Inability to adequately buffer trans IL-6 signaling may play a role in development of renal scarring after urinary tract infection

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Background

• Inflammation is an important defense against infection
  – Also responsible for local tissue damage

• IL-6 is induced in UTI
  – Signals through two pathways (Cis and Trans)
    • Cis/Classic: anti-inflammatory
    • Trans: pro-inflammatory

Hypothesis: activation of the trans IL-6 signaling pathway would be associated with the development of renal scarring in patients with a history of UTI
Methods

• We evaluated markers of *trans* IL-6 signaling in urine of pediatric patients

Patient Groups

- History of UTI
  (Culture positive: >50K of uropathogen)
- Healthy Controls (HC)
  (No history of UTI)

- No renal scarring (NS)*
- Renal scarring (S)*

*As documented on renal ultrasound and/or DMSA

• ELISAs: IL-6, soluble IL-6 receptor (R), sgp130
  – Sgp130 is a buffer of *trans* signaling

Lee et al, J Immunol 2011
Results

- Significantly more IL-6 in the urine of those with a history of UTI vs. Controls

![Graph showing IL-6 levels with statistical significance](image)
Results

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- No difference in IL-6R amongst groups

Lee et al. J Immunol 2011
Results

• Significantly more IL-6 in the urine of those with a history of UTI vs. Controls

• No difference in IL-6R amongst groups

• Significantly less sgp130 in those scarred compared to Controls
  – Less sgp130 in scarred vs not scarred (p=0.1446)
Conclusions

- Urine sgp130 is lower in those with renal scarring vs. controls
  - Basis to think *trans* IL-6 signaling plays a role in development of renal scarring

- Manipulation of *trans* IL-6 signaling may reduce the sequela of UTI
Conclusions

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• Manipulation of *trans* IL-6 signaling may reduce the sequela of UTI