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

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BPAC update of the Site Visit Review on May 12, 2022
For
Laboratory of Emerging Pathogens (LEP)
&
Laboratory of Molecular Virology (LMV)

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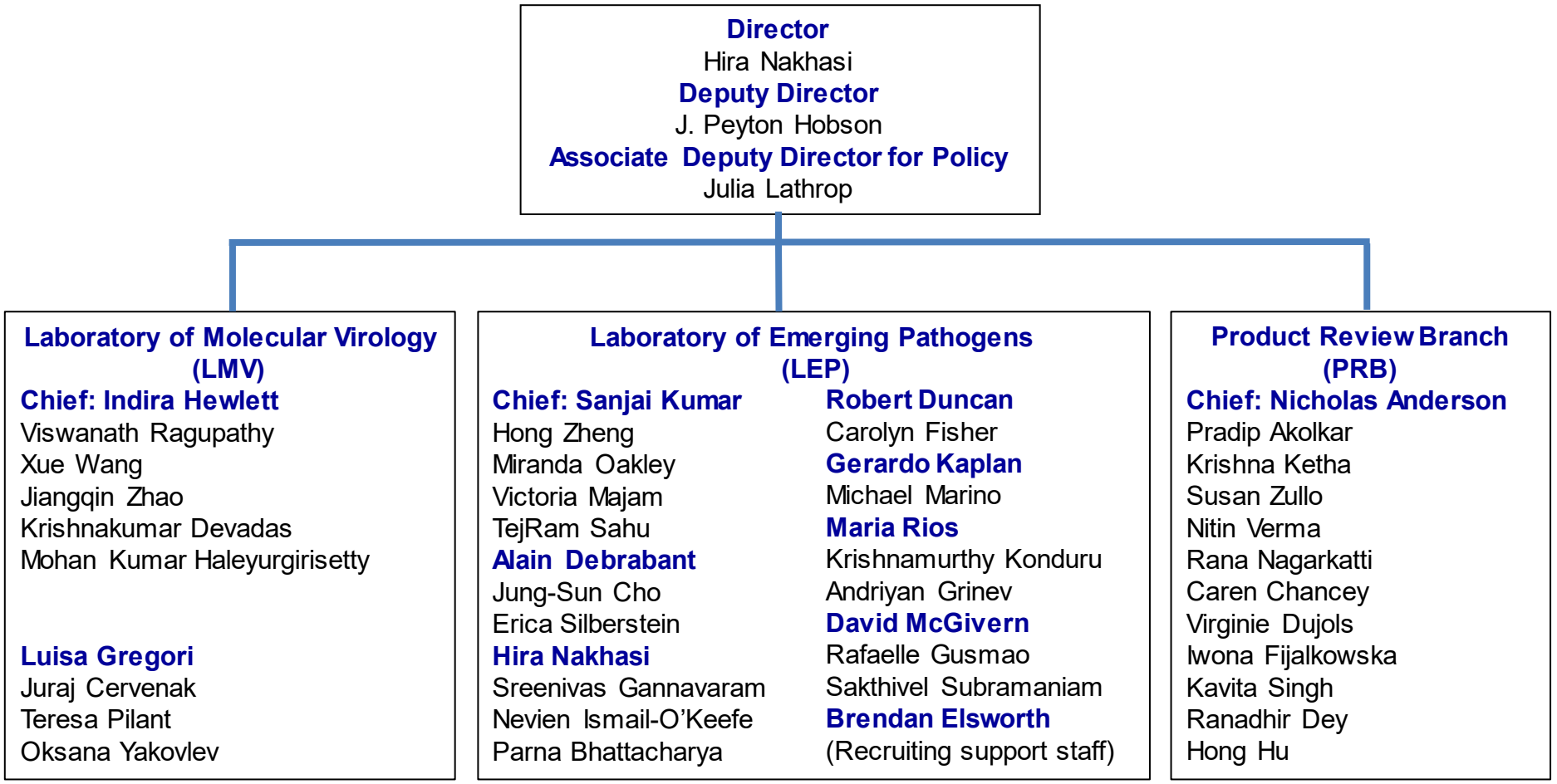
Division of Emerging and Transfusion Transmitted Diseases



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:
    - HIV-1/2/O, HCV, HBV, WNV, ZIKV** and *Babesia*
  - Current serological tests:
    - HIV-1/2, HCV, HBV, HTLV-I/II, *T.cruzi*, Syphilis, CMV

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

Overview of DETTD laboratories/branches

- Laboratory of Molecular Virology (LMV):
  - Focus on pathogenesis of retroviruses
- Laboratory of Emerging Pathogens (LEP)
  - Focus on emerging and reemerging blood borne parasitic, viral agents and tick-borne pathogens
- Product Review Branch (PRB)
  - Focus on review of regulatory submissions

DETTD Research and Regulatory activities

- **Plan and conduct mission-related research on:**
  - Pathogenesis of transfusion-transmitted infections of 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*, *Ehrlichia*)
    - Bacteria (*T. pallidum*)
    - Transmissible spongiform encephalopathies Agent (vCJD, CJD)

- **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 retroviral diagnostic devices

DETTD research and regulatory activities (cont'd.)

- **Provide source material for blood borne pathogens to:**
  - develop reference materials for validation of lot release testing for blood donor screening assays

- **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 for blood establishments and device manufacturers e.g., AABB; PPTA
  - 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

- Modulation of HIV Replication in Monocyte-Derived Macrophages (MDM) by Host Antiviral Factors, Secretory Leukocyte Protease Inhibitor and Serpin Family C Member 1, Induced by Steroid Hormones. (*Viruses. 2022*)

- Abnormal prion protein, infectivity and neurofilament light-chain in blood of macaques with experimental variant Creutzfeldt-Jakob disease. (*J Gen Virol. 2022)*

- Centrin-deficient *Leishmania mexicana* confers protection against Old World visceral leishmaniasis *(NPJ vaccines, 2022)*

- Comparative single-cell transcriptional atlases of *Babesia* species reveal conserved and species-specific expression profiles *(PLoS biology, 2022)*

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

- Development and characterization of secondary standards for nucleic acid amplification technology (NAAT) assays for detection of hepatitis E virus (*Journal of Clinical Virology, 2022*)
- Serum soluble mediator profiles and networks during acute infection with distinct DENV serotypes (*Front Immunol, 2022*)
- Tracking Ebolavirus genomic drift with a resequencing microarray. (*PLoS One 2022*)

Research and Regulatory accomplishments (FY21-22)

- Reviewed applications- ~422
  - BLAs, PMAs, BLA and PMA supplements, 510(k)s, INDs, IDEs, Presubmissions, Consult reviews
- Licensed several donor screening and cleared HIV diagnostic assays
- Research Publications- ~30
- Funding both (intramural and outside)-$2,278,063

Review of LMV and LEP PI's Research Programs held on May 12, 2022

Indira Hewlett (LMV): Improving Safety of the Blood Supply and Patient Management for HIV/AIDS by Developing Sensitive Diagnostic Tools and Investigating Disease Pathogenesis

Luisa Gregori (LMV): Detection of transmissible spongiform encephalopathy (TSE) agents and removal of bacteria in blood and blood components

Gerardo Kaplan (LEP): Diagnosis and Pathogenesis of Filoviruses (FV) and Hepatitis A Virus (HAV)

David McGivern (LEP): Diagnosis and Pathogenesis of Hepatitis Viruses that Threaten the Safety of Blood and Related Products

Maria Rios (LEP): Exploring Pathogenesis and Markers of Arbovirus Infections and Developing Reference Reagents to Improve Blood Safety

Thank You