AKINow Panel:
How to Build and Best Use Kidney Biorepositories

April 18, 2024

Welcome

LESLIE S. GEWIN, MD
**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.
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.

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: Renalytx
• 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
Panel discussion

Leslie S. Gewin, MD
Moderator

Panelists

Adriana M. Hung
MD, MPH

Sanjay Jain
MD, PhD

Chirag R. Parikh
MD, PhD, FASN
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?

### GENERAL POINTS

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<th>Purpose</th>
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<td>QA/QC in place</td>
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<td>Infrastructure – sample longevity</td>
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- Costs
- Broad sharing
- Standardized protocols
POTENTIAL SOURCES OF VARIABILITY

- Biological
- Technical
- Random

Variation

Reproducibility

Rigor

Transparency

QC

QUALITY CONTROL

(Recruitment, Tissue Interrogation, Pathologists)

El-Achkar...Jain, AJP, Phys Genomics, 2021

QUALITATIVE 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

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

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

The Million Veteran Program: Diversity in genetics

Genetically inferred ancestry in Participants with DNA (release 4: 658,220)

- 457,475 (70%)
- 61073 (9%)
- 123,260 (19%)
- 8761 (1%)
- 578 (0%)

Patient Count for APOL1 in MVP

- 121942
- 56289
- 15745

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.
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)

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

VETERANS HEALTH ADMINISTRATION
VA has created a data commons that is aimed to non-VA investigators; will be available in the near future.
How to Contribute

1. Navigate to https://phenomics.va.ornl.gov/
2. Create an account
3. Submit your phenotype using our phenotype web form

Million Veteran Program (MVP) (va.gov)
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 personalized 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**
- PRS/ Epidemiology & Outcomes
- Mobile/Fitbit/etc
- Implementation/ROR

email: Adriana.Hung@vumc.org
Thank You

AUDIENCE Q&A
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