Novel biomarkers for septic shock–associated

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Cincinnati Children’s Hospital Medical Center
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Cincinnati, OH, USA

Canada Critical Care Forum
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Monty Python's

And Now For Something Completely Different

The Best of Monty Python's Flying Circus
No NGAL, IL-18, L-FABP, KIM-1, etc.
Rationale
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• Current biomarkers for AKI are primarily derived from ischemia models.
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• The pathophysiology of sepsis–related AKI is mechanistically more complex than just ischemia.
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• The pathophysiology of sepsis–related AKI is mechanistically more complex that just ischemia.
• The performance of current biomarkers in predicting sepsis–related AKI is not
Using whole genome expression data (microarray) for the discovery of novel candidate biomarkers for septic shock–associated renal failure (SSARF)
Approach
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• Microarray-based gene expression data from 179 children with septic shock.
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• Microarray–based gene expression data from 179 children with septic shock.
• Data represent the first 24 hours of presenting to the ICU with septic shock.
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• Whole blood–derived RNA.
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• Data represent the first 24 hours of presenting to the ICU with septic shock.
• Whole blood–derived RNA.
• 31 patients with septic shock–
Definition of SSARF
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• >200% increase of serum creatinine, relative to the median normal value for age.
Definition of SSARF

- >200% increase of serum creatinine, relative to the median normal value for age.
- Persistent up to 7 days of ICU admission.
## Clinical Characteristics

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• ANOVA with corrections for multiple comparisons.
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• SSAKI vs. no SSARF.
• 100 gene probes differentially regulated between SSARF and no SSARF.
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61 unique and well-annotated genes
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21 up-regulated in SSARF, relative to no SSARF

Candidate SSARF Predictor Genes
### 21 genes up-regulated in SSARF vs. no SSARF

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Class Prediction Modeling
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- Can the expression patterns of the 21 gene probes predict SSARF?
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• Can the expression patterns of the 21 gene probes predict SSARF?
• Leave-one-out cross validation to predict SSARF and no SSARF “classes”.
Performance characteristics of class prediction modeling

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**Sensitivity**
- 98%
- CI 81 - 100%

**Specificity**
- 80%
- CI 72 - 86%
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- **Sensitivity**: 98% (CI 81 – 100%)
- **Specificity**: 80% (CI 72 – 86%)
- **PPV**: 50% (CI 37 – 63%)
- **+LR**: 4.8 (1.6 – 6.6)
- **NPV**: 99% (CI 95 – 100%)
- **-LR**: 0.04 (0.001 – 0.28)
Current technology may allow for the generation of mRNA expression data to conduct class prediction in a clinically relevant time frame.
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However, current biomarker development efforts are largely focused on serum/plasma protein measurements.
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## 21 genes up-regulated in SSARF vs. no SSARF

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Basu et al. Crit Care. 2011 (in
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Funding Acknowledgement

- NIH R01GM064619
- NIH RC1HL100474
- NIH R01GM096994
Thank You