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University of California  
San Francisco

advancing health worldwide™

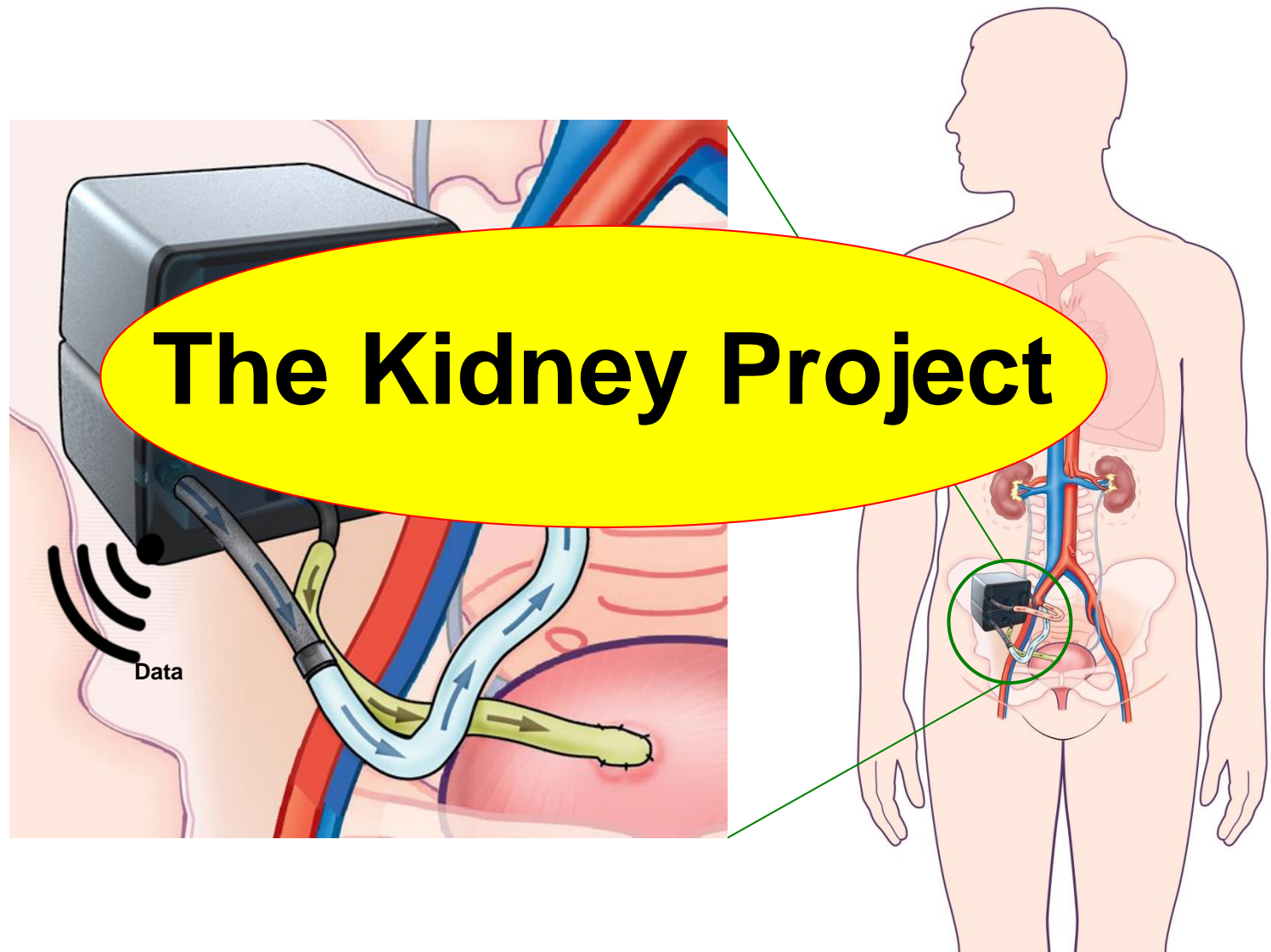
## Biohybrid Device for Implantable Renal Replacement Therapy

*AAKP/GWU Global Summit on  
Innovations in Patient-Centered  
Kidney Care*

Disclosure: Silicon Kidney



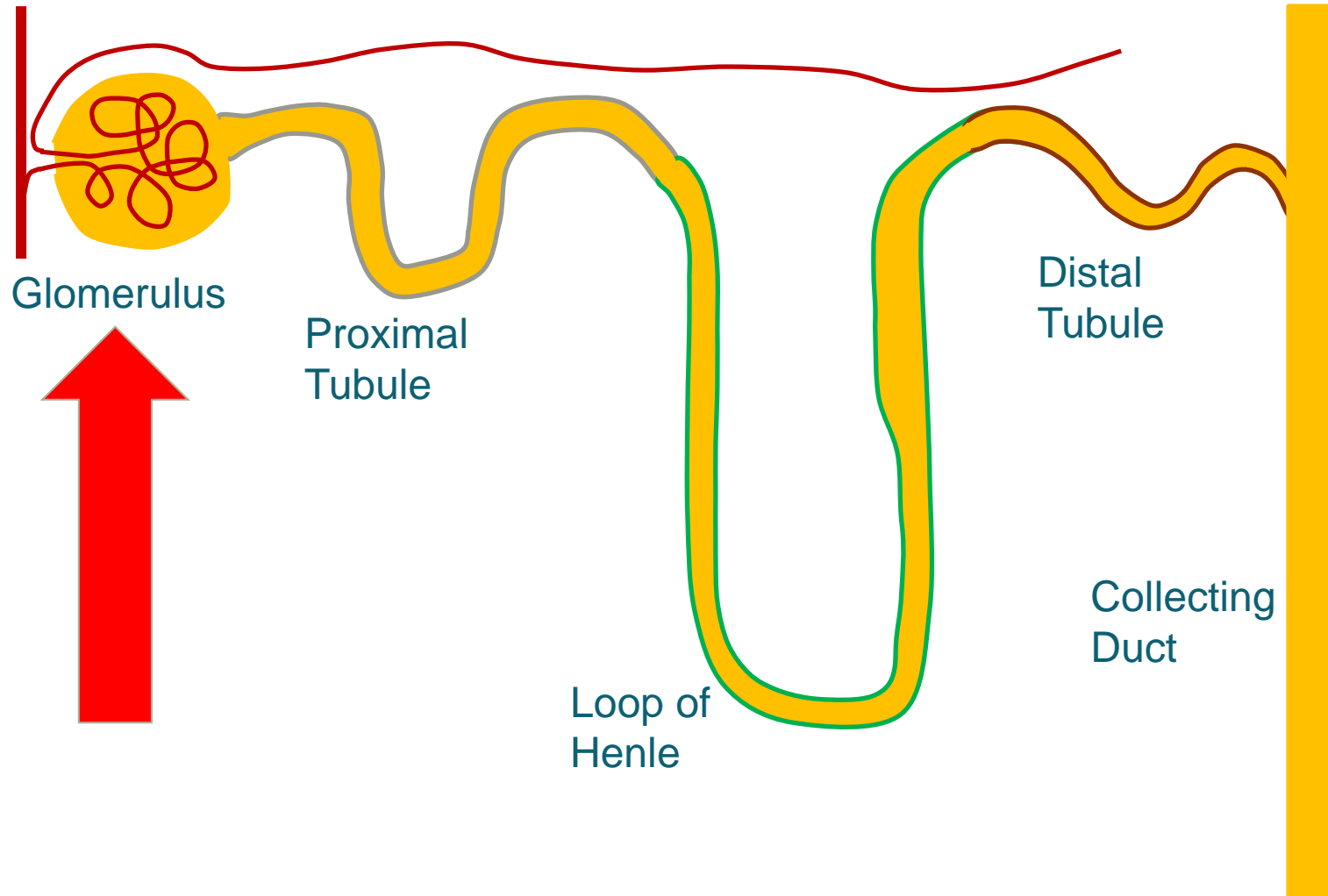
# Implantable Artificial Kidney



**The Kidney Project**

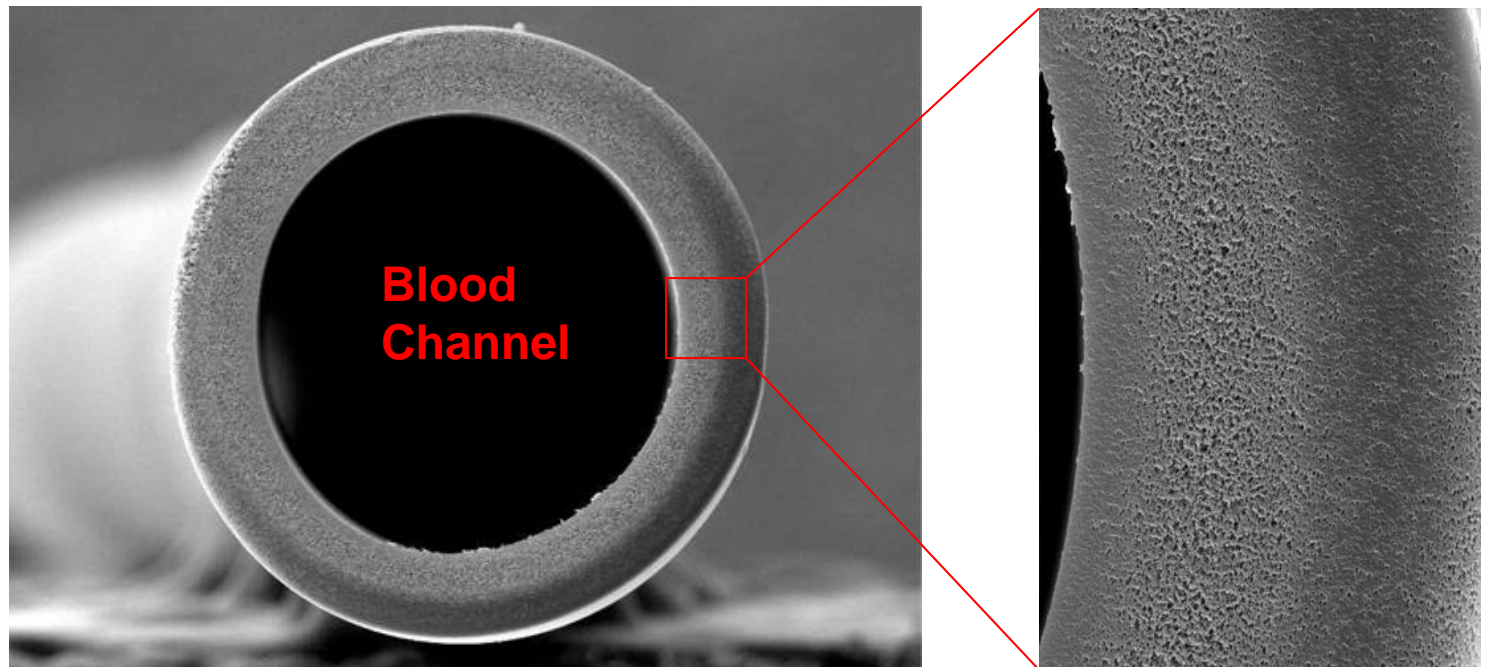
Data

# The Renal Filter Unit: the Nephron

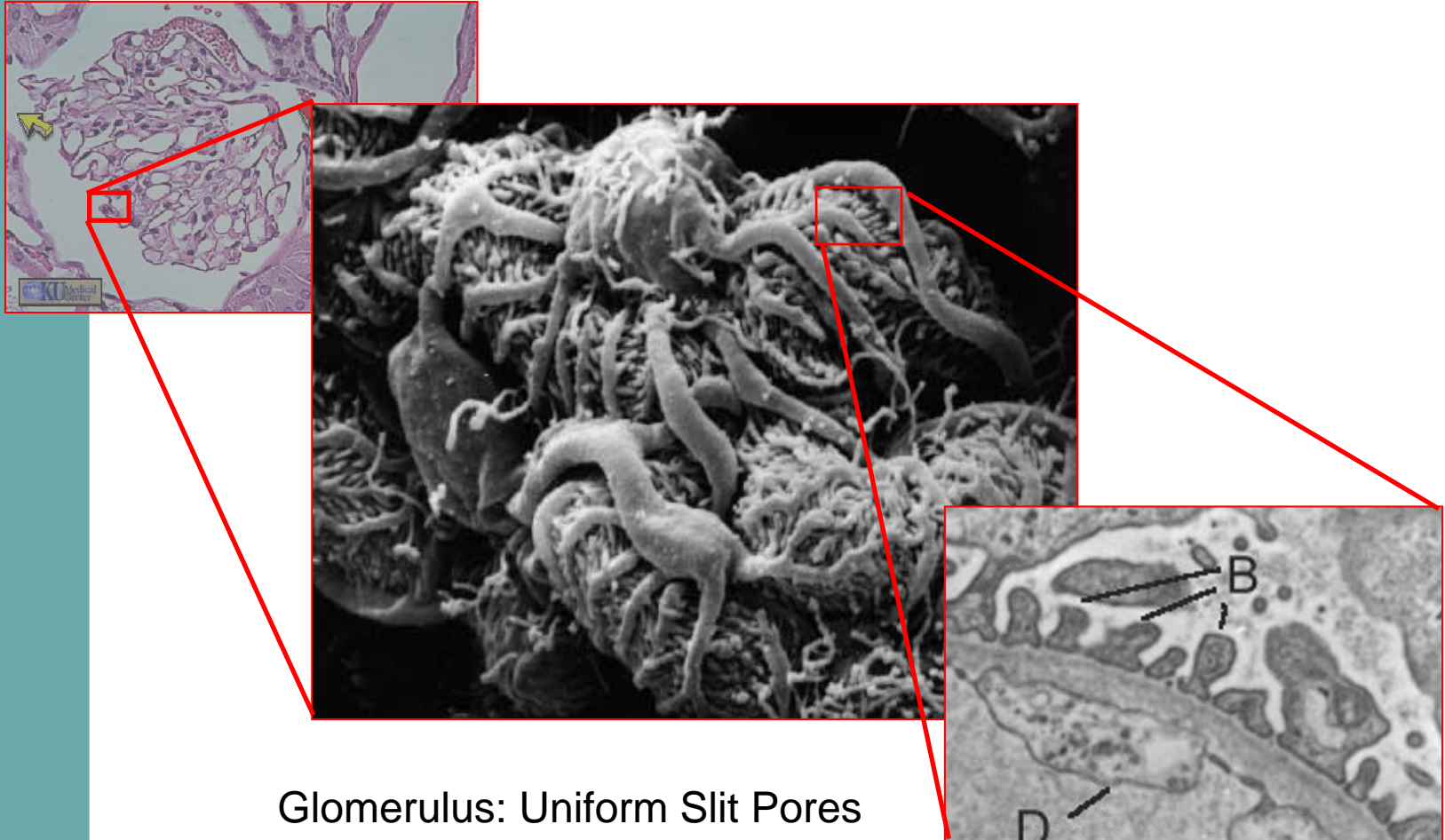


# Artificial Hemofilter

- **Hollow-fiber membranes have limitations**
  - thick porous polymer films have high resistance, non-uniform pore sizes and degrade over time upon exposure to body fluids



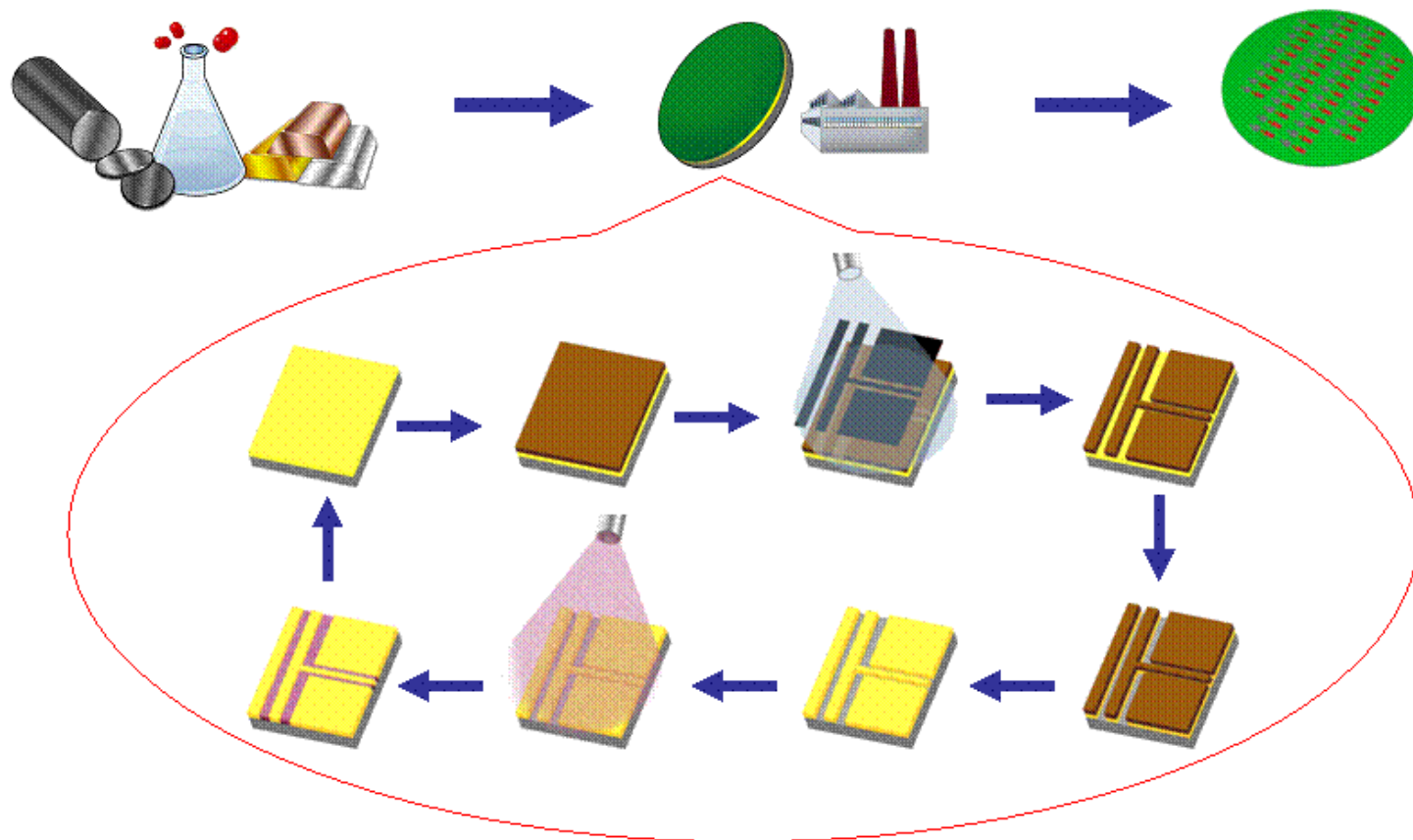
# Natural Hemofilter



Glomerulus: Uniform Slit Pores

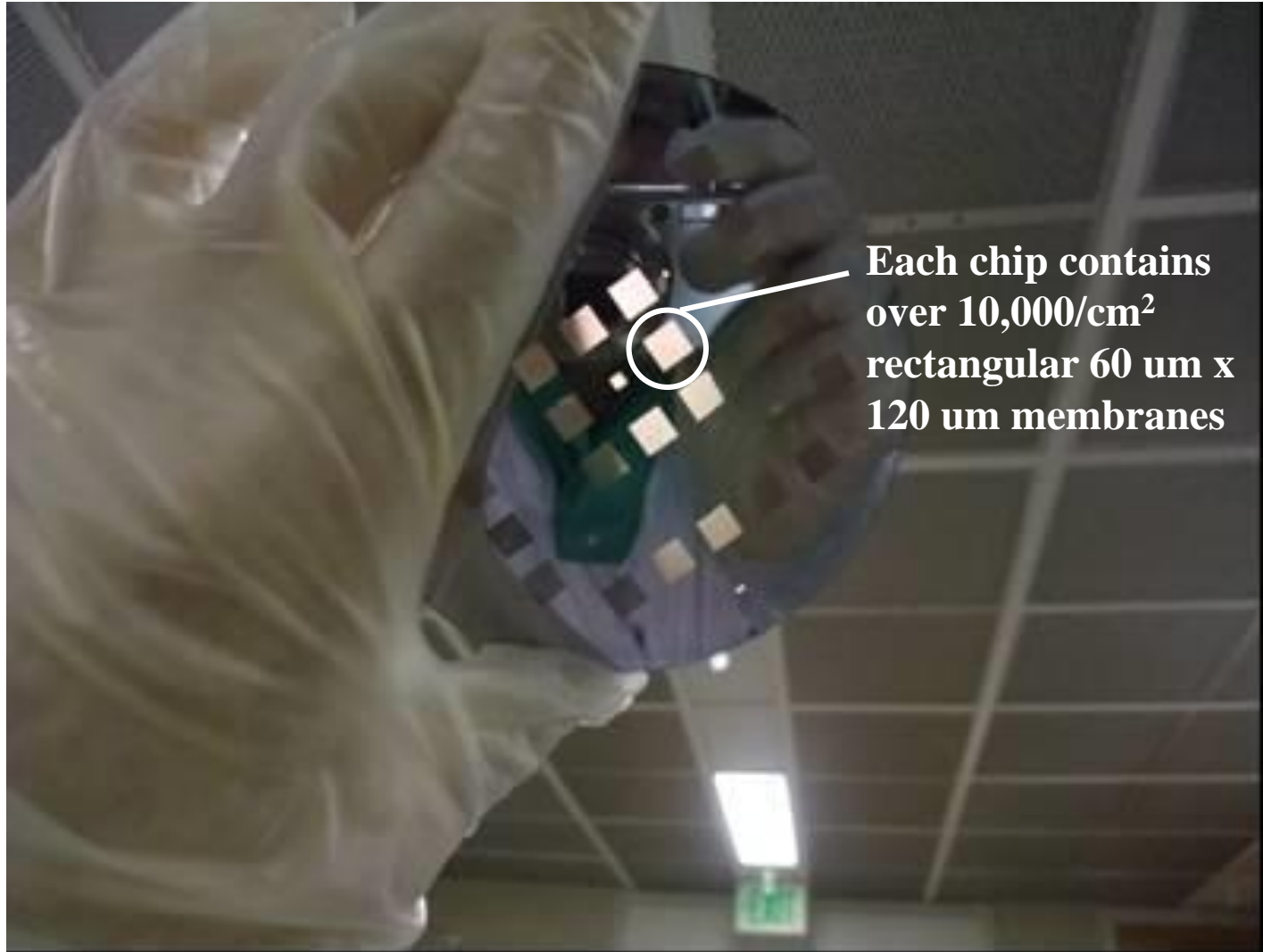


# Silicon Nanotechnology



**Leverage the extensive manufacturing infrastructure of the semiconductor industry (Intel, TSMC)**

# Silicon Membrane Wafer



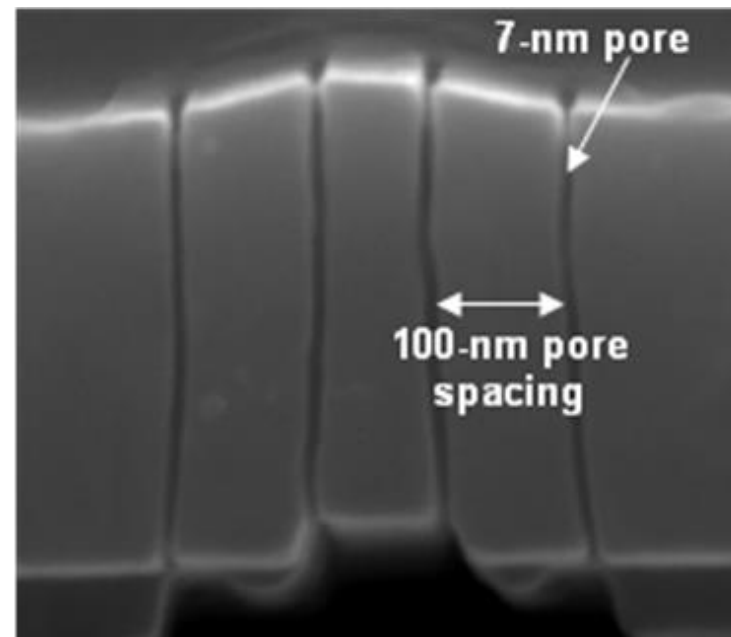
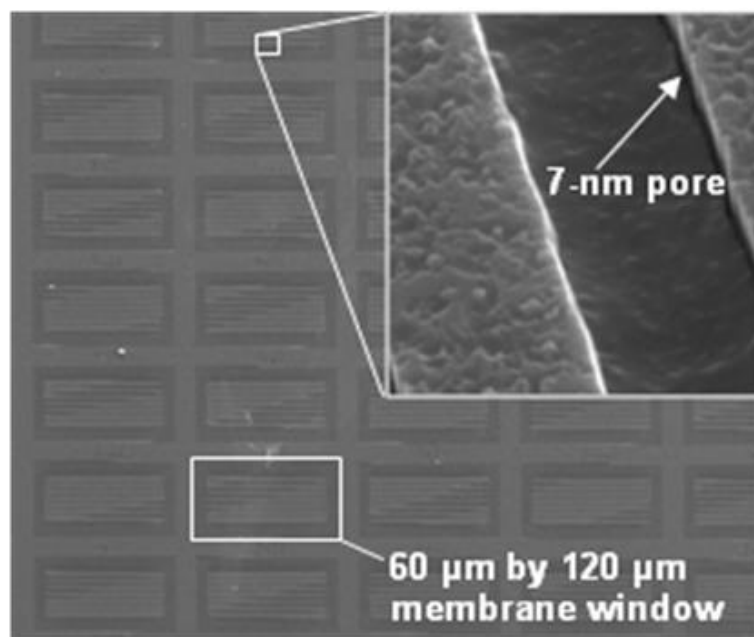
# Membrane Characteristics

- **High hydraulic permeability**
  - up to 600 ml/hr/mmHg/m<sup>2</sup>
- **High permselectivity**
  - over 80% middle-molecule clearance
  - less than 0.1% albumin passage

**No Pumps**

**Improved Clearance**

## SEM – Silicon Membranes





# Unique Hemocompatibility Challenges

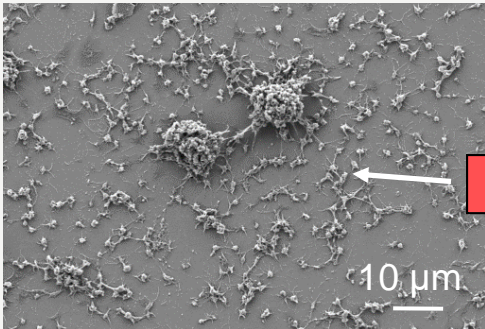
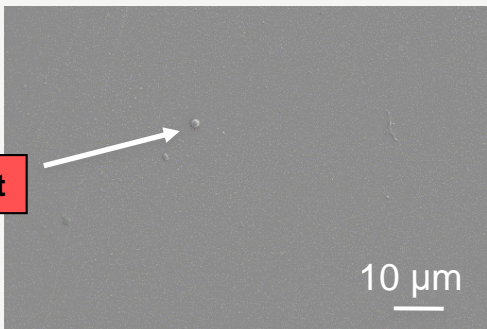
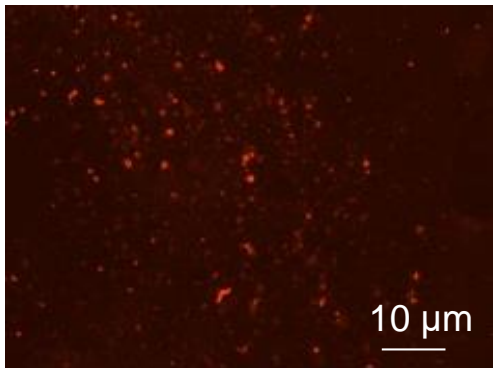

- **Pore Size (on order of 10nm)**
  - Ultrafiltration & Immunoisolation
- **Continuous blood contact**
  - Low flow rates
  - Low shear rates
- **Surface Protein Fouling**
- **Thrombus Formation**



## Strategy

- **Thin-film Surface Modifications**
  - Sub-5nm thick coatings
  - Long-term stability

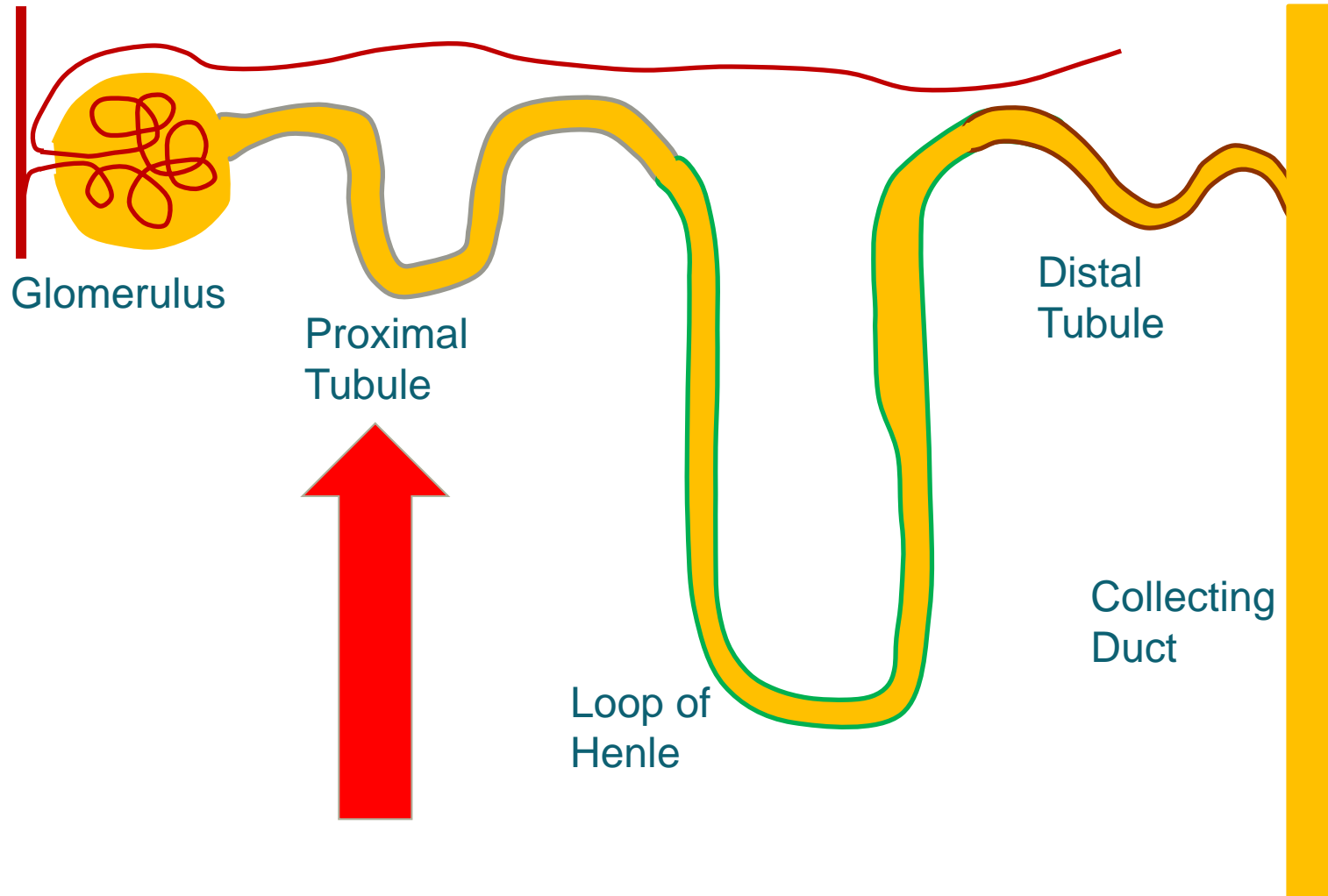
# Blood Compatibility

	Non-Coated Silicon	Coated Silicon
<b>Cell Adhesion (1000X)</b>		
<b>Platelet activation (CD62)</b>		

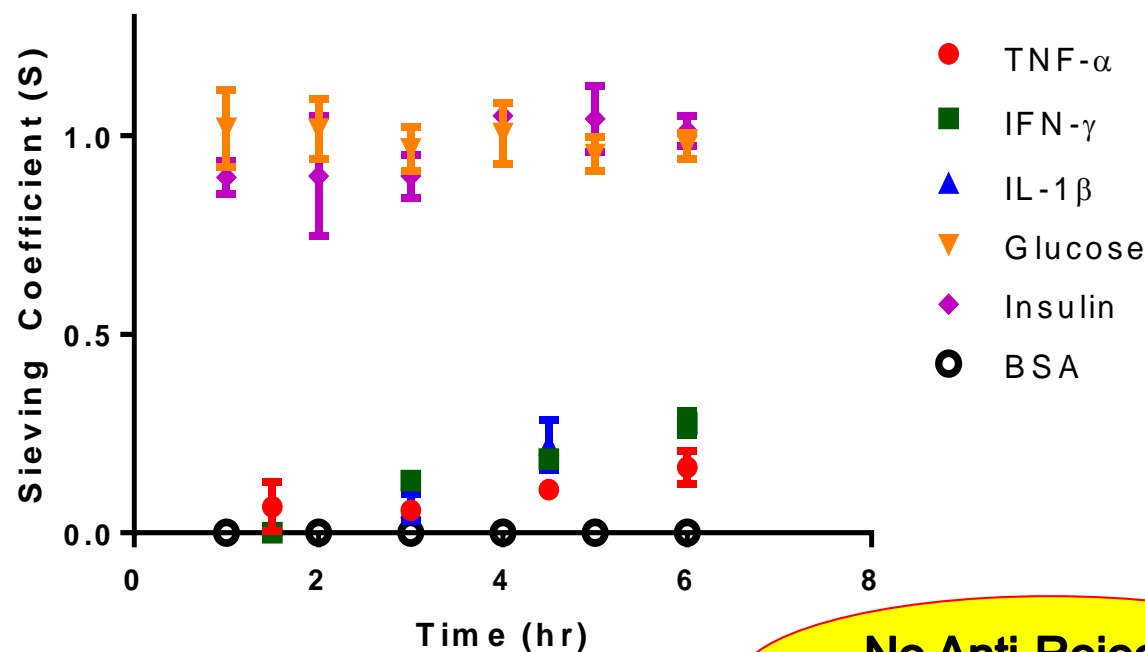
**No Blood  
Thinners**

***Minimal cell adhesion and platelet activation with polySBMA coatings.***

# The Renal Filter Unit: the Nephron



# Silicon Membrane Performance

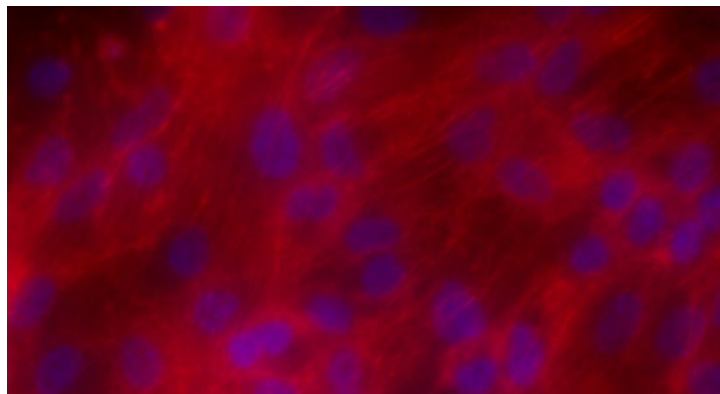


**No Anti-Rejection  
Drugs**

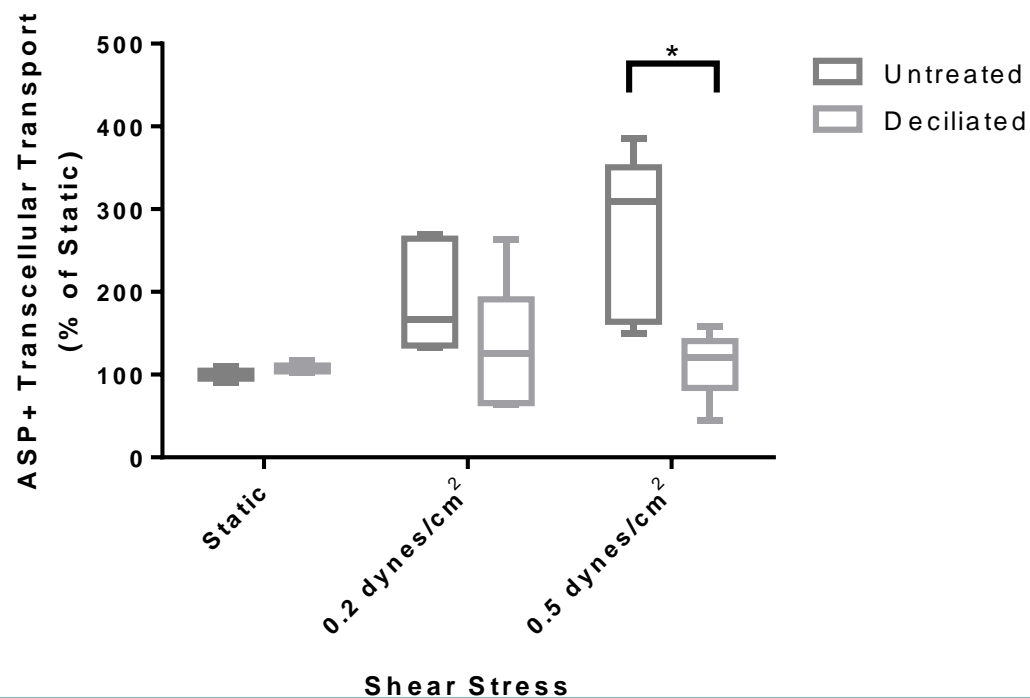
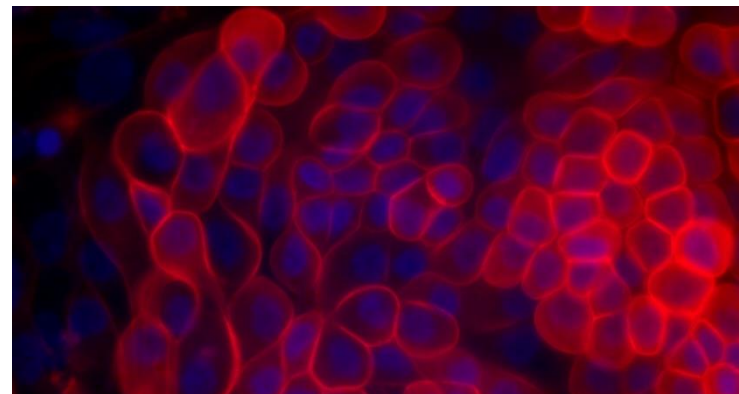
- 80% reduction in cytokine passage
- 100% passage of glucose and insulin
- No passage of BSA and antibodies

# Static vs Shear Conditions

Static Culture



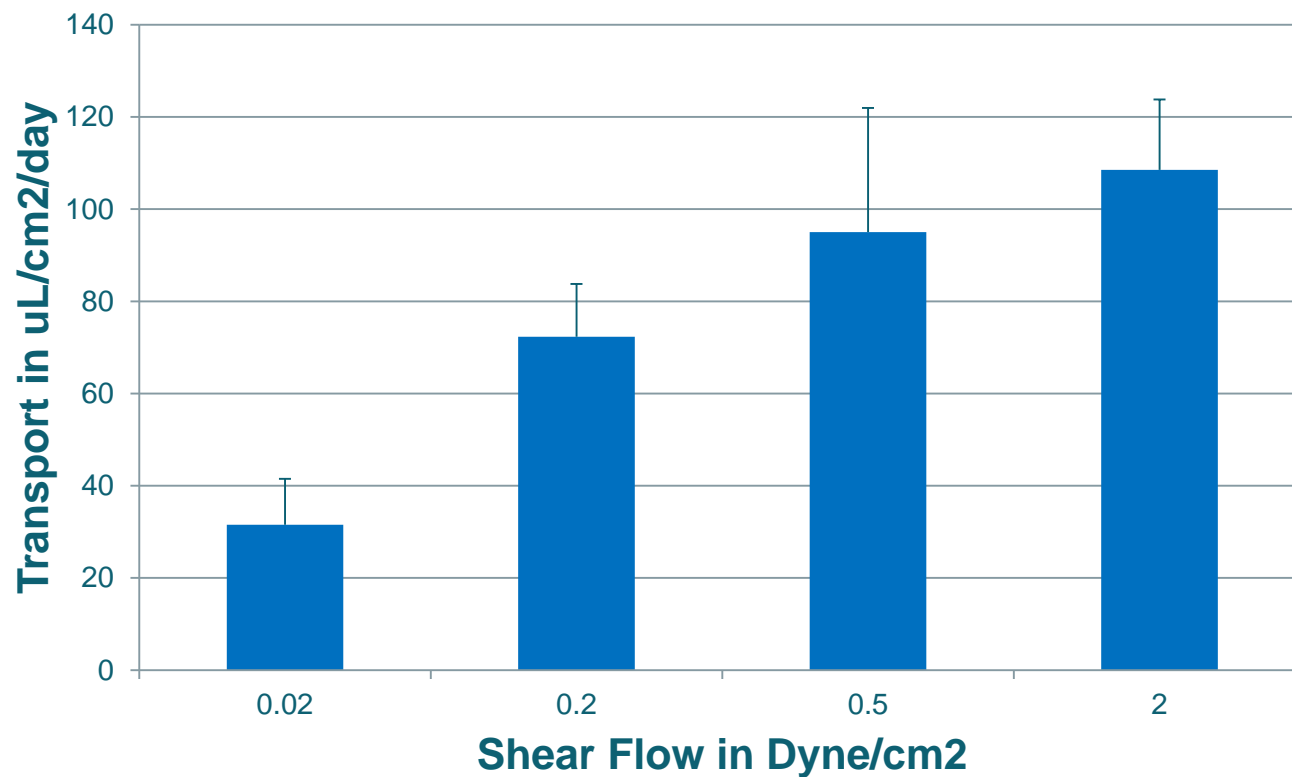
1 dyne/cm<sup>2</sup> x 6 hours



# Shear Effects

No Dialysate  
or Fluids...

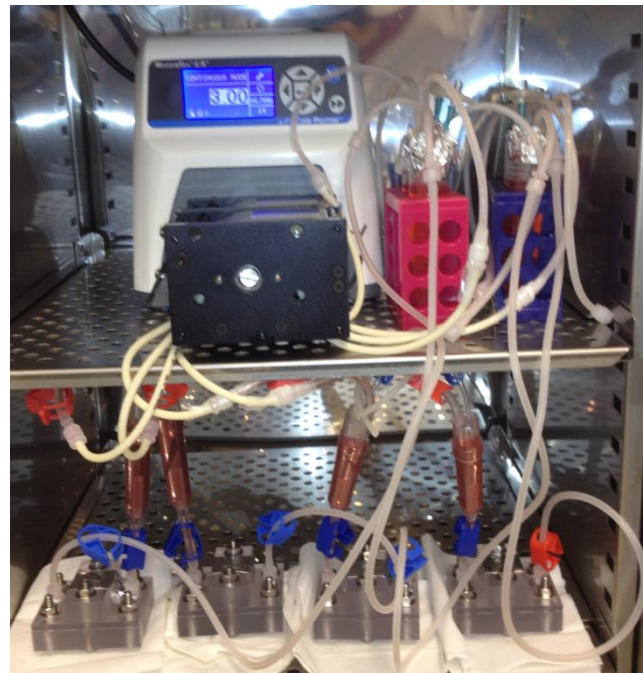
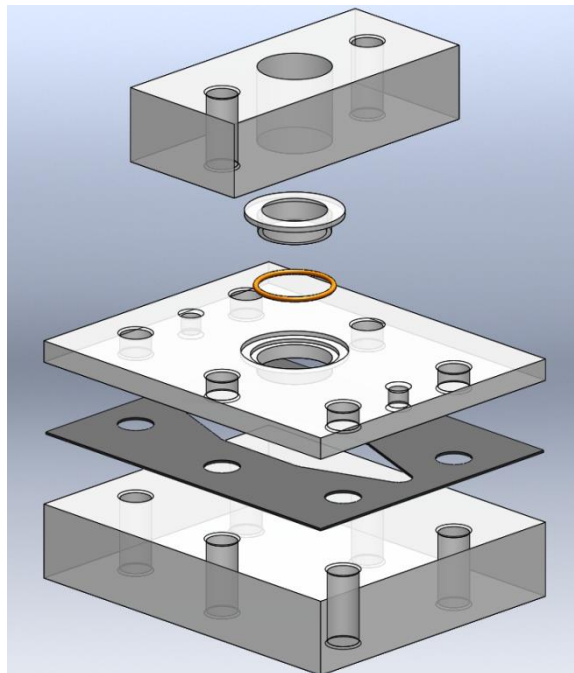
## Water Transport (LL-PCK1)



*Courtesy: Paul Brakeman, UCSF Pediatric Nephrology*

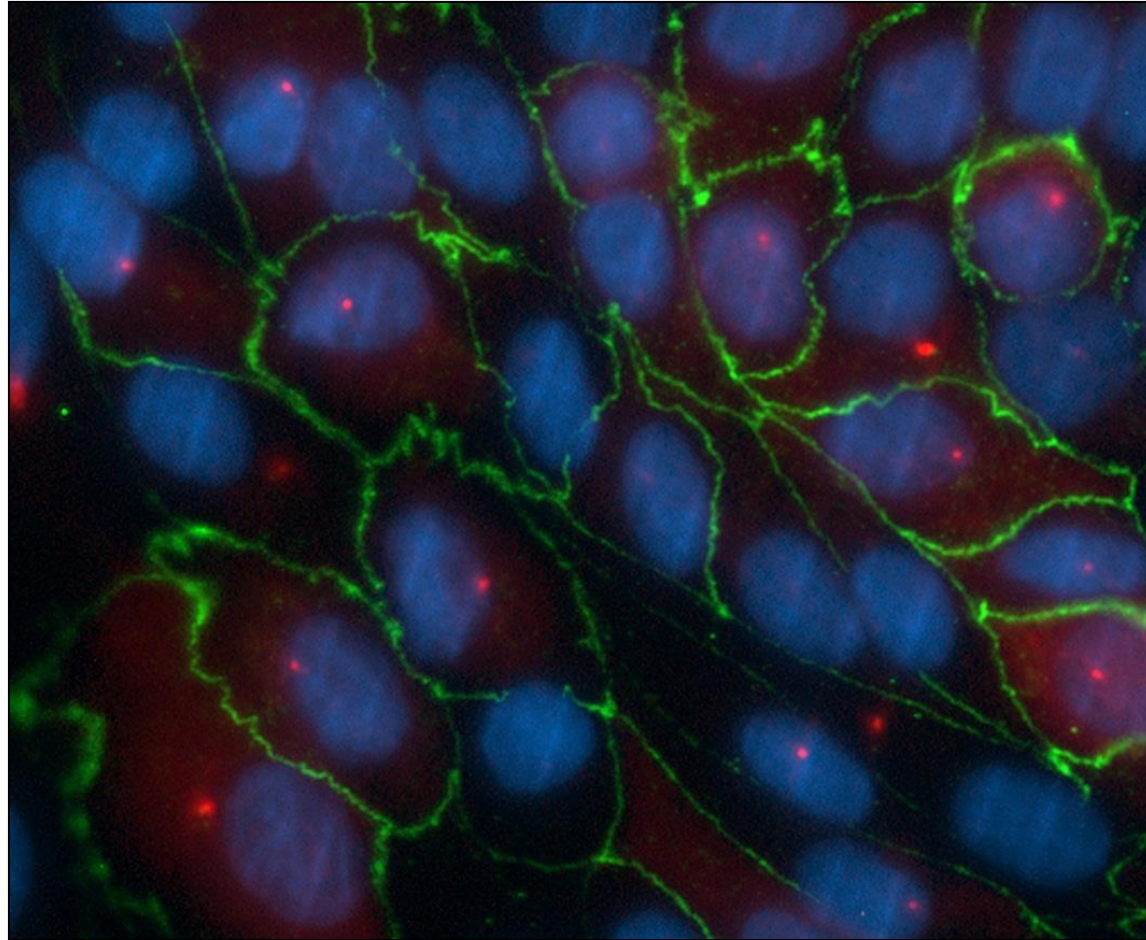


# Perfusion Flow Bioreactor



- **Bioreactor features**
  - microchannels for controlled shear stress on cells
  - membrane for cell support and transport pathway
  - basolateral chamber for membrane support and fluid collection

# HRTC on Silicon Membranes



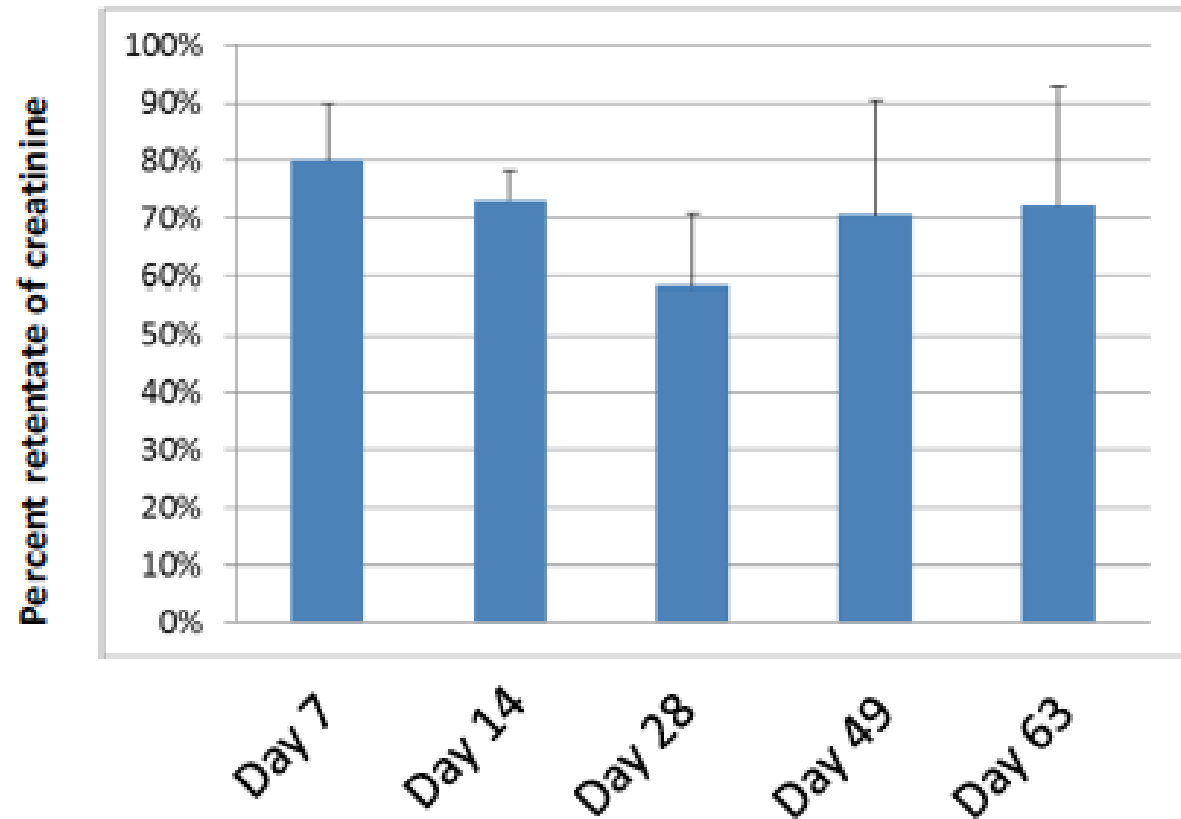
Blue – Nucleus

Green – Boundary

Red – Cilia

# Long-Term Barrier Function

## Creatinine Leakage (LL-PCK1)

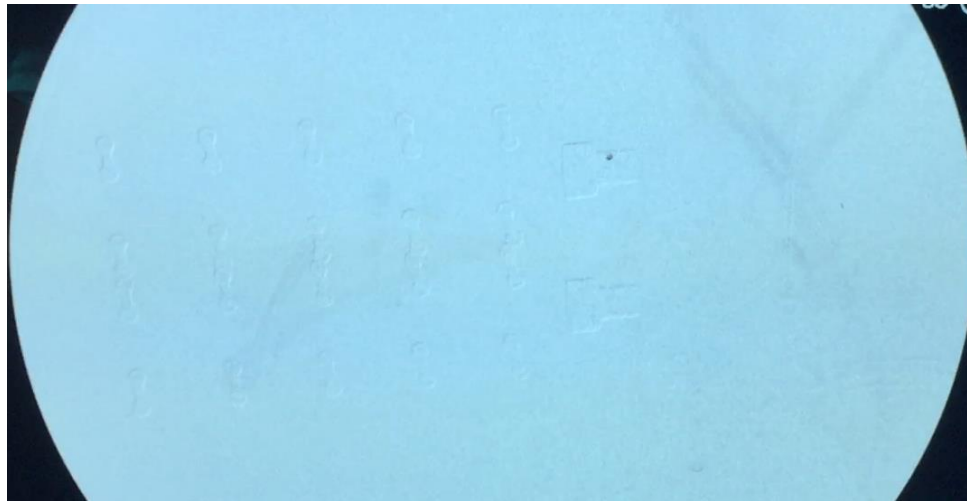


*Courtesy: Paul Brakeman, UCSF Pediatric Nephrology*

# Large Animal Testing

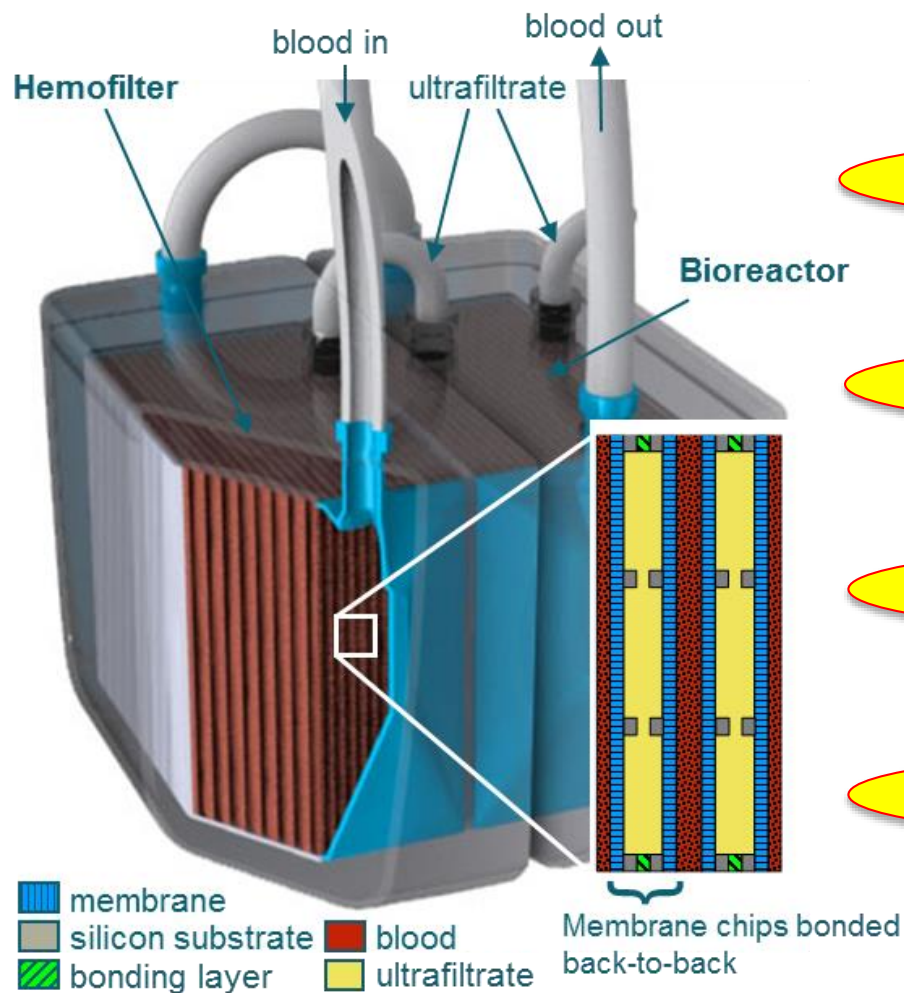


**No Pumps  
No Blood Thinners  
~1 month**





# Current Work: Scale-up and Integration



**No Catheters**

**No Dialysate**

**No Anticoagulants**

**No Immunosuppressants**

# Acknowledgements



JOHN & MARCIA  
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**The Kidney Project Team**  
<http://kidney.ucsf.edu>