

## Background

### Advancing HIV Cure Research:

The development of effective treatments or cures for a wide range of diseases requires translational studies that are directly relevant to human pathophysiology. The use of human biospecimens plays a key

role in accelerating scientific discoveries in HIV research by providing scientists with a direct experimental model system to advance understanding of HIV prevention, cure, co-morbidities, and therapeutic strategies. To address several complex issues facing HIV research, more comprehensive human tissue resources are needed.

### Key Objectives:

1. Discuss screening tools to identify, authorize, and recover biospecimens from HIV+ donors
2. Describe recovery protocols for HIV+ biospecimens to support areas of high impact HIV research
3. Report on the establishment of NDRI's HIV Human Tissue Resource (HHTR)

## NDRI is a Leading Partner for Research Placement

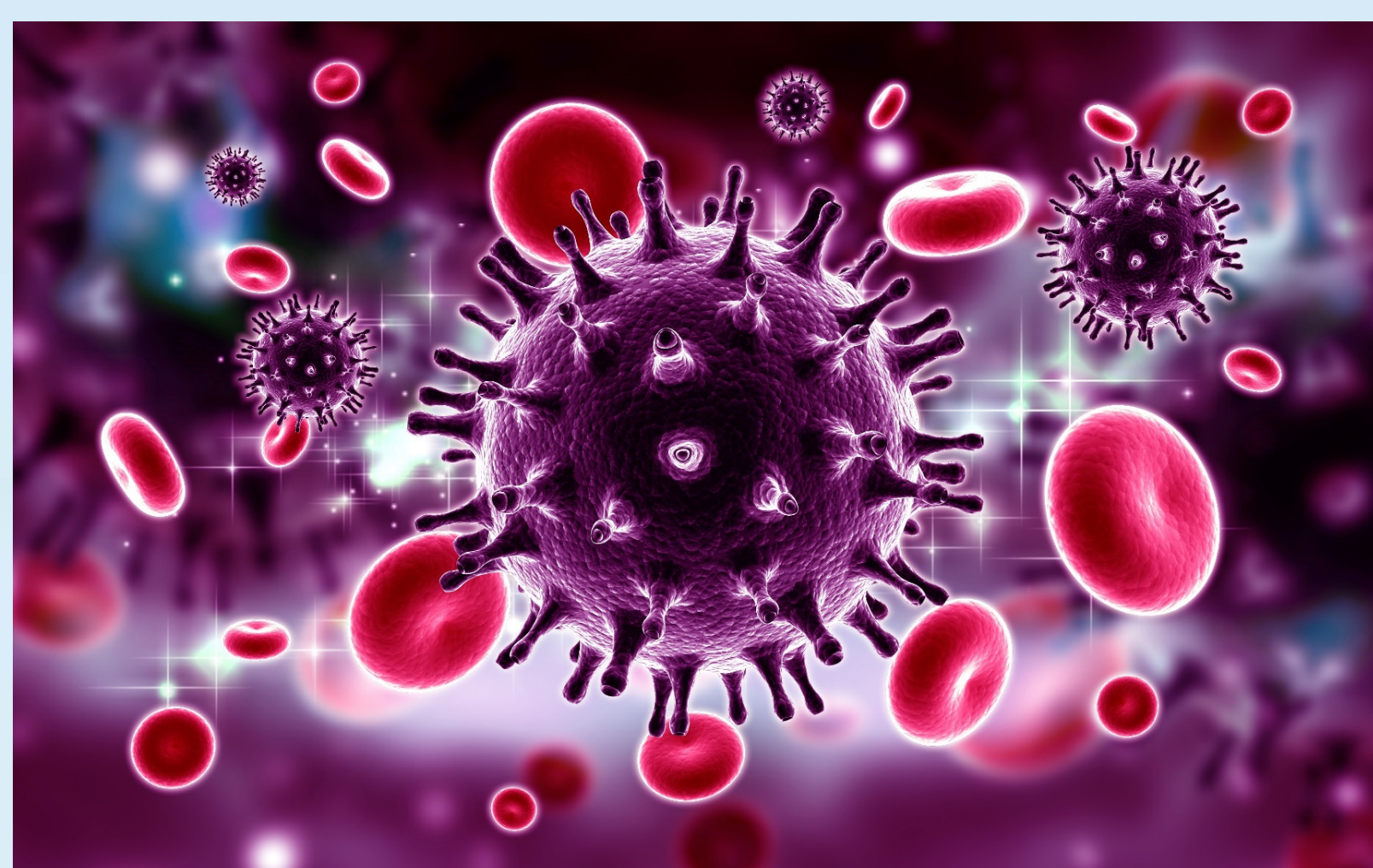


- ✓ A 501c3 corporation
- ✓ NIH funded for over 30 years
- ✓ 6,500 biospecimens/year to biomedical scientists
- ✓ Supporting 150 publications annually

## NDRI's Private Donor Program (PDP) Coordinates Donor Authorization and Tissue Recovery



**NDRI's Private Donor Program (PDP) Enables Screening and Recovery of Tissues from HIV+ Donors:** NDRI receives HIV referrals predominately from the Gift of Life Donor Program and screens them against their active HIV research project recovery protocols. NDRI's PDP then follows-up on eligible donors by working directly with the next-of-kin to obtain authorization for donation and a medical/social history. NDRI coordinates biospecimen recovery with PDP recovery specialists and ships tissue to approved researcher projects.



## HIV Replication Study Highlights the Impact of Human Biospecimen Collection for HIV Research

### Project Summary

- ❑ An NIH-led 14-month initiative studying persistent low-level HIV replication in tissue reservoirs (completed in September 2017)
- ❑ NDRI served as only tissue procurement contractor to coordinate the recovery of multiple (n~72) biospecimens per donor from 10 donors
- ❑ Referral sources for the HIV+ donors were **Gift of Life Donor Program** and the **Maryland Medical Examiner's (ME) Office**

### Study Results

**A large-scale HIV+ tissue collection is essential to fully characterize latent viral reservoirs:** This study's goal is to characterize the latent viral reservoirs in individuals with well-controlled disease in order to advance HIV cure research. Multiple frozen aliquots from 10 donors resulted in a comprehensive dataset for analysis.

- 185 HIV+ Donors Referred
- 24 HIV+ Donors Eligible
- 10 HIV+ Donors Recovered
- 729 Frozen Tissue Samples Collected

| Donor Eligibility                          |
|--------------------------------------------|
| • Age: 0-100                               |
| • HIV+                                     |
| • Known compliance with ART medication     |
| • Cause of death not due to HIV/AIDS       |
| • Co-infections with HCV or HBV acceptable |
| • CD4 count and viral load data preferred  |

| Tissues Collected |                   |
|-------------------|-------------------|
| • Blood           | • Liver           |
| • Brain           | • Lymph Node      |
| • Colon           | • Pancreas        |
| • CSF             | • Small Intestine |
| • Esophagus       | • Spleen          |
| • Heart           | • Stomach         |
| • Kidney          | • Tonsil          |

**Well-characterized HIV+ donors and multiple tissue types are essential to understand viral latency:** Donors were HIV+ with suppressed virus, identified by known ART compliance and/or CD4 count and viral load. Multiple regions of the tissues shown in the table were collected from each donor, resulting in a large scale, standardized tissue collection for the experimental analysis

### HIV Viral DNA/RNA was Detectable in All Tissues Analyzed at Varying Frequencies from ART-Compliant Donors

- ❑ Lymph Node (1/5)
- ❑ Colon (4/5)
- ❑ Spleen (3/5)
- ❑ Brain (3/5)
- ❑ Kidney (1/5)
- ❑ Liver (3/5)

**Evidence of HIV replication and reservoirs in tissue samples at autopsy from donors (n=5) on cART with undetectable HIV RNA in blood.** V. Natarajan<sup>1</sup>, Y. Badralmaa<sup>1</sup>, H.C. Lane<sup>2</sup> (1, Leidos Biomedical; 2, NIAID). Presented at AIDS 2018.

## Meeting Unmet Needs of the HIV Research Community

### Human Tissue and Organ for Research Resource (HTORR)



- ❑ NDRI's HTORR program has been funded by the NIH for > 30 years
- ❑ Goal is to provide human biospecimens to academic biomedical investigators
- ❑ Through HTORR, NDRI has supported HIV research with funding from NIAID

### Establishment of HIV Human Tissue Resource (HHTR)



### Supplemental NIH Funding Will Support a Valuable New Tissue Resource:

The Office of the Director at NIH awarded NDRI a supplement to its HTORR program to create the HHTR— a human biospecimen resource to support the advancement of HIV research. NDRI leads an advisory council made up of NIH, academic, and industry leaders in the field whose goal is to identify the areas of greatest need within HIV research. Gift of Donor Program will provide HIV donor referrals for the HHTR.

**Current Areas of Unmet Needs:** The HHTR Advisory Council have identified critical areas of unmet need that the HHTR can support.

- Well-characterized HIV+ Donors (e.g. Compliant vs Non-Compliant)
- Increased Donor Diversity (Minorities and Women)
- Multiple Tissues from One Donor

## Summary

1. HIV investigators require access to rigorous and uniformly collected human biospecimens to generate consistent and reproducible experimental data
2. The HIV Replication study provides a proof of concept model for supporting HIV studies requiring:
  - Biospecimens from well-characterized HIV+ donors
  - Complex and multi-biospecimen recoveries from HIV+ donors
3. HHTR will build upon this model to create a new resource that will address several unmet needs for HIV research community and support multiple groundbreaking and inventive HIV studies aimed at a cure

## Acknowledgements

The HIV Replication Study was funded through a contract by Leidos Biomedical. The HHTR is supported by NIH Grant 3U42OD011158-28S1. NDRI would like to thank the donors and their families for providing such valuable donations to advance HIV research.