Biomarkers for Predicting Progression to Chronic Kidney Disease after Acute Kidney Injury

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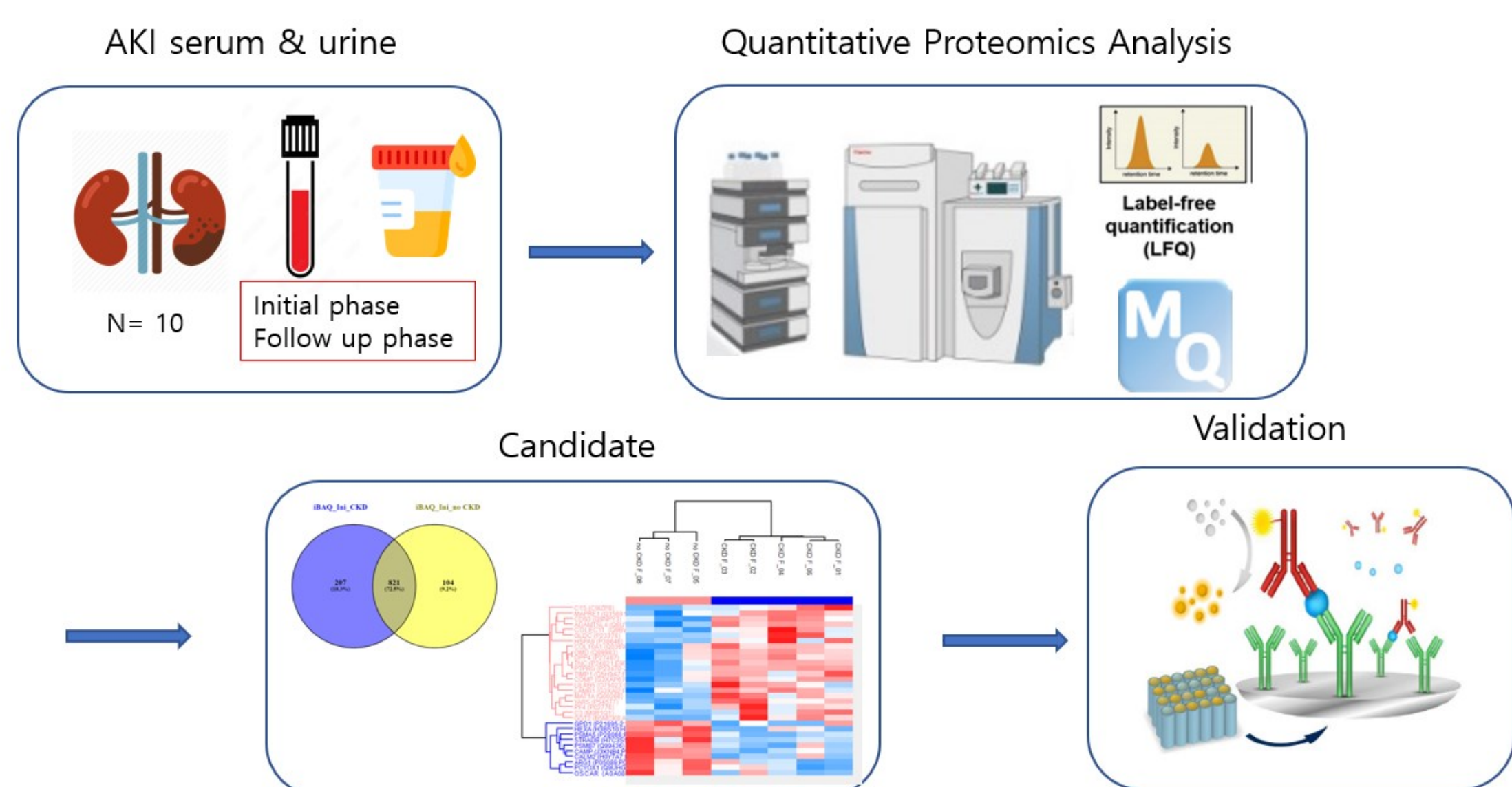
Introduction

- AKI is common in hospitalized patients
- Associate with progression of CKD (2-70%)
- Previous biomarker
  - ✓ inflammation (TNFR1/2, suPAR)
  - ✓ fibrosis (PIINP, MMP9)
  - ✓ injury (KIM-1, NGAL, IL-18, EGF)

- *Lack of data for pediatric patients*

Kidney International (2017) 92, 1071–1083; Clin J Am Soc Nephro (2008) 3: 881-886
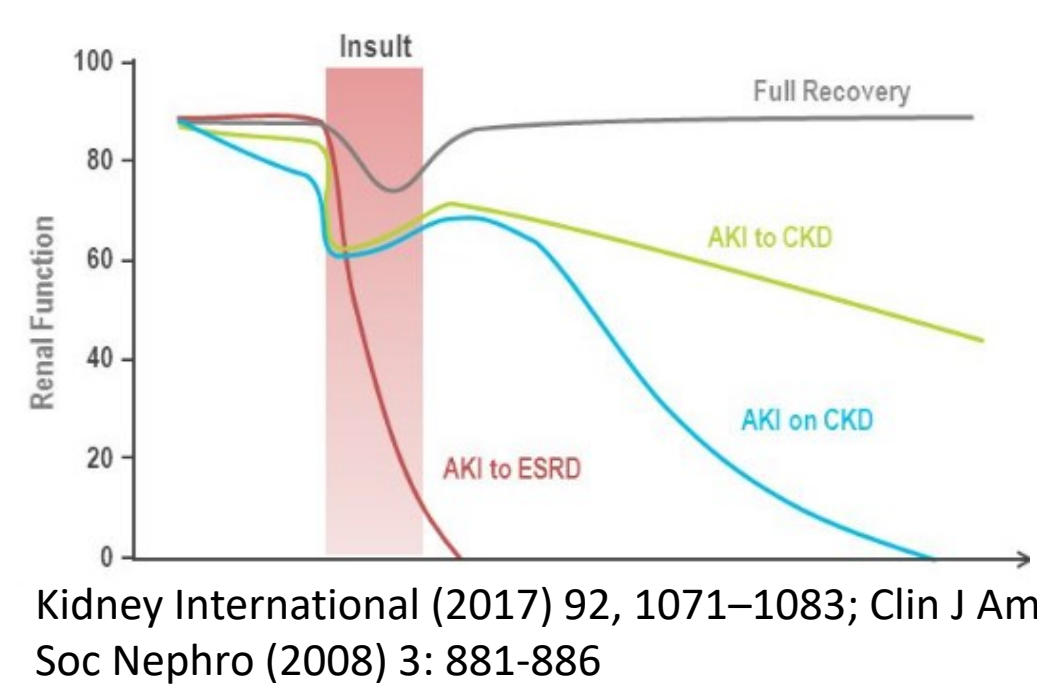
Methods and Materials

- 10 patients from SNUCH AKI cohort (n=807)
- Inclusion
  - Cause of AKI: Ischemic damage (cardiac surgery or hypoxia)
    - 6 progressed to CKD (CKD group)
    - 4 maintained normal kidney function (no CKD group)
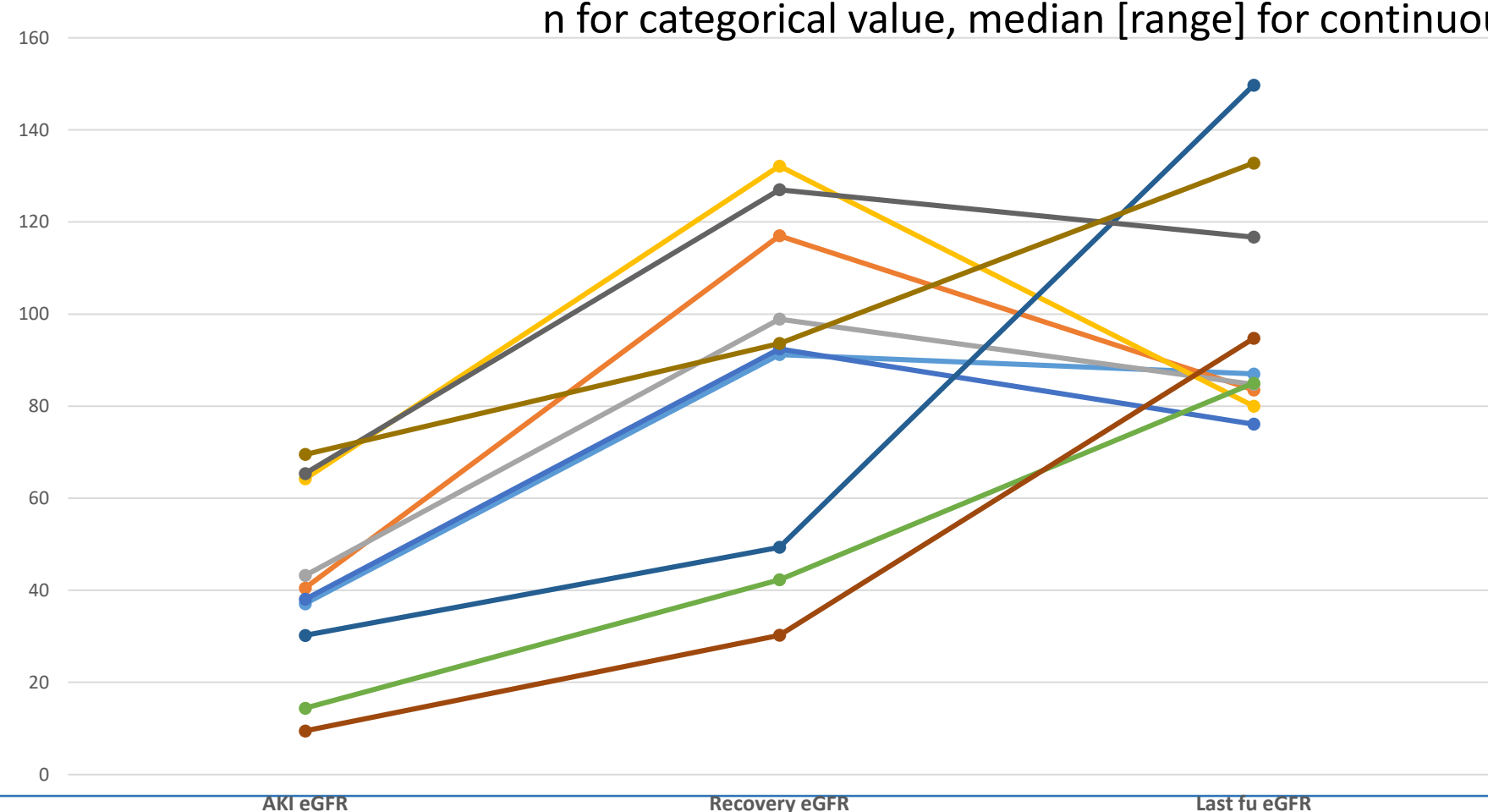 - Follow up period >2 years after AKI
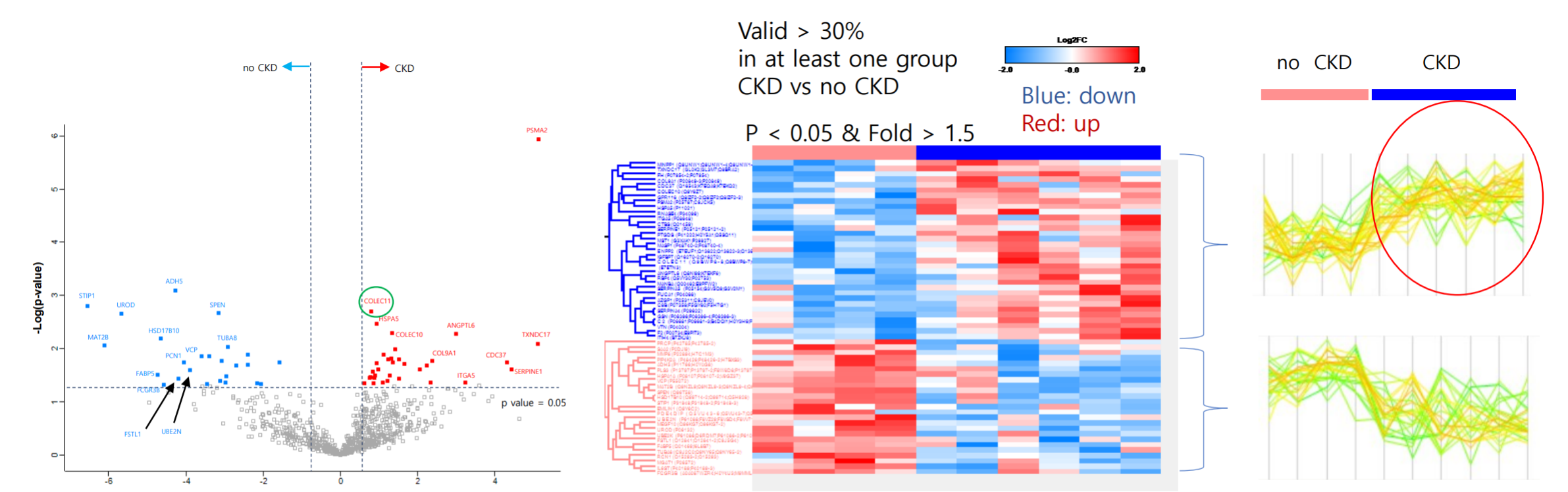
Workflow to discover biomarkers

AKI serum & urine — N= 10 — Initial phase / Follow up phase — Quantitative Proteomics Analysis — Label-free quantification (LFQ) — Candidate — Validation

Comparison between two groups

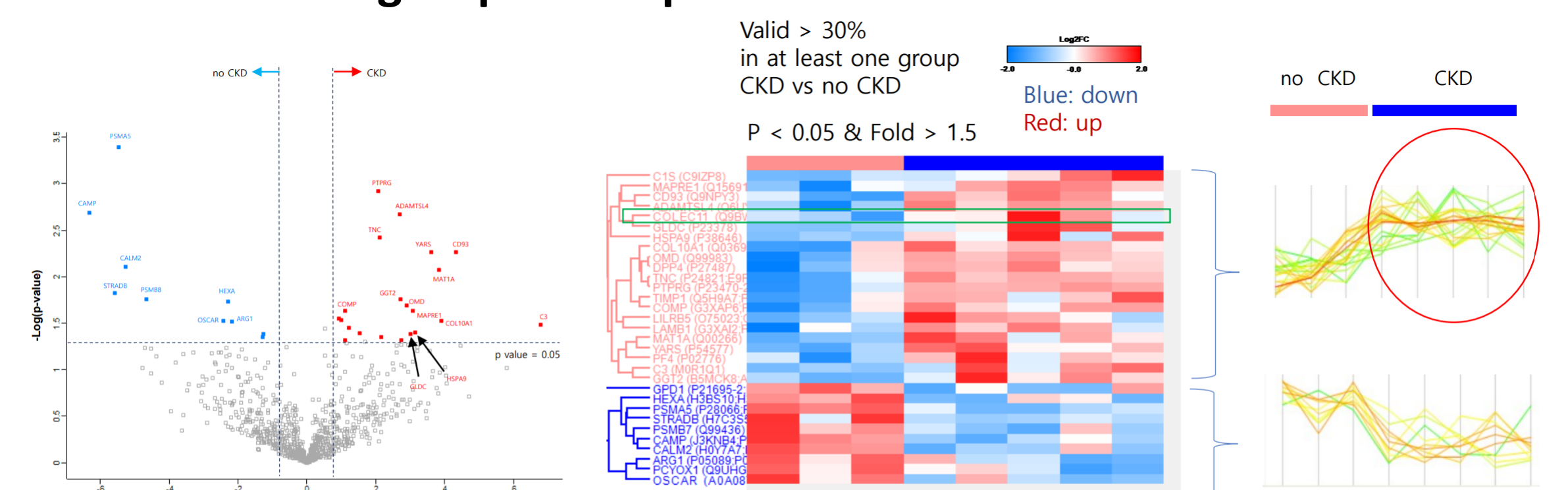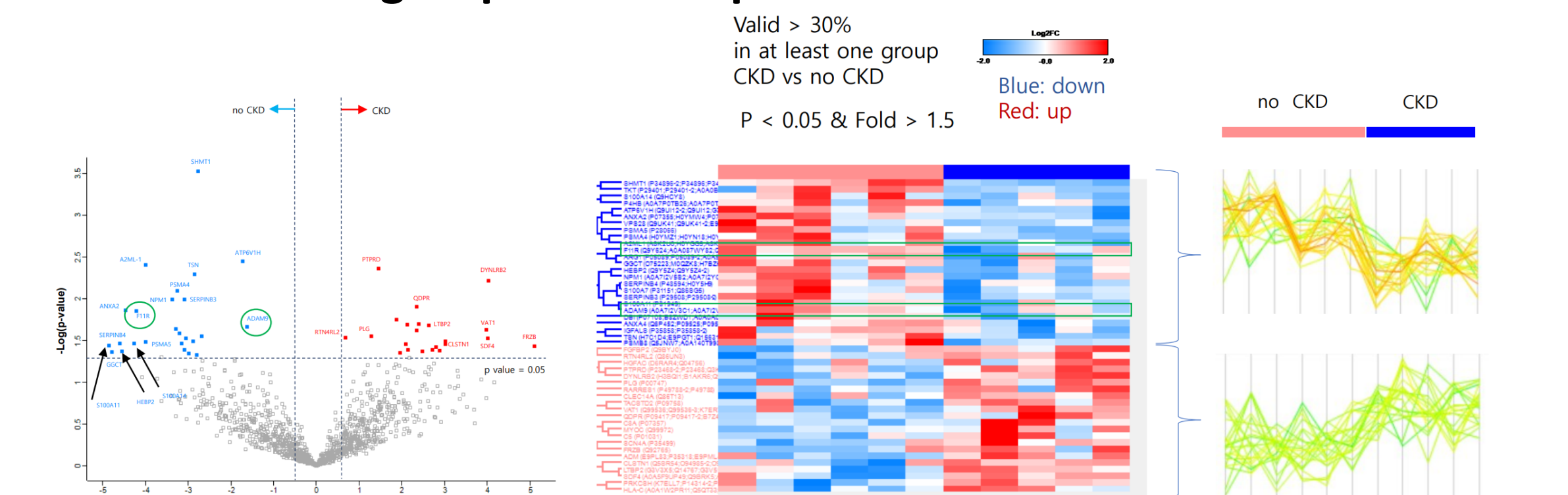|	CKD	No CKD	*P* value
M:F	4:2	1:2	0.524
Age at AKI	0.05 [0.00-9.70]	6.95 [0.00-15.90]	0.610
AKI stage			0.743
Stage 1	3	1	
Stage 2	1	2	
Stage 3	2	1	
FU period	4.56 [3.24-5.40]	4.50 [2.17-5.47]	1.000
eGFR at AKI	39.29 [14.41-64.22]	47.79 [9.46-69.51]	0.914
eGFR at recovery	95.67 [42.29-132.16]	71.49 [30.25-127.00]	0.610
eGFR at FU	84.13 [76.09-87.00]	124.75 [94.74-149.71]	0.010

n for categorical value, median [range] for continuous value

AKI eGFR — Recovery eGFR — Last fu eGFR

Results

CKD and no CKD groups in initial phase serum

Valid > 30% in at least one group CKD vs no CKD
P < 0.05 & Fold > 1.5
Blue: down / Red: up
no CKD / CKD

	Gene name	fold change
Initial	COLEC11	0.798430125

CKD and no CKD groups in FU phase serum

Valid > 30% in at least one group CKD vs no CKD
P < 0.05 & Fold > 1.5
Blue: down / Red: up
no CKD / CKD

	Gene name	fold change
Follow up	COLEC11	1.103047562

CKD and no CKD groups in initial phase urine

Valid > 30% in at least one group CKD vs no CKD
P < 0.05 & Fold > 1.5
Blue: down / Red: up
no CKD / CKD

	Gene name	fold change
Initial	F11R	-4.210321963
	ADAM9	-1.622138627

CKD and no CKD groups in FU phase urine

Valid > 30% in at least one group CKD vs no CKD
P < 0.05 & Fold > 1.5
Blue: down / Red: up
no CKD / CKD

	Gene name	fold change
Follow up	F11R	4.809455509
	ADAM9	-3.088713358

Conclusions

- We identified *3 candidate proteins* from serum and urine samples
  - COLEC11: **elevated** at **initial & fu** serum sample in **CKD group**
  - F11R: **decreased** at **initial** urine sample, **elevated** at **fu** urine sample in **CKD group**
  - ADAM9: **decreased** at **initial & fu** urine sample in **CKD group**
- Potential biomarkers identified in this study could provide a valuable opportunity *to predict AKI to CKD progression* in pediatric patients.
- Validation is needed to confirm this result