Sepsis and the Humoral Immune Response

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Sepsis: Clinical Definition and Relevance

- Systemic inflammatory response caused by infection
- Case mortality 30-50%
- 2nd most common cause of death in noncoronary ICUs and 10th overall cause of death
- Patients showed ongoing mortality due to suppressed immune function
- Survivors consistently demonstrate impaired quality of life
Previous Findings

➢ Global transient lymphopenia
➢ Asymmetric recovery of naïve Ag specific CD4 & CD8 T cell precursors
➢ Long lasting impairment in primary CD4 T cell dependent B cell responses
➢ Immunization induces auto-reactive antibodies
Cecal Ligation and Puncture (CLP) Model

➢ Infectious focus mimics perforated appendix/diverticulitis
➢ Similar cytokine response to septic patients

CLP Validation (Survival)
CLP Validation (Weight)

C57BL/6

Swiss Webster

Weight (% of Original)

Days Since Surgery

CLP
Sham

CLP
Sham
CLP Validation (Cell Numbers)
Influenza A PR8/35 Infection Study

CLP or Sham Surgery

Influenza Infection
10,000 PFU IP

Animals Euthanized Tissue Harvested

Day 0

Day 2

Day 30
α-Influenza A PR8/35 Antibodies (ELISA)
Conclusions and Future Directions

➢ CLP mimics clinical sepsis presentation

➢ CLP limits influenza specific antibody production
  ➢ Predominantly loss of class switching and IgG expansion

➢ Protection study utilizing serum from influenza infected mice

➢ Develop optimized method of imaging germinal centers in septic animals

➢ Further characterize antibody production following vaccination
Acknowledgements

➤ Griffith Lab
➤ Thomas Griffith, PhD
➤ Frances Sjaastad
➤ Tamara Kucaba
➤ Katherine Murphy, PhD

➤ Mescher Scholar Staff
➤ Daniel Mueller, MD
➤ Andrea Stewart