CD4⁺ T cell-derived NGAL mediates ischemia reperfusion-induced AKI

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Disclosures

• Nothing to disclose
Background

SA Lee et al., Nephron 2017;137(4):282-286. doi: 10.1159/000477181
Q1. How do CD4 T lymphocytes mediate the course of ischemic AKI
RNA-seq

qRT-PCR

Lcn2/NGAL markedly increases in kidney CD4⁺ T cells following IR-induced AKI

Submitted for review in *The Journal of Immunology* on Jun 17th, 2019.
Q1. How do CD4 T lymphocytes mediate the course of ischemic AKI

Q2. Does CD4 T cell NGAL serve any role in the course of ischemic AKI
Comparison of kidney & spleen CD4\(^+\) T cells from WT and NGAL KO mice

Submitted for review in *The Journal of Immunology* on Jun 17th, 2019.
**Lcn2/NGAL deficiency augments susceptibility to ischemic AKI in mice**

![Graph showing Serum Cr (mg/dL) vs Time after surgery (hr)](image)

**Graph a:**
- **WT** (blue line) shows a steady increase in Serum Cr over time.
- **NGAL KO** (red line) shows a higher and steeper increase compared to WT.

**Graph b:**
- Comparison of 24 hr serum creatinine (mg/dL) between WT and NGAL KO.
- NGAL KO group has significantly higher serum creatinine levels (*p* < 0.05).

**Images c and d:**
- **WT** and **NGAL KO** renal tissue sections.
- Arrows indicate necrotic tubules.
- **c:** Magnification of 50 μm.
- **d:** Comparison of % Necrotic tubule count between WT and NGAL KO.
- NS indicates no significant difference.

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Donor

WT

NGAL KO

Recipient

WT CD4+ T cells

KO CD4+ T cells

PBS

24hr

CD4 KO

24hr

WT
Adoptive transfer of Lcn2-deficient CD4$^+$ T cells aggravates ischemic AKI

Recipient: CD4 KO

**Figure a:**
- Serum Cr (mg/dL) over time after surgery (hr)
- PBS, WT, NGAL KO groups

**Figure b:**
- 24 hr serum creatinine (mg/dL)
- Groups: PBS, WT, NGAL KO

**Figure c:**
- Histological sections
- PBS, WT, NGAL KO

**Figure d:**
- % Necrotic tubule
- Groups: PBS, WT, NGAL KO

Submitted for review in *The Journal of Immunology on Jun 17th, 2019.*
Adoptive transfer of *Lcn2*-deficient CD4$^+$ T cells aggravates ischemic AKI

Recipient: WT

**a**

Serum Cr (mg/dL)

Time after surgery (hr)

**b**

24 hr serum creatinine (mg/dL)

PBS  WT  NGAL KO

**c**

PBS  WT  NGAL KO

% Necrotic tubule

PBS  WT  NGAL KO

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Q1. How do CD4 T lymphocytes mediate the course of ischemic AKI

Q2. Does CD4 T cell NGAL serve any role in the course of ischemic AKI

Q3. How does CD4 T cell NGAL protects mice from ischemic AKI
In vitro ischemia reperfusion induces higher IFN-γ in Lcn2-deficient CD4⁺ T cells

**Kidney**

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**Spleen**

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In vitro CD4\(^+\) T cell differentiation shows increased Lcn2 expression in Th1, Th2, and Th17 cells.
Q1. How do CD4 T lymphocytes mediate the course of ischemic AKI

Q2. Does CD4 T cell NGAL serve any role in the course of ischemic AKI

Q3. How does CD4 T cell NGAL protect mice from ischemic AKI

Q4. Is this finding reproducible in HUMAN kidney as well
Human kidney CD4⁺ T cells increase expression of NGAL after ischemic injury
**Summary**

**In vivo**
- **NGAL KO mice**
  - Reduced Treg numbers
  - Increased injury
- **NGAL KO CD4 T cell transfer**
  - Increased injury

**In vitro**
- **Lcn2/NGAL**
  - Hypoxia/reoxygenation
  - ↑ IFN-γ in NGAL KO CD4 vs. WT
- **Naive CD4 T cell**
- **Differentiated Th1, Th2, Th17 cells**
- **↑ Lcn2/NGAL**

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Conclusions

• CD4\(^+\) T cell-derived NGAL is an important underlying mechanism by which immune cells mediate AKI.

• Our study extends the importance of NGAL in AKI beyond diagnostics.

• Further exploration needs to be followed to find out the biological role of CD4\(^+\) T cell-derived NGAL in renal injury.