

Overview of Research and Regulatory Program of Division of Emerging and Transfusion Transmitted Diseases (DETTD)

Hira Nakhasi, PhD., FASTMH

Director DETTD

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Mission: Ensuring Blood Safety and Availability



- About 14 Million units are transfused annually*
About 10 million RBC; 2 million PLT and 2.4 million plasma
- Risk of transfusion-transmitted infections has been significantly reduced with the introduction of FDA licensed or cleared screening tests:
 - Current nucleic acid tests:
 - HIV1/2/O, HCV, HBV, WNV, ZIKV** and *Babesia*
 - Current serological tests:
 - HIV1/2, HCV, HBV, HTLVII, *T.cruzi*, Syphilis, CMV

*Jones et. al. Transfusion , 2020; ** Testing stopped due to reduce incidence

Division of Emerging and Transfusion Transmitted Diseases

Director

Hira Nakhasi, Ph.D.

Deputy Director

J. Peyton Hobson, Ph.D.

Associate Deputy Director for Policy

Julia Lathrop, Ph.D.

Associate Director for Managed Review

Sayah Nedjar, Ph.D.

Program Support Specialist

Alex Repace

Product Review Branch (PRB)

Acting Chief: Pradip Akolkar, Ph.D.

Pawan Jain
Krishna Ketha
Babita Mahajan
Susan Zullo
Nitin Verma
Rana Nagarkatti
Caren Chancey
Virginie Dujols
Iwona Fijalkowska
Kavita Singh
Nicholas Anderson

Laboratory of Bacterial and TSE Agents (LBTSEA)

Chief: David Asher, M.D.

Cyrus Betts
Juraj Cervenak
Luisa Gregori
Teresa Pilant
Oksana Yakovlev

Laboratory of Molecular Virology (LMV) Chief: Indira Hewlett, Ph.D.

Viswanath Ragupathy
Xue Wang
Jiangqin Zhao
Krishnakumar Devadas
Mohan Kumar Haleyrigisetty
Sherwin Lee

Laboratory of Emerging Pathogens (LEP) Chief: Sanjai Kumar, Ph.D.

Hong Zheng
Miranda Oakley
Victoria Majam
Alain Debrabant
Erica Silberstein
Robert Duncan
Carolyn Fisher
Hira Nakhasi
Sreenivas Gannavaram
Neven Ismail-O'Keefe
Parna Bhattacharya
Ranadhir Dey
Gerardo Kaplan
Maria Rios
Krishnamurthy Konduru
Andriyan Grinev
David McGivern
Rafaelle Gusmao
Sakthivel Subramaniam
(Vacant PI position)

Brief overview of DETTD laboratories/branches



- Laboratory of Molecular Virology (LMV):
 - Conducts mission-related research on pathogenesis of HIV, HTLV, and emerging retroviruses
- Laboratory of Emerging Pathogens (LEP)
 - Conducts mission-related research on emerging and reemerging blood borne parasitic, viral agents and tick-borne pathogens

Brief overview of DETTD laboratories/branches (cont'd)



- Laboratory of Bacterial and Transmissible Spongiform Encephalopathy Agents (LBTSEA)
 - Conducts mission-related research on bacteria and transmissible spongiform encephalopathy (TSE) agents

- Product Review Branch (PRB)
 - Conducts full-time review of regulatory submissions

DETTD regulatory research activities

- **Plan and conduct mission-related research on:**
 - Pathogenesis of transfusion-transmitted infections and blood-borne agents:
 - Human retroviruses (HIV-1 and HIV-2; HTLV-I/II)
 - Hepatitis viruses (A, B, C and E),
 - Arboviruses (West Nile virus, Dengue virus, Chikungunya virus and Zika virus),
 - Parasites (*Leishmania*, *Plasmodium*, *T. cruzi*)
 - Tick borne agents (Babesia, Anaplasma)
 - Bacteria (*T. pallidum*)
 - Transmissible spongiform encephalopathies Agent (vCJD)
- **Proactively ensure the safety of the blood supply by:**
 - Reviewing regulatory submissions (e.g., BLA, PMA, 510k, IND/IDE) for blood donor screening tests and HIV diagnostic tests
 - Evaluating new technologies for rapid and multiplex screening of the blood supply
 - Developing policy and guidance documents for blood donor screening tests and diagnostic devices

DETTD regulatory research activities (cont'd.)

- **Provide reference materials for validation of lot release testing**
- **Provide scientific and technical advice to other Agencies and Government components (e.g., CDC, DOD, DHHS)**
- **Outreach to stakeholders:**
 - Seek advice from Blood Product Advisory Committee
 - Participate in DHHS Advisory Committee on Blood Organ and Tissue Safety Availability
 - Serve as a liaison to committees of blood establishments and device manufacturers
 - Collaborate with World Health Organization as Collaborating Center for IVDs
 - Participate in horizon scanning of emerging and reemerging blood borne pathogens as a part of PHS subcommittee for EIDs.

Select examples of recent significant research publications



- Preclinical validation of a live attenuated dermatropic *Leishmania* vaccine against vector transmitted fatal visceral leishmaniasis (*Communications Biology*, 2021)
- *Babesia microti*: Pathogen Genomics, Genetic Variability, Immunodominant Antigens, and Pathogenesis (*Frontiers in Microbiology*, 2021)
- Human Placental Trophoblasts Are Resistant to *Trypanosoma cruzi* Infection in a 3D-Culture Model of the Maternal-Fetal Interface (*Frontiers in Microbiology*, 2021)
- Exosome mimicry by a HAVCR1-NPC1 pathway of endosomal fusion mediates hepatitis A virus infection (*Nature Microbiol.* 2020)

Select examples of recent significant research publications (cont'd)



- Effect of storage on survival of infectious *Treponema pallidum* spiked in whole blood and platelets. (*Transfusion*, 2021)
- The use of laser-based diagnostics for the rapid identification of infectious agents in human blood (*J. Applied Microbiol.* 2019)
- IRF3-mediated pathogenicity in a murine model of human hepatitis A (*PLoS Pathogen*, 2021)
- Comparison of miRNA Expression Profiles between HIV-1 and HIV-2 Infected Monocyte-Derived Macrophages (MDMs) and Peripheral Blood Mononuclear Cells (PBMCs) (*Int J Mol Sci*, 2020)
- Genomic and Phylogenetic Analysis of Zika Virus Isolates from Asymptomatic Blood Donors in the United States and Puerto Rico, 2016 (*Am J Trop Med Hyg*, 2020)

Regulatory and research accomplishments



- Reviewed applications- ~466
 - BLAs, PMAs, BLA and PMA supplements, 510(k)s, INDs and IDEs, Presubmissions
- Licensed several donor screening and cleared HIV diagnostic assays
- Research Publications- 22
- Secured funding both (intramural and outside)- \$2,489,423



Thank You