



THE UNIVERSITY OF ARIZONA
MEDICAL CENTER

The Protective Effects of Remote Ischemic Conditioning in a Septic Mouse Model

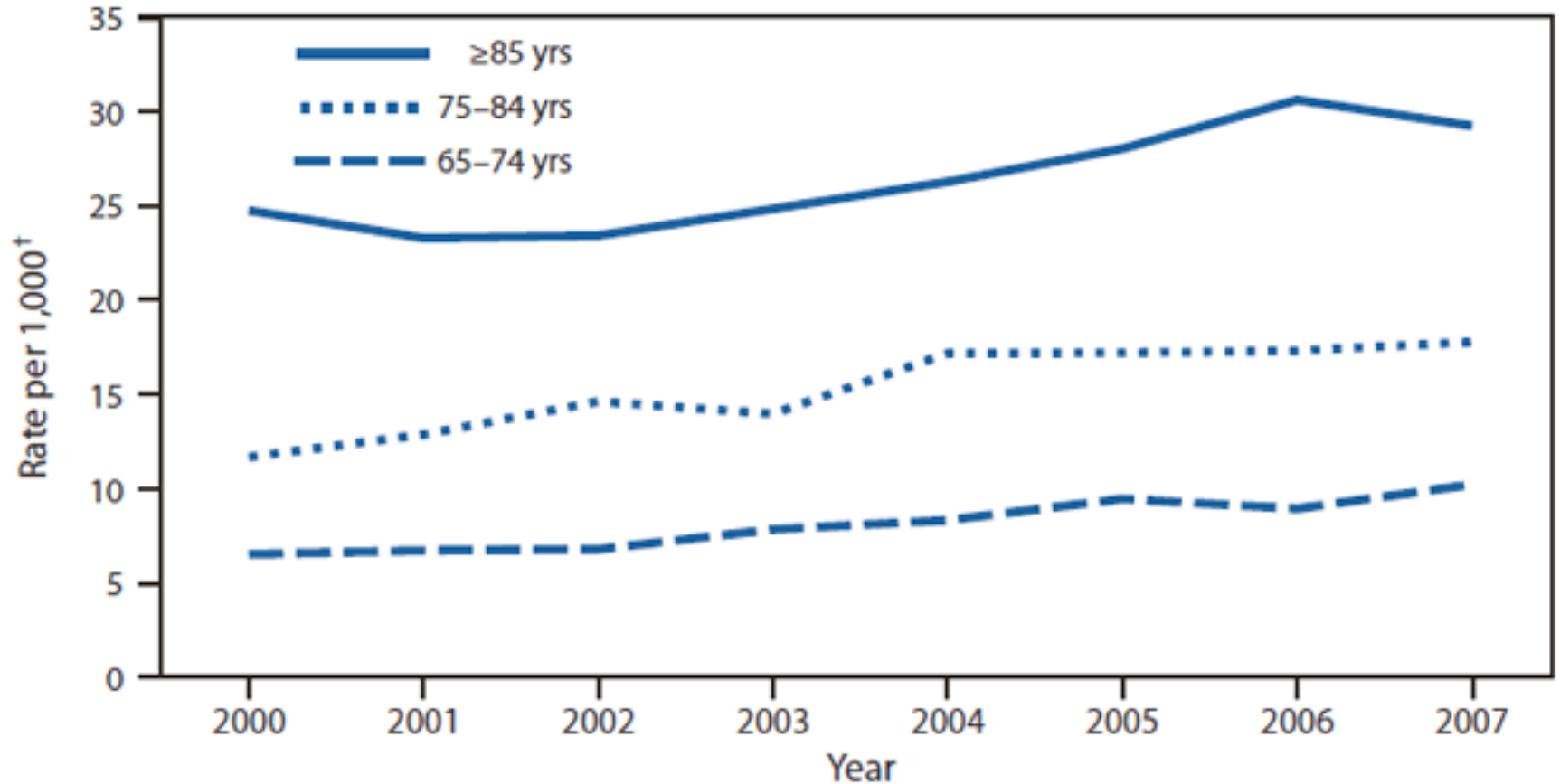
Joseph B, Khalil M, Kulvatunyou N, O’Keeffe T, Tang
A, Gries L, Latifi R, Rhee P

The University of Arizona



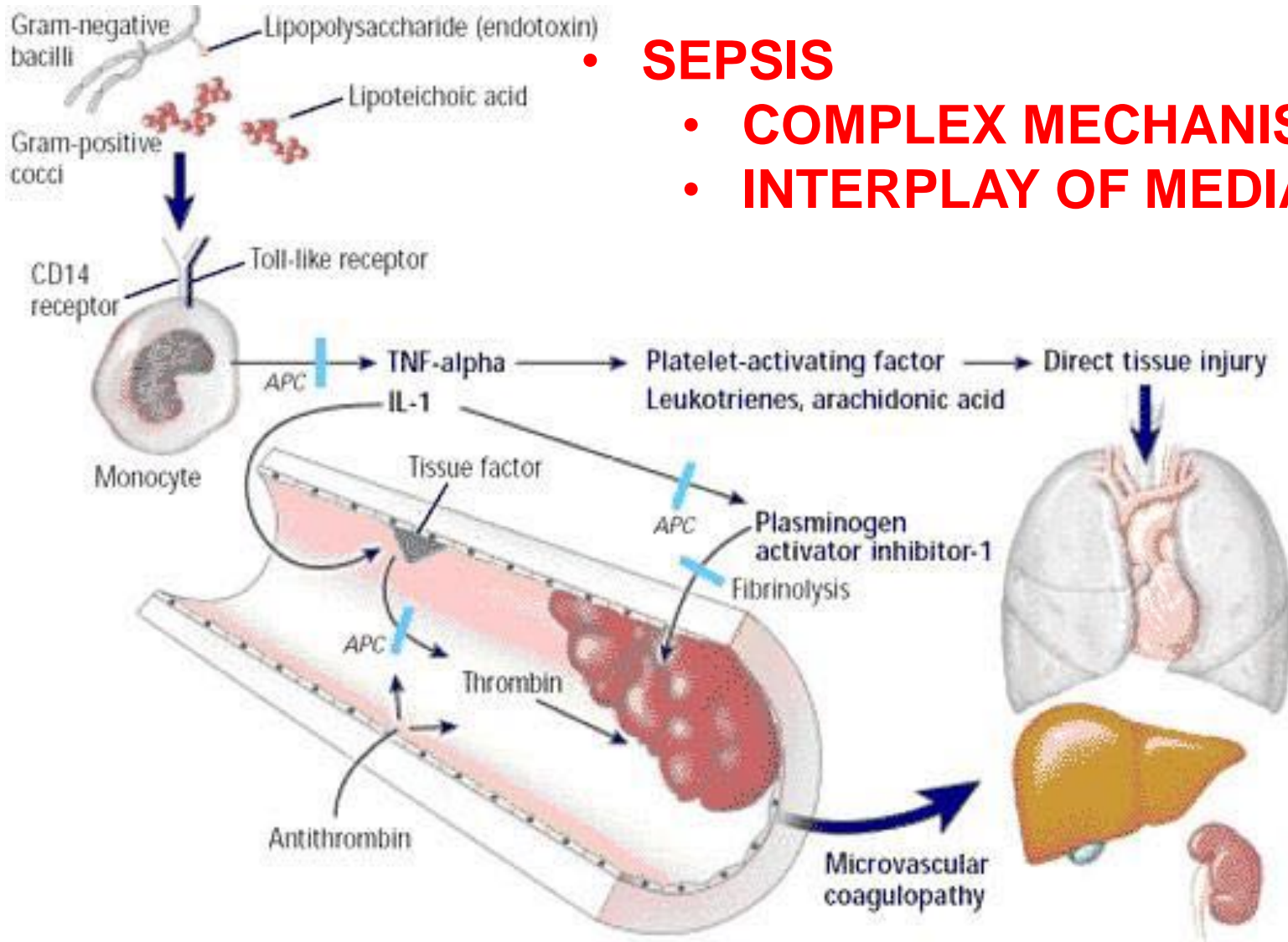
BACKGROUND

Hospital Admission with Sepsis

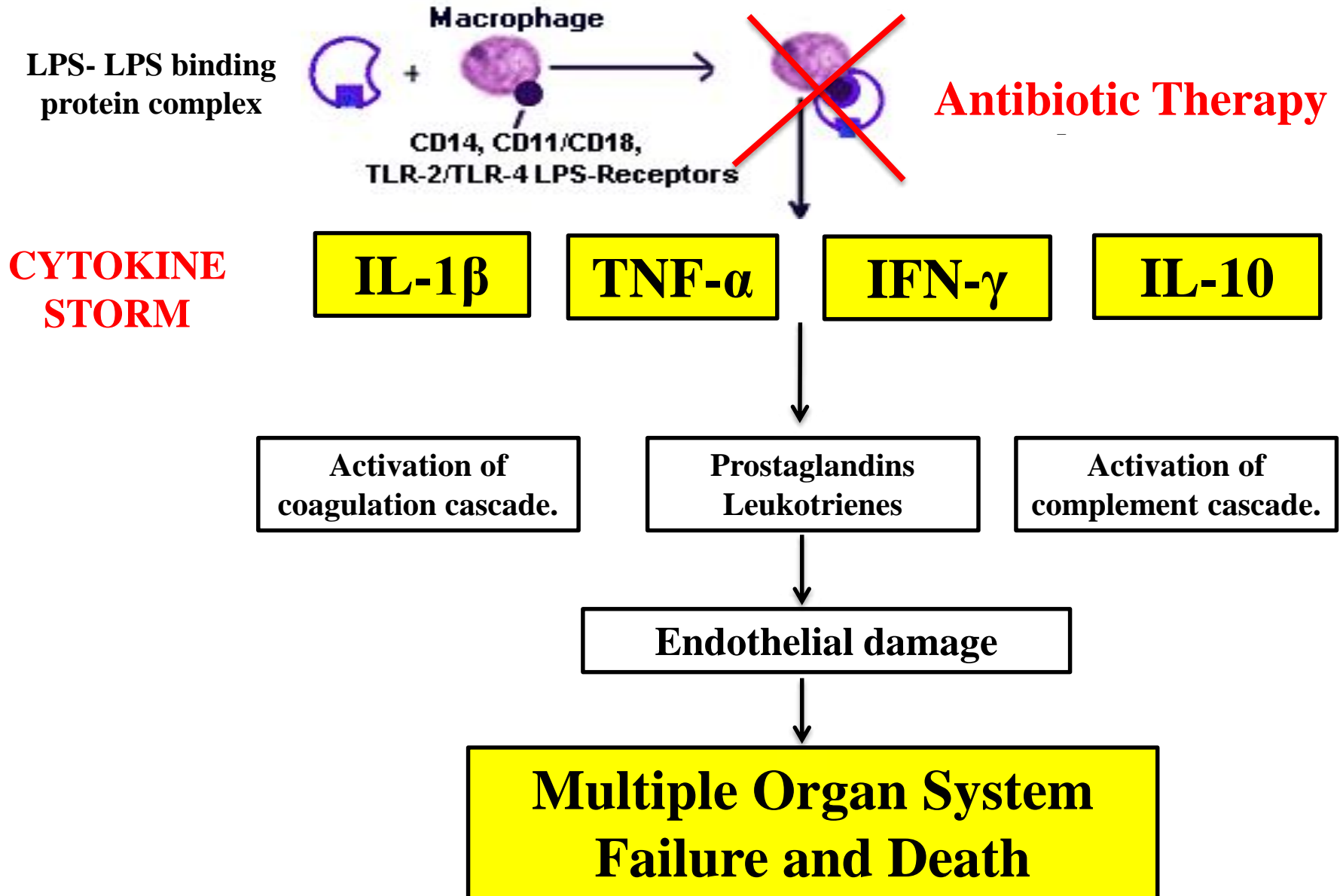


BACKGROUND

- **SEPSIS**
 - **COMPLEX MECHANISM**
 - **INTERPLAY OF MEDIATORS**



BACKGROUND





BACKGROUND

Monocyte deactivation in septic patients:
Restoration by IFN- γ treatment



- **Steroids**
- **Anti-oxidants**
- **Prostaglandins**
- **Mono-clonal Antibodies**
- **IL-1 receptor Antibodies**
- **Leukotriene Inhibitors**



Corticosteroids
and Septic Shock

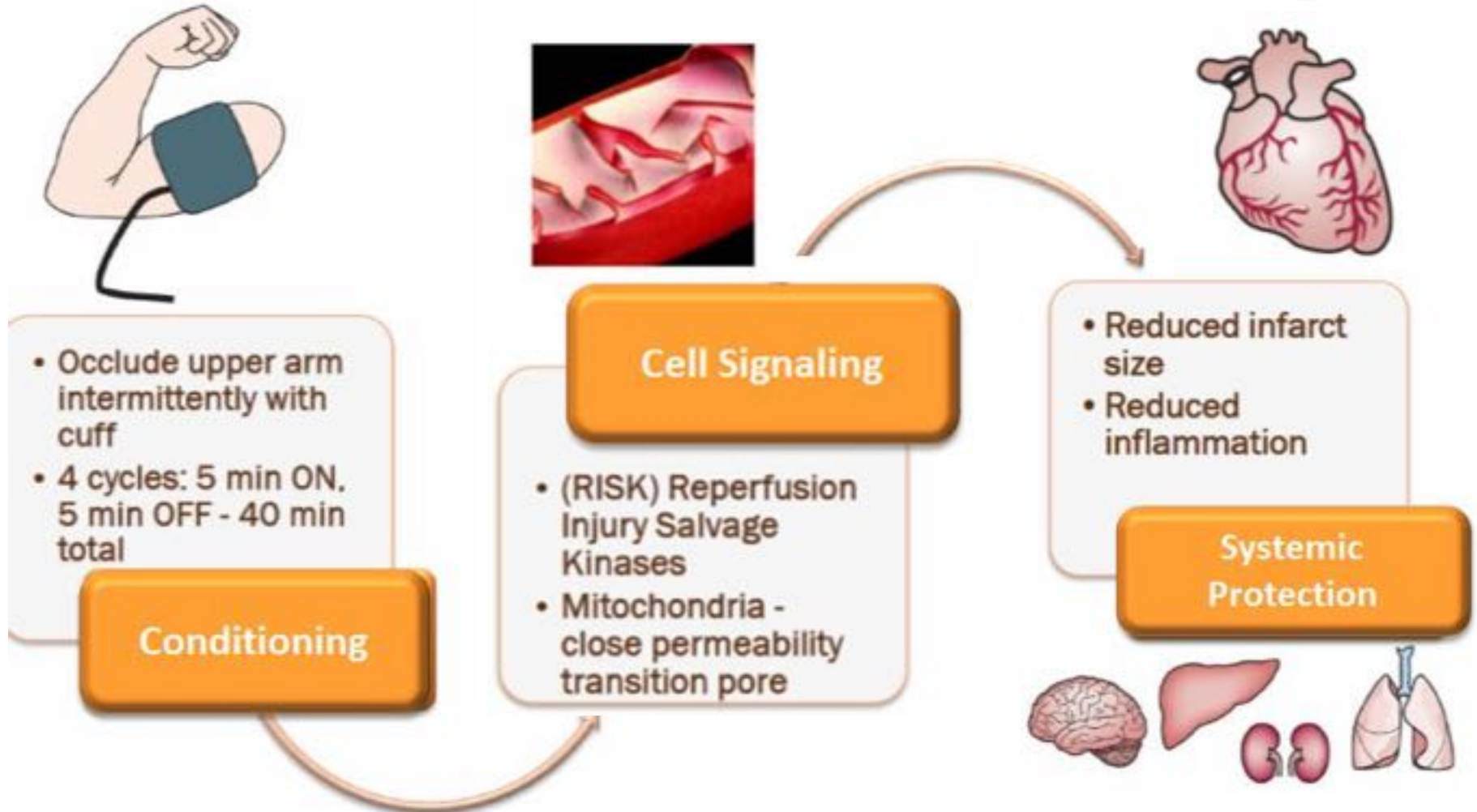
A Systematic Review

Ph.D.

MA



Remote Ischemic Conditioning





BACKGROUND

Postconditioning the human heart

Staat P, Rioufol G, Piot C, Cottin Y, Cung TT, L'Huillier I, Aupetit JF, Bonnefoy E, Finet G, André-Fouët X, Ovize M.

Circulation. 2005 Oct 4;112(14):2143-8.

Cardiac stress protein elevation 24 hours after brief ischemia or heat stress is associated with resistance to myocardial infarction

Marber MS, Latchman DS, Walker JM, Yellon DM.

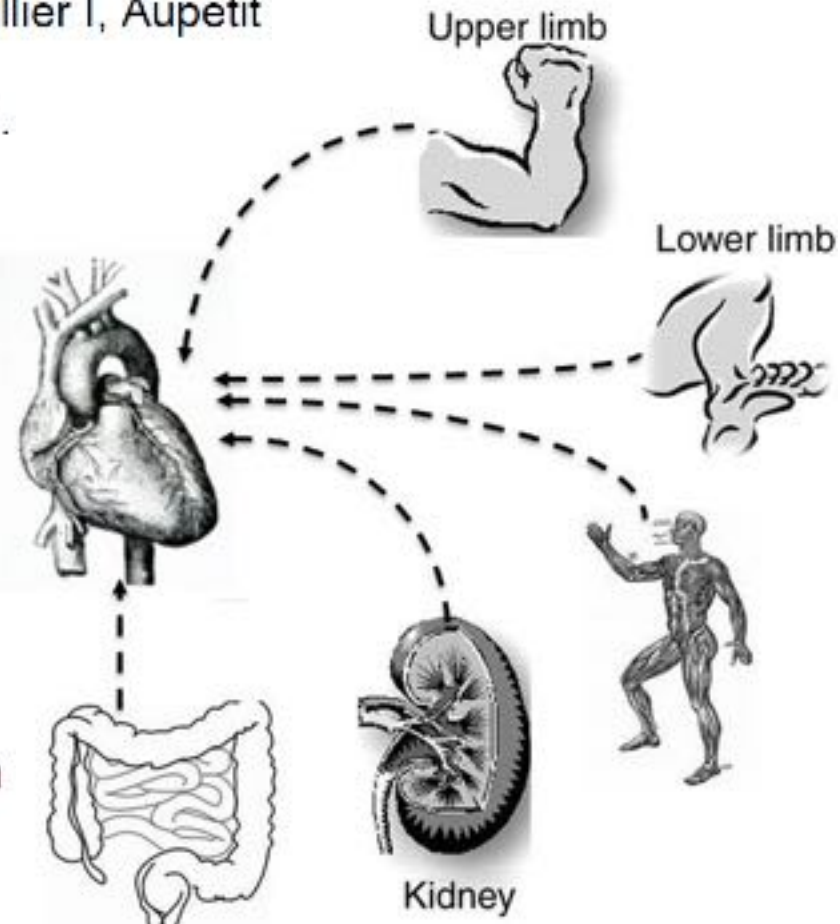
Circulation. 1993 Sep;88(3):1264-72.

Preconditioning with ischemia:

A delay of lethal cell injury in ischemic myocardium

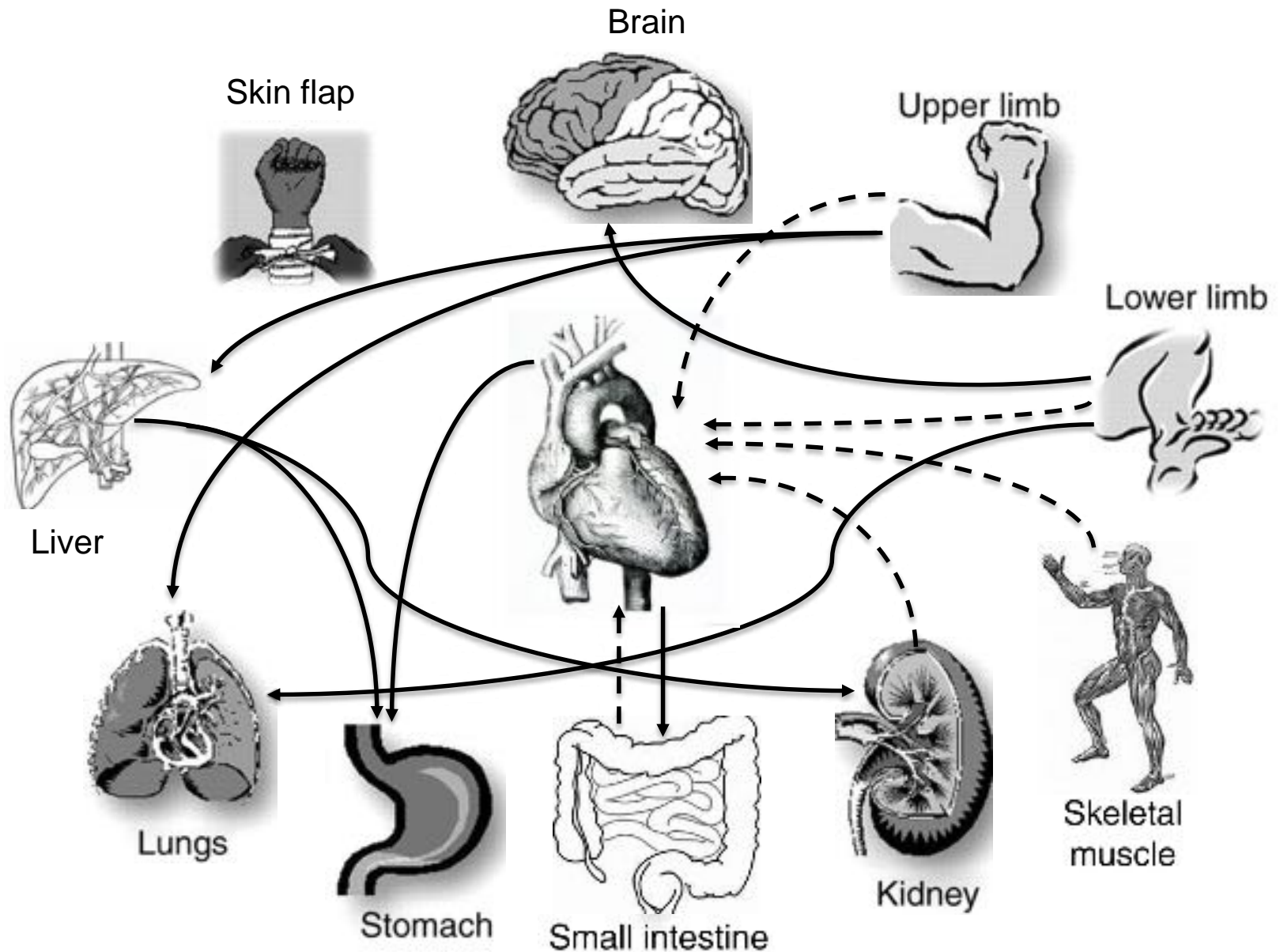
C E Murray, R B Jennings and K A Reimer

Circulation. 1986 Nov;74(5):1124-36.





BACKGROUND





BACKGROUND



Promising effects of ischemic preconditioning in renal transplantation

JOAN TORRAS, IMMACULADA HERRERO-FRESNEDA, NURIA LLOBERAS, MARTA RIERA,
JOSEP M^a CRUZADO, and JOSEP M^a GRINYÓ

Limb Remote Ischemic Preconditioning for Intestinal and Pulmonary Protection during Elective Open Infrarenal Abdominal Aortic Aneurysm Repair

A Randomized Controlled Trial

Cai Li, M.D.,* Yun-Sheng Li, M.D.,† Miao Xu, M.D.,* Shi-Hong Wen, M.D.,† Xi Yao, M.D.,† Yan Wu, M.D.,†
Chan-Yan Huang, M.D.,† Wen-Qi Huang, M.D.,‡ Ke-Xuan Liu, M.D., Ph.D.‡



Remote Ischemic Preconditioning: Making the Brain More Tolerant, Safely and Inexpensively

Michael A. Moskowitz and Christian Waeber

Remote Preconditioning Reduces Microcirculatory Disorders in Pancreatic Ischemia/Reperfusion Injury

Christina Oehmann, MD, Stefan Benz, MD, Oliver Drognitz, MD, Przemyslaw Pisarski, MD,
Ulrich T. Hopt, MD, and Robert Obermaier, MD



BACKGROUND

Remote Ischemic Conditioning

Neural

- Nitric oxide
- CGRP

Systemic

- Anti-apoptotic
- Anti-inflammatory

Humoral

- Opioids
- Angiotensin



HYPOTHESIS

Remote Ischemic Conditioning (RIC)
improves survival in septic mouse model

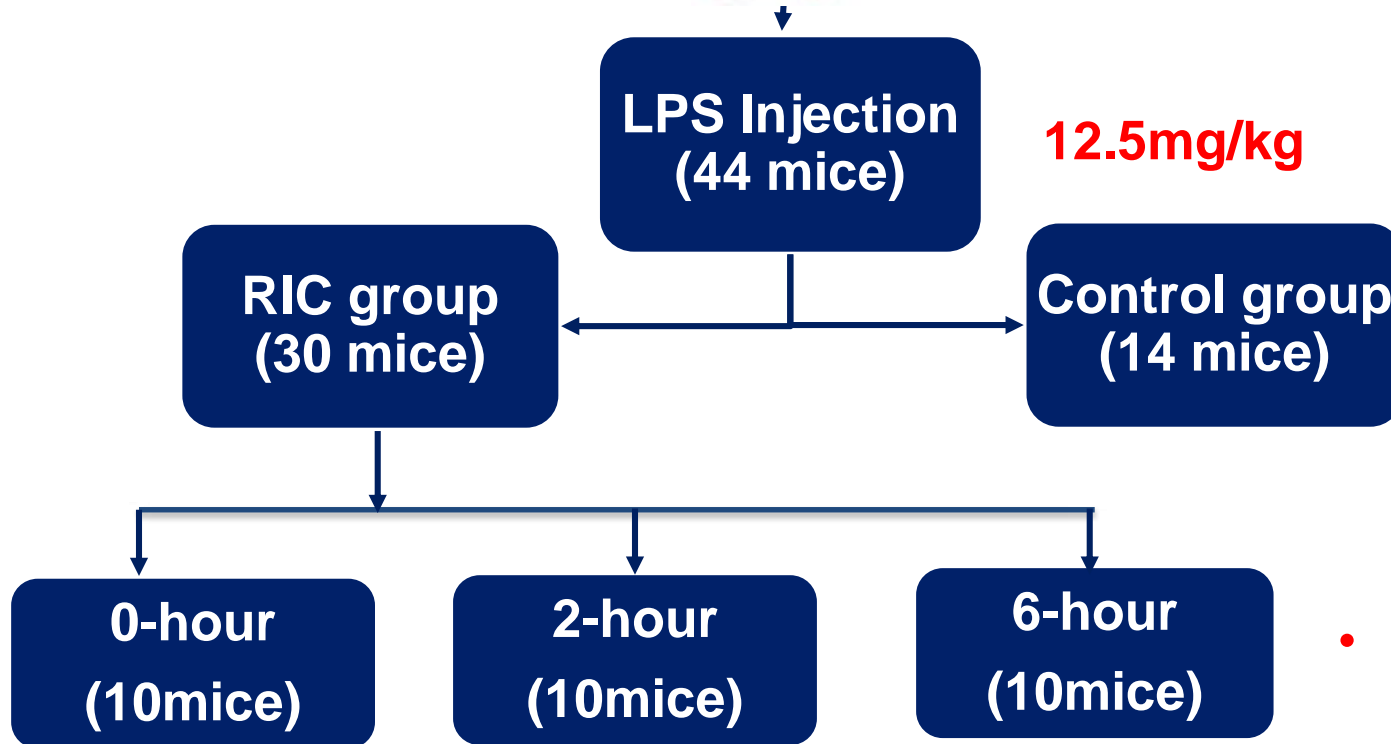
- **PRIMARY AIM:**
 - Survival advantage to RIC
 - Optimal timing for survival

- **SECONDARY AIM:**
 - Inflammatory profile



METHODS – PRIMARY AIM

8-12 week C57BL/6 mice



- Euthanized on 5th day

Kaplan Meier
Analysis

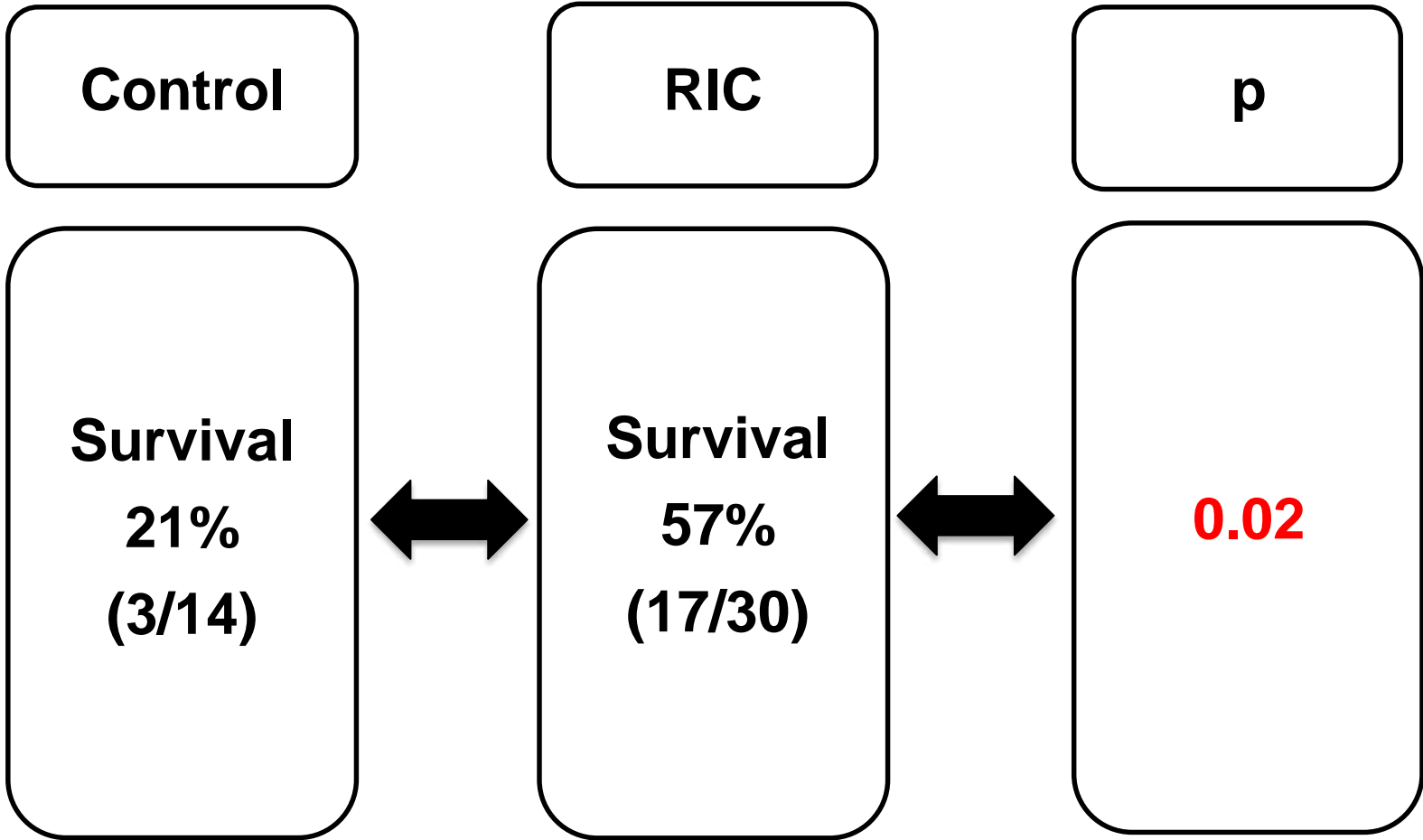
Outcome = Survival



- **RIC Group**
 - Femoral artery clamp
 - 6 cycles x 4 min cycles ischemia and reperfusion.

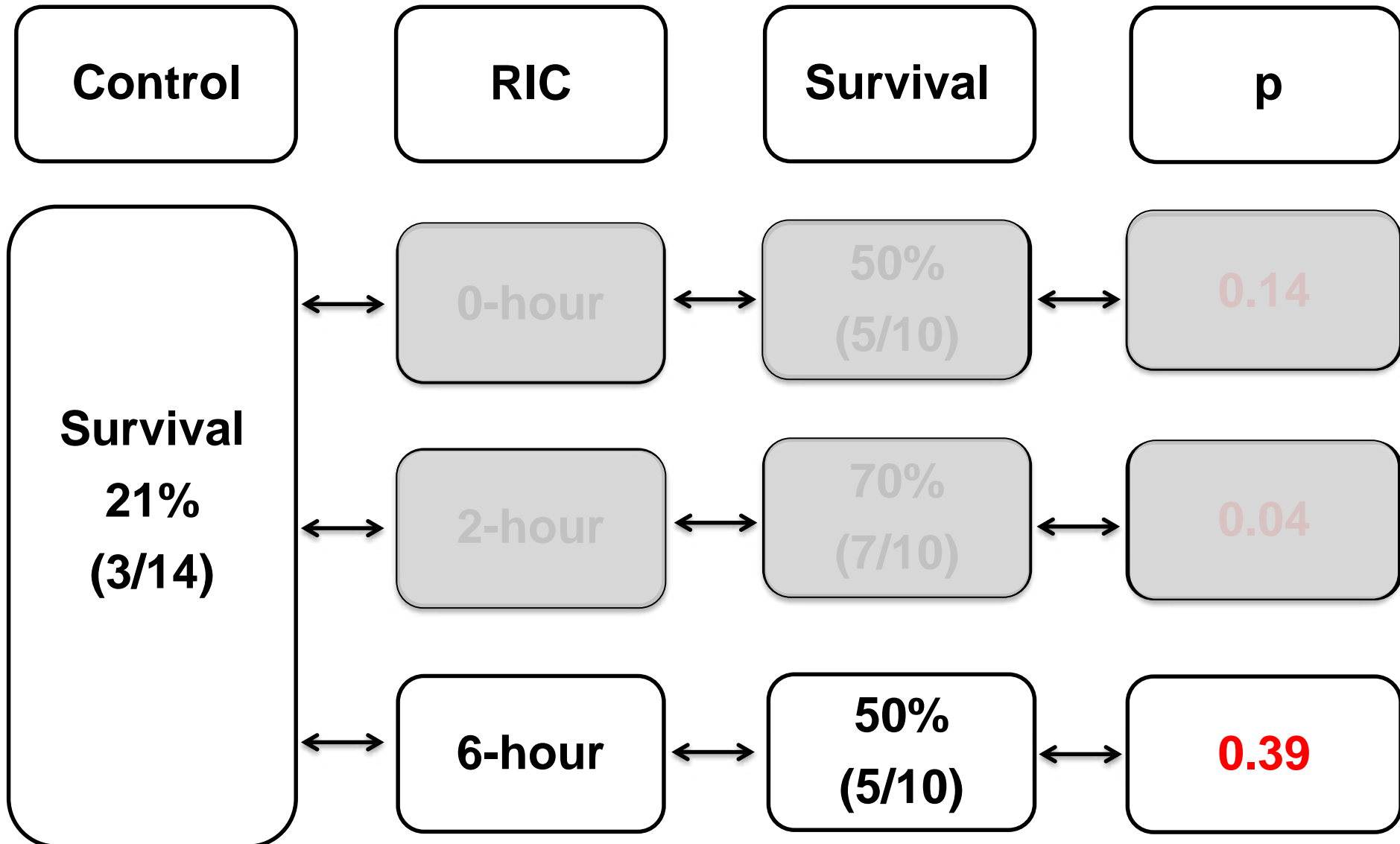


RESULTS- PRIMARY AIM





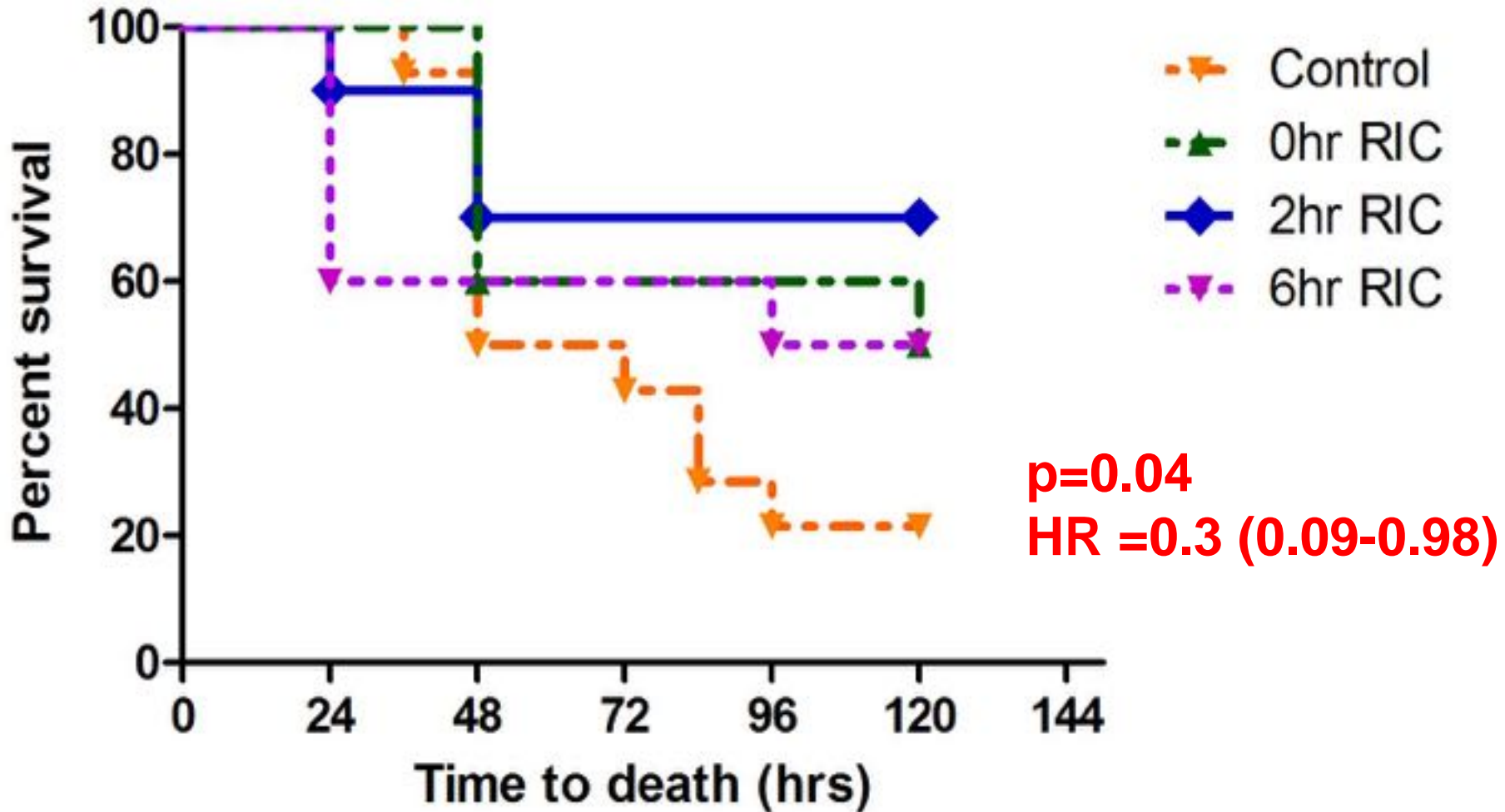
RESULTS- PRIMARY AIM





RESULTS- PRIMARY AIM

SURVIVAL





THE UNIVERSITY OF ARIZONA

College of Medicine

Tucson

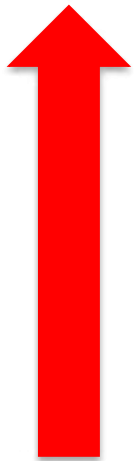
SECONDARY AIM

Inflammatory profile

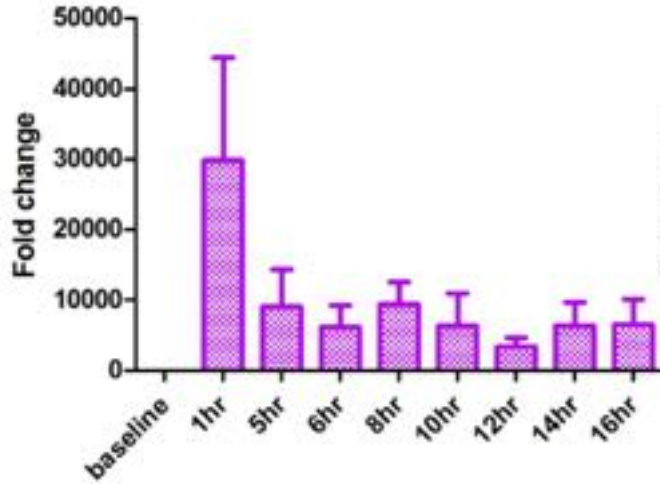




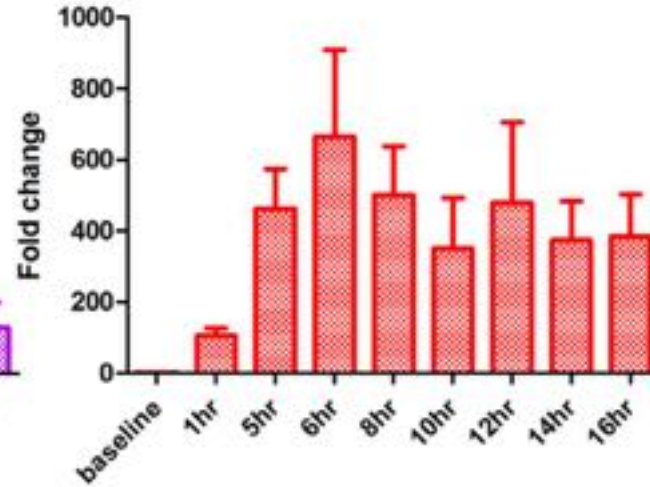
BACKGROUND – SECONDARY AIM



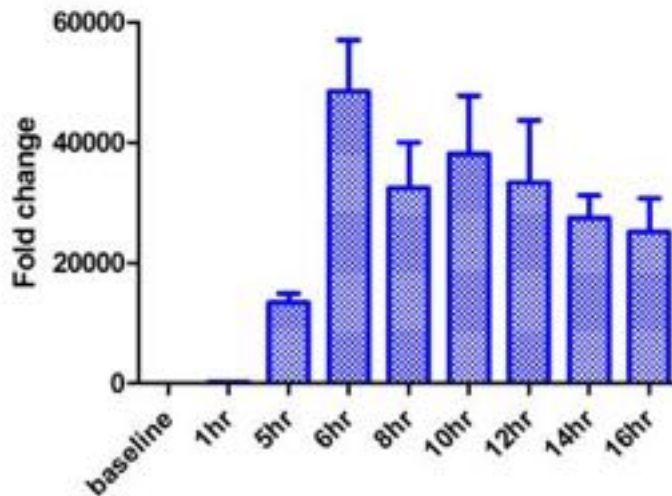
TNF - α



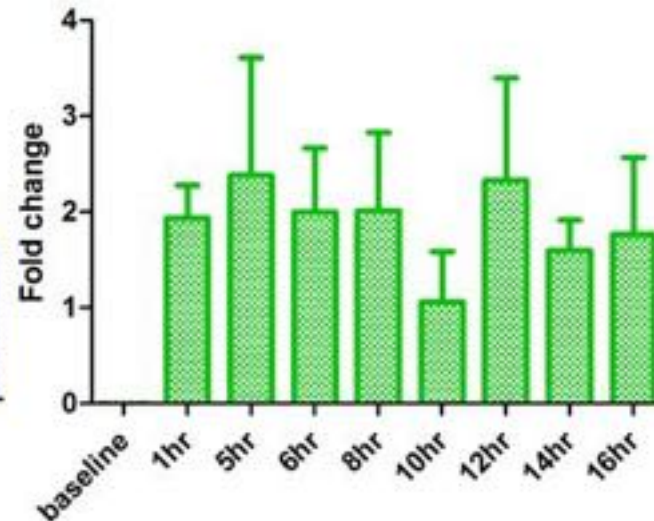
IL 1- β



INF - γ



IL - 10





METHODS – SECONDARY AIM



**ELISA Assay
(15 mice)**

**Baseline
(3 mice)**

**LPS
(12 mice)**

**0 hrs
(3 mice)**

**2 hrs
(3 mice)**

**4 hrs
(3 mice)**

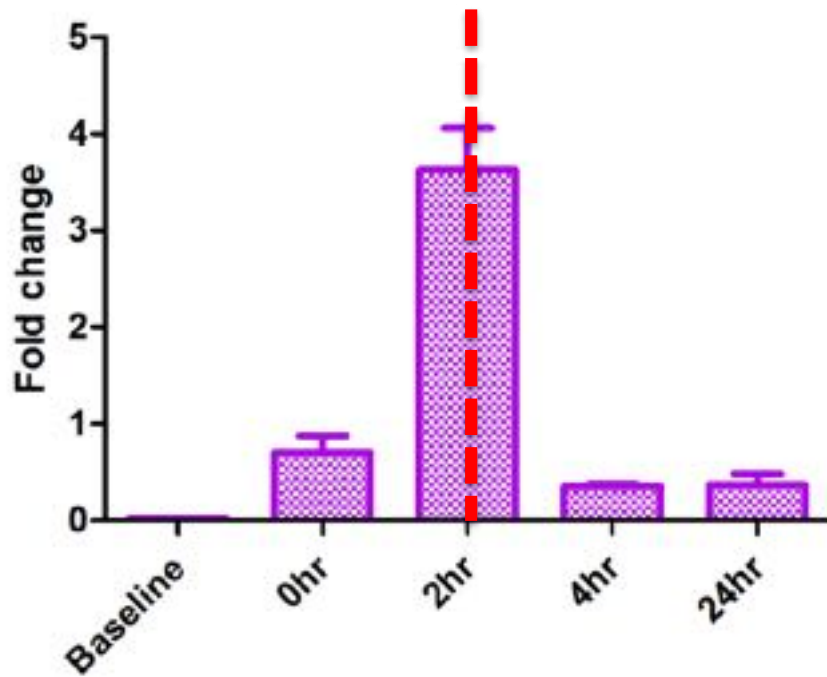
**24 hrs
(3 mice)**

RIC at 2 hours post LPS

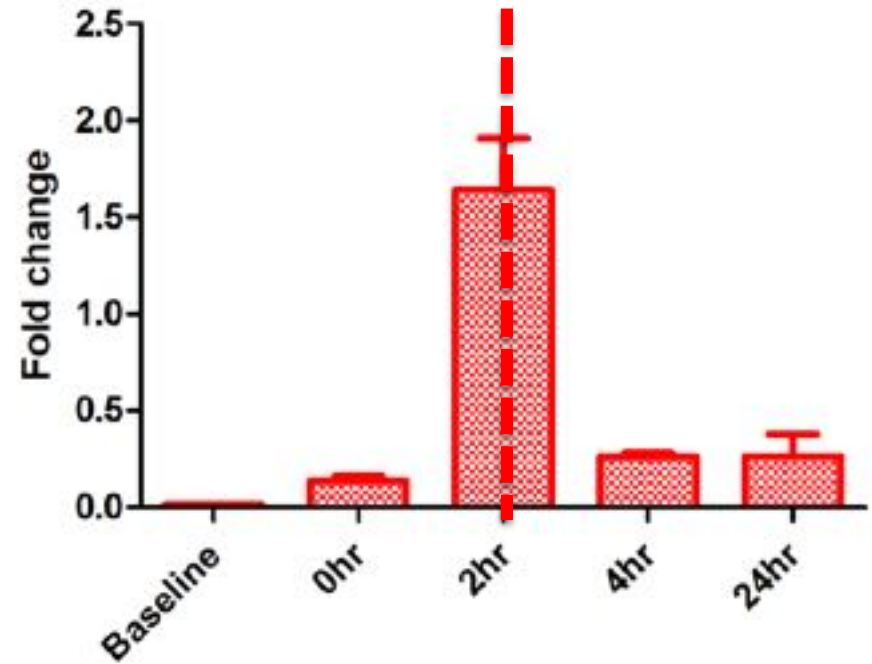


RESULTS – SECONDARY AIM

TNF - α



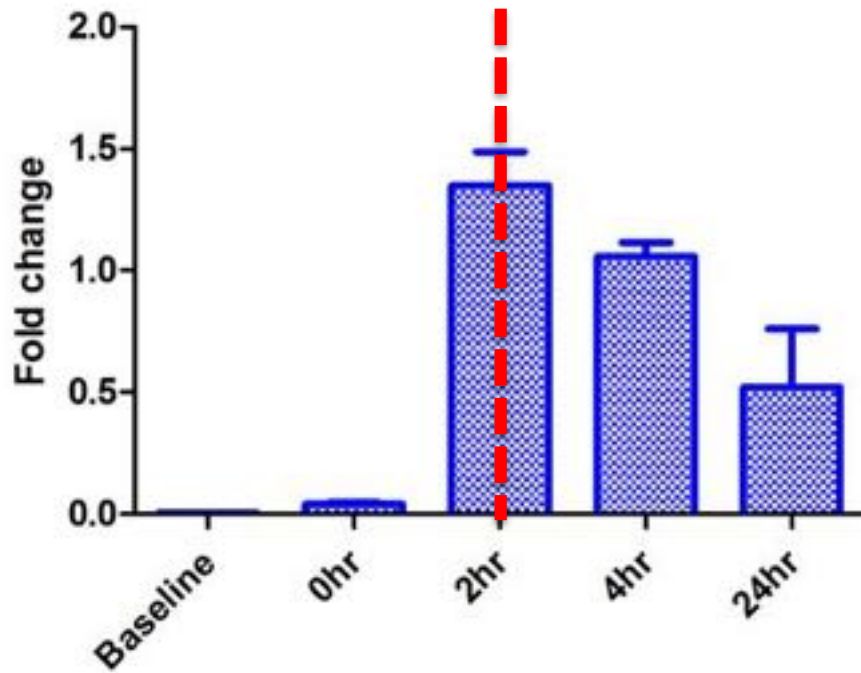
IL 1- β



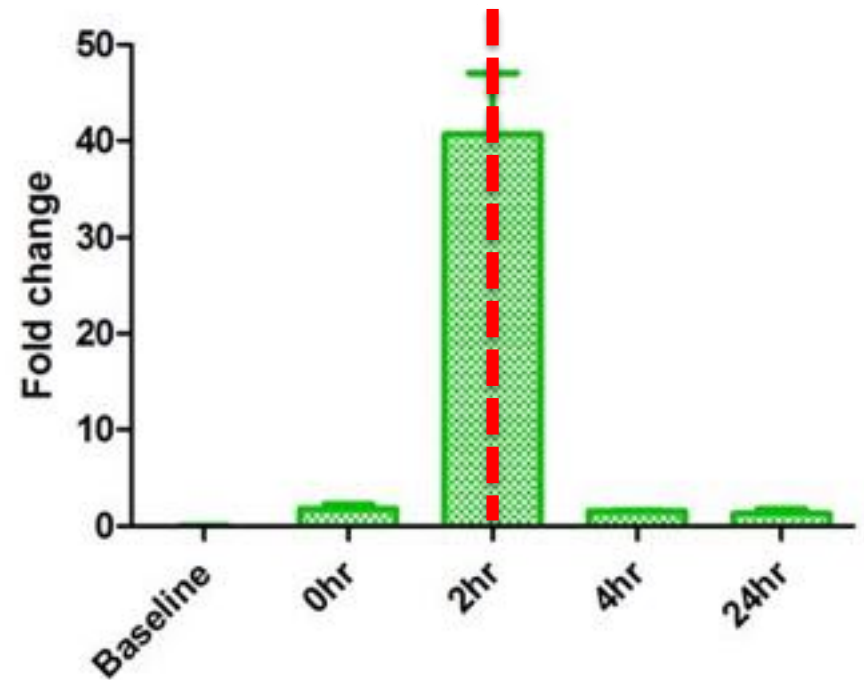


RESULTS – SECONDARY AIM

INF - γ



IL - 10



SUMMARY

- RIC provides survival benefit in septic mouse model
- 2 hours is the optimal timing for RIC
- RIC lowers inflammatory cytokines

CONCLUSIONS

- Early RIC is an effective therapy in a septic mouse model.
- RIC can have immunomodulatory role in sepsis.



THANKS

