Joint NEPTUNE-CureGN Ancillary Study Proposal Application

Please submit completed Ancillary Study Application with all supporting documents, including NIH biosketches for PIs, as a single PDF document to neptune-study@umich.edu; CureGN-AncillaryReview@arborresearch.org

Study Title	
PI Name	
Affiliation	
E-mail Address	
Mailing Address	
Co-Investigators' Names	
Proposed Start Date	
Proposed End Date	
Funding Source and Application Date:	☐ Internal funds from your own institution
	☐ NephCure Kidney International Pilot Program
	☐ Private sector funding (specify source)
	☐ Extramural/Intramural funding
	If already funded, specify agency and grant number:
	If planned submission, specify agency and application date:
CureGN Sponsor	
Is this a training proposal?	☐ Yes *Include with the application a paragraph from the mentor(s) indicating relevant experience, as well as commitment to the trainee.* ☐ No

Abstract (limit to one paragraph):

Part A. Study Design (5-page limit excluding references)

1. Background and rationale

2. Hypotheses and specific aims

3. Design and methods

4. Statistical Analysis. *For each study aim, describe the plan(s) for data analysis, stating the specific hypothesis that the statistical method will test or estimate. Make clear whether comparisons are within-subject or between-subject, and if or how controls will be included.*

5. Power analysis and sample size justification

6. Anticipated results and project timeline

7. References *Please include at the end of the application.*

8. NEPTUNE Data Sharing Plan
   All data from ancillary studies must be made available to the DACC through frequent data transfers. From there, it will be made available to the larger NEPTUNE consortium and other requesting third parties. The frequency and timing of these transfers should be stated in the study proposal for review by the Ancillary Studies Committee. The transfer of data must occur within 24 months from the time of transfer of samples or raw data sets, or at the time of publication if this occurs before 24 months. Exceptions to this rule must be requested at the time of initial application and review. The format of data transfer to the DACC must conform to standards compatible with the NEPTUNE data management platform and the NEPTUNE data management group.

   I agree to the NEPTUNE Data Sharing Policy (Please sign): _____

9. CureGN Data Sharing Plan
   Data (e.g. bioassays, PRO data, etc.) generated from ancillary studies are to be provided, in an agreed upon format, as soon as reasonably feasible and no longer than 6 months after data generation to the CureGN DCC for integration into the CureGN dataset. These data will be made available for use by other CureGN investigators. Data will also be transferred to the NIDDK data repository at the end of the study.

   I agree to the CureGN Data Sharing Policy (Please sign): _____

10.

Part B. Use of CureGN Data, Biomaterials and Infrastructure

B1. CureGN Requirements

B1a. Please indicate the CureGN resources you need *(Check all that apply)*

- ☐ Use existing clinical data
- ☐ Use existing procured samples
- ☐ Use existing patient-reported data
- ☐ Access to the Digital Pathology Repository
- ☐ Requires new clinical data collection
- ☐ Requires additional sample procurement
- ☐ Requires new patient-reported data collection

B1b. Please describe your proposed study population.

Select Population *(Check all that apply)*

- ☐ FSGS Cohort
- ☐ MCD Cohort
- ☐ MN Cohort
- ☐ IgA Cohort

- ☐ Incident (first kidney biopsy within 6 months of enrollment)
- ☐ Incident (first kidney biopsy at a CureGN site after 1/1/2015)
- ☐ Prevalent

- ☐ Adult
- ☐ Pediatrics

B1c. Provide the total number of adult and pediatric CureGN patients who meet your study requirements. *We encourage you to use tranSMART or work with a DCC member to assess case counts for your study design. If you need access to tranSMART, please contact CureGN-AncillaryReview@arborresearch.org.*

	FSGS	MCD	MN	IgA	Total
Adult					
Pediatric					

B2. CureGN Data Request

B2a. Indicate what existing CureGN data you will need for your proposed study: *(Check all that apply)*

- ☐ Demographics
- ☐ Comorbidities
- ☐ Family History
- ☐ Birth History
- ☐ Pregnancy History
- ☐ Prior Disease Course
- ☐ Medications
- ☐ Laboratory values/Clinical Information
- ☐ Hospitalizations and ER Visits
- ☐ Limited Physical Exam
- ☐ Patient-reported data (quality of life, adherence)
- ☐ Access to Whole Slide Images
- ☐ Other (specify: _____)

B3. CureGN Biospecimen Request

B3a. Will your proposed study require use of existing CureGN biospecimens? ☐Yes ☐No

If no, go to B4.

B3b. If yes, In the table below, provide the **minimum amount of sample**, at each visit, you are requesting for your proposed study. Due to the limited nature of all biospecimens, individual requests exceeding 10% of original stored volume may not be approved. *See https://curegn.org/publicdocuments/Biospecimens%20List.pdf for more information.*

		Visit	
Type of Specimen	**Volume Requested**	**Baseline**	**Annual** *(specify year)*
Whole blood for genomic DNA/ EDTA tube DNA			
Extracted genomic DNA			
Whole blood for genomic RNA/ PAXGene tube RNA			
Extracted genomic RNA			
EBV immortalized cell lines (PEDS ONLY)			
Plasma/ EDTA tube			
Plasma/ Sodium Citrate Tube			
Plasma/ Sodium Heparin (light protected)			
Serum/ Serum separator tube			
Spot urine cleared supernatant with Sodium Azide (NaN3)			
Spot urine cleared supernatant with Protease Inhibitor (PI)			
Spot urine pellet harvested in RNAlater stabilizing nucleic acids at RT			
24-hr urine collection container			

B3c. Justification for the request of limited and irreplaceable biomaterials:

1. Discuss how the proposed project will take advantage of the depth of larger CureGN clinical data set and make the case clearly that the proposed study will have significant scientific impact.

2. Provide preliminary data to support the proposal's hypothesis and technical feasibility. The ancillary studies committee may consider the use of CureGN biosamples to develop preliminary data in an iterative fashion in some cases. In this case, explain why alternative samples cannot be obtained from other sources.

3. Describe assay details and methodology, including amounts and type of samples (applicants should request the minimum volume required for their assays), anticipated assay variability, quality control (assay "robustness") assessment.

B4. Additional Study Visits, Additional Procedures or Specimen Acquisition in CureGN

B4a. Does your proposed study involve additional study visits, additional procedures or specimen acquisition beyond the core NEPTUNE protocol? *If no, go to B5.*

☐Yes
☐No

B4b. If yes, describe the rationale for additional procedures, specimens, or visits.

B4c. Does this ancillary study add new questionnaires/questions? *If yes, provide a copy of each proposed questionnaire/question with application.*

☐Yes
☐No

B4d. If yes, check all that apply:

☐Patient surveys
☐Clinical data (may be collected by patient interview)
☐Clinical data (chart review only)
☐Other (specify): _____

B4e. Use the table below to specify the proposed visit schedule and procedures (questionnaires, intervention, laboratory sampling and tests). Provide a subject level time estimate of additional study procedures (e.g., self-administered questionnaire x 10 minutes).

Procedure	Visit (Time)	Visit (Time)	Visit (Time)

Add rows as necessary

B4f. Use the table below to specify the proposed additional blood or urine collection beyond that collected in the CureGN protocol**.** *If no additional biosamples are proposed, go to B5.*

Specimen (Plasma, Serum, Urine, Other - specify)	**Sampling Times***	**Volume Requested**
Specimen 1 <SPECIFY>		
Specimen 2 <SPECIFY>		
Specimen 3 <SPECIFY>		

* Specify CureGN Visit # or additional visit time

Add rows as necessary

B4g. Describe assay details and methodology including amounts and type of samples (applicants must request the minimum volume required for the assay), anticipated assay variability, quality control (assay "robustness").

B5. Other Ancillary Study Considerations		
B5a.	Will the ancillary study require the DCC to perform study monitoring activities? *(e.g., study coordinator training, IRB and/or other regulatory assistance, label creation and delivery, etc.)*	☐Yes ☐No
B5b.	Will any additional effort or personnel time be expected of the CureGN DCC? *(Check all that apply)* ☐CureGNLink questionnaire changes ☐CureGN Link functionality changes ☐Custom SAF ☐Other (describe)	
B5c.	Where will the data analyses be conducted? ☐The DCC will conduct all analyses, OR ☐The ancillary study team will design and conduct the analysis with quality review from the DCC, OR ☐The DCC will conduct some analyses, and the ancillary study investigator (ASI) team will conduct others. *Please explain.*	
B5d.	For analyses conducted by DCC, will the resulting manuscript(s) be submitted by the DCC or other institution? ☐DCC ☐Other, specify:	
B5f.	Describe any additional burden to PCCs or study sites *(e.g., study coordinator training, interface with participants, sample kit creation and delivery or shipping, etc.)*	
B5j.	Indicate if the study has an active Investigational New Drug (IND) or Investigational Device Exemption (IDE) number:	

	Number	**Responsible Investigator(s) or Sponsor(s)**
IND		
IDE		

B5k.	Does this research have the potential to be used when applying for an IND or IDE to the FDA?	☐Yes ☐No

Part C. Use of NEPTUNE Data, Biomaterials, and Infrastructure

C1. NEPTUNE Requirements

C1a. Please indicate the study resources you need *(Check all that apply)*

- ☐ Existing clinical data
- ☐ Existing procured samples
- ☐ Existing Microarray data
- ☐ Existing RNAseq data (specify glom, tub, or both)
- ☐ Existing WGS data
- ☐ Access to the DPR
- ☐ Controls for genomic data from living donor and tumor nephrectomy *(note clinical data is not available)*
- ☐ Requires new clinical data collection
- ☐ Requires additional sample procurement
- ☐ Requires new patient-reported data collection

C1b. Please describe your proposed study population.

Select Population *(Check all that apply)*

- ☐ FSGS Cohort
- ☐ MCD Cohort
- ☐ MN Cohort
- ☐ Non-Biopsy Cohort

- ☐ Adult
- ☐ Pediatrics

C1c. Provide the total number of adult and pediatric NEPTUNE patients who meet your study requirements. *We encourage you to use tranSMART or work with a DACC member to assess case counts for your study design. If you need access to tranSMART, please contact neptune-study@umich.edu.*

	FSGS	MCD	MN	Non-biopsied Pediatrics	Total
Adult					
Pediatric					

C1d. Please provide inclusion/ exclusion criteria

C2. NEPTUNE Data Request

C2a. Indicate existing NEPTUNE data you will need for your proposed study. *(Check all that apply)*
Please use tranSMART or contact the DACC to review NEPTUNE datasets. Data elements selected should be referenced in the analysis plan for justification of request.

	Visits		
Data Category	Baseline	Follow-up	Specify which Foll.-up Visits
Demographics	☐		
Age of disease onset	☐		
Kidney disease duration	☐		
Socioeconomic Status/Healthcare			
Healthcare	☐	☐	
SES Status	☐	☐	
Clinical Data and Measurements			
Renal function and proteinuria	☐	☐	
Physical exam	☐	☐	
Lab results	☐	☐	
Symptoms in the last 2 weeks	☐	☐	
Patient-reported data	☐	☐	
Endpoints	☐	☐	
APOL1 Risk Haplotype	☐	☐	
Morphology data	☐	☐	
Morphometry data	☐	☐	
NS Classification data	☐	☐	
Medical History and Medications			
Medical History	☐		
Family Medical History	☐	☐	
Pregnancy History	☐	☐	
Medications	☐	☐	

☐Other, *please specify:*

C3. NEPTUNE Biospecimen Request

C3a.	Will your proposed study require use of existing NEPTUNE biospecimens? *If no, go to C4.*	☐Yes ☐No

C3b. If yes, in the table below, provide the **minimum amount of sample**, at each visit, you are requesting for your proposed study. Due to the limited nature of all biospecimens, individual requests exceeding 10% of original stored volume may not be approved. *See NEPTUNE website for more information.*

Visit Sequence	Biopsy	Base-line	4 Mos.	8 Mos.	12 Mos.	18 Mos.	24 Mos.	30 Mos.	36 Mos.	42 Mos.	48 Mos.	54-60 Mos.
Plasma (EDTA)												
Plasma (Sodium Citrate)												
Plasma (Sodium Heparin)												
Serum SST												
Serum SST (light-sensitive)												
24hr Urine (PI)												
24hr Urine Untreated												
Urine Clean Catch (PI)												
Urine Clean Catch (NaN3)												
Urine Pellet (PI)												
Urine Pellet RNA Later												
DNA PAXgene Tube												
RNA PAXgene Tube												

C3c. Justification for the request of limited and irreplaceable biomaterials:

4. Discuss how the proposed project will take advantage of the depth of larger NEPTUNE clinical data set and make the case clearly that the proposed study will have significant scientific impact.

5. Provide preliminary data to support the proposal's hypothesis and technical feasibility. The ancillary studies committee may consider the use of NEPTUNE biosamples to develop preliminary data in an iterative fashion in some cases. In this case, explain why alternative samples cannot be obtained from other sources.

6. Describe assay details and methodology including amounts and type of samples (applicants should request the minimum volume required for their assays), anticipated assay variability, quality control (assay "robustness") assessment.

C4. Additional Study Visits, Additional Procedures or Specimen Acquisition in NEPTUNE

C4a. Does your proposed study involve additional study visits, additional procedures or specimen acquisition beyond the core NEPTUNE protocol? *If no, go to B5.*

☐Yes
☐No

C4C. If yes, describe the rationale for additional procedures, specimens, or visits.

C4c. Does this ancillary study add new questionnaires/questions? *If yes, provide a copy of each proposed questionnaire/question with application.*

☐Yes
☐No

C4d. If yes, check all that apply:

☐Patient surveys
☐Clinical data (may be collected by patient interview)
☐Clinical data (chart review only)
☐Other (specify): _____

C4e. Use the table below to specify the proposed visit schedule and procedures (questionnaires, intervention, laboratory sampling and tests). Provide a subject level time estimate of additional study procedures (e.g., self-administered questionnaire x 10 minutes).

Procedure	Visit (Time)	Visit (Time)	Visit (Time)

Add rows as necessary

C4f. Use the table below to specify the proposed additional blood or urine collection beyond that collected in the NEPTUNE protocol**.** *If no additional biosamples are proposed, END.*

Specimen (Plasma, Serum, Urine, Other - specify)	**Sampling Times***	**Volume Requested**
Specimen 1 <SPECIFY>		
Specimen 2 <SPECIFY>		

* Specify NEPTUNE Visit # or additional visit time

Add rows as necessary

C4g. Describe assay details and methodology including amounts and type of samples (applicants must request the minimum volume required for the assay), anticipated assay variability, quality control (assay "robustness").