

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*](mailto:neptune-study@umich.edu)*;* [*CureGN-AncillaryReview@arborresearch.org*](mailto: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.

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

1. 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.

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

**Part B. Use of CureGN Data, Biomaterials and Infrastructure**

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| **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*](mailto: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: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_) |

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| **B3. CureGN Biospecimen Request** | | | | |
| **B3a.** | **Will your proposed study require** use of existing CureGN biospecimens?  *If no, go to B4.* | | Yes  No | |
| **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*](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"). | | |

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| **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**

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| **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*](mailto: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:*

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **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*](https://drive.google.com/file/d/1khCTCD2YAwveJ-CDK7XODO6MwhH0LuP_/view?usp=sharing) *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:   1. 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. 2. 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. 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. | | | | | | | | | | | | | |

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| **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"). | |