Development of a Uremic Pig Model for ESKD Innovation

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Outline

• **WHY** we need a uremic pig model
• **HOW** we developed and validated our uremic pig model
• **WHAT** we (as a community) could do with such a model
WHY a pig model?

- Relative lack of ethical issues
- Easy availability
- Size similarities (devices and clearances)
- Widely used for cardiovascular research (biological and molecular reagents and probes)
- Animal of choice for xenotransplants
WHY we need a uremic pig model

• The time is right

• Large number of national and local initiatives (bench to bedside) that are focused on kidney innovation

  - Rebuilding the Kidney Initiative: deep dive into the cellular circuits that could be manipulated to create organoids and kidneys!
  - KHI roadmap for innovative RRT
  - Kidney X: provide funding for the technical construct described in the roadmap
  - AAKHi: implantable bioartificial kidney
  - Center for Dialysis Innovation (KRI)
  - Kidney and Vascular Innovation Program (focus on cardiovascular health in CKD and ESKD)
A uremic pig model will help all these initiatives in the context of:

- Safety
- Technical feasibility
- Robust efficacy signal
- For innovative novel therapies
Using the right animal model

Sick Patients ≠ Young healthy pig
Stable creatinine in the advanced CKD range
Increased levels of expected uremic toxins

![Graphs showing increased levels of P-cresol Sulfate and Indoxyl Sulfate in Uremia 42D compared to Control.](image)

![Graph showing increased Plasma AGE Concentration (ug/ml) in Uremic 42D compared to Control.](image)
Increased levels of other potential uremic toxins (secretory ability)
what can we use this model for?

- Identify uremia specific druggable or deviceable targets that could impact on the morbidity, mortality and quality of life of CKD and ESKD patients
  - Identification of uremic toxins
  - Better understanding of uremic vascular biology and the vascular response to injury
- Real world experimental testing of novel therapies
Many of the products being showcased today could benefit from the availability of an uremic pig model

- Clearance of protein bound uremic toxins (Tumlin)
- Continuous dialysis with improved toxin removal (Stamatialis)
- Improved devices for dialysis access (Connolly)
- Displacer enhanced hemodialysis (Kotanko)
Summary

• Robust real world model for experimental studies of novel kidney disease therapies (like to add diabetes to the model)

• Presence of such an animal model could nicely complement multiple on going initiatives in the kidney disease space

• Just because its there does not mean you have to use it!

• It should be used when there is biological plausibility that the pathways that are being targeted by novel therapies (or the therapies themselves) could be modulated or modified by the presence of uremia
Thanks

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