Accelerating Military Medical Research via Project-driven Human Biospecimen Collection and Analysis

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NDRI
Empowering Research and Discovery

Background

Advancing Military and Civilian Translational Medicine: Medical research supported by the DoD is variegated, and spans many platforms from translational studies to basic science. This research is challenging for numerous reasons, but species-specific differences in genomic, transcriptomic, and proteomic profiles are emerging as major hindrances for both military and civilian translational medicine. Experimental analysis on primary human tissues provides an alternative method to overcome this challenge, but acquiring appropriate biospecimens to develop human model systems is a critical impediment for most investigators.

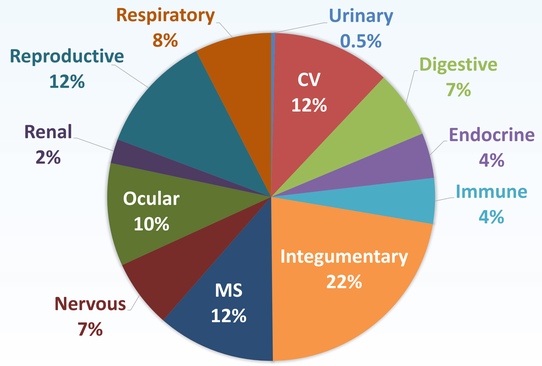
Key Objectives:

1. ***Discuss access to primary human biospecimens to be used as an experimental model system for translational research***
2. ***Describe advances in scientific methodologies and biospecimen procurement practices that have enabled the use of human biospecimens for areas of high impact research***

NDRI Provides Superior Access to Human Biospecimens

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

NDRI Provides Normal and Diseased Human Biospecimens From Any Body System



Biospecimen Diversity Enables a Wide Spectrum of Disease Research: In the last 3 years, NDRI shipped over 19,000 samples to over 600 investigators. The pie chart shows the proportion of tissues shipped by body system. Tissues include both normal and diseased samples, representing 100 distinct common and rare diseases.

Standardized Human Tissue Collection Allows for Rigorous Experimental Analysis

The Genotype-Tissue Expression (GTEx) Project Highlights the Impact of Human Tissue Research

- **658 Donors**
- **Avg 28.3 Tissues per Donor (median=26)**
- **>80,000 Tissue Samples Collected**

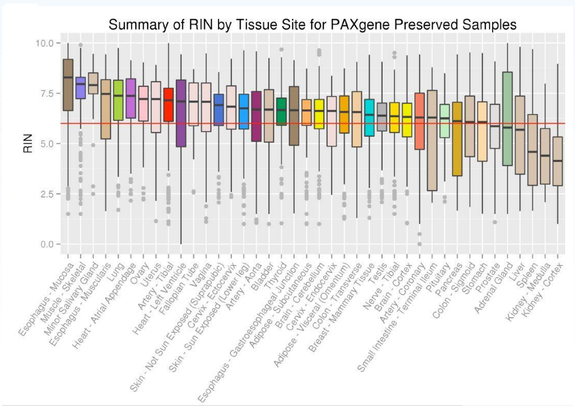
Project Highlights

- An NIH-led initiative studying genetic variation and the regulation of gene expression in a range of human tissue types
- NDRI served as the lead tissue procurement contractor for the project, responsible for 658 out of ~1000 donors collected

Tissue Site Detail	Abbreviation	Color	n	RIN Mean	RIN SD	Sample Ischemic Time (min) Mean	Sample Ischemic Time (min) SD	Age Mean
★Adipose - Subcutaneous	ADPSBQ		94	6.9	0.6	421.9	318.3	48.2
Adipose - Visceral (Omentum)	ADPVSC		19	7.2	0.6	401.4	303.1	46.9
Adrenal Gland	ADRNLG		12	8.3	0.8	172.8	107.2	51.4
Artery - Aorta	ARTAORT		24	7.8	0.8	262.0	178.3	50.8
Artery - Coronary	ARTCRN		9	7.5	0.7	312.4	307.9	55.3
★Artery - Tibial	ARTTBL		112	7.5	0.7	486.7	350.0	47.9
Brain - Amygdala	BRNAMY		23	6.9	0.8	NA	NA	51.2
Brain - Anterior cingulate cortex (BA24)	BRNACC		17	7.0	0.7	NA	NA	51.4
Brain - Caudate (basal ganglia)	BRNCDT		36	7.5	0.8	NA	NA	52.5
Brain - Cerebellum [PAXgene]	BRNCHA		30	7.4	1.0	868.9	300.9	51.6
Brain - Cerebellar Hemisphere [Frozen]	BRNCHB		24	7.6	1.1	NA	NA	49.7
Brain - Cortex [PAXgene]	BRNCTXA		23	7.1	0.9	837.2	280.3	51.3
Brain - Frontal Cortex (BA9) [Frozen]	BRNCTXB		24	7.5	0.9	NA	NA	55.1
Brain - Hippocampus	BRNHPP		24	6.9	0.7	NA	NA	51.1
Brain - Hypothalamus	BRNHPT		23	7.0	0.9	NA	NA	51.4
Brain - Nucleus accumbens (basal ganglia)	BRNNCC		28	7.4	0.6	NA	NA	53.4
Brain - Putamen (basal ganglia)	BRNPTM		20	7.3	0.9	NA	NA	49.5
Brain - Spinal cord (cervical c-1)	BRNSPC		16	7.1	0.7	NA	NA	52.5
Brain - Substantia nigra	BRNSNG		25	6.8	0.7	NA	NA	53.8
Breast - Mammary Tissue	BREAST		27	7.0	0.7	645.6	425.4	50.3
Cells - EBV-transformed lymphocytes	LCL		39	9.9	0.2	59.7	502.0	46.2
Cells - Transformed fibroblasts	FIBRBLS		14	9.5	0.5	544.5	478.4	49.2
Colon - Transverse	CLNTRN		12	7.5	0.8	236.5	137.0	46.3
Esophagus - Mucosa	ESPMCS		18	8.6	0.7	330.9	219.6	51.7
Esophagus - Muscularis	ESPMSL		20	7.9	0.6	310.6	273.3	48.5
Fallopian Tube	FLLPNT		1	6.1	NA	520.0	NA	51.0
Heart - Atrial Appendage	HRTAA		25	7.5	0.7	492.3	323.9	51.0
★Heart - Left Ventricle	HRTLV		83	7.9	0.9	380.9	334.4	48.0
Kidney - Cortex	KDNCTX		3	6.8	0.4	583.0	585.0	56.3
Liver	LIVER		5	7.6	0.9	365.2	321.8	42.8
★Lung	LUNG		119	7.6	0.9	447.0	380.4	48.9
★Muscle - Skeletal	MSCLSK		138	7.9	0.6	486.1	358.1	49.2
★Nerve - Tibial	NERVET		88	7.0	0.7	463.8	315.6	49.4
Ovary	OVARY		6	7.3	0.7	401.0	248.4	43.5
Pancreas	PNCREAS		19	6.8	0.7	200.4	115.3	49.3
Pituitary	PTTARY		13	7.3	0.6	841.3	305.5	51.9
Prostate	PRSTTE		9	6.8	0.7	231.1	84.0	50.2
Skin - Not Sun Exposed (Suprapubic)	SKINNS		23	7.2	0.7	557.2	388.2	48.7
★Skin - Sun Exposed (Lower leg)	SKINS		96	7.0	0.7	498.5	364.0	49.0
Stomach	STMACH		12	7.4	0.9	250.0	131.6	47.8
Testis	TESTIS		14	7.0	0.9	293.6	236.3	52.4
★Thyroid	THYROID		105	7.0	0.7	428.5	391.7	49.2
Uterus	UTERUS		7	7.4	1.0	313.3	184.3	48.7
Vagina	VAGINA		6	7.8	1.1	414.5	234.4	54.0
★Whole Blood	WHLBLD		156	8.1	0.8	238.4	498.2	49.7
All			1641	7.5	0.9	418.9	394.2	50.2

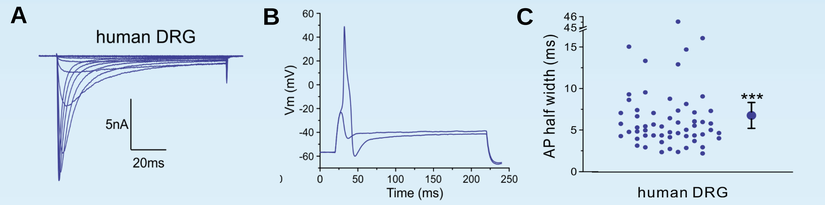
GTEx collection approach yielded an extensive data set of high quality RNA to evaluate gene expression across multiple tissues: Characteristics of a subset of RNA-sequenced samples from the GTEx pilot phase (n=270 donors) are shown. The red stars indicate the tissues prioritized for RNA sequencing. RIN values of >6 were obtained from 96% of the GTEx samples.

RNA quality varies by tissue type: Box plots of RNA quality as measured by RIN for all the PAXgene preserved tissues sampled for the GTEx project. Some tissues, such as muscle, lung, and esophagus, have well-preserved RNA. Other tissues, such as kidney, colon, and spleen, generally have poorly preserved RNA.



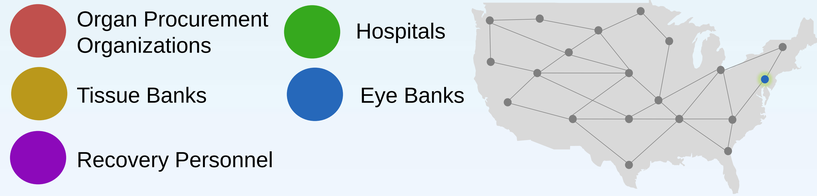
Data from *GTEx Consortium. The Genotype-Tissue Expression (GTEx) pilot analysis: Multitissue gene regulation in humans. Science 2015 May: 348(6235):648-660.*

Human DRGs are Suitable for Electrophysiological Analysis



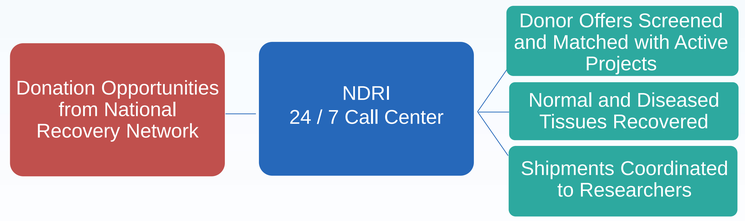
Human DRG neurons recovered from organ donors maintain functionality *in vitro* and provide a reliable model system for evaluating responses to mechanical, thermal, and chemical stimuli. A. Representative Nav1.8 current family traces recorded in the voltage-clamp mode from a human DRG. Cells were held at -60 mV and stepped to a range of potentials (-60 to +40 mV in 5 mV increments) for 100 ms. **B.** Representative action potential traces recorded in the current-clamp mode from a human DRG neuron. The resting membrane potential for human DRG neurons was -55.0±0.8 mV (n=59), which was depolarized by 6 mV. Action potentials were elicited by 200-ms step depolarizing current injections from resting membrane potential. **C.** For human DRG neurons, the mean half-width of the action potential was 6.83±0.78 ms (n=59). Data from *Han C et al J Neurophysiol 2015;113: 3172-3185.*

NDRI's Network Enables Biospecimen Diversity



Recovery Network: The Centers for Medicare and Medicaid Services (CMS) mandate that US medical centers refer all acute deaths to organ, tissue, and eye donation organizations. NDRI partners with this nationwide network to screen donors for biomedical research use, allowing for the authorization and collection of tissues from individuals with a documented history of specific medical conditions and/ or diseases that match authorized research donors to specific research protocols.

NDRI: A Valued Partner for Military Medical Research



Donation to Discovery: NDRI receives biospecimen donor profiles from deceased, living, and pre-registered research donors. Our 24/7 fulfillment staff matches potential donors with active researcher protocols to allow NDRI to place multiple tissues with a wide range of investigators. This approach yields highly suitable biospecimens for accelerating the development of new medical therapies and treatments for wounded service members and civilians.