Role of innate immune responses in early hepatic ischemia-reperfusion injury
Neutrophils have a pivotal role in the pathogenesis of hepatic ischemia-reperfusion injury (IRI).

- Activate by chemokines, migrate across the endothelium to the hepatocytes.
- Tissue injury: release ROS, proteinases, and cationic peptides.
- Inhibition of neutrophil infiltration can protect against hepatocellular injury.

Background

1. Complex interactions between Natural Killer (NK) cells and neutrophils

2. NK cells may be critical in the process of neutrophil recruitment to the site of tissue injury

Murine model of partial liver ischemia – Hanging weight model

A. Before hepatic ischemia

B. During hepatic ischemia

Murine model of partial liver ischemia – Hanging weight model
Liver IRI in the setting of altered NK cell function

![Graphs showing AST and ALT levels in WT and SCID^B mice](image)
Liver IRI in the setting of altered NK cell function
Liver IRI in the setting of altered NK cell function
Antibody-mediated neutrophil depletion in the setting of altered NK cell function
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Control – No IRI
WT – CB17- ND – 4i/24r
SCIDb – ND – 4i/24r
Cytokine profile following liver injury with combined immunodeficiency and neutrophil depletion
Summary

1. Mice with severe combined immunodeficiency and dysfunctional NK cells develop significant liver IRI

2. Neutrophil depletion aggravates hepatic IRI

3. A persistent inflammatory response is observed despite the absence of critical leukocytes
Future directions – Hypoxia and innate responses: The link to extracellular adenosine production

Role of **adenosine receptors** (Adora 2a and 2b) in liver IRI