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TITLE: Multispecies, Integrative GWAS for Focal Segmental Glomerulosclerosis

PRINCIPAL INVESTIGATOR: Dr. Ali G. Gharavi

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Fort Detrick, Maryland 21702-5012

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6. AUTHOR(S)
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7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
TRUSTEES OF COLUMBIA
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8. PERFORMING ORGANIZATION REPORT NUMBER

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13. SUPPLEMENTARY NOTES

14. ABSTRACT The goal of this project are to identify genetic determinants of focal segmental glomerulosclerosis (FSGS) using genomewide association studies in mouse strains. We have shown that the development nephropathy in the HIV-1 transgenic mice (TgFVB) is highly strain dependent. Linkage mapping in murine crosses have shown that there are at least 4 FSGS susceptibility loci among inbred strains. Furthermore, F1 hybrids between TgFVB and other inbred strains show highly variable penetrance of nephropathy, indicating the feasibility of mapping genes using F1 hybrids for association mapping. In the past funding periods, we have generated 459 F1 hybrids between TgFVB and 15 inbred strains and have determined variable susceptibility to kidney disease based on genetic background, with C57Bl6/J, A/J, DBA/1J, NZO/HILtJ, C3H/HeJ and CBA/J mice showing highest prevalence of injury as measured by proteinuria, and urinary NGAL levels. The increased prevalence of pathology, measured by glomerulosclerosis, was observed on the WSB/EiJ, CBA/J, DBA/1J, C3H/HeJ, and A/J genetic backgrounds. By performing serial analysis of proteinuria, we have also determined the optimal timepoint for assessment of kidney disease in the f1 progeny. The initial QTL analysis shows the genes within a Chr 6 interval that maps to a previously identified QTL, and this contains the *Ptpro* gene. In addition, annotation of the genes located within the shared haplotype intervals using the Molecular Signature Database demonstrates a significant enrichment for transcriptional targets of NFAT and FOXO4. Once the final cohort has been generated, we will perform a GWAS to detect susceptibility loci for FSGS and compare results to the ongoing GWAS in humans.

15. SUBJECT TERMS:
NONE LISTED

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
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1. **INTRODUCTION:** Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.

The glomerular filtration barrier amongst mammals is highly conserved, and mouse models are highly relevant to understanding the human pathogenesis of FSGS. Frequent candidate genes identified in the mouse models have been implicated in the cause of human disease, demonstrating the importance of genes identifies in the mouse FSGS model are highly relevant to human disease. The development of nephropathy in HIV-1 transgenic mice are highly strain dependent, breeding these mice onto diversity out cross mice strains will enable us to preform GWAS for FSGS in mice to identify new genes. Cross-annotation of findings with transcriptomic analyses and human GWAS results will increase power to detect new FSGS causal genes.

2. **KEYWORDS:** Provide a brief list of keywords (limit to 20 words).

FSGS, GWAS, Nephropathy, Mouse Kidney Disease

3. **ACCOMPLISHMENTS:** The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction.

What were the major goals of the project?
List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

Specific aim 1: A Genome-wide association study for common single nucleotide polymorphisms and rare copy number variations in 7,559 FSGS and over 50,000 controls.
See progress report from Dr Sanna-Cherchi

Specific aim 2: A GWAS for FSGS in mice.
2a. Generated HIV-1 transgenic F1 hybrids between TgFVB and other inbred and outbred strains of mice. **Completed**
2b. Preform detailed assessment of severity of kidney disease based on histopathology, proteinuria, and urine NGAL production at 6 weeks of age. **In progress (see interim analyses table 1): will be completed after Year 3 completion of genotyping.**
2c. Preform genome-wide genotyping and quantitative GWAS for FSGS in mice. **Preliminary analysis completed by July 2019 on 16 transgenic strains (see interim analyses). Analysis on transgenic strains 20 currently in progress**

Specific aim 3. Cross annotation between human and mouse GWAS and identification of downstream dysregulated pathways and networks.
In progress, expected to be completed by June 2020.

What was accomplished under these goals?
For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive

and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

We generated transgenic F1 hybrids between the TgFVB mice and 20 inbred strains of mice, characterizing the phenotypes based on the proteinuria, urine NGAL and the histopathology. Following collection of urine, the level of proteinuria, hematuria and urine NGAL (uNGAL) was determined for each of the Tg-F1 hybrids. Upon euthanasia of the mice, the kidneys are prepared for histopathological analysis and for RNA extraction, serum has been collected and stored in three vials for metabolic and immunological analysis, and the urine, spleen and feces are collected and bio-banked at this time point. NGAL is measured in the urine before at and the time point of proteinuriadetection in the TG-F1 mice. Kidney sections for histopathology have been processed and stained with Periodic acid Schiff (PAS).
Currently in 17 strains of mice we have completed the pathology (% glomerulosclerosis (GS), % Casts, % tubular atrophy and fibrosis, % interstitial inflammation), and 20 strains for urine analysis (NGAL, proteinuria, and hematuria) and serum analysis (BUN, IgA and IgG). Our data has demonstrated, that not all the Tg-F1 hybrids develop proteinuria (Table 1). The Tg-F1 hybrids derived from the A/J, C3H/HeJ, C57BL/6J, CBA/J, DBA/1J and NZO/HILtJ mice had increased numbers of Tg-mice positive for proteinuria compared to the Tg-F1 hybrids generated from the other strains of mice

Table 1: Phenotypic characterization of the Tg-F1 hybrids derived from different mouse strains.

F1-hybrid	# pups	Male	Female	Transgene	M-Transgene (% proteinuria)	F-Transgene (% proteinuria)	GS > 10% (% Tg-mice)
129S1/SvimJ	36	19	17	24	11 (27%)	13 (46%)	8 (33%)
A/J	23	11	12	8	3 (100%)	5 (100%)	8 (100%)
C3H/HeJ	36	14	22	17	9 (100%)	8 (100%)	17 (100%)
C57BL10/J	26	14	12	11	6 (0%)	5 (0%)	0 (0%)
C57BL/6J	44	18	26	18	8 (50%)	10 (50%)	4 (22%)
C57BL/6NJ	32	15	17	20	9 (0%)	11 (0%)	1 (5%)
C57L/J	34	13	21	17	6 (50%)	11 (27%)	5 (29%)
C58/J	16	10	6	10	5 (40%)	5 (60%)	4 (40%)
CAST/EiJ	10	3	7	7	1 (0%)	6 (50%)	1 (14%)
CBA/J	27	14	13	18	10 (70%)	8 (50%)	18 (94%)
DBA/1J	27	14	13	14	5 (80%)	9 (88%)	13 (92%)
DBA/2J	32	13	19	12	7 (28%)	5 (40%)	12 (50%)
NOD/ShiLt	30	17	13	11	6 (33%)	5 (20%)	6 (55%)
NZO/HILtJ	24	12	12	12	6 (100%)	6 (80%)	12 (100%)
WSB/EiJ	11	5	6	6	1 (100%)	5 (60%)	5 (84%)
BALB/C	50	27	23	25	16(50%)	9(23%)	5(20%)
KK/HiJ	42	21	21	12	5(100%)	7(100%)	In-progress
LP/J	28	10	18	9	3(0%)	6(0%)	In-progress
NZB/BINJ	27	14	13	9	5(40%)	4(50%)	In-progress

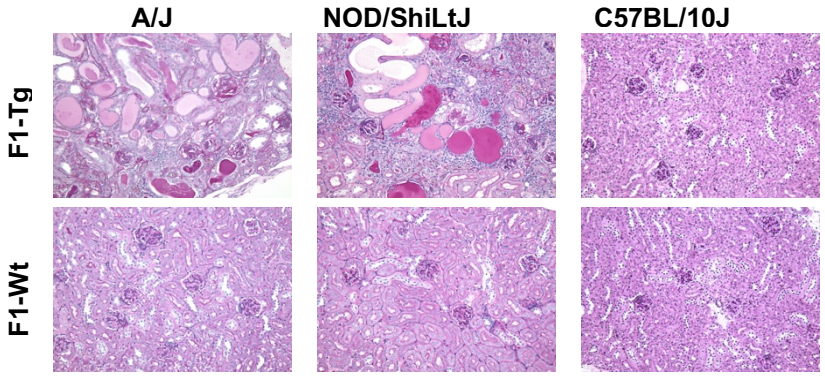

Figure 1: Periodic acid–Schiff stained histology of F1-A/J mice that highly sensitive to the Tg resulting in severe glomerulosclerosis (Upper left panel), NOD/ShiLtJ intermediate glomerulosclerosis (Upper middle panel) panel) and F1-C57BL/10J mice that are resistant to the transgene resulting in no glomerulosclerosis (Upper right panel). The F1-A/J, F1-NOD/ShiLtJ and F1-C57BL/10J Wt mice are shown in the left, middle and right lower panel respectively.

Mapping genetic susceptibility to collapsing FSGS in mouse model. Although mice do not possess an *APOL1* ortholog, HIV-1 transgenic mice on the FVBN/J background (TgFVB) display virtually all the clinical and molecular features of collapsing variant of FSGS, indicating that alternative genetic lesions, in the absence of *APOL1*, can predispose to this disease (**Figure 2**). To map genes for glomerulosclerosis, we generated F1 hybrids between TgFVB and 16 inbred strains (over 555 F1 hybrids generated). F1 hybrids between 129S1/SvImJ, C57BL/6J, C57BL/10J, C57BL/J, C58/J and CAST/EiJ are completely protected from disease, while the other F1 hybrids have evidence of disease. To map loci predisposing to collapsing FSGS, we performed a GWAS using 450,000 SNPs, searching for haplotype distribution patterns that matched the high/low strain susceptibility pattern.

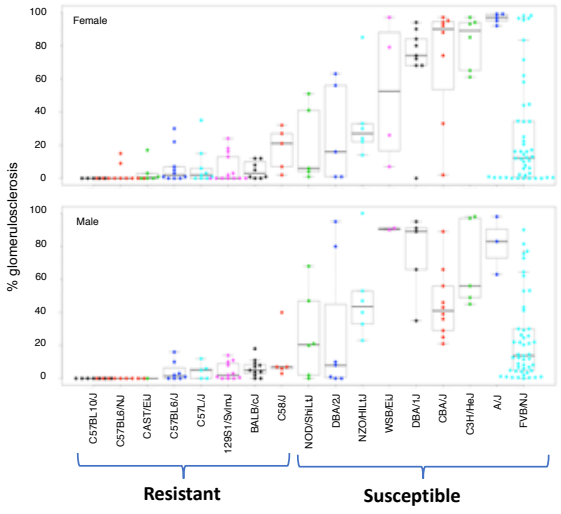

Figure 2: significant interstrain variation in glomerulosclerosis in 16 inbred strains (N=10-20 per strain). There were no differences by sex.

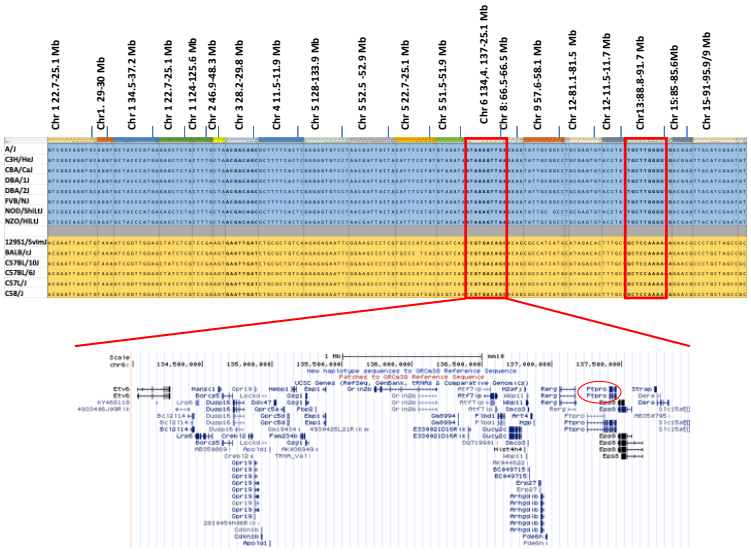

Figure 3: Top panel show haplotypes matching the strain susceptibility pattern. The intervals coinciding with known QTLs are shown in red boxes. The lower panel shows the genes within a Chr 6 interval that maps to a previously identified QTL, and this contains the *Ptpro* gene (highlighted in red)

This search identified 20 discrete segments, totaling 30.7 Mb of mouse genome that have a haplotype distribution that exactly matches the strain susceptibility pattern (Figure 4, p= 9 x 10^{-5}). Thus, the analysis of 16 inbred strains remarkably reduced the search space to 1.1% of the mouse genome. The quantitative comparison of GS severity between high and low susceptibility strains is highly significant (p= 5 x 10^{-23}). These haplotypes vary in size between 0.5 to 4.1 Mb, delineating a tractable number of candidate genes (107 genes, ~5 genes per interval). These include two intervals that coincide with QTL loci we had previously mapped using segregating crosses. Notably, the Chr 6 interval contains the *Ptpro* gene, encoding a podocyte protein implicated in Mendelian FSGS (**figure 3**).

In addition, annotation of the genes located within the shared haplotype intervals using the Molecular Signature Database demonstrates a **significant enrichment for transcriptional targets of NFAT (18 targets, p= 1 x 10^{-9}) and FOXO4 (9 targets, p = 2 x 10^{-6}, Figure 4). Both NFAT and FOXO4 pathways have been implicated in podocyte dysfunction and glomerulosclerosis Figure 4**. Moreover, NFAT modulation via cyclosporine ameliorates FSGS in some patients. These findings indicate that differential activation of NFAT and FOXO4 may underlie contrasting susceptibility to FSGS in this model, enabling analysis of the mechanisms of response to cyclosporine or FOXO4 modulators such as sirtuins. In addition, because of the highly structured nature of the inbred strain genomes, some of these intervals likely have a matching haplotype just by chance. Analysis of additional strains, currently under way, will help distinguish true from false positive signals and refine these intervals. We expect that with data from each additional strain, false positive intervals will be reduced by 50% and significantly reduce candidates.

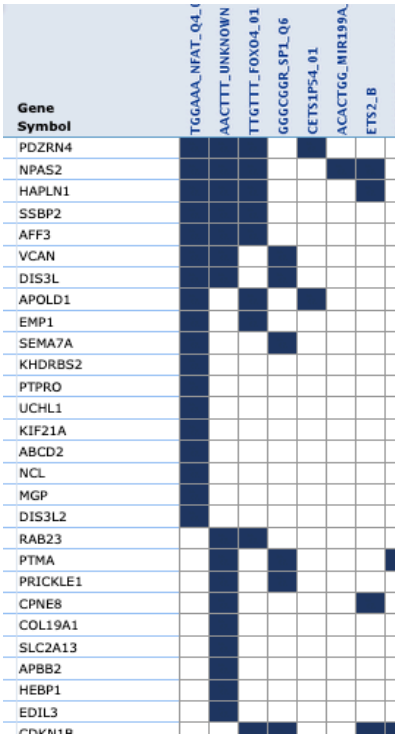

Figure 4: Positional candidates are highly enriched for targets of *NFAT* (p=1 x10 -9) and *FOXO4* (2 x 10-6).

With the partnering PI project (see Dr. Sanna-Cherchi's report), we conducted a multiethnic GWAS comparing 2,639 cases and 16,765 ethnically matched. **In the combined meta-analysis** (2,639 cases), we discovered significant associations for *APOL1* (OR=2.87, P= 7.68×10^{-31}), which were driven solely by African individuals (OR=2.82, P=1.45×10^{-37}), the *HLA-DQA*1 locus (OR=1.43, P= 3.2×10^{-22}), and **two novel loci** on chr.1q42.2 (OR=1.34, P=3.29×10^{-08}) and chr.16q21 (OR=2.72, P=2.07×10^{-8}). **After conditional analysis** on the top two SNPs at *APOL1* and *HLA* loci, a second independent *HLA* genome-wide significant signal was discovered (OR=1.36, P=2.18×10^{-10}). **Among adult-onset patients** (n=1,391), the strongest signals were at the *APOL1* locus (OR=3.14, P=1.82×10^{-21}) and a **novel locus** on chr.14q21.3 (OR=1.54, P=1.62×10^{-8}). The *HLA-DQA1* locus was the highest among **pediatric cases** (OR=2.01, P=4.06×10^{-32}). The *HLA* signal in Caucasians was genome-wide significant also in adults (OR=1.33; P=1.20×10^{-8}). Analysis of rare CNVs in the same cohort identifies known and novel disease causing structural variants. in 3.6% of the cases. Cross-annotation of these loci with the results from the mouse GWAS will increase our power to detect true associations and novel genes.

What opportunities for training and professional development has the project provided?
If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. "Training" activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. "Professional development" activities result in increased knowledge or skill in one's area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

This award provides additional training to Dr. Steers, an Instructor of Medical Sciences in my lab to utilize and learn additional skill sets.

Results generated in association with this award will be presented at conferences, seminars and research meetings by Dr. Steers.

This award provides training for post-bac students and summer students who are currently working in the laboratory who intend to go on the graduate education.

How were the results disseminated to communities of interest?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

Presentations/Abstracts

1. NJ. Steers NJ, Na YJ, DeMaria ND, Lam WY, D'Agati VD, Gharavi AG. Interstrain variation in severity of nephropathy and immunoglobulin levels in HIV-1 transgenic mice. ASN FR-PO1019. American Society of Nephrology Kidney Week, 2018

2. Ahram D, Gilles C, Mitrotti A, …. Gharavi A, Hildebrandt F, Sampson MG, Sanna-Cherchi S. HLA Alleles Confer Risk to Primary Idiopathic Nephrotic Syndrome in Individuals of Caucasian Ancestry. ASN SA-PO593. American Society of Nephrology Kidney Week, 2017

3. Ahram D, Gilles C, Mitrotti A, …. Gharavi A, Hildebrandt F, Sampson MG, Sanna-Cherchi S. HLA Alleles Confer Risk to Primary Idiopathic Nephrotic Syndrome in Individuals of Caucasian Ancestry. Human Genetics in New York (Sept 12 2017)

4. Ahram D, Gilles C, Mitrotti A, …. Gharavi A, Hildebrandt F, Sampson MG, Sanna-Cherchi S. Multiethnic GWAS for Idiopathic Nephrotic Syndrome in Adults and Children. ASN PO1002-3. American Society of Nephrology Kidney Week, 2019

What do you plan to do during the next reporting period to accomplish the goals?
If this is the final report, state "Nothing to Report."

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

Report at end of three years of funding, granted a no-cost extension for the fourth year, provide a final report after the fourth year.

Finalize the mouse genotyping and perform the full GWAS.

4. **IMPACT:** Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

What was the impact on the development of the principal discipline(s) of the project?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge,

theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

In the first 3 years of funding we identified several new loci and genes associated to nephrotic syndrome in human and mouse, and we are currently finalizing analyses and preparing manuscripts describing our findings. The study makes use of novel methods to find new genes involved in kidney diseases and the pathogenesis of FSGS in mammals that might have repercussions in diagnosis, clinical management, and treatment.

What was the impact on other disciplines?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

Nothing to report

What was the impact on technology transfer?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:

- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

Nothing to Report

What was the impact on society beyond science and technology?

If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:

- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

Nothing to Report

5. **CHANGES/PROBLEMS:** The Project Director/Principal Investigator (PD/PI) is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:

Changes in approach and reasons for change
Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.

Nothing to Report

Actual or anticipated problems or delays and actions or plans to resolve them
Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

Nothing to Report

Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

Nothing to Report

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Significant changes in use or care of human subjects

Nothing to Report

Significant changes in use or care of vertebrate animals.

Nothing to Report

Significant changes in use of biohazards and/or select agents

Nothing to Report

6. **PRODUCTS:** List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."

- **Publications, conference papers, and presentations**
  Report only the major publication(s) resulting from the work under this award.

  Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

  Nothing to Report

  Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: Author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

  Nothing to Report

  presentation produced a manuscript.

1. Ahram D, Gilles C, Mitrotti A, …. Gharavi A, Hildebrandt F, Sampson MG, Sanna-Cherchi S. HLA Alleles Confer Risk to Primary Idiopathic Nephrotic Syndrome in Individuals of Caucasian Ancestry. ASN SA-PO593. American Society of Nephrology Kidney Week, 2017

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American Society of Nephrology Kidney Week, 2019

4. NJ. Steers NJ, Na YJ, DeMaria ND, Lam WY, D'Agati VD, Gharavi AG. Interstrain variation in severity of nephropathy and immunoglobulin levels in HIV-1 transgenic mice. ASN FR-PO1019. American Society of Nephrology Kidney Week, 2018

- **Website(s) or other Internet site(s)**
  List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Nothing to Report

- **Technologies or techniques**
  Identify technologies or techniques that resulted from the research activities. In addition to a description of the technologies or techniques, describe how they will be shared.

Nothing to Report

- **Inventions, patent applications, and/or licenses**

Identify inventions, patent applications with date, and/or licenses that have resulted from the research. State whether an application is provisional or non-provisional and indicate the application number. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

Nothing to Report

- **Other Products**

  Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment, and/or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:

  - *data or databases;*
  - *biospecimen collections;*
  - *audio or video products;*
  - *software;*
  - *models;*
  - *educational aids or curricula;*
  - *instruments or equipment;*
  - *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
  - *clinical interventions;*
  - *new business creation; and*
  - *other.*

Nothing to Report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?
Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change."

Example:

Name:	*Mary Smith*
Project Role:	*Graduate Student*
Researcher Identifier (e.g. ORCID ID):	*1234567*
Nearest person month worked:	*5*
Contribution to Project:	*Ms. Smith has performed work in the area of combined error-control and constrained coding.*
Funding Support:	*The Ford Foundation (Complete only if the funding support is provided from other than this award.)*

Name:	Ali Gharavi
Project Role:	Principal Investigator
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest person month worked:	1.2

Contribution to Project: Dr. Gharavi was responsible for achieving the overall goals of the study. He supervised mouse genetic studies at Columbia University and will collaborate with Dr. Sanna-Cherchi (partnering PI) on the human genetic studies.

Funding Support: Dr. Gharavi's funding portfolio currently includes NIH Grants 5UM1DK100876-04, NIH 5R01MD009223-03, 5R01DK082753-07, 5U54DK104309-03, 5U01HG008680-02, 2R01DK080099-06A1, 1R21DK109690-01and 1UG3OD231183-01 and USAMRAA Grant PR151419.

Name:	Iulina Ionita-Laza
Project Role:	Co- Investigator
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest person month worked:	.22

Contribution to Project: sequencing data, analysis of datasets GWAS

Funding Support: Dr. Ionita-Laza's funding portfolio currently includes NIH Grants 5R01MH095797-04, 5R21MH106888-02, 5R01MH106910-02, 5R01HG008980-02, 5R01AR065963-03, 1P50AR070588-01, 5R01DK080099-07, USAMRAA Grant PR151419.

Name: Vivette D'Agati
Project Role: Co-Investigator
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: .84

Contribution to Project: Dr. D'Agati perform standardized review and scoring of kidney biopsies for enrolled patients and mouse samples.

Funding Support: Dr. Agati's funding portfolio currently includes NIH Grants
1 UM1 DK100876-01, 1R01MD009223-01, 1R24DK103032-01, 1R01DK106436-01A1
USAMRAA Grant PR151419.

Name: Nicholas Steers
Project Role: Associate Research Scientist
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 9.0

Contribution to Project: Dr. Steers performed the GWAS in the TgFVBxDO F1 mice, under the supervision of Dr. Ionita-Laza and Dr. Gharavi.
Funding Support: N/A

Name: Wan Yee Lam
Project Role: Tech
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 6.0

Contribution to Project: Wet lab experiments, DNA preparation and plating. Processed mouse husbandry and genotyping and processing samples for histopathology.
Funding Support: N/A

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

Nothing to Report

What other organizations were involved as partners?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

- *Nothing to report*

Nothing to Report

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: For collaborative awards, independent reports are required from BOTH the Initiating PI and the Collaborating/Partnering PI. A duplicative report is

acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to **https://ers.amedd.army.mil** for each unique award.

Dr. Gharavi and Dr. Sanna-Cherchi will submit cognate reports.

QUAD CHARTS: If applicable, the Quad Chart (available on https://www.usamraa.army.mil) should be updated and submitted with attachments.
N/A

9. **APPENDICES:** Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.