

tengion®

Regenerative medicine
brought to life.

***Multivariate Analysis of Preclinical Data
from the Tengion Neo-Kidney Augment™***

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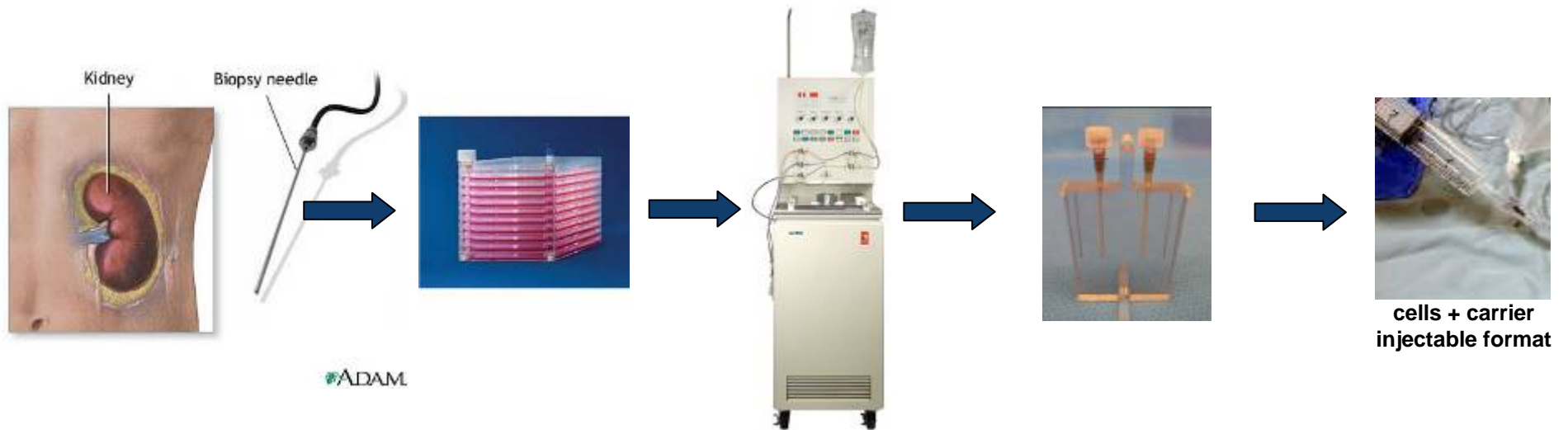
** Corresponding Author*

Neo-Kidney Augment Overview

Intended to delay the need for dialysis or transplantation

100,000 new dialysis patients each year in the US

- 350,000 currently on dialysis
- 20% annual mortality
- \$77,000 annual cost per patient per year
- \$39 billion in direct US costs annually for end stage kidney disease



Biopsy

*Cell Isolation & Culture
(2-3 weeks)*

*Cell Selection
(<1 day)*

*Dose Preparation
(2 weeks)*

Delivery

tengion®

NKA Tested in Four CKD Animal Models

Nephrectomized Lewis Rat (Kelley et al., 2010 AJPrenal Physiol 299 (5))

- *Aggressive preclinical model of chronic kidney disease*
- *Preserved functional kidney mass, slowed progression, improved survival at 6 months*

Diabetic ZSF1 Rat

- *Aggressive diabetic, obese, hypertensive rat model of kidney failure*
- *Slowed kidney failure progression and improved survival at 1 year*

Human Kidney Cells in Nude Rat

- *Chronic kidney failure model*
- *Reversed kidney failure at 3 months*

Nephrectomized Dog

- *Aggressive preclinical model of chronic kidney disease*
- *Early observations from ongoing large animal study consistent with small animal results*

Experimental Design

Diabetic ZSF1 Rat



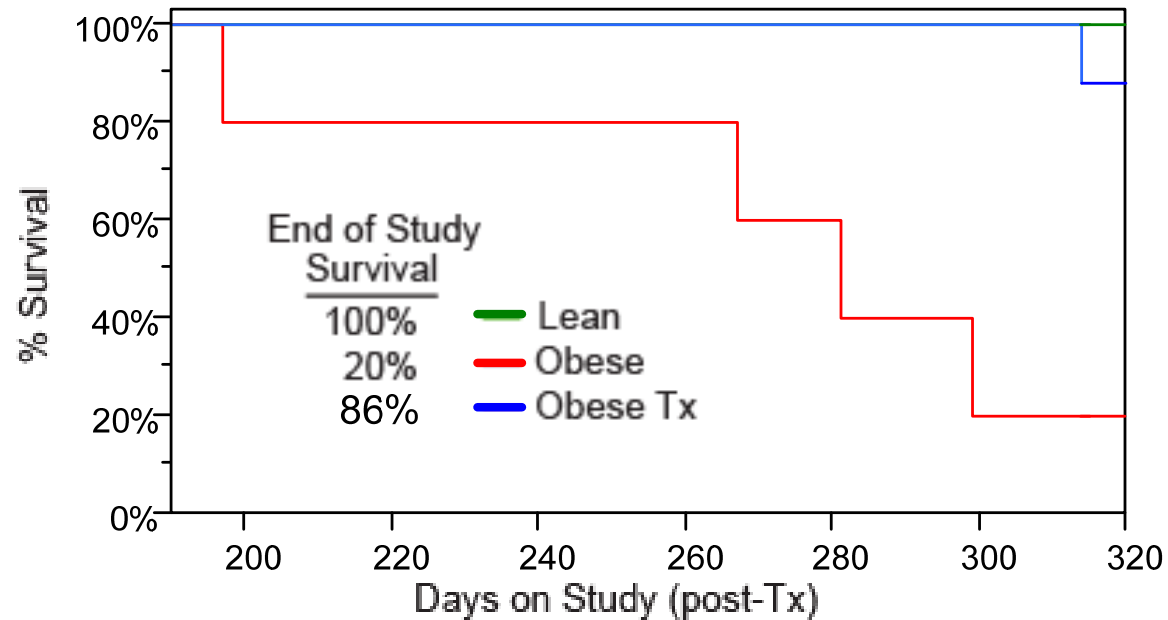
- Rat strain with leptin receptor deficiency
- Aggressive Metabolic Syndrome causing progressive loss of kidney function
- Seven rats treated with syngeneic Selected Renal Cells versus five untreated control rats
- Measured survival, serum chemistry, urinalysis over 45 weeks

NKA Improved Survival

Statistically Significant Effect on Survival

-Log Rank Test $p=0.0036$

NKA Treatment Extended Rat Lifespan 11 to 27%



How to characterize treatment effect and translate to clinic?

Blood and Urine Chemistry Analysis

Blood Markers:

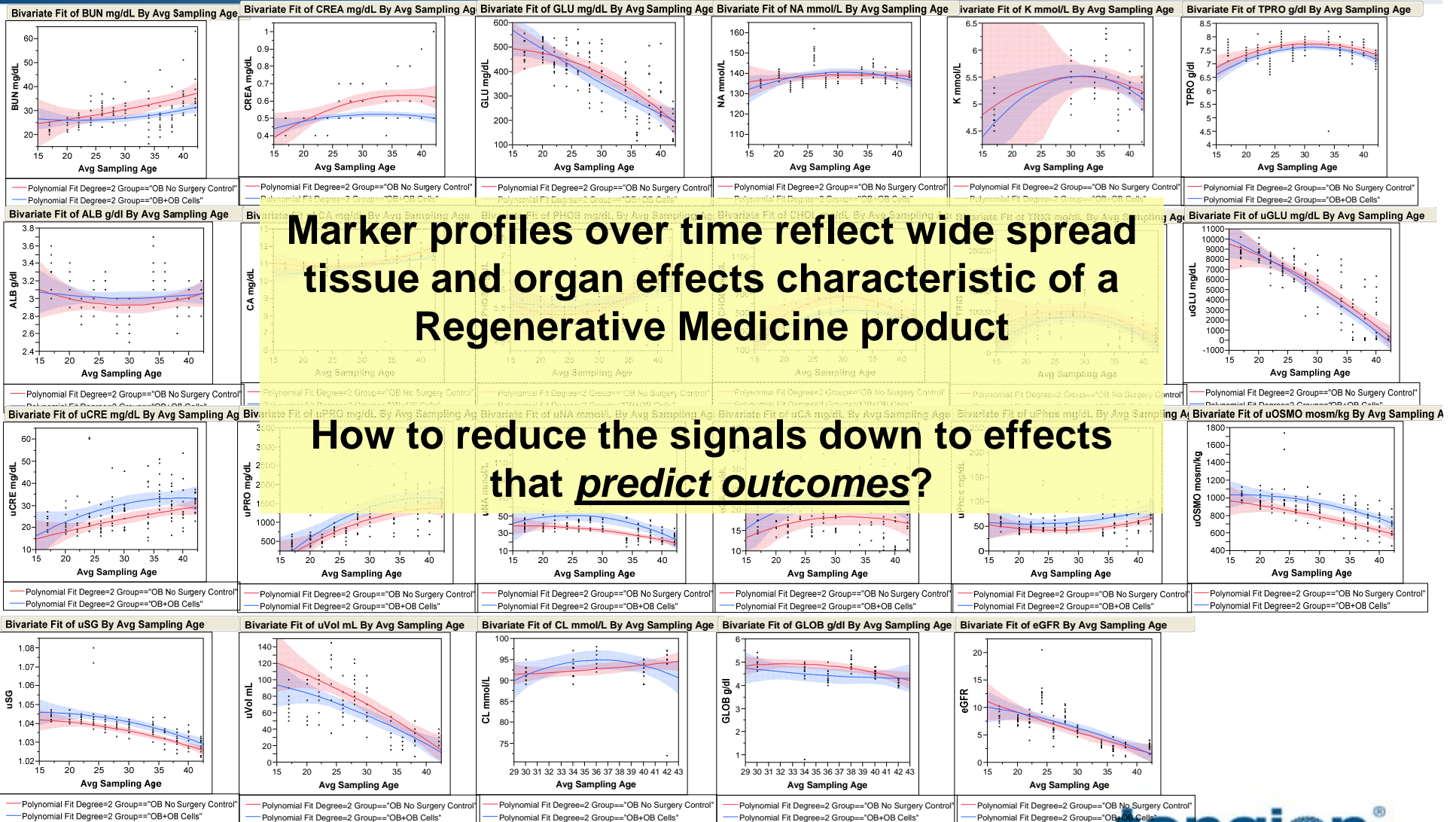
Blood Urea Nitrogen (BUN)
Creatinine
Glucose
Total Protein
Albumin
Cholesterol
Triglyceride
Globulin
Potassium
Sodium
Calcium
Phosphate
Chloride

Urine Markers:

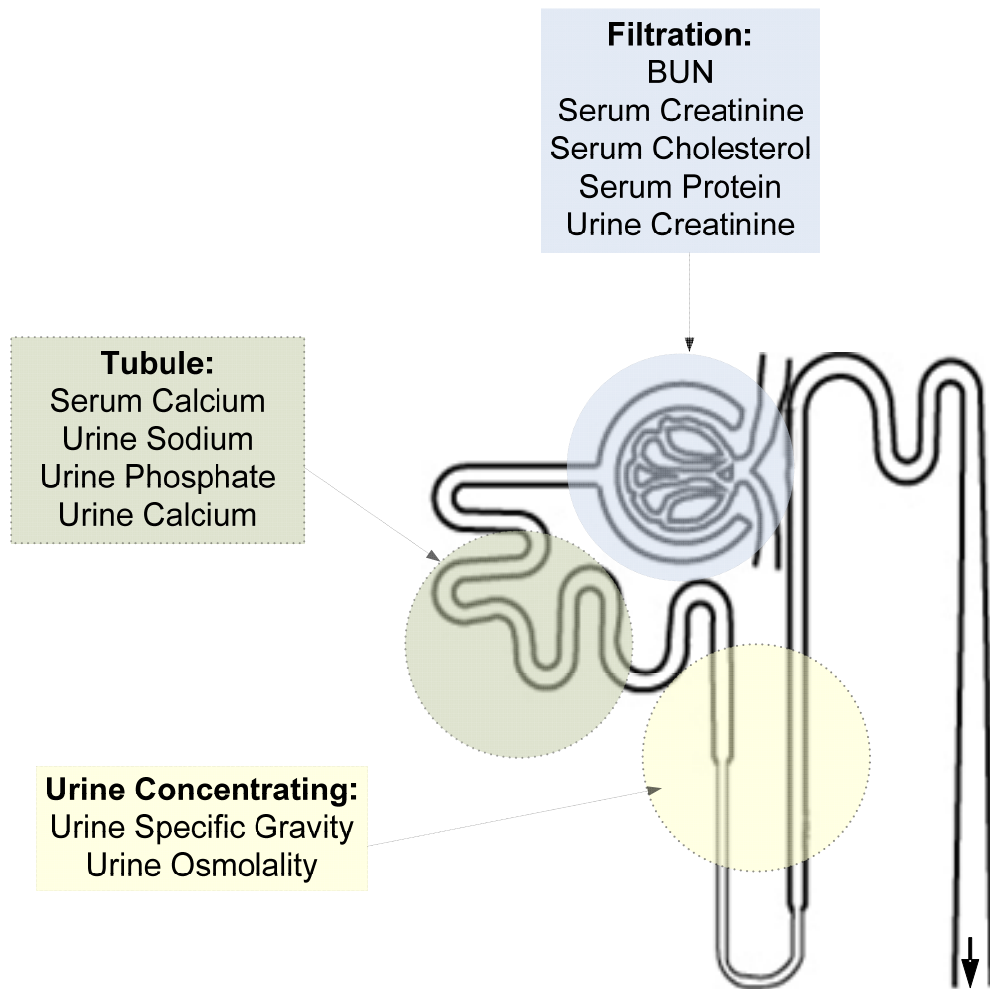
Creatinine
Glucose
Protein
Sodium
Calcium
Phosphate
Osmolality
Specific Gravity
Urine Volume
Estimated Glomerular Filtration (eGFR)

Tested multiple markers to identify relevant signals for product development and clinical translation

Raw Data Analysis



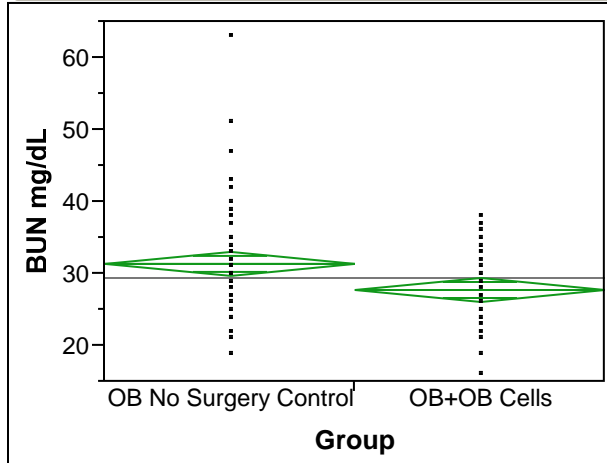
Functional Composite Measures



Categorize and combine markers for related kidney functions by calculating composite measures representing different renal “compartments”

Screening Markers by ANOVA

Oneway Analysis of BUN mg/dL By Group

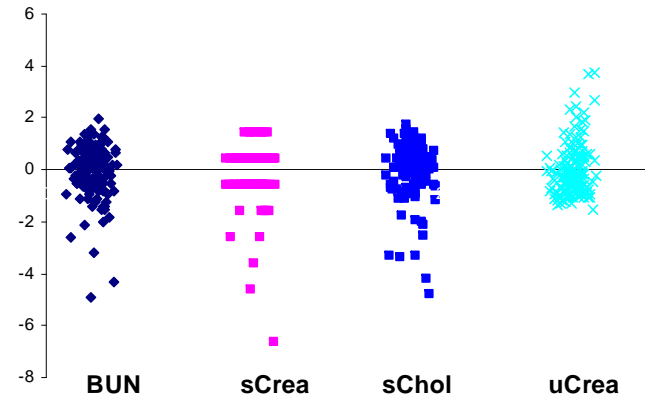
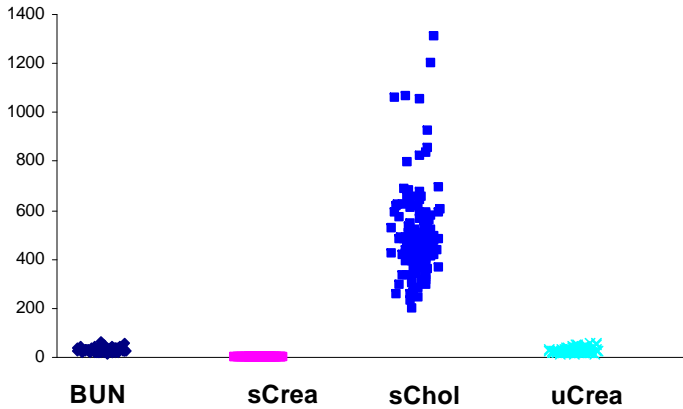


Identified nine markers with significant treatment effects by ANOVA

Biomarker	P value	Biomarker	P value
BUN	0.0039	uCRE	0.0291
CREA	<.0001	uPRO	0.2427
GLU	0.6665	uNA	0.002
NA	0.5814	uCA	0.0018
K	0.9486	uPhos	0.0457
TPRO	0.0093	uOSMO	0.0001
ALB	0.3333	uSG	0.0019
CA	0.0031	uVol	0.3321
PHOS	0.9379	CL	0.9543
CHOL	0.0002	GLOB	0.0902
TRIG	0.1123	eGFR	0.2503
uGLU	0.6476		

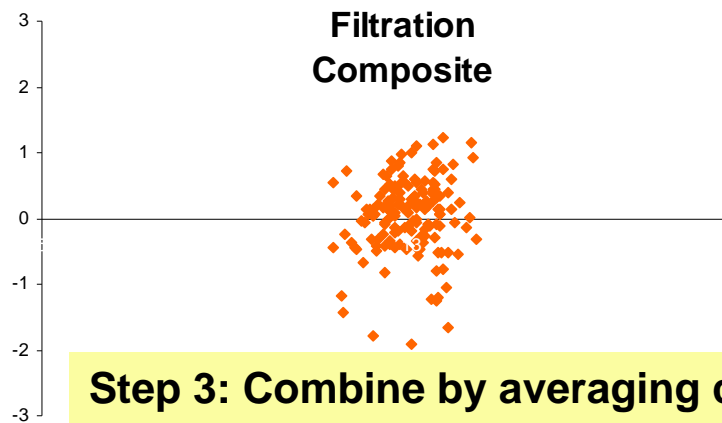
Composite Calculation

Converting raw data into functional composites



Step 1: Identify related components

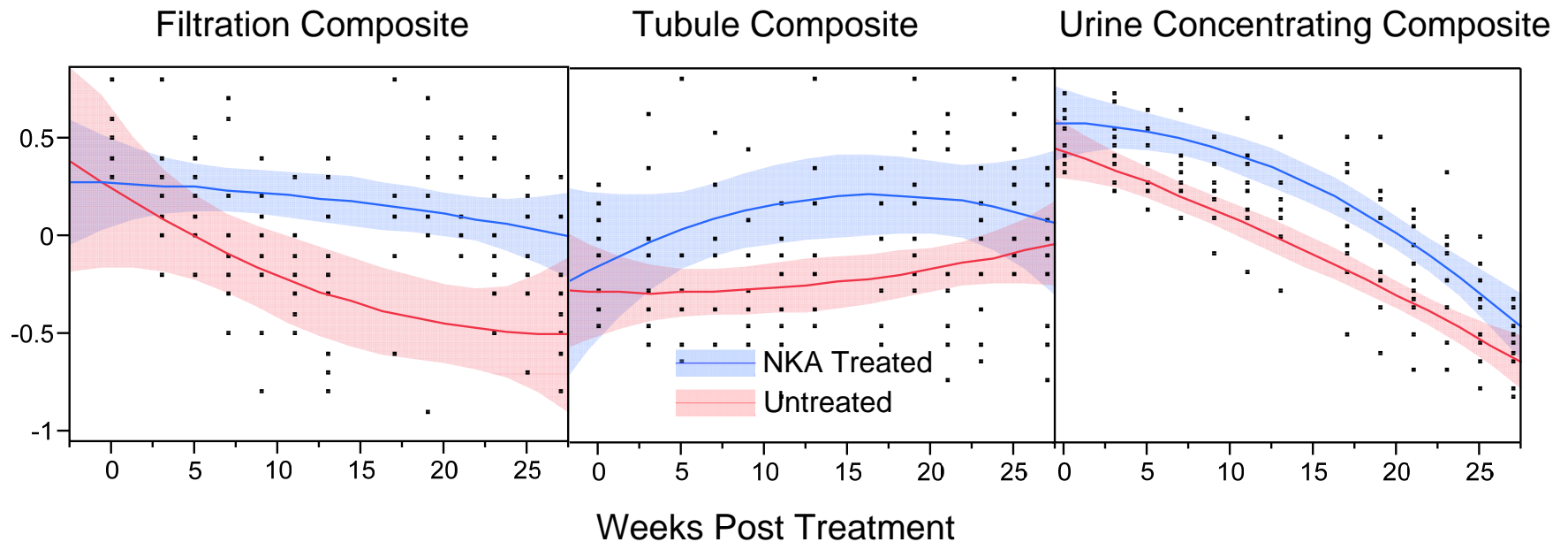
Step 2: Center and scale raw data



Step 3: Combine by averaging components

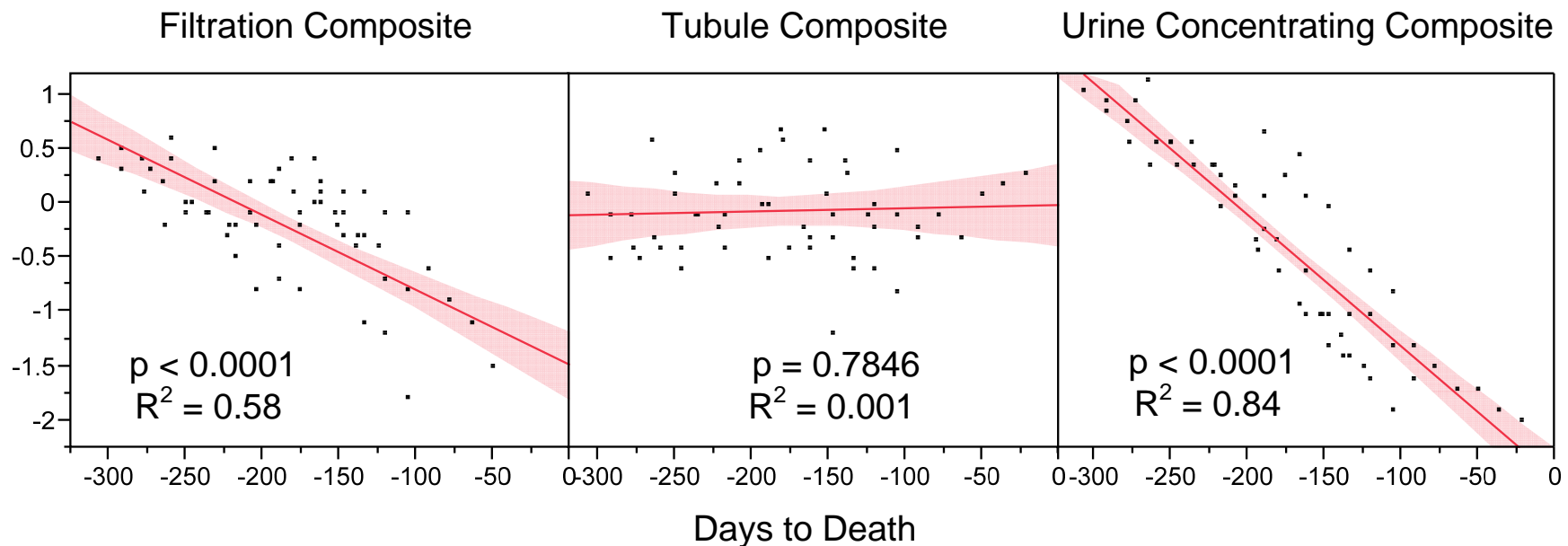


Composite Profile Over Time



- The composites illustrate the effects of treatment on kidney function over time
- Each composite has a unique profile characteristic of the functional compartment regeneration and disease progression

Validation of Composites



- **Filtration and Urine Concentrating composites strongly correlate to survival time in expired animals**
- **Tubule composite result suggests the effects in this compartment do not directly impact survival in this model**

Conclusion

- **Treatment with the Neo-Kidney Augment regenerates multiple tissue compartments and significantly improves survival in the diabetic rat model**
- **The calculated multivariate composites illustrate the impact of treatment over time, demonstrating improvement in Filtration (i.e. Serum Creatinine, BUN etc.) and maintenance of other kidney functions**
- **The Filtration and Urine Concentrating composite values significantly predict the time to death of the subject animals**