

14th PAN ARAB TRANSFUSION MEDICINE CONFERENCE QATAR 2024



Inspiring
Transfusion
Excellence Across
Arab Nations

Joint-Provider



Under the Patronage of

وزارة الصحة العامة
Ministry of Public Health
دولة قطر - State of Qatar



30 November to 2 December 2024

Sheraton Grand Doha Resort & Convention Hotel,
Doha, Qatar

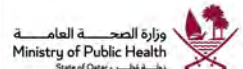
Big Data Studies in Transfusion Medicine

Michael P. Busch, MD, PhD
Vitalant Research Institute
University of California, San Francisco

Joint-Provider



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Disclosure Statement

I make the following declaration in relation to this CPD Activity :

- This complies with the Ministry of Public Health in Qatar Department of Healthcare Professions MoPH-DHP accreditation standards.
- There is NO Conflict of Interest.
- There is no plagiarism or copyright infringement.
- The content is balanced and free of bias, either commercial or non-commercial.

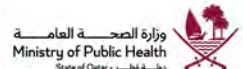
14th PAN ARAB TRANSFUSION MEDICINE
CONFERENCE QATAR 2024

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1980s

1987 – AIDS Epidemiologic Study of Blood Donors
 1986 – Transfusion-Related Viral Infections and Immune Response
 1986 – Effectiveness of HIV-1 Screening
 1986 – Development/Evaluation of New Screening Tests for HTLV-III
 HIV-1 Antibodies/Antigens/Nucleic Acids
 1984 – Transfusion Safety Study (TSS)

1989 – Retrovirus Epidemiology Donor Study, REDS-I
 1988 – Removal/Inactivation of Viruses in Blood
 1988 – Natural History of AIDS in Homosexual Man ("San Francisco Men's Health Study")
 1987 – Epidemiologic Study of Heterosexual Transmission of HIV from Persons with
 Transfusion-Associated Infections ("Partner Study")

1990s

1999 – Pathophysiology of HTLV-I and HTLV-II Infection "HOST"
 1996 – Donor Leucocyte Activation/Proliferation Post-Transfusion
 1994 – Viral Activation in Transfusion Study, VATS
 1992 – Impact of Homologous Blood Transfusion on HIV Replication and Disease in vivo (AABB NBF)
 1992 – HIV Diversity/Pathogenesis in Donor/Recipient Clusters

2000s

2004 – Acute HCV Infection in Injection Drug Users
 2004 – Natural History & Pathogenesis of WNV in Viremic Blood Donors
 2003 – Natural History of Acute and Chronic HCV in Blood Donors
 2002 – Immunologic and Virologic Features of Early HIV Infection (OPTIONS)

2009 – Viral/immune Parameters of Dengue and WNV in Donors
 2006 – Mechanisms and Clinical Effects of Microchimerism in Transfused Trauma Patients
 2004 – Retrovirus Epidemiology Donors Study, Part II (REDS-II)

2010s

2014 – Multiplex treatment-Outcomes Test for Chagas Disease
 2014 – Chikungunya Seroprevalence Study in Puerto Rico Following a 2014 Outbreak
 2014 – Validation of Ultra-Sensitive Assays for Quantifying HIV Persistence (RAVEN)
 2012 – HIV Incidence Testing using Multiple Biological Specimens (CEPHIA)
 2012 – Screening and Confirmatory Testing for Human Babesia-SBIR Phase II
 2011 – Recipient Epidemiology and Donor Evaluation Study-III – Central Laboratory
 2010 – Impact of Early Antiretroviral Therapy on HIV Persistence and Inflammation
 2010 – External Quality Assurance Program Oversight (EQAPOL)

2019 – The Impact of Illness and Medical Treatments on the Alloantibody Response to Platelet Transfusion
 2019 – NIAID Virology Quality Assurance (VQA)
 2018 – REDS-IV-Pediatric
 2017 – RedeS
 2016 – ZIKV Supplement to REDS-III
 2015 – amfAR Institute for HIV Cure Research

2020s

2021 – SARS-CoV-2 Options to EQAPOL
 2021 – Transfusion-Transmissible Infections Monitoring System (TTIMS)
 2020 – SARS-CoV-2 Supplement to REDS-IV-Pediatric
 2020 – National SARS-CoV-2 Seroincidence Studies in Blood Donors & Research Donor Cohort Studies
 2020 – Assessing Donor Variability and New Concepts in Eligibility (ADVANCE) Study

2022 – Innate Sensing of the Cell-Free DNA & the Interferon-Mediated Control of HIV *in Vivo*
 2022 – Hematopoietic & Immune Development in the Human Chorion
 2021 – ACTIV Integration of Host-targeting Therapies for COVID-19 Administrative Coordinating Center (C3PO)
 2020 – Transfusion-Related Immunomodulation Influences Infectious Disease Outcomes

Objectives

1. Surveillance and Response to Emerging Infectious Diseases:

- Use of cross-sectional and longitudinal donor samples from repeat blood donors for serosurveillance for known and emerging infectious diseases (EIDs)
- Potential extension to source plasma donors to inform response to EIDs
- Rapid access to convalescent plasma with high-titer Abs for hyperimmune IVIG preparations as well as B cell sourcing for production of monoclonal Ab or novel recombinant polyclonal Ab therapeutics

1. Apply “omics” technologies to improve blood donor retention and transfusion efficacy.



Part 1

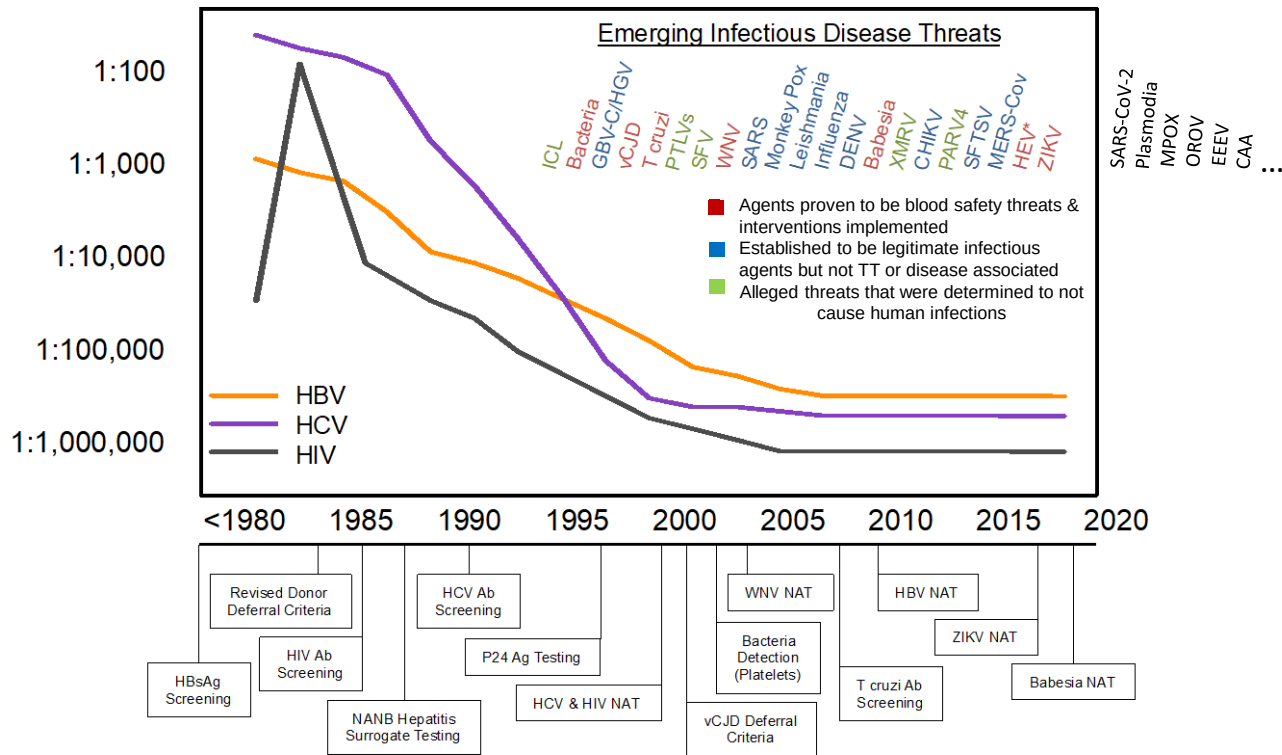
Surveillance and Response to Emerging Infectious Diseases

Surveillance and Response to EIDs

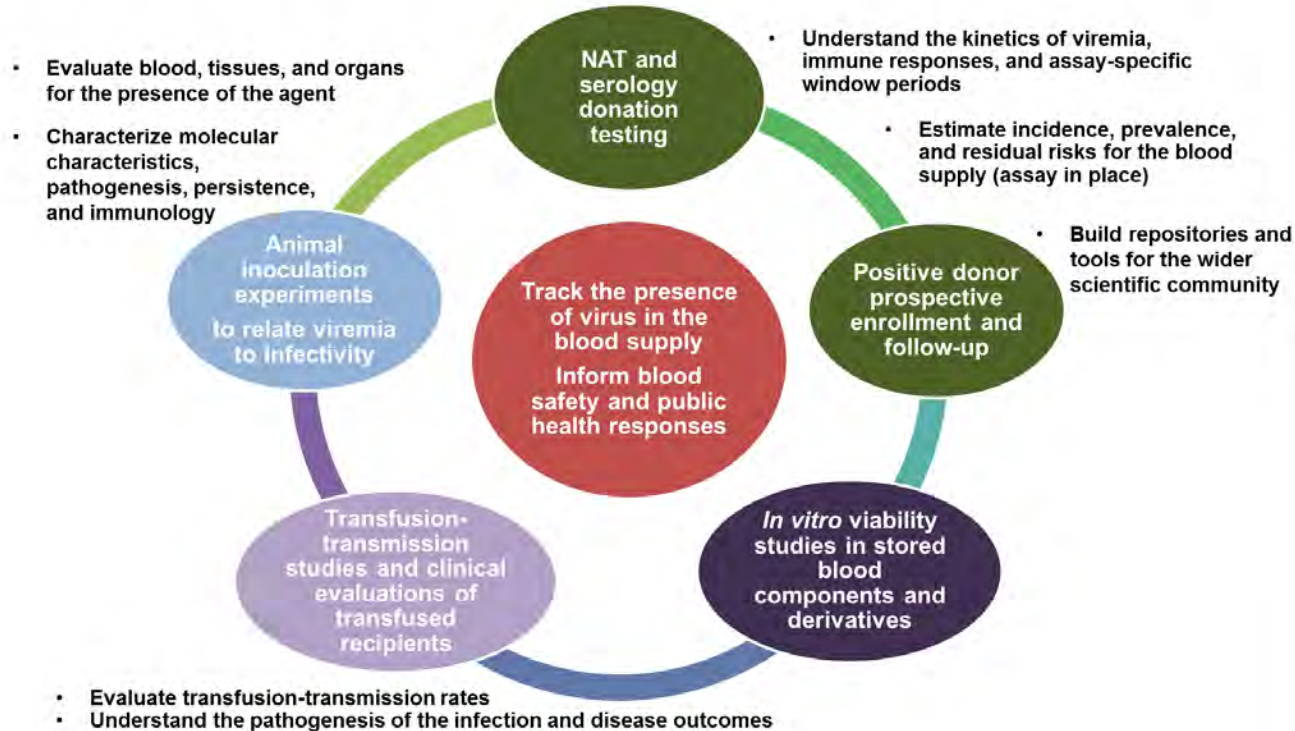
- Responding to previous outbreaks and EID threats
- Infrastructure, testing capacity and research expertise
- Response to evolving SARS-CoV-2 pandemic
 - SARS-CoV-2 serological assay comparative evaluations
 - Early studies under NHLBI REDS-IV-P program (no TT risk; no risk from receipt of Ab+ blood; pilot serosurveys)
 - CDC Nationwide Blood Donor Serosurveillance (cross-sectional design; 7/2020 – 12/2021)
 - CDC Nationwide Blood Donor Cohort (longitudinal design; surveys of participants; capture VI and RI; CoP)
 - 2023 Repeat Donor Cohort (transition to prospective testing of trimmed NBDC)
- New 5-year CDC Cooperative Agreement for expansion of US donor serosurveillance to other respiratory viruses using highly multiplexed array or NA-tagged antigens/NGS “seroplex” technologies
- Proposed study of highly pathogenic avian H5N1 influenza virus exposure (sero-prevalence/incidence) in U.S. blood and plasma donor populations



Risks of major transfusion-transmitted viral infections and emerging infectious agents of concern to blood safety



Assessing the risk of transfusion-transmission for newly discovered pathogens

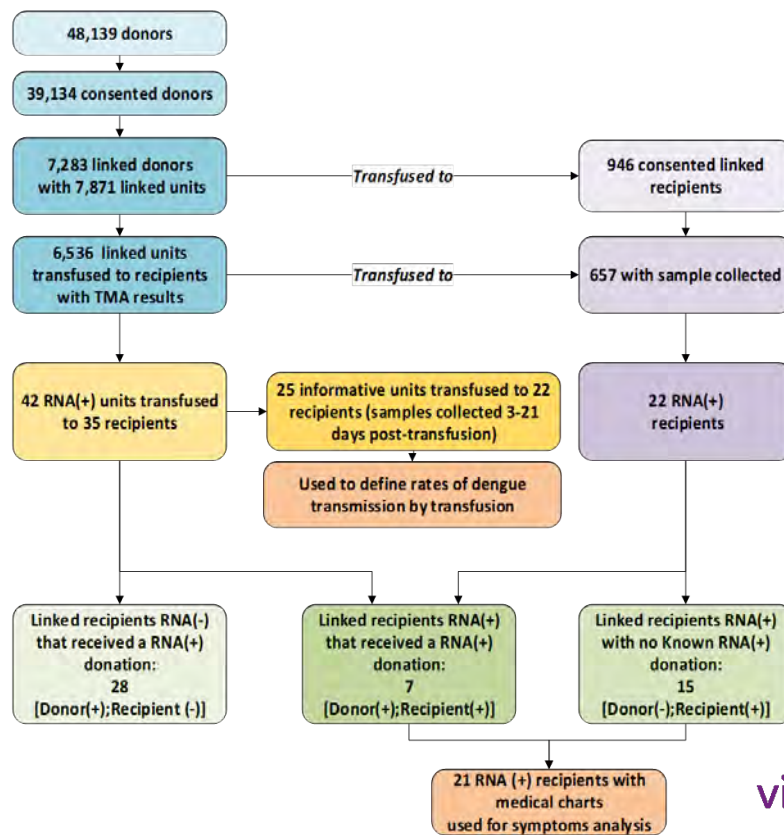


Dengue Transfusion-Transmitted Study in Brazil

2012 Rio de Janeiro and Recife



- DENV-4 viremia in 0.51% of donors in Rio de Janeiro and 0.80% in Recife.
- **Rate of TT: 37.5% (95% CI 15–64%)**
- **Symptomatic infection and severity not different between TT and mosquito acquired infections**
- Multiple DENV serotype 4 introduced during the outbreak



J Infect Dis. 2016 Mar 1;213(5):694-702

J Infect Dis. 2016 Jul 1;214(1):49-54.

Sci Rep. 2017 Nov 9;7(1):15216.

Zika Virus Response Studies Led by VRI

Assay Characterization

Relative analytical sensitivity of donor nucleic acid amplification technology screening and diagnostic real-time polymerase chain reaction assays for detection of Zika virus RNA

TRANSFUSION 2017;57:734-747

Mars Stone,¹ Marion C. Lanteri,^{1,2} Sonia Bakkour,¹ Xutao Deng,¹ Susan A. Gale,³ Jeffrey M. Linnen,⁴ Jorge L. Muñoz-Jordán,⁵ Robert S. Lanciotti,⁶ Maria Rios,⁷ Pierre Gallian,^{4,8} Didier Musso,¹⁰ José E. Levi,¹¹ Ester C. Sabino,¹² Lark L. Coffey,¹³ and Michael P. Busch^{1,2}

PLOS NEGLECTED TROPICAL DISEASES

Standardized evaluation of Zika nucleic acid tests used in clinical settings and blood screening

Mars Stone^{1,2*}, Sonia Bakkour^{1,2}, Eduard Grebe^{1,2}, Devy M. Emperador^{1,2}, Camille Escadafal¹, Xutao Deng¹, Honey Dave¹, Cassandra Kelly-Cirino¹, Eve Lackritz¹, Diana P. Rojas¹, Graham Simmons^{1,2}, Ingrid B. Rabe¹, Michael P. Busch^{1,2}



Article

Comparative Evaluation of Select Serological Assays for Zika Virus Using Blinded Reference Panels

Devy M. Emperador^{1,2}, Mars Stone^{2,3,4}, Eduard Grebe^{2,5}, Camille Escadafal^{1,6}, Honey Dave¹, Eve Lackritz¹, Cassandra Kelly-Cirino^{1,7}, Ingrid Rabe¹, Diana P. Rojas^{1,8}, Michael P. Busch^{2,9,10} and Graham Simmons^{2,3,4,11}



Learning about Zika virus epidemiology and diagnostics from blood donor studies

*Lyle R Petersen, M Cristina Cassetti

www.thelancet.com/infection Vol 20 December 2020

Natural History and Surveillance

Zika virus RNA and IgM persistence in blood compartments and body fluids: a prospective observational study

Mars Stone, Sonia Bakkour, Marion C Lanteri, Donald Brambilla, Graham Simmons, Roberta Bruhn, Zhanna Kaidarova, Zsong-Hae Lee, Jose Orlando Alsina, Phillip C Williamson, Susan A Gale, Lisa L Pate, Jeffrey M Linnen, Steve Kleinman, Michael P Busch, for the NHLBI Recipient Epidemiology Donor Evaluation Study REDS-III Program

www.thelancet.com/infection Published online July 13, 2020

Evolving viral and serological stages of Zika virus RNA-positive blood donors and estimation of incidence of infection during the 2016 Puerto Rican Zika epidemic: an observational cohort study

Phillip C Williamson, Brad Rigganstaff, Graham Simmons, Mars Stone, Val Winkler, Girish Laxmi, Jyoti Ahuja, Sonu Winkler, Christian Winkler, Lisa L Pate, Susan A Gale, Steven Kleinman, Michael P Busch

www.thelancet.com/infection Published online July 13, 2020

The Journal of Infectious Diseases

MAJOR ARTICLE



Surveillance for Zika, Chikungunya, and Dengue Virus Incidence and RNAemia in Blood Donors at 4 Brazilian Blood Centers During 2016–2019

Brian Custer,^{1,2} Eduard Grebe,^{1,2} Renato Bacchetti,¹ Sonia Bakkour,^{1,2} Mars Stone,^{1,2} Ligia Cognan,¹ Cecilia Alencar,¹ Luiz Amorim,¹ Paulo Loureiro,^{1,2} Anna Barbara Carneiro-Pereira,¹ Alayne Mendonça-Junior,¹ Thelma Gonçalves,¹ Kai Guo,¹ Kristin W. Linney,¹ Jeffrey M. Linnen,¹ Gus Brambilla,¹ Chris McClure,¹ Michael P. Busch,^{1,2} and Ester C. Sabino,¹ for the Recipient Epidemiology and Donor Evaluation Study (REDS-III) International Component Brazil

Blood, Organ and Tissue Safety

Received: 10 October 2021 | Revised: 5 December 2021 | Accepted: 5 December 2021
DOI: 10.1111/inf.137543

DONOR INFECTIOUS DISEASE TESTING

TRANSFUSION

Plasma transfusion–transmission of Zika virus in mice and macaques

Koen K. A. Van Rompay^{1,2} | Lark L. Coffey² | JoAnn L. Yee¹ | Anil Singupuri² | Jackson Stuart² | Marion C. Lanteri³ | Felicia Santa Maria³ | Kai Lu⁴ | Inderdeep Singh⁴ | Sonia Bakkour⁴ | Mars Stone^{4,5} | Phillip C. Williamson⁶ | Marcus O. Muench^{4,5} | Michael P. Busch^{4,5} | Graham Simmons^{4,5}

Received: 13 January 2022 | Revised: 14 February 2022 | Accepted: 24 February 2022
DOI: 10.1111/inf.14003

ORIGINAL RESEARCH

TRANSFUSION

Reprogramming of red blood cell metabolism in Zika virus–infected donors

Alexis Catala^{1,2} | Mars Stone^{3,4} | Michael P. Busch^{3,4} | Angelo D'Alessandro^{1,2}



RESEARCH ARTICLE

Zika Virus Tissue and Blood Compartmentalization in Acute Infection of Rhesus Macaques

Lark L. Coffey^{1*}, Patricia A. Pesavento¹, Rebekah I. Kaesler², Anil Singupuri¹, Jennifer Watanabe², Rie Watanabe¹, JoAnn Yee², Eliza Bliss-Moreau^{2,3}, Christina Cruzen², Karl L. Christe², J. Rachel Reader², Wilhelm von Morgenland², Anne M. Gibbons², A. Mark Allen², Jeff Linnen², Kai Gao², Eric Delwart², Graham Simmons², Mars Stone², Marion Lanteri², Sonia Bakkour², Michael Busch², John Morrison², Koen K. A. Van Rompay^{2*}

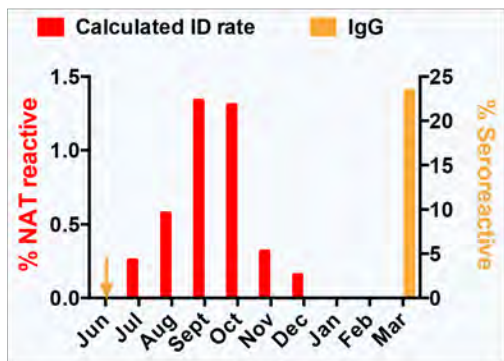
Annals of Internal Medicine

ORIGINAL RESEARCH

Screening the Blood Supply for Zika Virus in the 50 U.S. States and Puerto Rico A Cost-Effectiveness Analysis

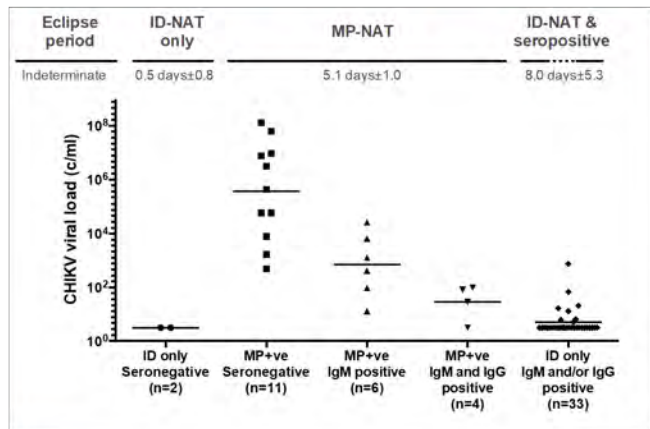
W. Alton Russell, MS; Susan L. Stramer, PhD; Michael P. Busch, MD, PhD; and Brian Custer, PhD

High Incidence of Chikungunya Virus and Frequency of Viremic Blood Donations during Epidemic, Puerto Rico, 2014



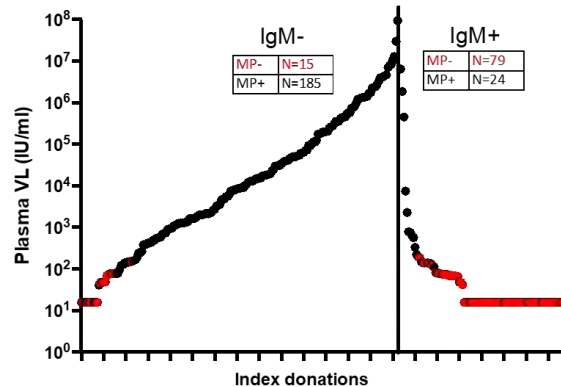
Simmons et al, EID 2016

Dynamics of CHIKV viremia in blood donations

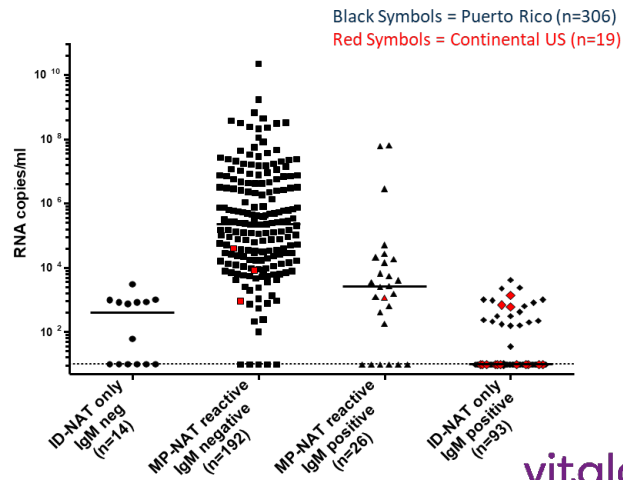


Simmons et al, EID 2016

Zika Plasma VL pre/post seroconversion

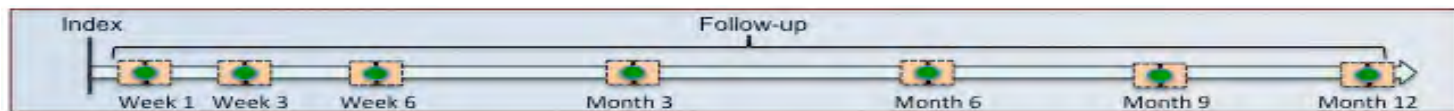


viremia duration of 9.9 days (SD $\pm$ 3.9)

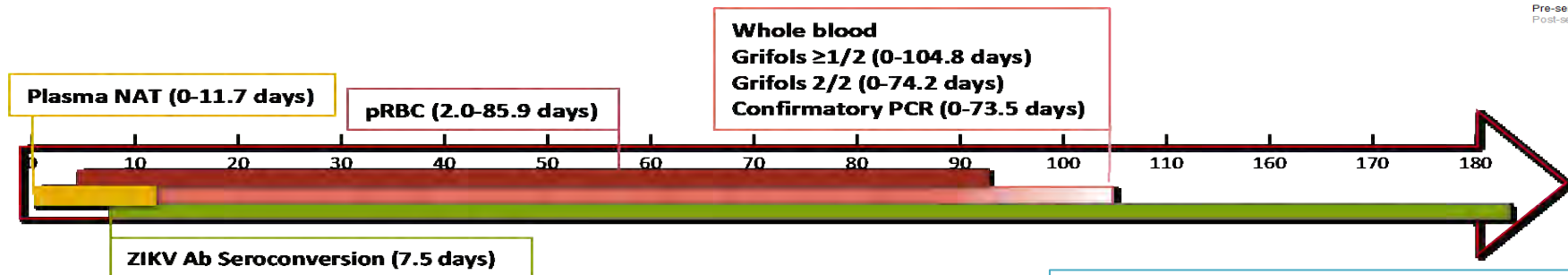
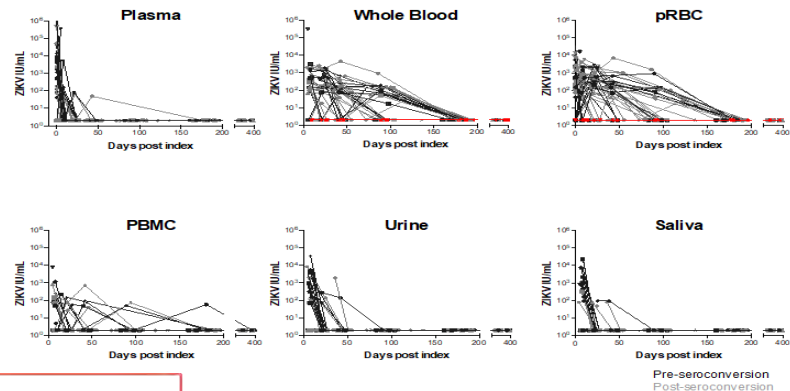


Williamson et al. Lancet ID 2020

US Natural History Cohort of Zika Virus RNA+ Blood Donors



- Evolution of viral and immunological markers
- Distribution and compartmentalization in blood and body fluids
- Clinical outcomes post donation
- Sharable biorepository
 - Characterize assay performance and provide standards for assay development



Learning about Zika virus epidemiology and diagnostics from blood donor studies

Lyle R Petersen, M Cristina Cassetti

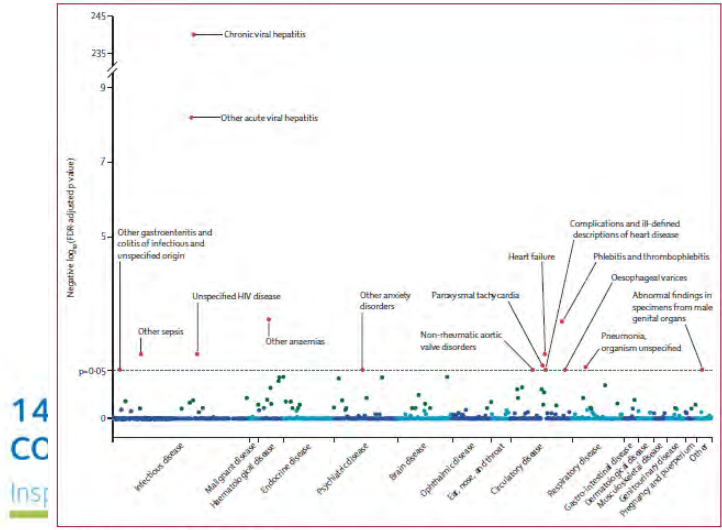
Lancet Infect Dis, 2020



Using routine health-care data to search for unknown transfusion-transmitted disease: a nationwide, agnostic retrospective cohort study

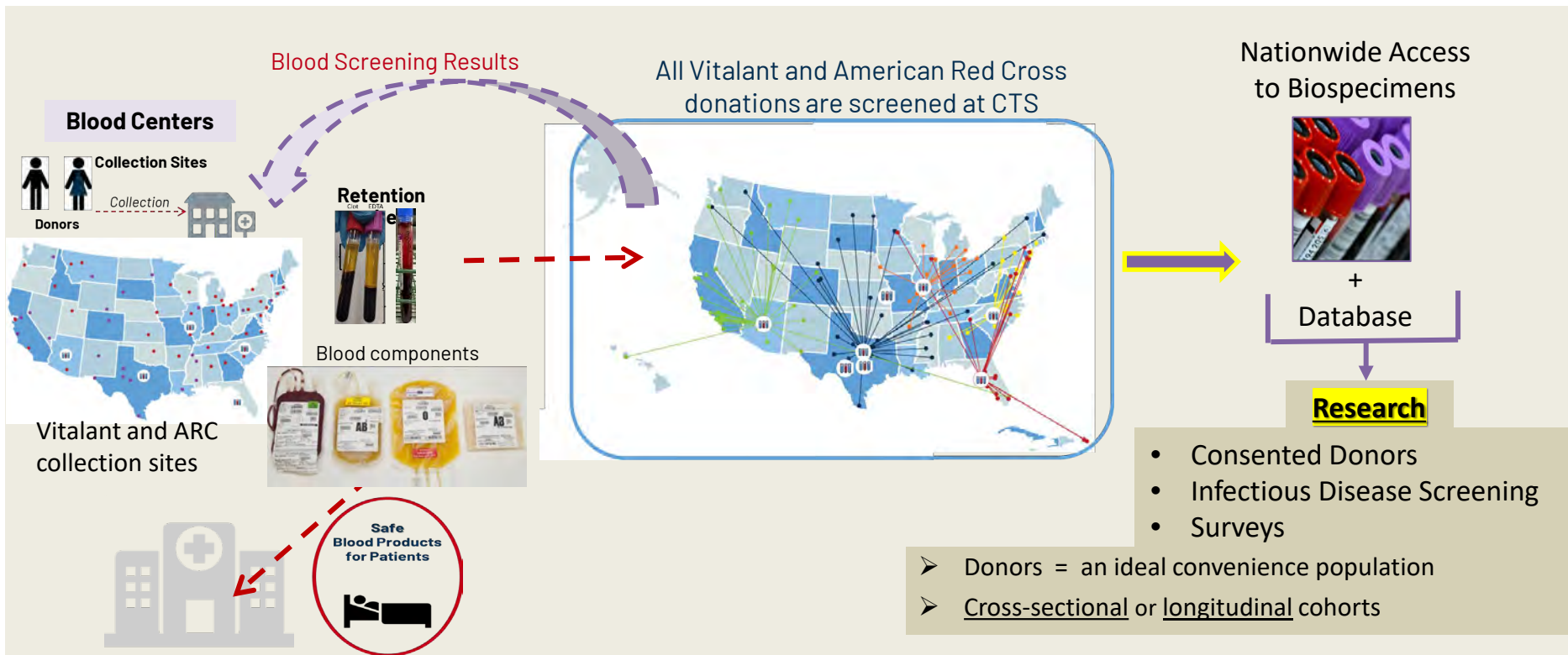
Torsten Dahlén, Jingcheng Zhao, Michael P Busch, Gustaf Edgren

- 1.7 million transfused patients, median follow-up 4.5 years
- 1,155 unique outcomes (ICD-8—10)

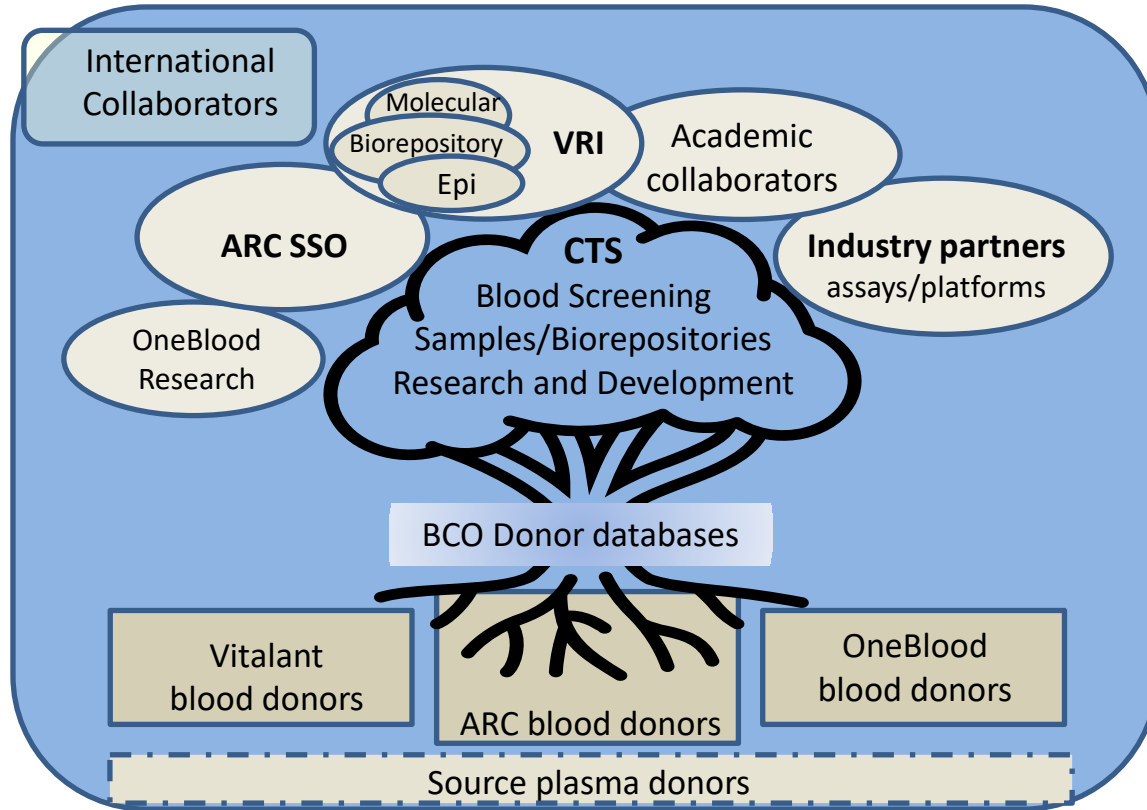


Disease group	Disease category	Raw-P	FDR-P	No. events Exposed	No. events Unexposed
Infectious Disease	Herpesvirus (herpes simplex) infections	0.05	0.54	525	8,978
	Streptococcal sepsis	0.047	0.53	541	15,110
	Streptococcus and Staphylococcus as the cause of diseases classified elsewhere	0.012	0.27	2,969	37,901
	Dermatophytosis	0.045	0.52	368	5,027
	Unspecified viral hepatitis	0.016	0.32	20	969
	Tularaemia	0.018	0.33	4	194
	Acute hepatitis A	0.022	0.37	3	267
	Purpura and other haemorrhagic conditions	0.025	0.4	1,526	24,322
Hematological Disease	Iron deficiency anaemia	0.028	0.42	4,554	95,894
	Acute posthaemorrhagic anaemia	0.014	0.31	1,955	48,716
	Other coagulation defects	0.005	0.15	1,015	19,205
	Other hereditary haemolytic anaemias	0.039	0.52	308	16,590
	Immunodeficiency with predominantly antibody defects	0.0028	0.095	34	1,359
	Other disorders involving the immune mechanism, not elsewhere classified	0.0018	0.074	35	2,205
	Combined immunodeficiencies	0.002	0.076	2	268
	Hypofunction and other disorders of pituitary gland	0.045	0.52	197	7,194
Endocrine Disease	Other specified diabetes mellitus	0.042	0.52	1,304	19,994
	Type 2 diabetes mellitus	0.019	0.35	21,643	79,778
	Other hypothyroidism	0.019	0.35	4,860	47,141
	Adrenogenital disorders	0.028	0.42	2	453
Psychiatric Disease	Other mental disorders due to brain damage and dysfunction and to	0.0023	0.061	1,775	27,596
	Dementia in Alzheimer disease	0.036	0.5	651	18,638
	Other neurotic disorders	0.012	0.27	368	3,799
	Mental and behavioural disorders due to use of opioids	0.016	0.32	86	5,494
	Mental and behavioural disorders due to use of hallucinogens	0.04	0.52	4	647
	Severe mental retardation	0.0021	0.076	2	633
	Other degenerative diseases of basal ganglia	0.044	0.52	2	1,408
	Nerve root and plexus compressions in diseases classified elsewhere	0.044	0.52	56	2,796
Brain Disease	Other disorders of brain	0.0018	0.074	1,323	20,390
	Sleep disorders	0.024	0.4	9,867	26,324
	Alzheimer disease	0.041	0.52	1,762	30,641
	Other acute disseminated demyelination	0.0091	0.23	27	2,381
Ophthalmic Disease	Visual impairment including blindness (binaural or monocular)	0.041	0.52	379	13,493
	Otitis externa	0.02	0.35	2,523	15,166
Ear, Nose and Throat	Essential (primary) hypertension	0.0059	0.16	113,547	141,558
	Atrial fibrillation and flutter	0.029	0.42	40,103	129,856
	Acute myocardial infarction	0.0046	0.14	23,974	87,041
	Other cardiac arrhythmias	0.0074	0.19	10,035	47,013
	Cardiac arrest	0.0059	0.16	9,264	53,070
	Aortic aneurysm and dissection	0.031	0.44	2,107	25,747
	Hypertensive heart disease	0.013	0.27	833	20,013
	Pleural effusion, not elsewhere classified	0.023	0.39	2,849	37,943
Respiratory Disease	Bacterial pneumonia, not elsewhere classified	0.012	0.27	14,994	79,481
	Nasal polyp	0.047	0.53	560	5,701
	Chronic sinusitis	0.027	0.5	477	5,379
	Pneumocystosis due to dust containing silica	0.0039	0.12	1	215
Gastro-intestinal Disease	Gastro-oesophageal reflux diseases	0.015	0.31	10,008	38,105
	Other female pelvic inflammatory diseases	0.042	0.52	2	1,382
	Obstetric death of unspecified cause	0.05	0.54	1	128
	Abnormalities of heart beat	0.027	0.42	5,944	33,217

Using Donor Samples After Blood Screening for Public Health Surveillance



Joining Efforts in Research - The US Research Consortium



1. Maintaining Blood Safety
2. Conducting Donor-Based Research
3. Innovative Technologies in Blood Screening

- Positioned for large-scale funding
- Further driving innovation to inform EID surveillance and response
- Technology Horizon Scanning

➤ **Public Health Surveillance**

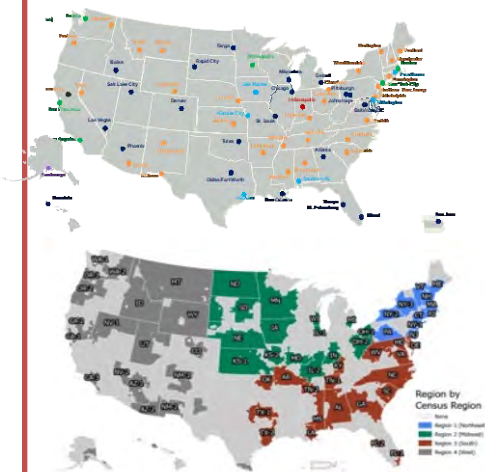
Responding to Evolving SARS-CoV-2 Pandemic

NBDS cross sectional donor serosurveillance

~152,000 monthly donations, 17 BCOs

Track infections, Vx, hybrid immunity

Nationally representative weighted seroprevalence

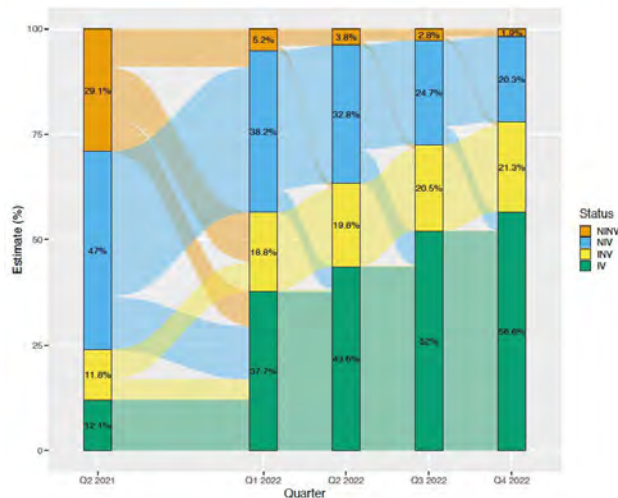


NBDC longitudinal donor cohort

~142,000 routine donors

Vx breakthrough and reinfections, Vx effectiveness, Correlates of protection, impact of VoC, surveys

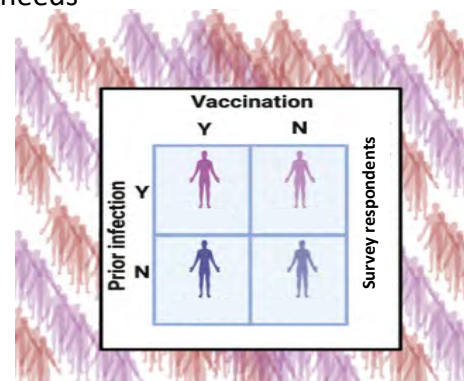
Revised seroprevalence estimates



2023 Repeat Donor Cohort

~45,000 informative donors

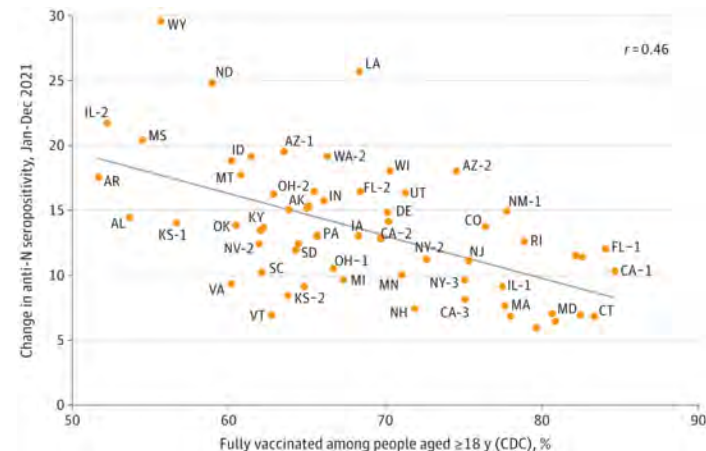
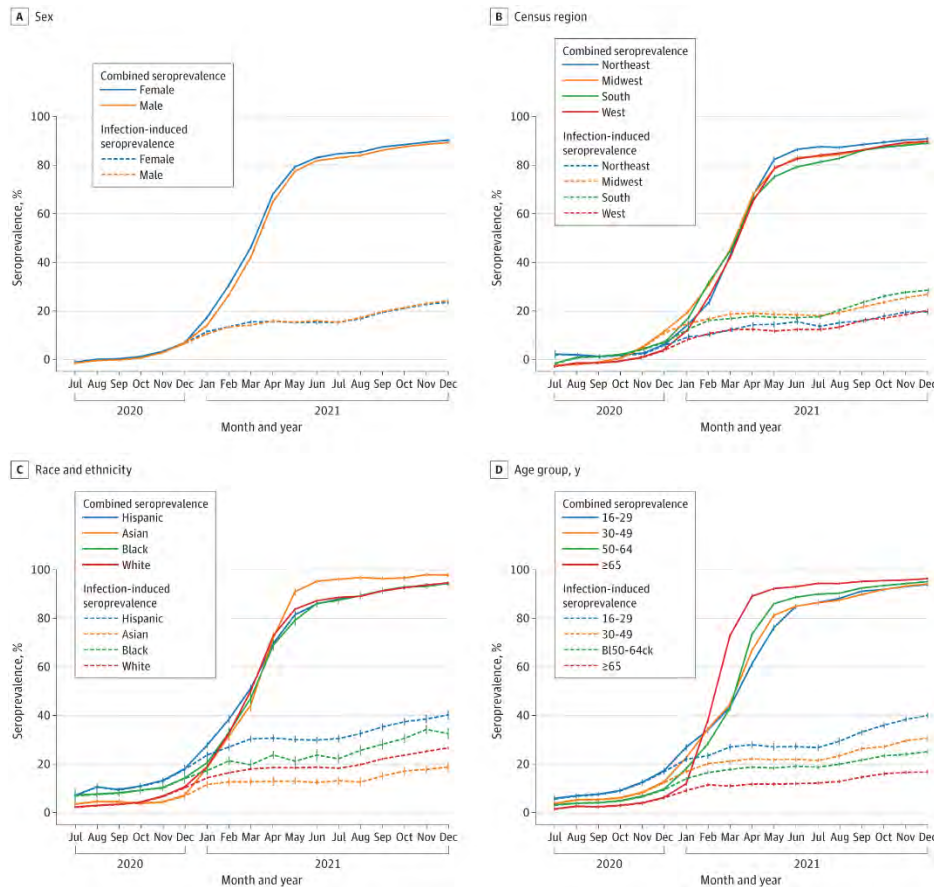
Self funded sample and survey data acquisition, real time quarterly testing
Inform current and future public health needs



June 13, 2022

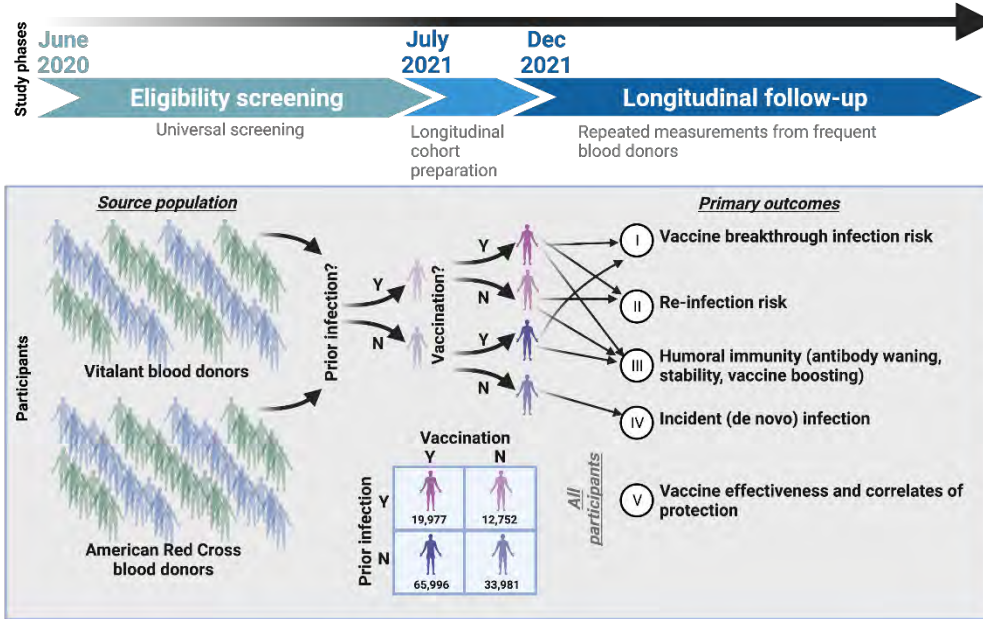
Updated US Infection- and Vaccine-Induced SARS-CoV-2 Seroprevalence Estimates Based on Blood Donations, July 2020–December 2021

Jefferson M. Jones, MD, MPH¹; Jean D. Opsomer, PhD, MBA²; Mars Stone, PhD³; Tina Benoit, MPH¹; Robyn A. Ferg, PhD²; Susan L. Stramer, PhD, MS⁴; [Michael P. Busch, MD, PhD³](#)
 JAMA. 2022;328(3):298-301. doi:10.1001/jama.2022.9745



Association between December 2021 vaccination rate and increase in infection-induced seroprevalence during 2021 by Study Region, US, January – December 2021

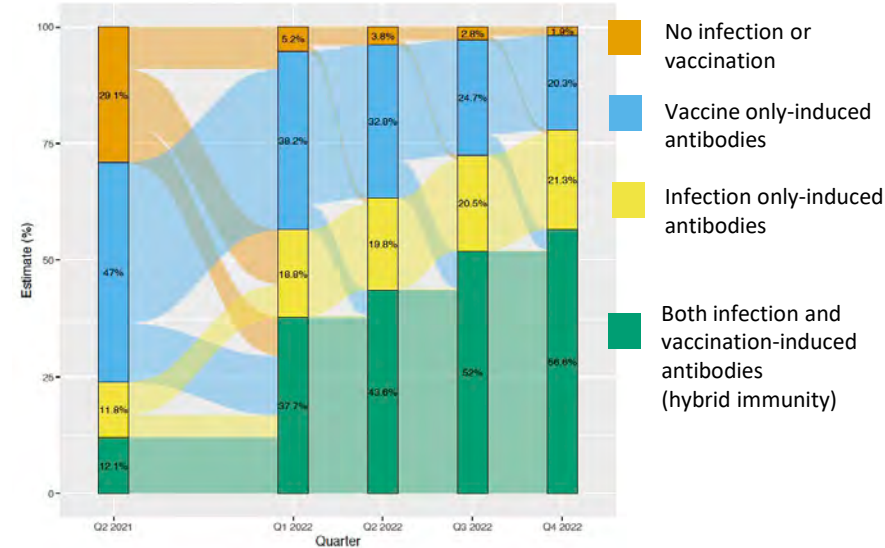
NBDC: Longitudinal Study to Characterize Evolving Immunity, Identify Breakthrough and Reinfections, and Correlates of Protection



a Initial implementation date of donor surveys with questions regarding self-reported vaccine status: September 2020 (Vitalant), December 2020 (American Red Cross)

~75,000 donors donate per quarter, providing
~120,000 donations per quarter

Single quarterly samples per donor tested for NC Ig and S IgG; longitudinal samples from subsets tested for variant specific bAbs (MSD) & nAbs (RVPNT)

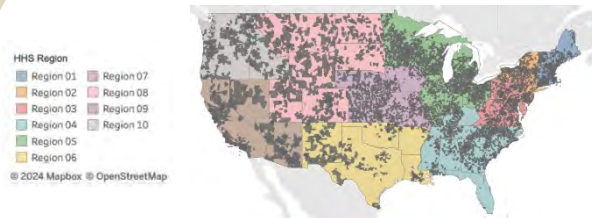


New funding opportunity by CDC (\$26.5 M for 5 years - 2024-2029)

This project will *establish* and *sustain* a national longitudinal cohort of 50,000 repeat blood donors with the purpose of monitoring changes in antibody titers against common or novel respiratory viruses:

- 1) Estimating the national burden of incident SARS-CoV-2, RSV, Influenza, Human Metapneumovirus, EVD-68 infections and other EIDs;
- 2) Determining antibody thresholds for protection across multiple respiratory viruses;
- 3) Assessing state- or region-specific population-level immunity to/risk for infection through tracking median antibody titers within various populations;
- 4) Monitoring waning immunity and changes in immune capabilities in the context of ongoing viral evolution.

2023 Repeat Donor Cohort (n=45,000)



Respiratory Viruses program:

- SARS-CoV-2
→ RSV, Flu, Metapneumo, EVD-68...

Innovative technologies:

- Horizon scanning
✓ “Seroplex” assays!

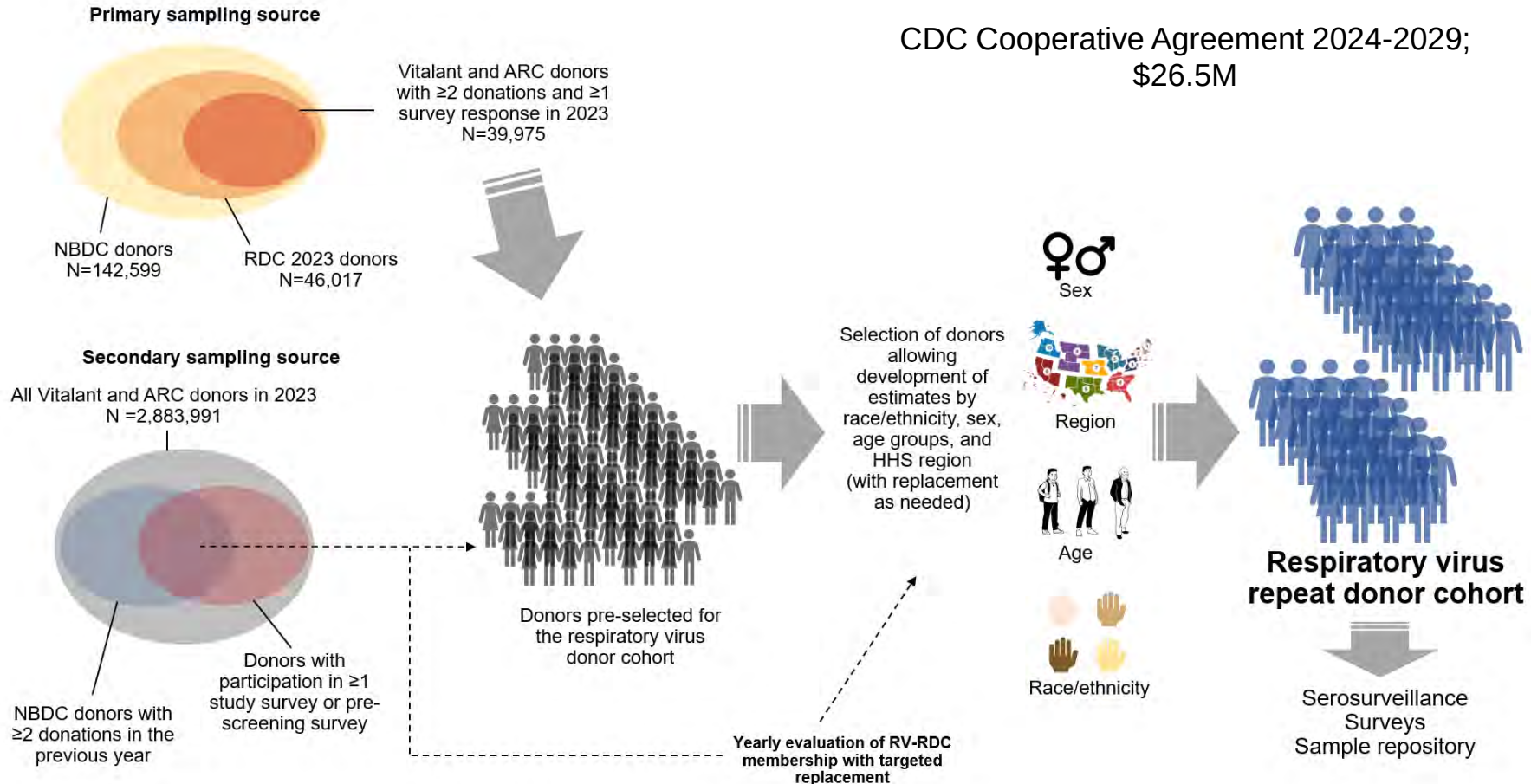
Getting closer to making “concepts” a reality

ICE FORUM

**A Global Immunological
Observatory to meet a time of
pandemics**

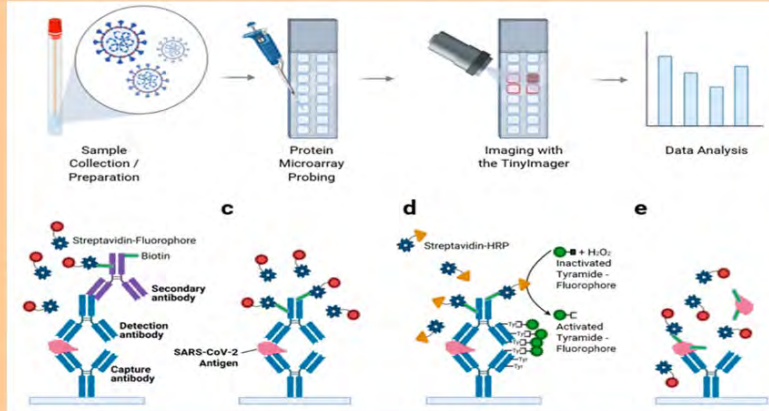
MICHAEL J MINA^{†*}, C JESSICA E METCALF^{†*}, ADRIAN B MCDERMOTT,
DANIEL C DOUEK, JEREMY FARRAR AND BRYAN T GRENFELL

Respiratory virus repeat donor cohort surveillance program



Innovative Technology Horizon Scanning: applications for donor screening and public health surveillance

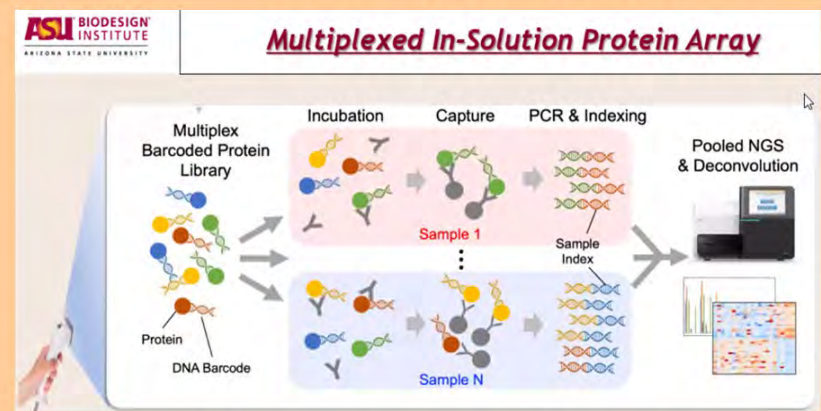
Protein Array-type x2



16 samples/run, 30 Antigens/run, 3-6 logs dynamic

- **Ab chip by UC Irvine – Felgner P.**
(Beck S et al. Biomedicines. 2022)
- **V-plex (15 Ag) by MesoScaleDiscovery – Sigal G.**

MISPA-type x3



2,000 samples/run, 200 Antigens/run, 3-6 logs dynamic

- **MISPA by ASU – LaBaer J.** (Song L et al. Microbiol Spectr. 2024)
- **PepSeq by ASU – Altin J.** (Henson SN et al. Nat Protoc. 2023)
- **MIPSA by Infinity Bio. – Larman B.** (Infinity Bio.com)

- **Driving scientific innovation in blood screening**
- **Positioning for scale up of public health surveillance and response to EIDs**
- **Building donor repositories for "immunologic observatory"**

Convalescent Blood and Plasma Donors for Generation of Immunotherapies

- Convalescent plasma for direct transfusion (analogous to CCP)
- Convalescent plasma for fractionation and production of hyperimmune IVIG
- PBMC for isolation of B cells to generate hybridomas for pathogen-specific mAbs
- Collaboration with Gigagen/Grifols to produce recombinant polyclonal Ab therapies

GigaGen Awarded U.S. BARDA Contract to

Develop Recombinant Polyclonal Antibody Therapies for Botulinum Neurotoxins and an Additional Biothreat

The contract will provide an initial commitment of \$19.6 million and up to \$135.2 million over a six-year period, supporting drug manufacturing and phase 1 trials for the two programs.

GigaGen's recombinant polyclonals are part of Grifols' robust innovation strategy and commitment to delivering the next generation of antibody drugs for patients and healthcare professionals.

The award, valued at up to \$135.2 million, is to develop a recombinant polyclonal antibody therapy for botulinum neurotoxins (BoNT) and a second biothreat of interest to the agency that will be determined at a later time.

Generation of recombinant hyperimmune globulins from diverse B-cell repertoires

Sheila M. Keating^{1,15}, Rena A. Mizrahi^{1,15}, Matthew S. Adams^{1,14}, Michael A. Asensio¹,

New technologies in therapeutic antibody development: The next frontier for treating infectious diseases

Antiviral Research 227 (2024) 105902

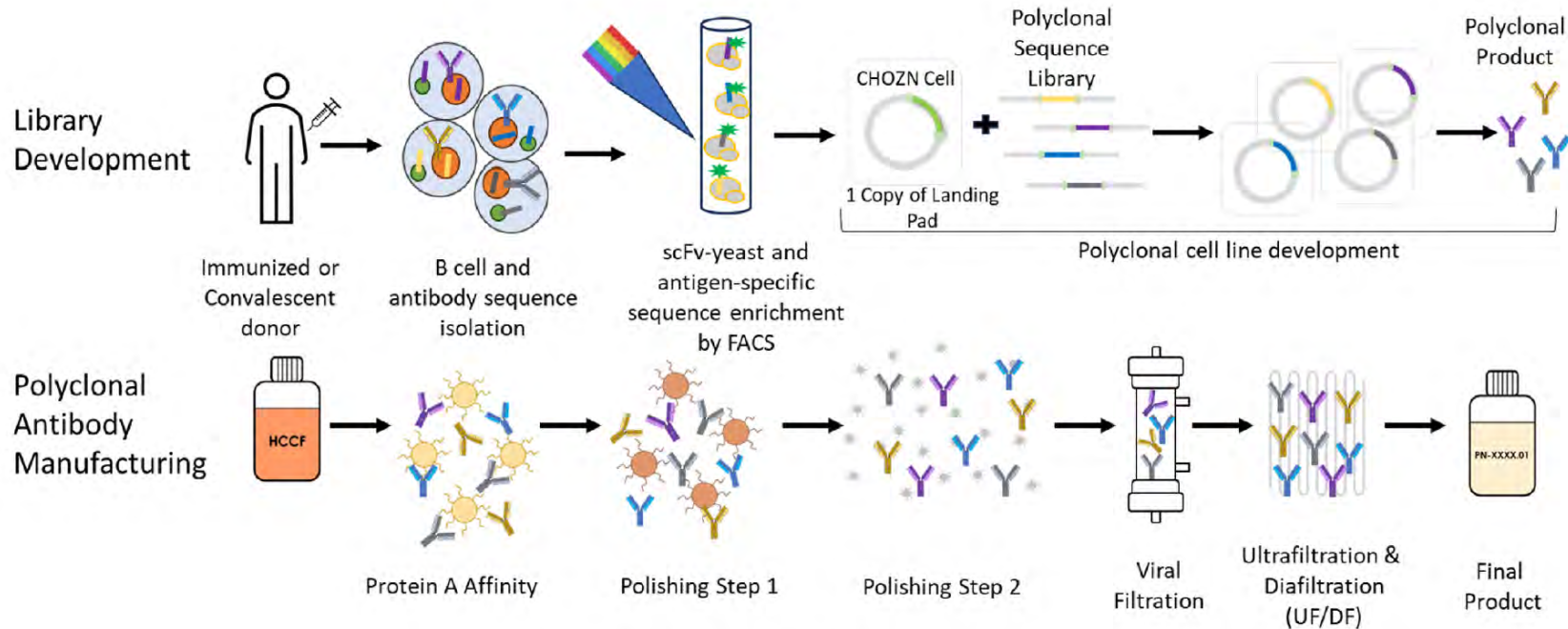
Sheila M. Keating^{a,*}, Brett W. Higgins^b

^a GigaGen, Inc. (A Grifols Company), 75 Shoreway Road, San Carlos, CA, 94070, USA

^b Grifols, 125 Shoreway Road, San Carlos, CA, 94070, USA

A Potent Recombinant Polyclonal Antibody Therapeutic for Protection Against New Severe Acute Respiratory Syndrome Coronavirus 2 Variants of Concern

Nicholas P. Wayham,¹ Ariel R. Niedecken,² Jan Fredrik Simon,³ Yao Y. Chiang,⁴ Angelica V. Medina-Cacurella,⁵ Rena A. Mizrahi,⁶ Ellen K. Wagner,⁷ Ashley Gray,⁸ Hana Segal,⁹ Peyton Witte,¹⁰ Alexis Enstrom,¹¹ Kristina Bountarova,¹² Sabrina M. Nelson,¹³ Tessa Weinberger,¹⁴ David Tan,¹⁵ Michael A. Asensio,¹⁶ Aleagu Subramanian,¹⁷ Young Weon Lim,¹⁸ Adam S. Adler,¹⁹ and Sheila M. Keating¹

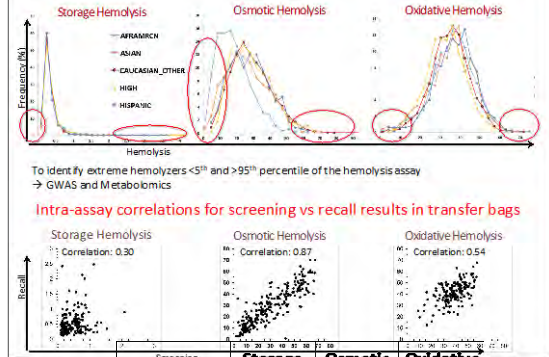
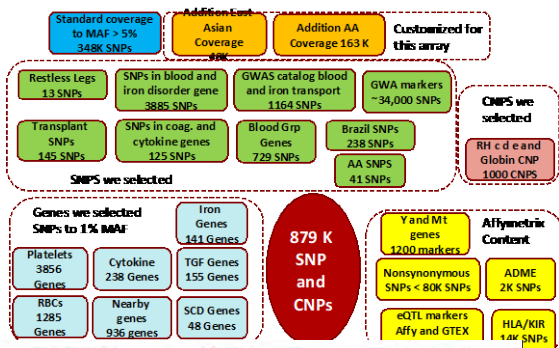


Part 2

Applying “omics” technologies to improve blood and plasma donor retention and transfusion component and PDMP efficacy

REDS-III RBC-Omics Study

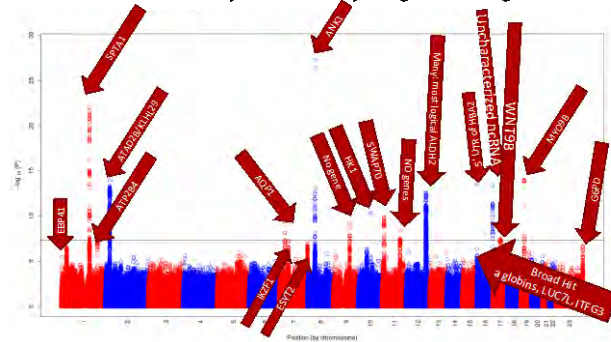
Affymetrix Axiom genome wide SNP array



Strain	Storage Hemolysis	Osmotic Hemolysis	Oxidative Hemolysis
African			
Asians	0.69	<0.0001	0.41
High-intensity	<0.0001	0.84	<0.0001

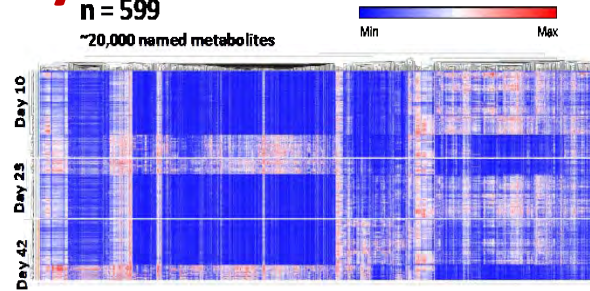
↑ > hemolysis vs Caucasian donors

↓ < hemolysis vs Caucasian donors



n = 599

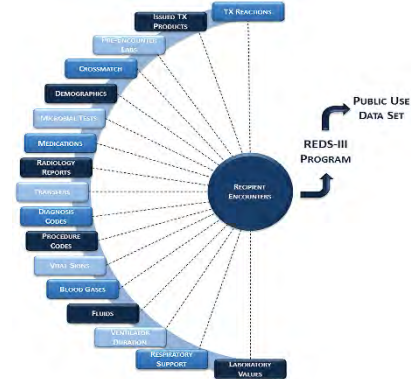
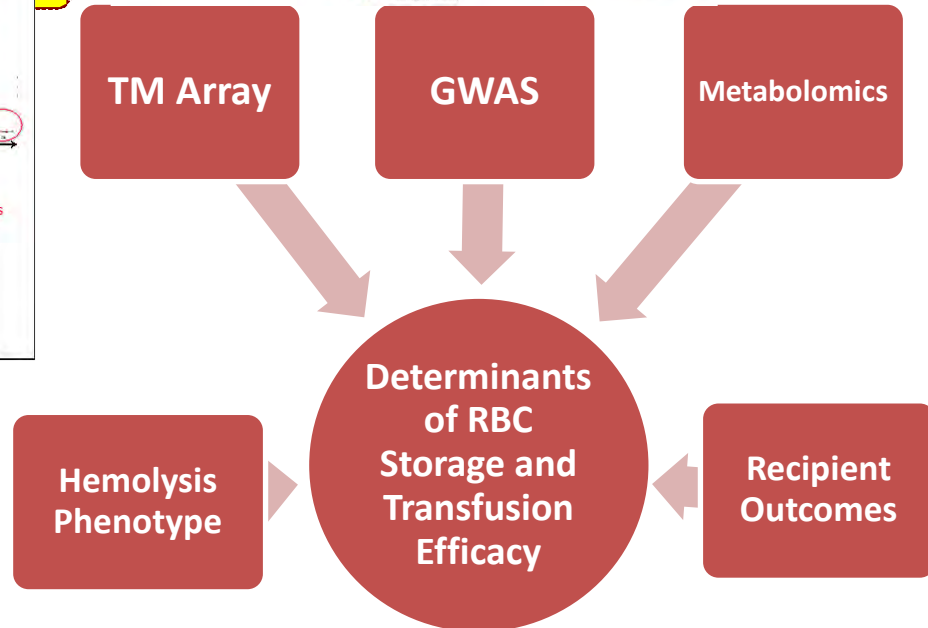
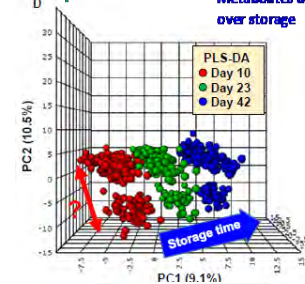
~20,000 named metabolites



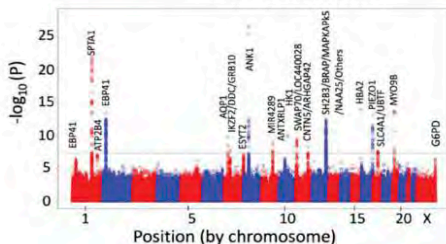
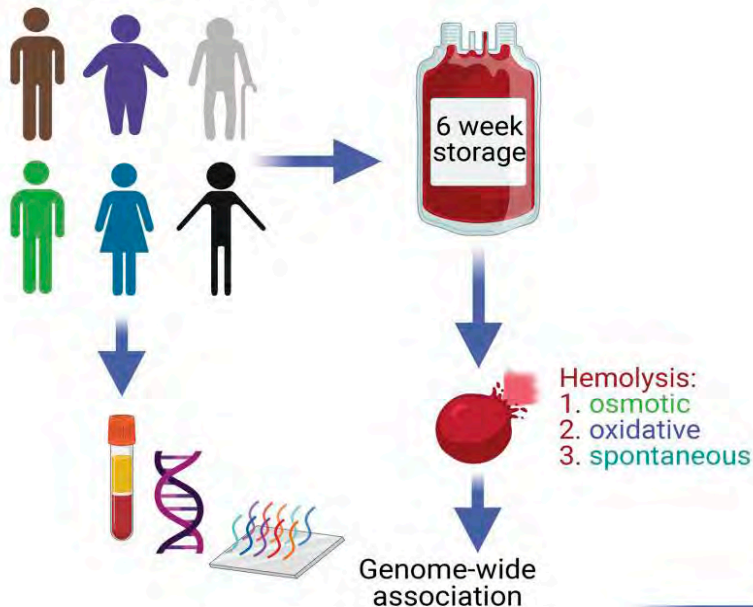
Metabolites increasing over storage

Donor-specific

Metabolites decreasing over storage



>12K racially diverse
Blood donors
(NHLBI RBC-Omics)

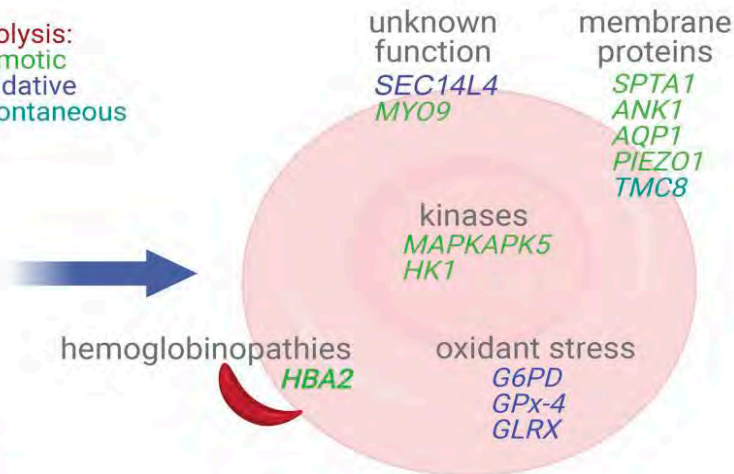


JCI

Multiple-ancestry genome-wide association study identifies 27 loci associated with measures of hemolysis following blood storage

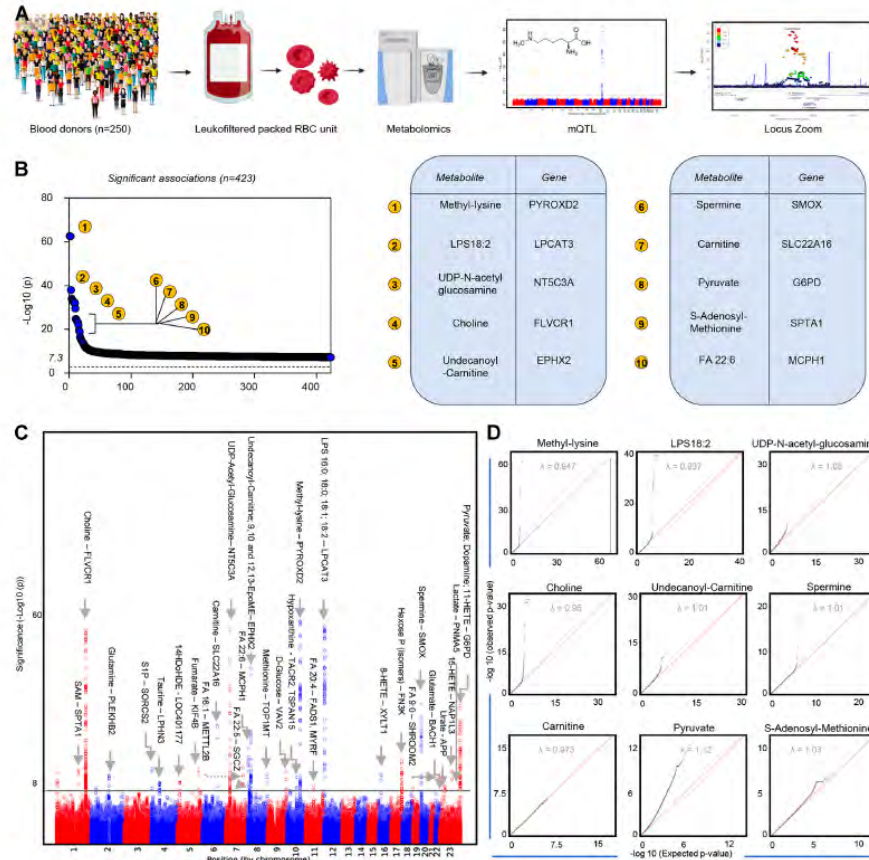
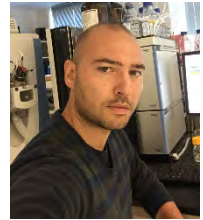
Grier P. Page, ... , Mark T. Gladwin, the National Heart, Lung, and Blood Institute (NHLBI) Recipient Epidemiology Donor Evaluation Study–III (REDS–III)

J Clin Invest. 2021

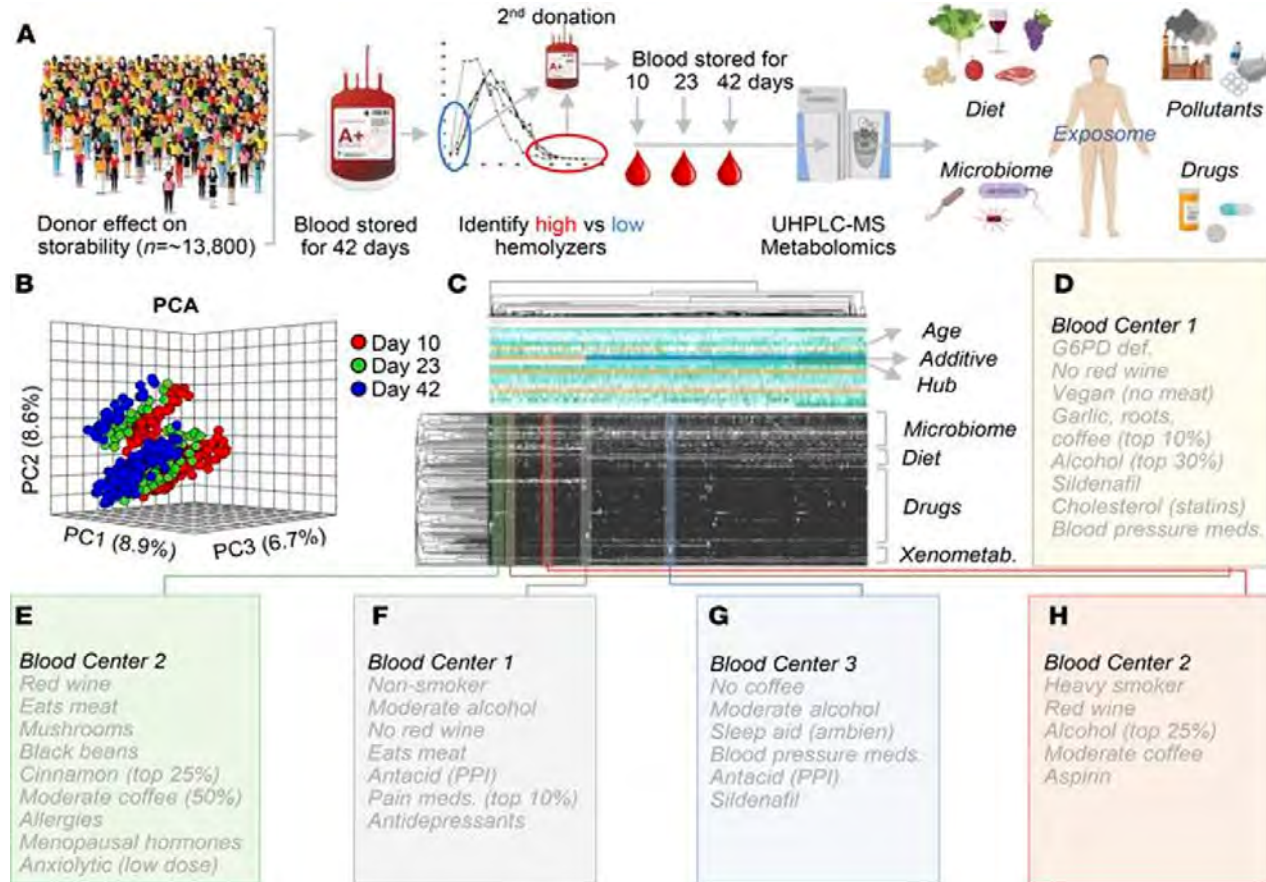


Genome-wide metabolite quantitative trait loci analysis (mQTL) in red blood cells from volunteer blood donors

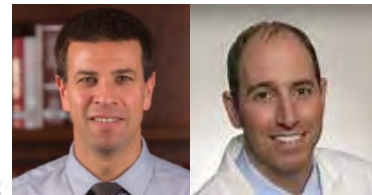
Amy Moore¹, Michael P. Busch², Karolina Dziejulska³, Richard O. Francis⁴, Eldad A. Hod⁴, James C. Zimring³, Angelo D'Alessandro^{4,5,6} , and Grier P. Page^{1,*} 



Blood donor "Exposome"



Donor, component and recipient factors influencing RBC transfusion efficacy

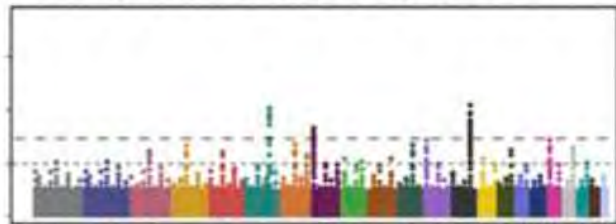


Retrospective cohort study of 46,705 transfusion recipients who received 102,043 single-unit RBC transfusions from 2013-2016 at 12 hospitals

Donor genetic polymorphisms



G6PD, SEC14L4, HBA2, MYO9B

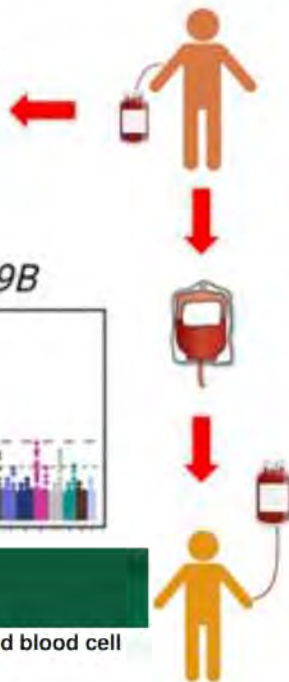


JCI insight

Donor genetic and non-genetic factors affecting red blood cell transfusion effectiveness

Nareg H. Roubinian, ... , Michael P. Busch, Eldad A. Hod

JCI Insight, 2021, <https://doi.org/10.1172/jci.insight.152598>



Blood Donor

Sex
RhD status
Hemoglobin
Tobacco use

Component

Collection Method
Leukoreduction
Storage solution
Gamma irradiation
Storage duration

Transfusion Recipient

Sex
Age
Race
Body mass index

Combinations of blood donor metabolomic and genetic factors remain associated with hemoglobin increments

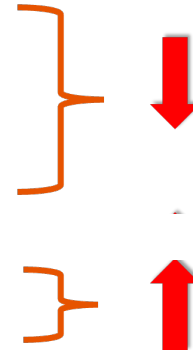
Kynurenine SNP (-0.12 g/dL)

L-Carnitine (-0.08 g/dL)

PFK SNP (-0.10 g/dL)

Urate SNP (-0.13 g/dL)

L-Citrulline (0.08 g/dL)

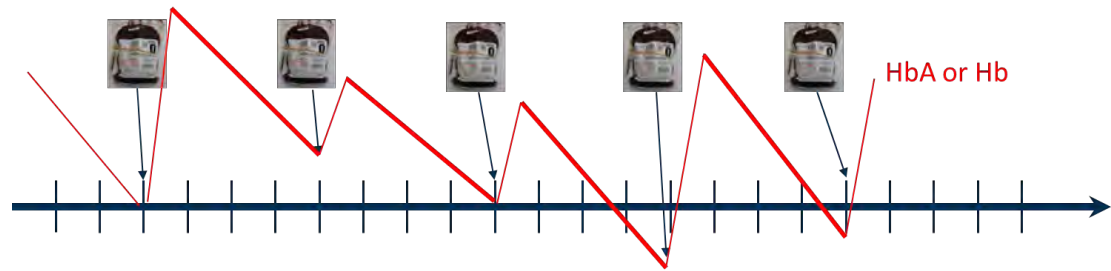


Red Blood Cell – IMProving trAnsfusions for Chronically Transfused recipients (RBC – IMPACT)

Objective:

Assess how donor, component, and recipient factors contribute to RBC efficacy in chronically and episodically transfused patients

Conducted in US and Brazil
REDS-IV-P programs



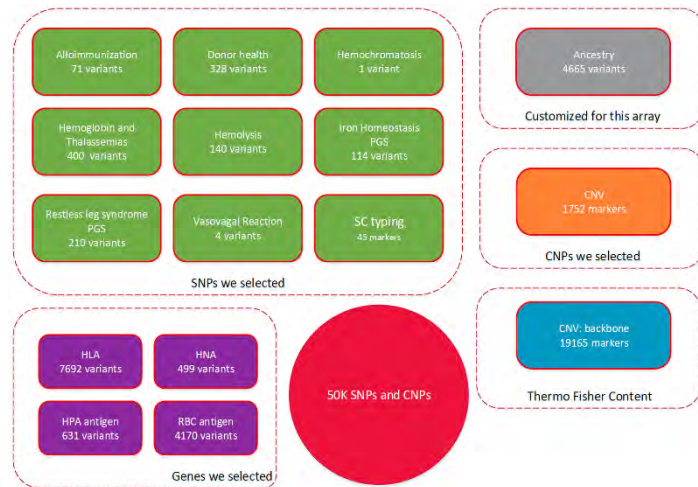
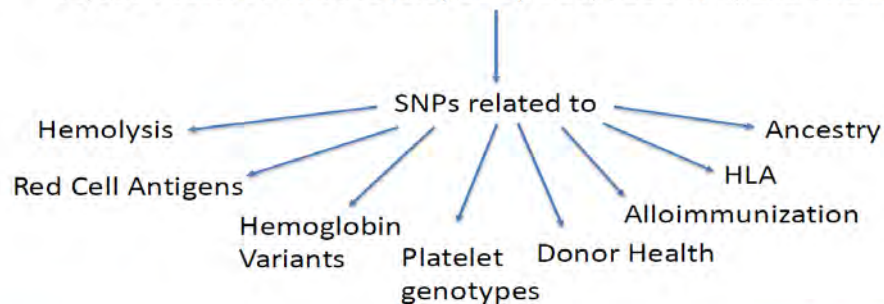
Specific genetic donor factors influence RBC survival of units transfused to patients with SCD (measured by HbA) and Thalassemia (measured by total Hb)

Effectiveness of transfusion = RBC survival

Precision Transfusion Medicine Array

PTM Array

50,000 Feature PTMA developed by BGC, REDS-IV-P, and ThermoFisher



REDS-IV-P content

Iron Homeostasis Polygenic Trait/Risk Scores (PGS):

- **Variants:** 114
- **Source:** EdA priority list

Restless leg syndrome PGS:

- **Variants:** 210
- **Source:** EdA priority list

Vasovagal Reaction:

- **Variants:** 4
- **Source:** EdA priority list

Total REDS= 328

Plus Ancestry for Brazilian/South American Pop

REDS-IV-P content

Hemolysis:

- **Variants:** 140
- **Criteria:** all category 1, 2, 3, 4 in prioritized list from REDS-III

Alloimmunization:

- **Variants:** 53
- **Criteria:** all “must have” and “nice to have” in alloimmunization list REDS-III Brazil

Hemoglobin:

- **Variants:** 269
- **Source:** Hemoglobin variants from “TAG” list provided by REDS-IV-P investigators
- **Criteria:**
 - Observed in gnomAD + TF already has a working probe (n=30)
 - Observed in gnomAD (n=199)
 - Unobserved in gnomAD + TF already has a working probe (n=40)

Total REDS = 462

ISBT TTID and Big Data Working Parties



A Safe and Effective Blood and Plasma Supply

Precision Transfusion Medicine

Informing Public Health, Biology and Disease Pathogenesis



***Thank you for the invitation to participate in your
meeting and hospitality in Qatar!!!***

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CONFERENCE QATAR 2024**

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