DEVELOPMENT OF NEW BIOCHIP ARRAYS FOR THE DETERMINATION OF BIOMARKERS RELATED TO ACUTE KIDNEY INJURY APPLIED TO THE EVIDENCE INVESTIGATOR ANALYSER

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INTRODUCTION

Acute Kidney Injury (AKI) is a syndrome characterized by the loss of the excretory function within a few hours of renal insult. AKI occurs in nearly 20% of all hospitalized patients and is most common in critically-ill patients with a subsequent increased risk of Chronic Kidney Disease. Increased serum creatinine and decreased urine output are used to diagnose AKI utilizing Kidney Disease: Improving Global Outcomes guidelines. However, serum creatinine is a non-specific and trailing index of AKI, therefore there is a need for more sensitive and timely biomarkers of AKI. Biochip Array Technology, by employing discrete miniaturized assays on the biochip surface, allows the determination of multiple analytes from a single sample and therefore increases the test result output and the information output per sample.

The objective of this study was to develop new biochip arrays for the simultaneous determination of AKI biomarkers – clusterin, cystatin C, Kidney Injury Molecule 1 (KIM-1) and Neutrophil Gelatinase-Associated Lipocalin (NGAL) for application in clinical test settings. The application to the dedicated benchtop semi-automated biochip analyser Evidence Investigator allows the analysis of up to 54 biochips at a time.

METHODOLOGY

Chemiluminescent sandwich immunoassays were employed and applied to the Evidence Investigator analyser. Sensitivity, recovery, intra-assay and inter-assay precision, specificity, and interference were evaluated in accordance with Clinical and Laboratory Standards Institute (CLSI) guidelines. A test method comparison, between the developed biochip immunoassays and commercially available individual enzyme-linked immunosorbent assays (ELISA), was completed using a cohort of 39 urine samples from normal subjects.

RESULTS

Cross-reactivity analysis determined that each individual assay was specific for its target, no cross-reactivity was observed with non-panel homologous proteins (cross-reactivity <1%). No significant interference was found with common interferents tested.

SENSITIVITY

Biomarker	Functional Sensitivity	Upper Limit of Quantification
Clusterin	10.82 ng/mL	1000 ng/mL
Cystatin C	0.87 ng/mL	180 ng/mL
KIM-1	54.60 pg/mL	4000 pg/mL
NGAL	0.40 ng/mL	100 ng/mL

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RECOVERY

Biomarker	Level 1 Recovery (%)	Level 2 Recovery (%)	Level 3 Recovery (%)
Clusterin	110.92	98.38	98.59
Cystatin C	100.77	98.79	97.42
KIM-1	104.57	94.65	97.89
NGAL	106.52	103.18	100.92

18726.104RDRT

PRECISION

Intra-assay Precision		
Biomarker		% Mean Coefficient of Variation (%CV)
Clusterin (ng/mL)	Level 1	8.09
	Level 2	
	Level 3	
Cystatin C (ng/mL)	Level 1	8.92
	Level 2	
	Level 3	
KIM-1 (pg/mL)	Level 1	7.94
	Level 2	
	Level 3	
NGAL (ng/mL)	Level 1	5.15
	Level 2	
	Level 3	

19.832.104RDRT

PRECISION

Inter-assay Precision		
Biomarker		% Mean Coefficient of Variation (%CV)
Clusterin (ng/mL)	Level 1	8.30
	Level 2	
Cystatin C (ng/mL)	Level 1	7.44
	Level 2	
KIM-1 (pg/mL)	Level 1	10.00
	Level 2	
NGAL (ng/mL)	Level 1	7.61
	Level 2	

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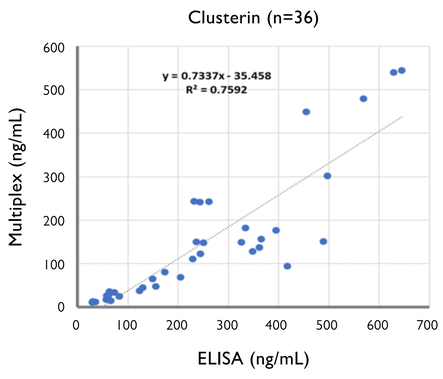
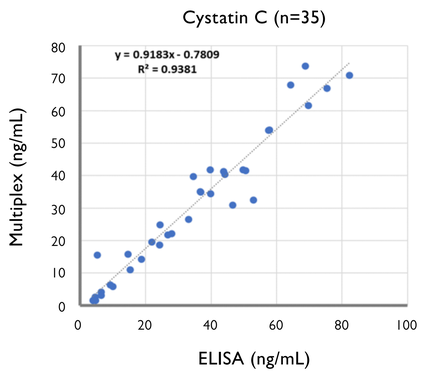
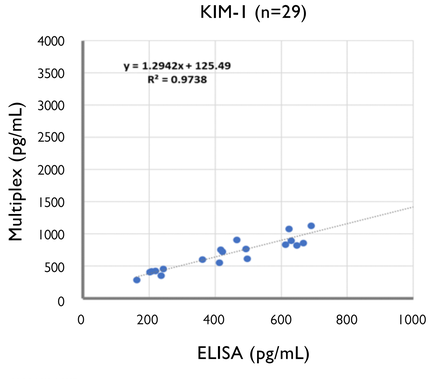
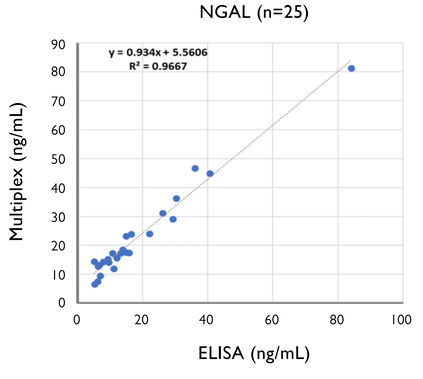
METHOD COMPARISON









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CONCLUSION

This study indicates optimal analytical performance of AKI related immunoassays on the biochip platform. This provides a valuable and reliable multi-analytical tool, indicating clinical utility with potential for the early and rapid detection of AKI on the Evidence Investigator platform.