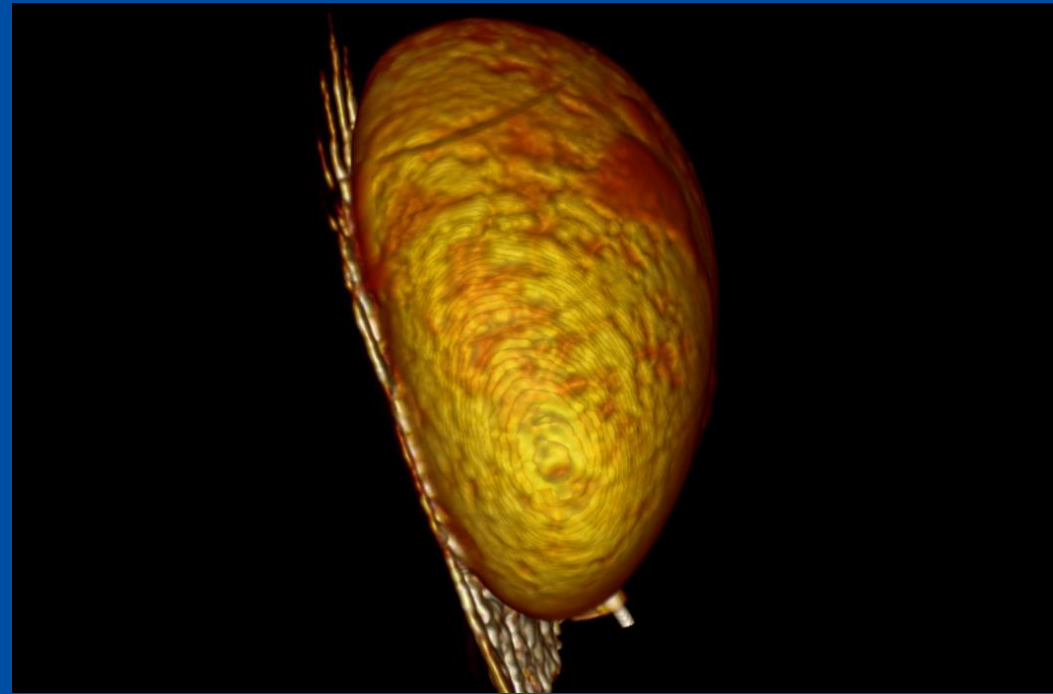
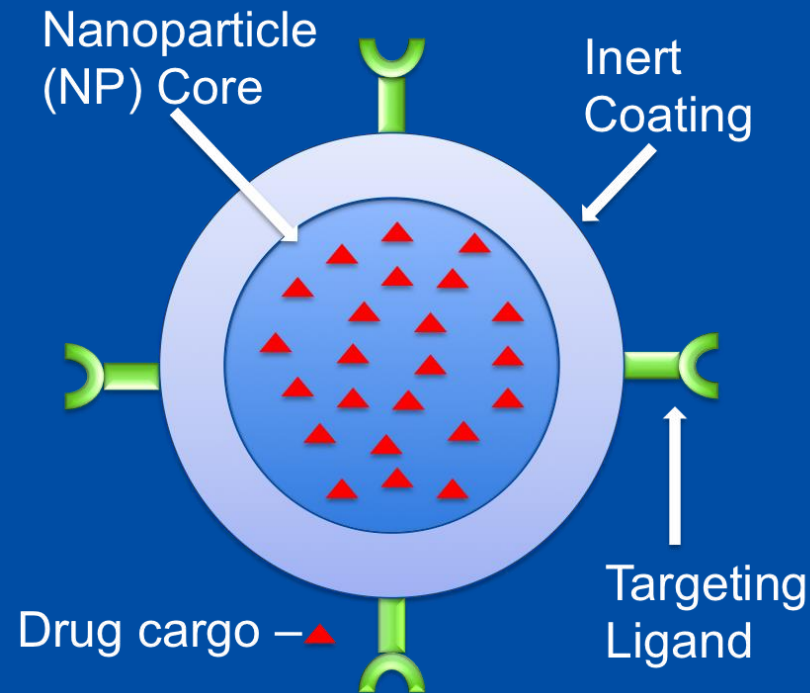


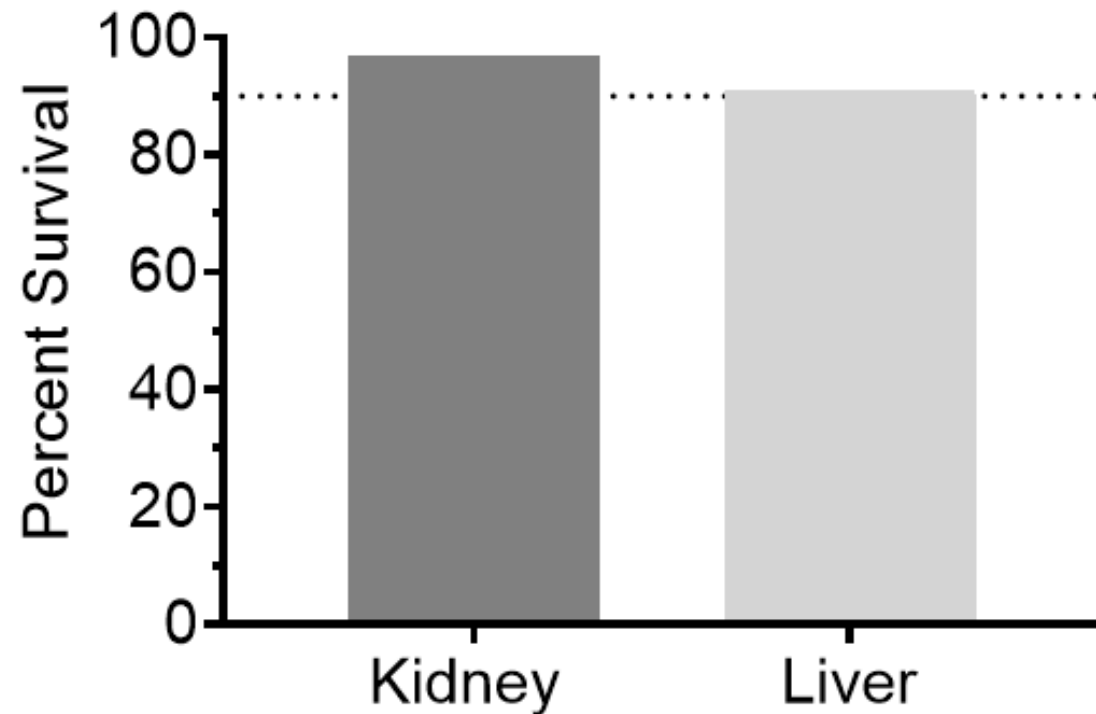
# Monobody-Linker Technology as a Catalyst to Transform Access to Organ Transplantation



# Our Motivation:

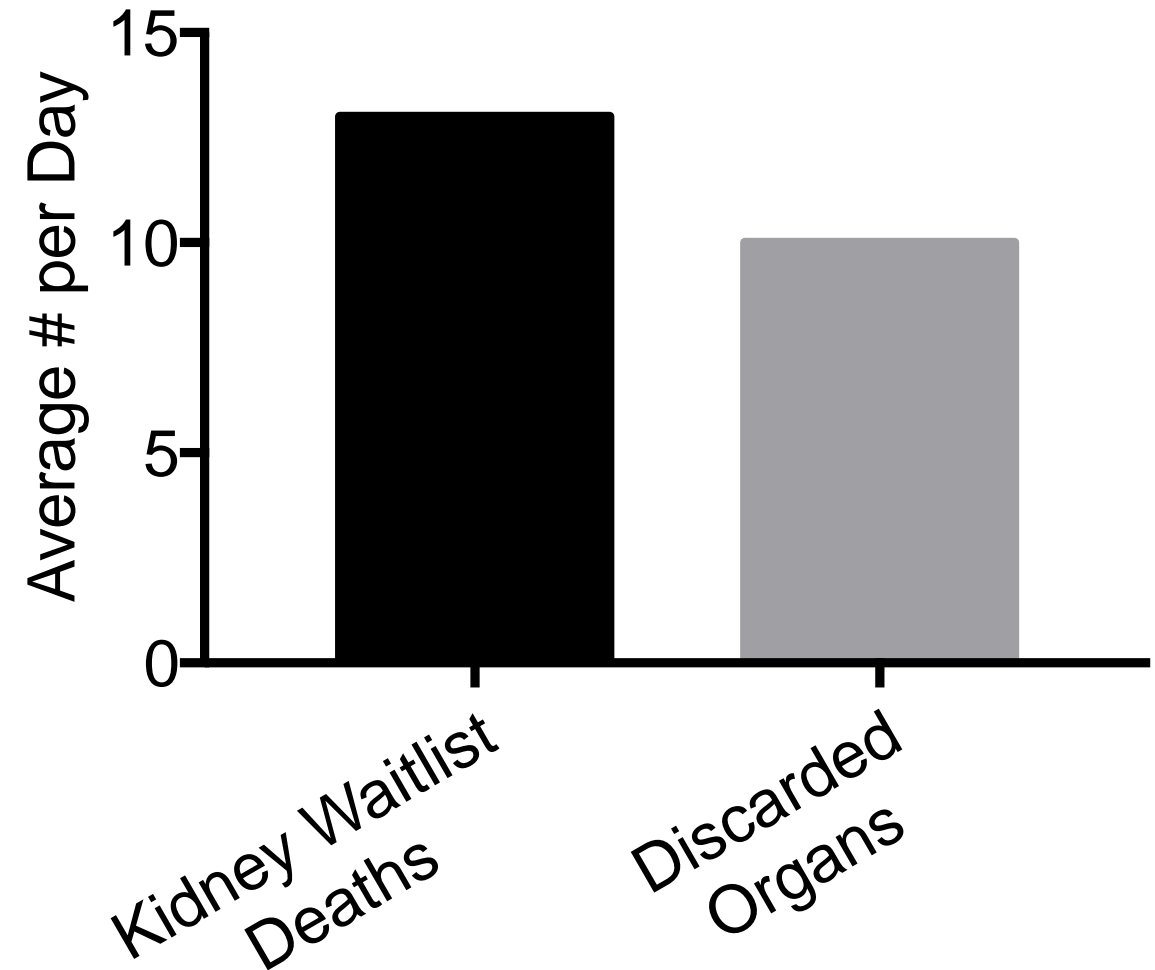
## Improving Access to Organ Transplant

### 1 Year Transplant Recipient Survival



#### Comparative Survival Without Transplant:

- Kidney – ~30% survival for typical 6-8 year wait
- Liver – 27% Survival at 3 months



# Our Approach:

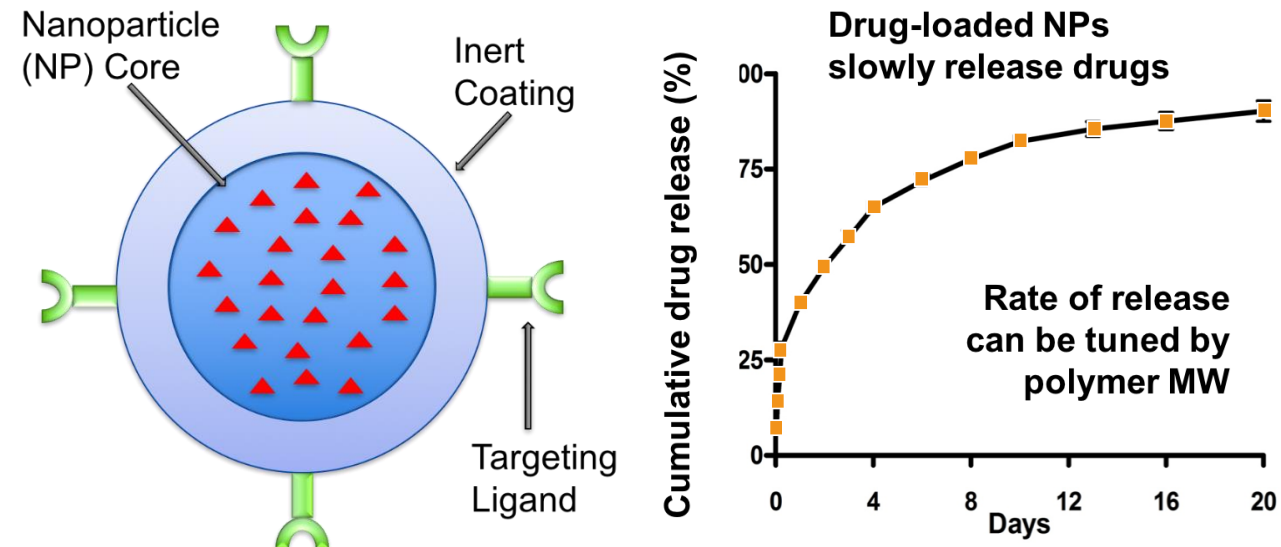
## Vascular-targeted nanomedicines delivered ex vivo



**Ex Vivo Organ Perfusion has Emerged as a Clinical Platform for Organ Repair**

### **Characteristics of Ideal Therapy for Ex Vivo Organ Repair:**

- Potential for sustained effect
- Modular adaptability for different drugs
- Capacity for robust retention on vascular-endothelium throughout organ



# Our Comprehensive Team of Experts

## Transplant/Vascular Immunology

- **Jordan Pober MD/PhD, Yale University:** World leader in human translational immunology with decades of experience in defining biologic pathways of injury related to organ transplant

## Targeted Nanomedicine Development

- **Mark Saltzman PhD, Yale University:** World leader in nanomedicine based drug delivery, member of two national academies (Medicine, Engineering), founder of Yale CBIT, several patents & startup co.
- **Shohei Koide, PhD, NYU:** World leader in protein engineering, Inventor of Monobody Technology, extensive experience with therapeutic Ab development (1 Ab nearing IND), 19 issued patents
- **Greg Tietjen, PhD, Yale:** Emerging leader in therapeutic delivery during ex vivo human organ perfusion, built a robust pipeline for preclinical research in non-transplanted human organs

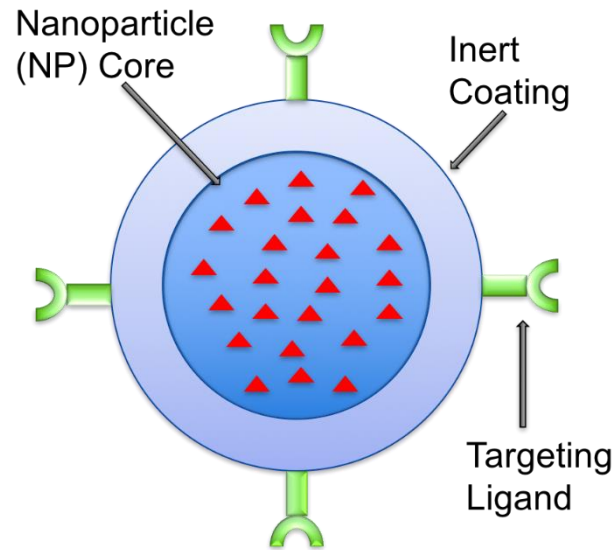
## Clinical Organ Transplant and Ex Vivo Organ Perfusion

- **Peter Friend, MD, Oxford University:** Pioneer of normothermic liver perfusion, scientific founder of OrganOx and co-inventor of best-in-class liver perfusion device
- **Mike Nicholson, MD, Cambridge University:** Pioneer of normothermic kidney perfusion, currently running largest multi-center randomized control of kidney machine perfusion

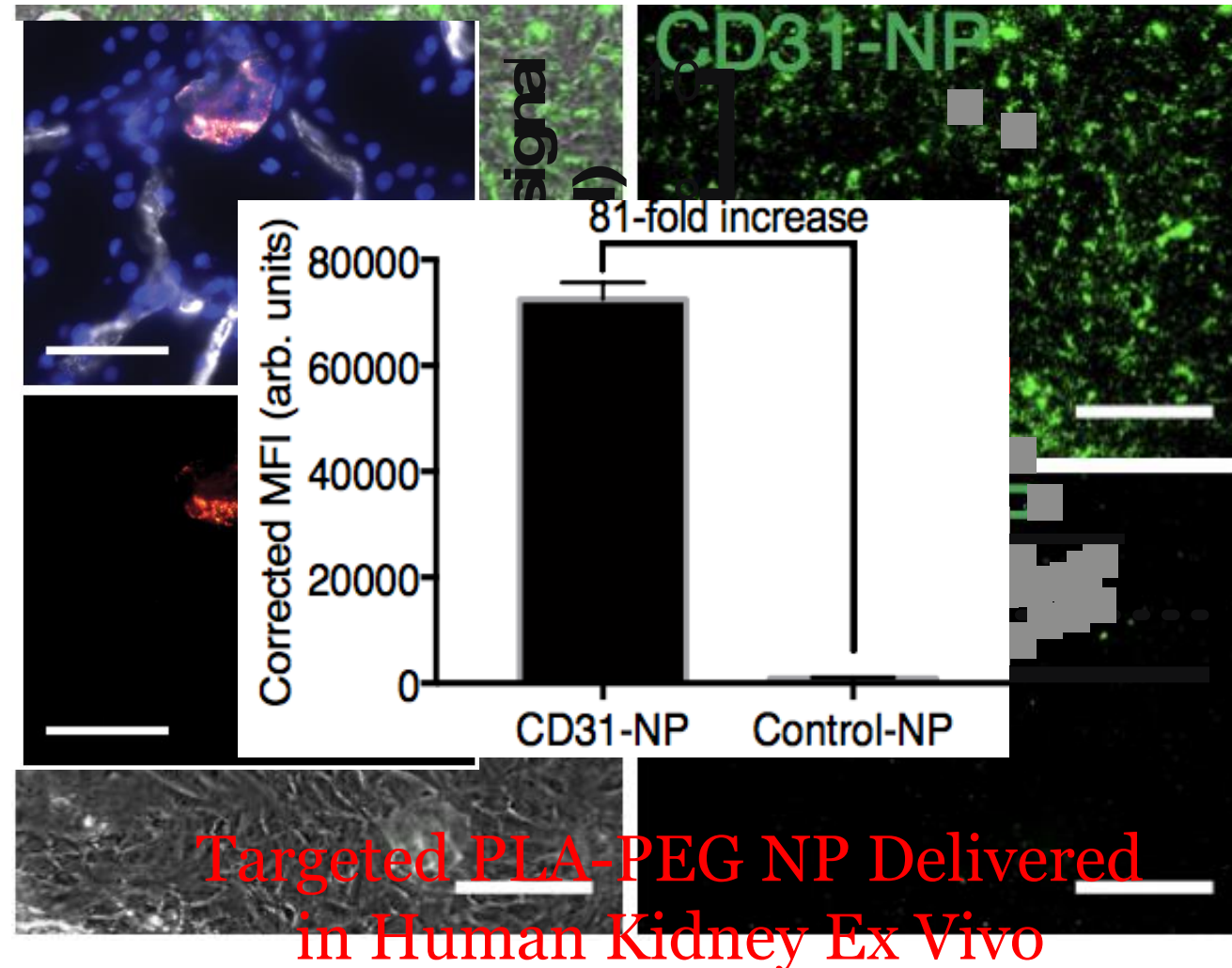


# The Problem:

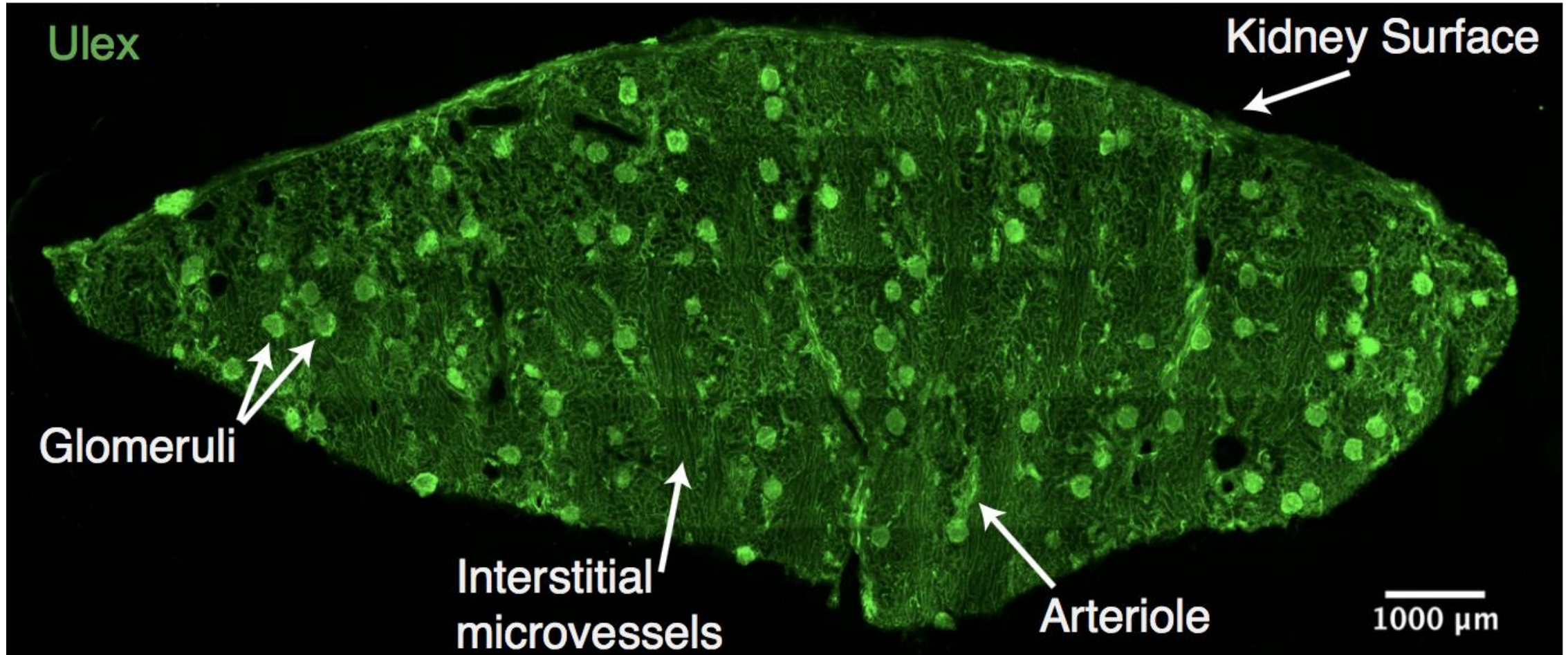
## Getting Nanomedicines to the Cells that Need Them



Translating this to a complex  
Achieving effect NP-targeting  
vascular network in a human  
in a petri dish is easy!  
organ is really hard!



# The Problem: Getting Nanomedicines to the Cells that Need Them



Human Organs are Very Complex and Competitive Environment!

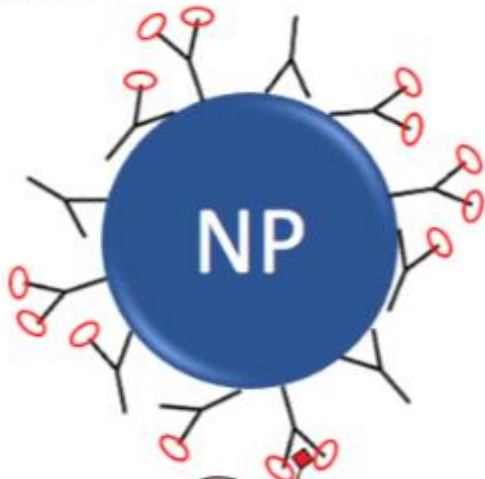


# Our Solution: Monobody-Linker Technology



Antibody  
(Ab)  
150 kDal

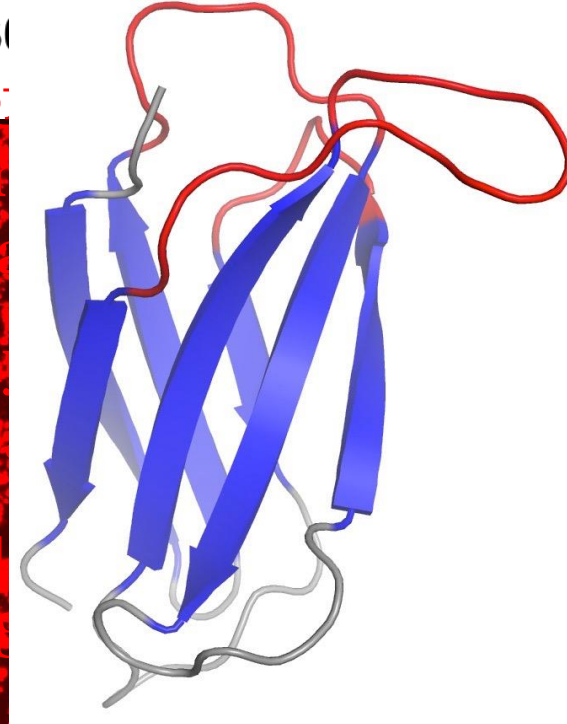
Standard approach:  
*Ab-NPs*



## Benefits of

MFI (PECY5)

- Obtain dramatic
- High affinity
- Can't be



NP

on  
eting  
nt Abs

out need to  
poke Abs

**Monobody Binding Protein**

(invented by Shohei Koidei)

Ab standard approach allows for  
engineered terminal cysteine

# Market Opportunity

## Phase I: Ex Vivo Organ Delivery

- Transplant Market ~\$3 billion
- Cost per transplant:
  - Kidney: \$418,400
  - Liver: \$812,500
- Current # on Wait list:
  - ~114,000 patients
- Current # of Transplants/year
  - ~30,000

## Phase II: In Vivo Delivery

- Pre-clinical validation in human organs could enable targeted in vivo delivery
- Diagnostic and Therapeutic possibilities in wide array of indications
- Nanomedicine market projected to be ~\$350 billion by 2025



# How We Intend to Use Blavatnik Funds

- ❖ Requesting \$300k for preclinical validation to enable clinical trials
- ❖ CRO for large scale production of Monobody-NP and in vitro validation
- ❖ Ex Vivo validation in human liver and kidney (Tietjen and Friend Labs) with CRO analysis of biopsies
  - Phase I: NP target and dose optimization
  - Phase II: Evaluation of Therapeutic Efficacy
- ❖ Candidate therapeutic encapsulants:
  - Small Molecule: Rapamycin
  - siRNA: MHC knockout

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