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Strategies for the Prevention or Treatment of Acute Kidney Injury in COVID-19 Infection

A forum to bring together investigators in the field interested in discussing drug development pathways, and how to plan and execute **meaningful clinical trials**

Drs. Robert Star, Paul Kimmel, and Ivonne Schulman

March 26, 2020

Agenda

11:00 – 11:05am Introduction (Dr. Robert Star)

11:05 – 11:45am Discussion (Drs. Kimmel and Schulman)

- What is your **current experience** with COVID associated AKI incidence and outcomes in hospital and especially ICUs?

  Start first with China, Washington State, California, and New York.
- What is **needed now**, for the fall?
- Are **agents/drugs 'shovel ready'** for Phase 2 testing?

11:45 – 11:55am Questions to NIDDK program officers

- NIH Resources – NCATS screening platforms, Notice of Special Interest (NOSI)

11:55 - Noon Concluding comments (Dr. Star

- Interest in future meetings
- Volunteer leaders

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COVID-19 AKI Epidemiology

Knowns – initial preliminary data

- AKI incidence in patients with COVID-19 ranges from 0.5% (hospital) to 23% (ICU)
- AKI develops at a median of 7 to 15 days after admission

Unknowns

- More detailed incidence, risk factors, clinical course, short- and longer-term outcomes
- Homogeneity or heterogeneity of AKI
- What observational data are needed; especially **to properly plan a study**?

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Pre-clinical studies

Knowns

- ACE2 is a viral receptor for COVID-19, facilitating entry into cells
- ACE2 is highly-expressed in the proximal tubule
- Kidney pathology in 6 autopsies (China): severe acute tubular necrosis and leukocyte infiltration; SARS-CoV2 antigen accumulated in kidney tubules

Unknowns

- **Disease pathogenesis in humans**
- Intervention target: COVID-19 infection, or COVID-19 related AKI
- Efficacy in cells, organoids, small and large animals that **mimic human disease**
- Animal PK/PD, toxicoloty, dose and schedule for any potential ACE2-targeted therapeutic
- **Informative (companion) biomarkers** for pathway detection and amelioration

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Clinical Studies

Mostly unknowns

- **Human disease pathogenesis**
- Need **Phase 1 study in COVID-19 patients**?
- Phase 2 Study design decisions for a study in very ill patients
  - In whom (inclusion/exclusion) or when (early or late) might intervention be effective?
  - Possible primary outcome (that might respond to therapy)
  - What **doses and dosing schedules** to test
  - Effect of **intervention on COVID-19** viremia, immune system, cytokine storm
  - Adequate power
  - Number of **available patients** that meet inclusion/exclusion criteria

Human Subjects & Clinical Trials

- Guidance for NIH-funded Clinical Trials and Human Subjects Studies Affected by COVID-19 - NOT-OD-20-087 (https://grants.nih.gov/grants/guide/notice-files/NOT-OD-20-087.html)
- FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Pandemic Link to Non-U.S. Government Site - Click for Disclaimer https://www.fda.gov/regulatory-information/search-fda-guidance-documents/fda-guidance-conduct-clinical-trials-medical-products-during-covid-19-pandemic

NIH resources

- NIAID infection, viral transmission
- NCATS screening platforms
- Non Human Primate models – oversubscribed
- NIBIB assay development

- CALL US

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Funding Opportunities Specific to COVID-19

NOT-AI-20-030	Notice of Special Interest (NOSI) regarding the Availability of Urgent Competitive Revisions for Research on the 2019 Novel Coronavirus (2019-nCoV)	National Institute of Allergy and Infectious Diseases (NIAID) National Institute of General Medical Sciences (NIGMS)
NOT-HL-20-757	Notice of Special Interest (NOSI): Availability of Administrative Supplements and Revision Supplements on Coronavirus Disease 2019 (COVID-19)	National Heart, Lung, and Blood Institute (NHLBI)
NOT-DA-20-047	Notice of Special Interest (NOSI) regarding the Availability of Administrative Supplements and Urgent Competitive Revisions for Research on the 2019 Novel Coronavirus	National Institute on Drug Abuse (NIDA)

NIDDK NOSI not yet available

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Small Business Funding Opportunities

The Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs allow US-owned and operated small businesses to engage in federal research and development that has a strong potential for commercialization.

Phase I	Phase I awards are intended to establish the technical merit, feasibility, and commercial potential of the proposed research and research and development (R/R&D) efforts.
Phase II	Phase II awards are intended to continue the R/R&D efforts initiated in Phase I. Funding is based on the results achieved in Phase I and the scientific and technical merit and commercial potential of the project proposed in Phase II.
Fast-Track	Fast-track incorporates a submission and review process in which both Phase I and Phase II grant applications are submitted and reviewed together as one application.
Direct Phase II (SBIR only)	Phase II award to a small business concern that did not receive a Phase I award for that research/research & development.

PA-19-272	**SBIR** Omnibus/Parent Clinical Trial Not Allowed Funding Opportunity Announcement
PA-19-270	**STTR** Omnibus/Parent Clinical Trial Not Allowed Funding Opportunity Announcement
PA-19-273	**SBIR** Omnibus/Parent **Clinical Trial Required** Funding Opportunity Announcement

FOAs: https://sbir.nih.gov/funding#omni-sbir

SBIR vs STTR: https://sbir.nih.gov/about/critical Receipt and Review Schedule: https://sbir.nih.gov/apply/submission-dates

Eligibility: https://sbir.nih.gov/about/eligibility-criteria

Application Types: https://sbir.nih.gov/apply/application-types

KUH SBIR Contact: daniel.gossett@nih.gov

Next Receipt Dates: April 6, September 5

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Office of Biomedical Advanced Research and Development Authority (**BARDA**) Broad Agency Announcement (BAA)

a. AOI 7.7.1	**Diagnostic Assay** for human coronavirus using existing FDA-cleared platforms
b. AI 7.7.2	**Point-of-Care Diagnostic Assay** for detection of SARS-CoV-2 virus
c. AOI 7.7.3	**Diagnostic Assay** for detection of COVID-19 disease (SARS-CoV-2 infection)
d. AOI 8.3	COVID-19 **Vaccine**
e. AOI 9.2	COVID-19 **Therapeutics**
f. AOI 9.3	**Immunomodulators** or therapeutics targeting **lung repair**
g. AOI 9.5	**Pre-exposure and Post-exposure Prophylaxis**
h. AOI 10	**Respiratory Protective Devices**
i. AOI 11	**Ventilators**

BARDA will **only accept submissions related** to the **SARS-CoV-2 virus or the COVID-19** disease until further notice. https://beta.sam.gov/opp/d1b6e601426e4e4c943235babdd4133a/view

Opportunity from HHS/BARDA, not NIH. Direct questions to POCs in BAA.

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Concluding Thoughts

- Interest in future virtual forums?
- Volunteers to lead future virtual forums?

- NIH website (Google NIH COVID Research) https://www.nih.gov/health-information/coronavirus
- https://grants.nih.gov/grants/natural_disasters/corona-virus.htm

- Contact Ivonne Schulman Ivonne.Schulman@nih.gov