# AKINow Panel:

## How to Build and Best Use Kidney Biorepositories

*April 18, 2024*

ASN
American Society of Nephrology

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# Welcome

***LESLIE S. GEWIN, MD***

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# Agenda

**Introductory Remarks**
*Leslie Gewin, MD*

**Panel Discussion**
*Adriana M. Hung, MD, MPH*
*Sanjay Jain, MD, PhD*
*Chirag R. Parikh, MD, PhD, FASN*

**Audience Q&A**
*Leslie S. Gewin, MD and panelists*

**Closing Remarks**
*Leslie S. Gewin, MD*

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# Zoom Housekeeping

**Presentation will last 60 minutes.**

**Session is recorded.**
Recording and resources will be uploaded onto the EPC website.

**Audio is muted.**
Use the Q&A icon or chat function to ask the presenters questions and read their responses.

**How did we do?**
Survey will be shown at the end of the webinar.

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# Disclaimer

*This AKINow panel discussion is provided as information and education and should not be construed as medical advice or recommendations for patient care. The information expressed is that of the speaker(s) and contributor(s) only. Clinicians are to use their own training, clinical observations, and judgment to make all diagnostic and treatment decisions. The ASN Alliance (including ASN) does not offer medical advice.*

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# Faculty Disclosures

**Leslie S. Gewin, MD**

**Employer:** Washington University in St. Louis School of Medicine, St. Louis VA Hospital
**Research Funding:** NIH, VA; Longer Life Foundation
**Honoraria:** Daiichi Sankyo
**Advisory or Leadership Role:** Editorial boards for JASN, Kidney360, and American Journal of Physiology Renal Physiology, and Frontiers in Nephrology; External Scientific Advisor, Kidney Institute of New Mexico; Executive Council for Women in Nephrology and Council member for Southern Society of Clinical Investigation, member of AKINow Workgroups

**Adriana M. Hung, MD, MPH**

**Employer:** Vanderbilt University and Veterans Affairs
**Research Funding:** VHA CSR&D Merit "Genetics of Kidney Disease & Hypertension, Risk Prediction and Drug Response"; Vertex Grant to VUMC
**Advisory or Leadership Role:** Co-Chair, Million Veteran Program (MVP) Publication and Presentations Committee and Co-chair of the MVP Phenomic Working Group

**Sanjay Jain, MD, PhD**

**Employer:** Washington University in St. Louis School of Medicine
**Advisory or Leadership Role:** HUBMAP, KPMP

**Chirag R. Parikh, MD, PhD, FASN**

- **Employer:** Johns Hopkins Medicine
- **Ownership Interest:** Renalytix
- **Research Funding:** National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK); National Heart, Lung and Blood Institute (NHLBI)
- **Advisory or Leadership Role:** Principal Investigator: TRIBE-AKD Network; Steering Committee, KPMP

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# Panel discussion

*Leslie S. Gewin, MD*
*Moderator*

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PANELISTS

## Panelists

**Adriana M. Hung**
**MD, MPH**

**Sanjay Jain**
**MD, PhD**

**Chirag R. Parikh**
**MD, PhD, FASN**

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# How to build and best use kidney biorepositories

Sanjay Jain MD, PhD
sanjayjain@wustl.edu
*Professor, Medicine (Nephrology)*
Director, Kidney Translational Research Center – KTRC

- *Who is it for?*
- *How to make it happen?*
- *Do we need to think about applications not currently perceived?*
- *Can we sustain it?*

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## GENERAL POINTS

**Purpose**
- Cell diversity
- Gene networks
- Cell throughput
- Cell rarity
- Pathobiology
- Biomarkers
- Validations

**Source**
- Deceased Donor
- Living Donor
- Surgical Resection
- Biopsy
- Fluid samples

$f(\text{trash})=\text{trash}$ (in vivo / vitro)

$f(\text{trash})=\text{trash}^2$ (in vivo / vitro)

$f(\text{trash})=\text{trash}^3$ (in vivo / vitro plus omics)

**Factors**
- Accessibility
- Patient burden
- Metadata – general health
- Sampling
- Timely preservation
- QA/QC in place
- Infrastructure – sample longevity
- Broad sharing
- Standardized protocols
- Costs

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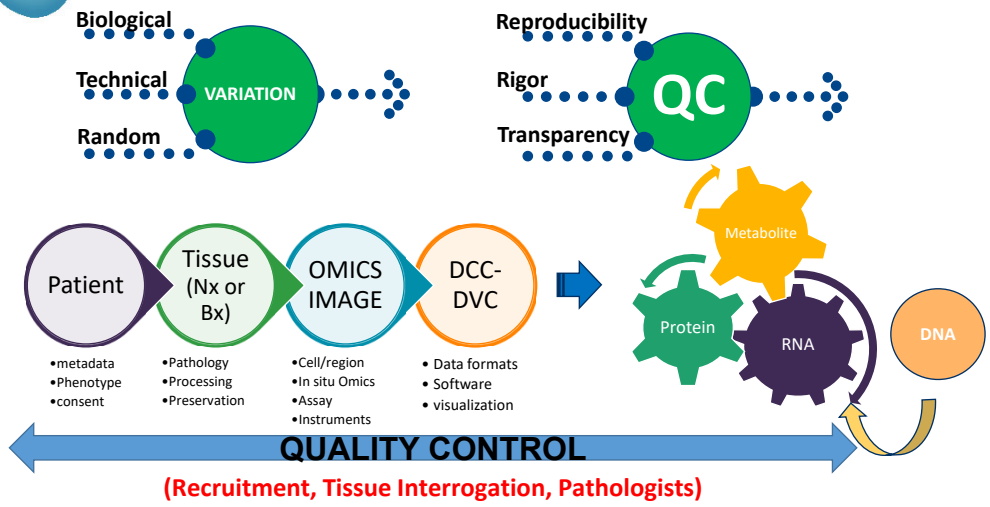
## POTENTIAL SOURCES OF VARIABILITY




*El-Achkar…Jain, AJP, Phys Genomics, 2021*

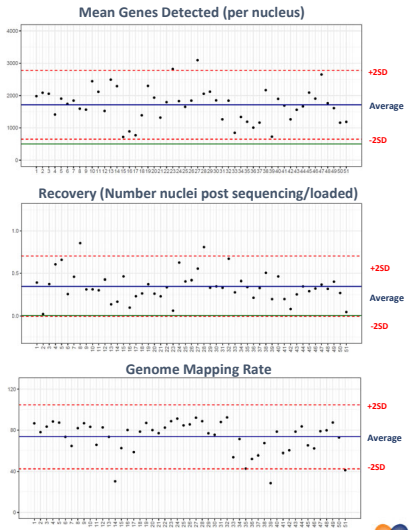


## QUANTITATIVE METRICS TO ASSESS TISSUE QUALITY

- Procurement time (warm ischemia, cold ischemia)
- **Preservation and Processing (perfusate, media, fixative, freezing, time, shipping)**
- Tissue morphology (composition, age-appropriate histopathology – inflammation, fibrosis, vascular disease, artifacts, cell death, epithelial injury); percent or scale
- **Molecular (what should these be for RNA, Protein, Metabolites…?)**

## ASSAY PERFORMANCE AND DRIFT OVER TIME

***Some metric to assess robustness of procedures for the use desired***

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# National repositories (MVP, BioVU)versus building your own repository

*Adriana M. Hung*
*Professor of Medicine*

*Vanderbilt Precision Nephrology -KidPhenGen*
*Division of Nephrology and Hypertension*
*Vanderbilt University Medical Center*

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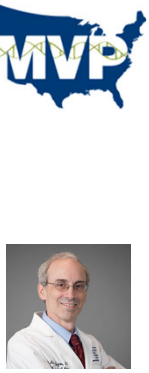
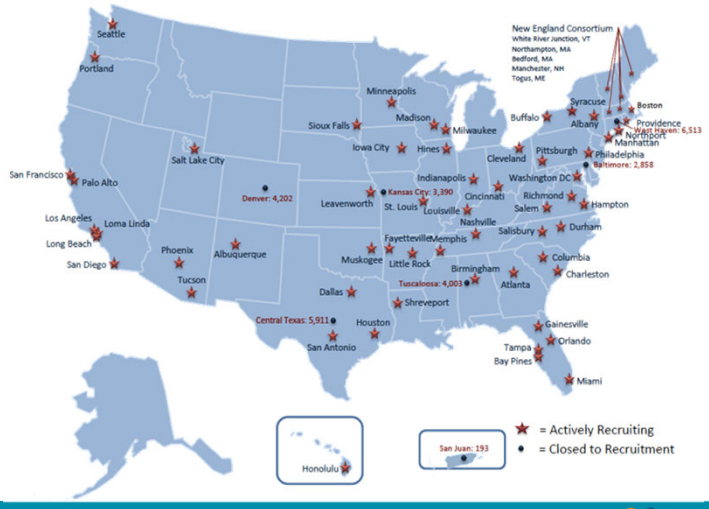
## The Million Veteran Program: >1,000,000 participants

❖ Clinical cohort of US military veterans enrolled at 65 (**~80 VAMC)** since 2011



Chief, Division of Aging
Professor, Harvard Medical School

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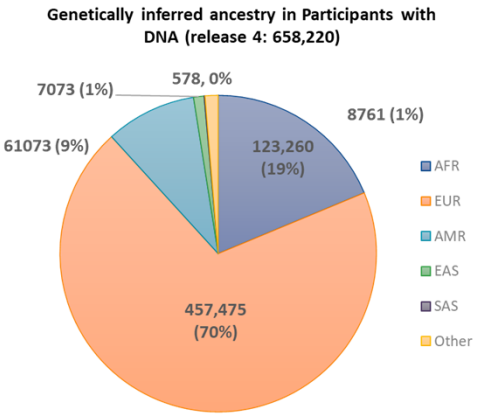
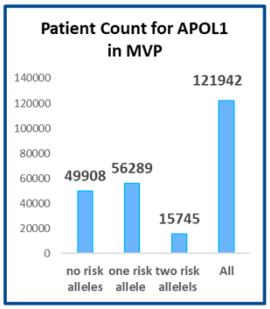
## The Million Veteran Program: Diversity in genetics

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**The role of APOL1 in AKI in patients with COVID-19**

**The characterization of N264K a protective variant that represent the genetic proxy of an APOL1 blocker**

**The role of G6PD deficiency in diabetes complications.**

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## Current Omics Plans

- ❑Genotyping for all MVP sample (n=658,220 for release 4)
  - MVP array (Affymetrix +custom chosen)
- ❑WGS: 182,000 (10K pilot 80x)
- ❑Methylation: 42,000 (currently available)
  - MVP array (Affymetrix +custom chosen)
  - MVP Ethic array
- Exomes: 250,000
- Metabolomics: 20,000 to 10,000
- Proteomics (pilot on 1000 individuals)

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## Million Veteran Program (MVP)

- Enroll up to one million users of the VHA into an observational mega-cohort
  - Blood collection for storage in biorepository for future research
  - Collect self-reported health and lifestyle information
  - Access to electronic medical record
  - Ability to recontact participants

Million Veteran Program

VETERANS HEALTH ADMINISTRATION

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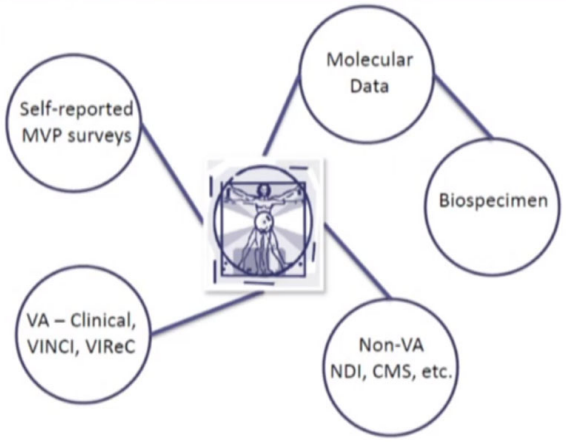
# MVP Data Universe

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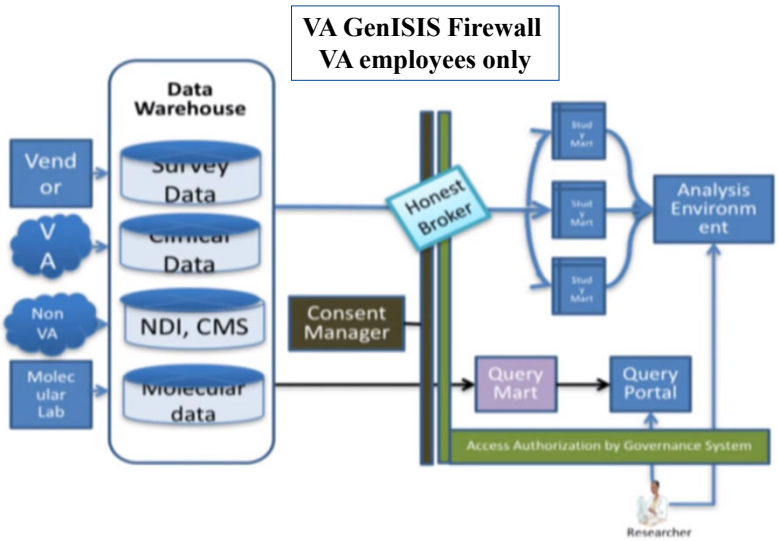
# System Architecture




VA has created a data commons that is aimed to non-VA investigators; will be available in the near future

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CIPHER

CENTRALIZED INTERACTIVE PHENOMICS RESOURCE

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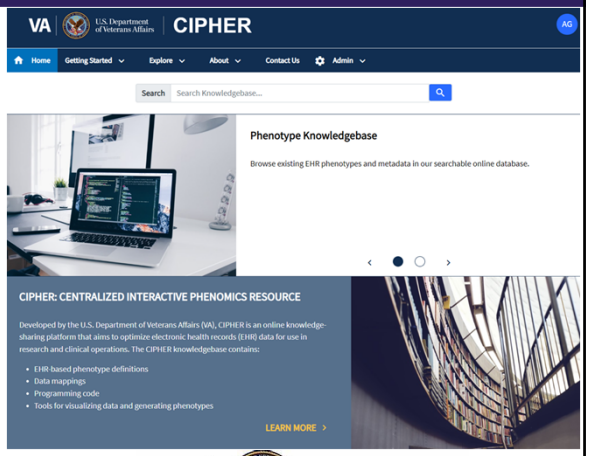
CIPHER@va.gov | phenomics.va.ornl.gov




Million Veteran Program (MVP) (va.gov)

VA U.S. Department of Veterans Affairs

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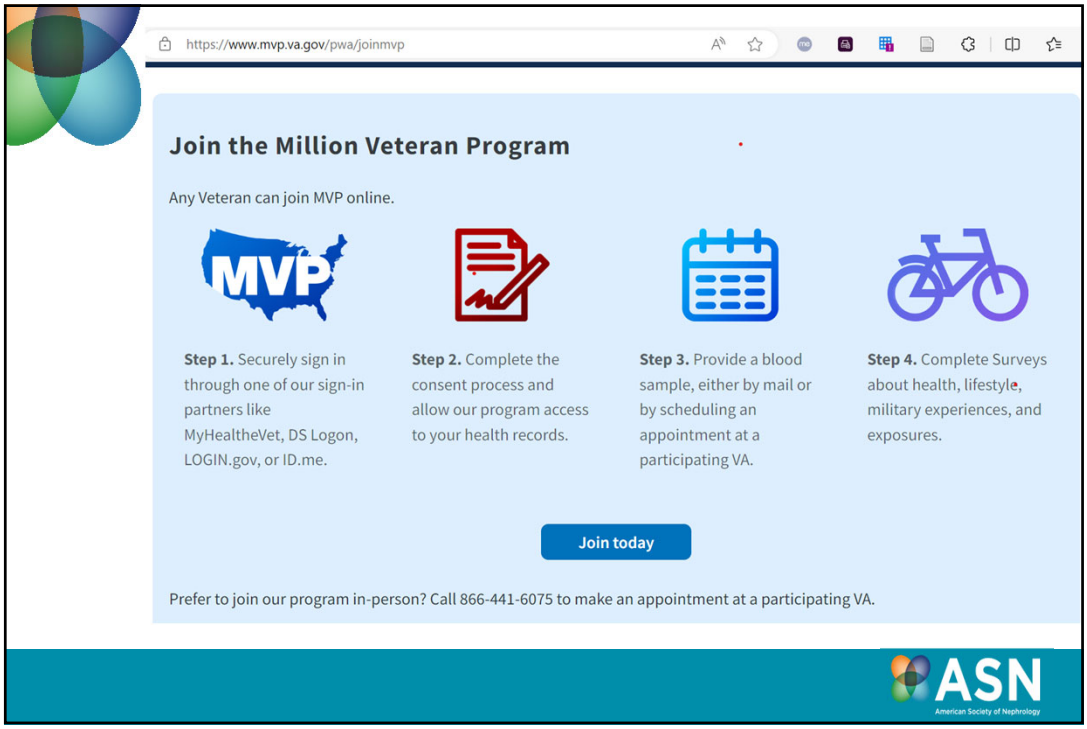


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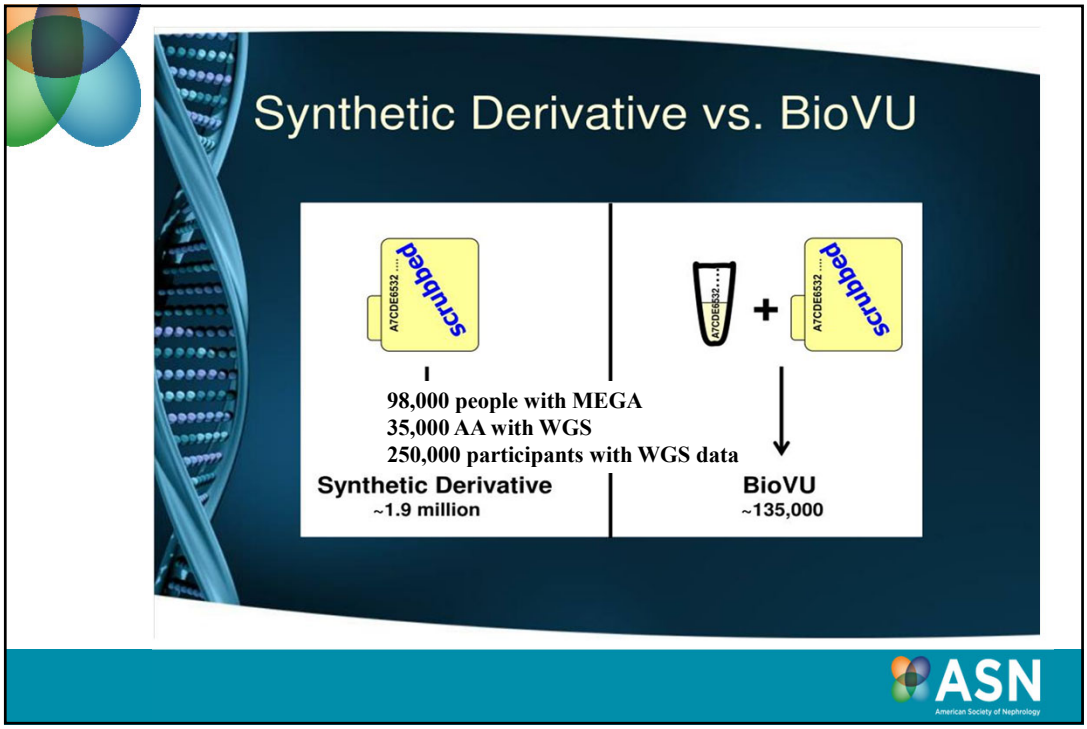


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## Question & collaborations:


**Kidney Phenomics & Genomics (KidPhenGen) / Precision Nephrology**

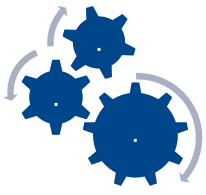
Understanding the genetic and environmental factors that contribute to chronic kidney disease (CKD) progression and outcomes in CKD to improve the care we provide through personalize medicine and reduce kidney outcomes inequalities

### Precision phenomics

***VA e-kidney Bx repository***
***Progression phenotypes***
Phenomics risk score (pair WGS)
Urine/ imaging/ discovery.

### Discovery & integrative Omics

**GWAS/WES/WGS and fine mapping**
**Transcriptomic/metabolomics/proteomics/epigenetics**
**Functional genomics**



### Precision prescribing

**Pharmacoepidemiology**
**Emulation trials**
**Pharmacogenomics**
**MR & the druggable genome**

### Individual risk prediction & Environmental exposures

**PRSs/ Epidemiology & Outcomes**
**Mobile/Fitbit/etc**
**Implementation/ROR**

*email: Adriana.Hung@vumc.org*

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# Thank You

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## AUDIENCE Q&A

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Thank you for attending today's AKINow panel discussion!
Please contact ASN with any questions:
Email: epc@asn-online.org
Website: epc.asn-online.org
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