523-31. PMC ID 4497764.
- Briney BS, Willis JR, **Crowe JE Jr**. Human peripheral blood antibodies with long HCDR3s are established primarily at original recombination using a limited subset of germline genes. ***PLoS ONE*** 2012; 7: e36750. PMC ID: 3348910.
- Joyner AS, Willis JR, **Crowe JE Jr**, Aiken C. Maturation-induced cloaking of neutralization epitopes on HIV-1 particles. ***PLoS Pathogens*** 2011; 7: e1002234. PMC ID: 3169560.

Scientific Metrics

- Google Scholar *h*-index: 58; cited 11,479 times (04/12/2017)
  i10 index (papers with more than 10 citations) = 179 (04/12/2017)
- ResearchGate *h*-index: 51; RG score: 46.58 (highest percentile tier [>97.5%]).
- **Thomsen Reuters, Science Citation Index**; *h*-index: 47 (04/12/2017)

Identifiers

- **ORCID ID:** 0000-0002-0049-1079
- **ResearcherID:** B-5549-2009
- **Scopus Author ID:** 26642993000
- **International Standard Name Identifier (ISNI):** 0000 0003 5201 8432

Complete List of Published Work in: James Crowe - NCBI MyBibliography

D. Ongoing Research Support

U19 AI117905-01, NIH/NIAID Crowe and Meiler (Co-PI) 06/01/2015 - 05/31/2020
Structure Based Design of Antibodies and Vaccines
The purpose of this grant is to develop new computational modeling methods for the design of novel antibodies and antigens.

R01 AI114816, NIAID/NIH Crowe & Diamond [WUSTL] (Co-PI) 02/10/2015 - 01/31/2020
Structural and Functional Basis of Ultrapotent CHKV Neutralization by Human MAbs
The purpose of this grant is to study the structural and functional basis of ultra-potent CHKV neutralization by human mAbs isolated from humans.

R01AI127828, NIH/NIAID Crowe & Diamond [WUSTL] (Co-PI) 01/01/2017 – 12/31/2021
Human Neutralizing Antibodies for Zika Virus
The purpose of this grant is to study the structural and functional basis of Zika virus neutralization by human mAbs isolated from humans.
Selected for funding; 10th percentile score.

1U19AI109711-01, NIH/NIAID CETR Geisbert (PI; UTMB) 03/01/2014-02/28/2019
Advancements of Treatments for Ebola and Marburg Virus Infections
My Role: PI of Research Project 3, Therapeutic Human Monoclonal Antibody Treatments for Filoviruses.

HHSN272201400024C Contract, NIAID Crowe 09/30/14 - 09/29/2019
Genetic and Structural Basis for Virus Neutralization
This is a B cell epitope-mapping contract focused on H7 influenza epitopes.

HHSN272201400018C Contract, NIAID 09/30/14 - 09/29/2019
B Cell Epitope Mapping of Viral and Parasitic Antigens
Role: Vanderbilt subcontract PI, (overall PI is Daved Fremont, Washington University at St. Louis)

HHSN272201400058C Contract, NIAID 09/30/14 - 09/29/19
B-cell Epitope Discovery and Mechanisms of Antibody Protection for HCV and EBOV Envelope proteins

Role: Vanderbilt subcontract PI (overall PI is Ben Doranz, Integral Molecular)

HHSN2720100007C Contract, NIAID

Center of Excellence for Influenza Research and Surveillance (CEIRS) 10/01/2014-09/30/2019

PI: The Human Influenza Immunome Project

Role: Vanderbilt subcontract PI and Project PI (overall PI is Andrew Pekosz, Johns Hopkins University))

The purpose of this project is to study the human influenza B cell immunome using repertoire sequencing.

HDTRA1-13-1-0034 Crowe (PI) 04/01/2013- 03/31/2018

Defense Threat Reduction Agency (Department of Defense)

Human monoclonal antibodies against Ebola and Marburg viruses

The purpose of this award is to isolate and study human monoclonal antibodies to filoviruses.

2R01AI073755-06, NIAID/NIH Diamond (PI; Wash Univ) 06/18/2013 – 05/31/2018

Antibody-Based Protection Against Dengue Virus

Role: Co-Investigator, PI of Vanderbilt subcontract

The goal of this project is to study the function of antibodies against dengue virus.

5P30 DK058404-11, NIH/NIDDK Peek (PI) 06/1/2012 - 05/31/2017

Molecular and Cellular Basis of Digestive Disease; Core Director

This is our Digestive Diseases Research Center. My role is to direct the flow cytometry shared resource.

1R01AI114816-01A1, NIAID/NIH Crowe and Diamond (WUSTL) 04/01/2015 - 03/31/2020

Structural and Functional Basis of Ultrapotent CHKV Neutralization by Human MAbs

The purpose of this project is to study the structural and functional basis of ultra potent CHKV neutralization by human mAbs isolated from humans.

1R43AI118087-01 Yondola (PI; Avatar) 02/15/2015-01/31/2018 NCE

Role: Co-Investigator, PI of Vanderbilt subcontract

This is a grant lead by Avatar to develop and test influenza stem vaccine constructs. Our role is to provide human monoclonal antibodies for validating the stem constructs.

1 P01 AI106695 Harris (PI; UC Berkeley) 07/29/2015-06/30/2020

Role: Co-Investigator, PI of Vanderbilt subcontract

This is a program project to study the human host immune response to dengue infection and reinfection in a Nicaraguan cohort, and in a vaccine trial. Our role is to serve as the antibody core to make human monoclonal antibodies from human B cells.

DARPA, BA-14-38 Ahmed (PI; Emory**)** 02/12/2015-02/11/2018

Role: Co-Investigator, PI of Vanderbilt subcontract

This grant is focused on characterizing the human antibody response to Ebola infection in survivors of Ebola treated at Emory University. Our role is to isolate human antibodies to Ebola and provide to the consortium.

DARPA, BA-14-38 Simon (PI; Inovio) 03/12/2015-01/07/2017

Role: Co-Investigator, PI of Vanderbilt subcontract

The purpose of this grant is to develop and test DNA vectored delivery of antibody genes in humans. Our role is to provide antibody genes for human monoclonal antibodies to Ebola virus and Marburg virus.

Completed in Last Three Years

R01 Al 090656, **R21 AI098592, P01 AI078064, HDTRA1-10-1-0067, R01 GM 094198, R21 AI103834, R56 AI110750, R01 AI106002**