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Hsp72 is an early and sensitive biomarker to detect acute kidney injury

*Jonatan Barrera-Chimal^{1,2}, Rosalba Pérez-Villalva^{1,2}, Cesar Cortés-González^{1,2},
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Accepted November 08, 2010

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Molecular Medicine

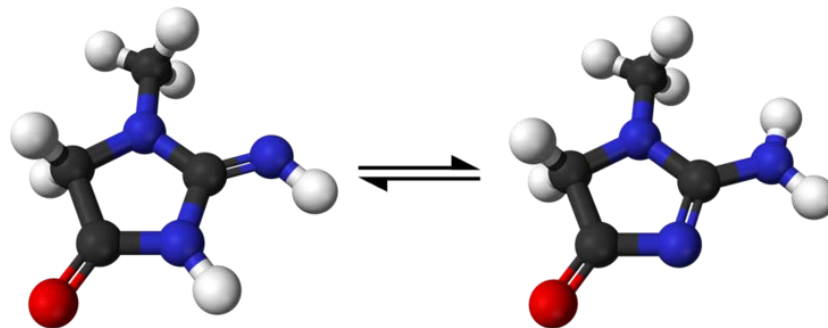
IMPACT FACTOR
2011
10.3

- 
- Background Acute Kidney Injury
 - Background Heat Shock Response
 - Manuscript

Acute Kidney Injury

Reduction of kidney function within 48 h:

- absolute increase in serum creatinine ≥ 0.3 mg/dl
- percentage increase in serum creatinine ≥ 50 % (1.5 from baseline)
- reduction in urine output (< 0.5 ml/kg per h for minimum 6 hours)



Acute Kidney Injury

RIFLE criteria

- **Risk:** GFR decrease >25%, serum creatinine increased 1.5 times or urine production of <0.5 ml/kg/hr for 6 hours
- **Injury:** GFR decrease >50%, doubling of creatinine or urine production <0.5 ml/kg/hr for 12 hours
- **Failure:** GFR decrease >75%, tripling of creatinine or creatinine >4 mg/dl or urine output below 0.3 ml/kg/hr for 24 hours
- **Loss:** persistent AKI or complete loss of kidney function for more than 4 weeks
- **End-stage:** complete loss of kidney function for more than 3 months

Acute Kidney Injury

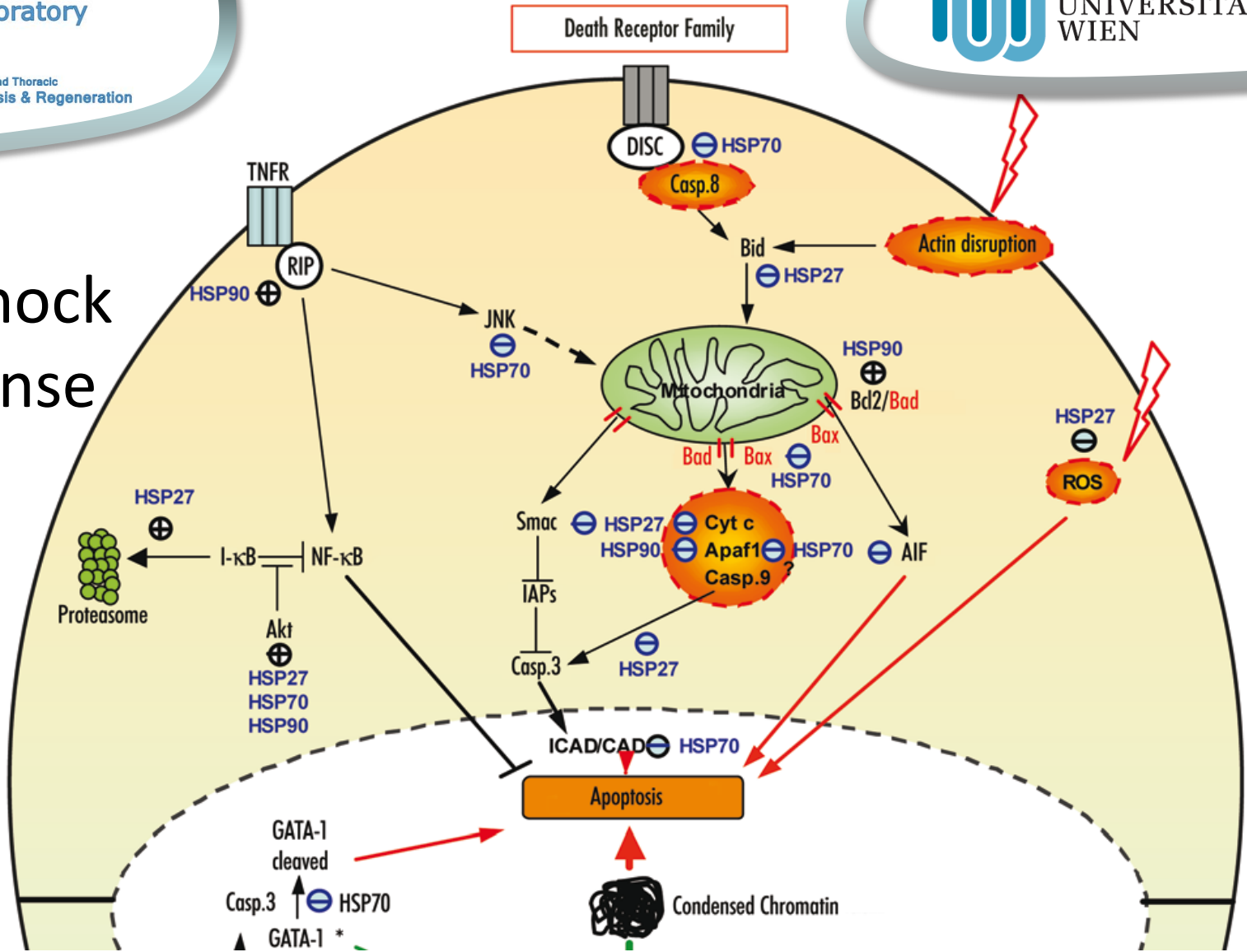


Dialysismachine 5008 produced from Fresenius Medical Care

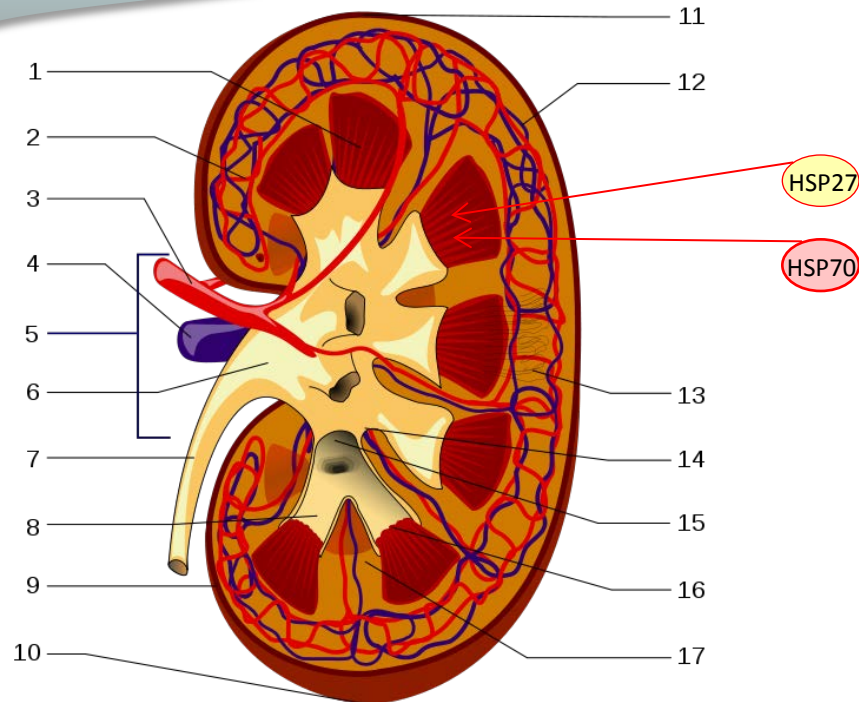
Therapie

- Intravenous fluid
- Norepinephrine/Dobutamine
- Diuretics (furosemide, fluid overload)
- Renal replacement therapy

Heat Shock Response

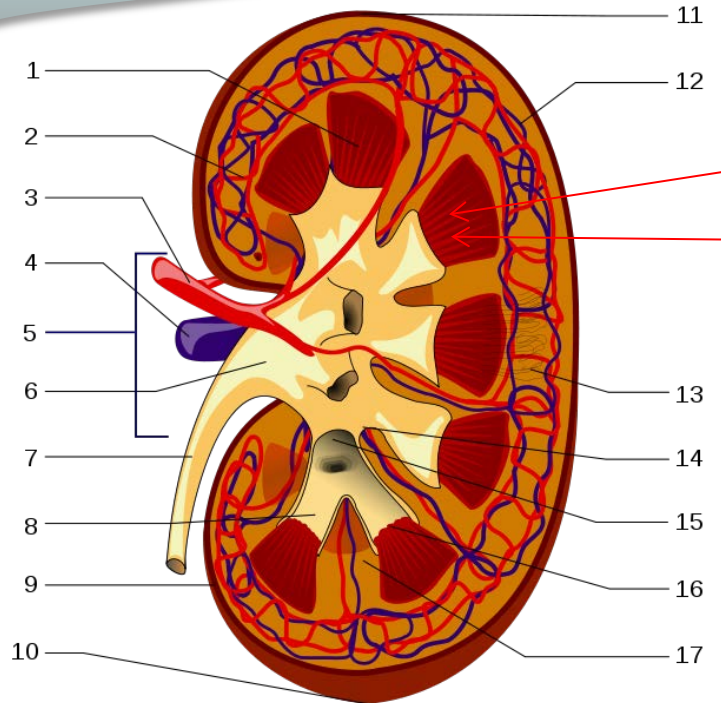


Heat Shock Response

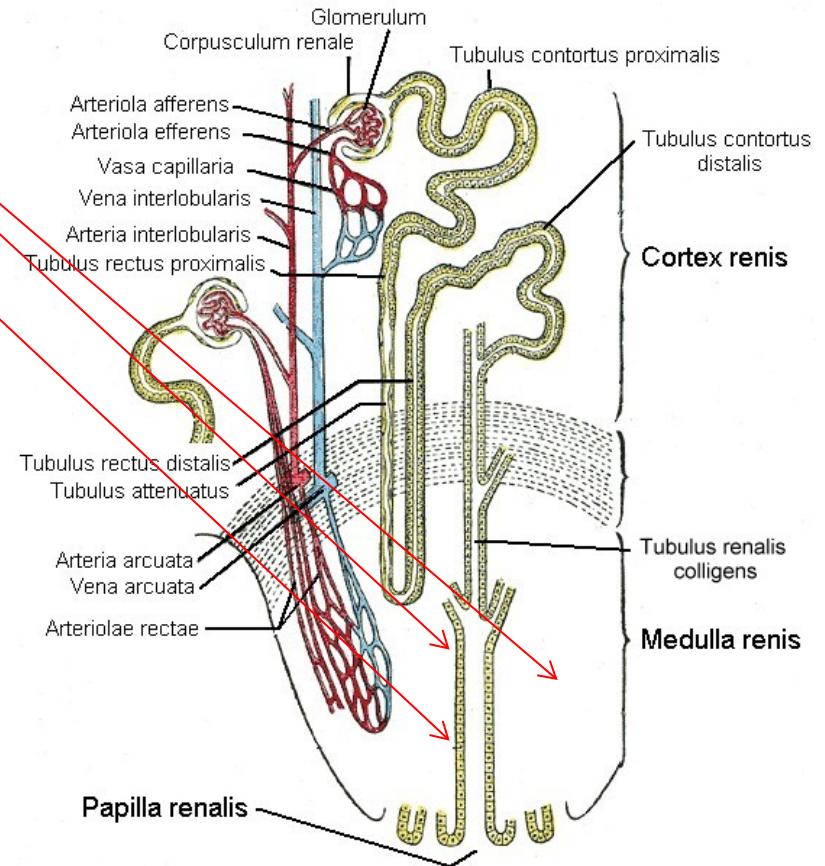


- | | |
|----------------------------|----------------------------|
| 1. Renal pyramid | 2. Interlobular artery |
| 3. Renal artery | 4. Renal vein |
| 5. Renal hilum | 6. Renal pelvis |
| 7. Ureter | 8. Minor calyx |
| 9. Renal capsule | 10. Inferior renal capsule |
| 11. Superior renal capsule | 12. Interlobar vein |
| 13. Nephron | 14. Minor calyx |
| 15. Major calyx | 16. Renal papilla |
| 17. Renal column | |

Heat Shock Response



- | | |
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Schematic drawing of the anatomy of the kidney modified from by Uwe Gille 18:36, 12 August 2005 (UTC), wikipedia, oct. 2012

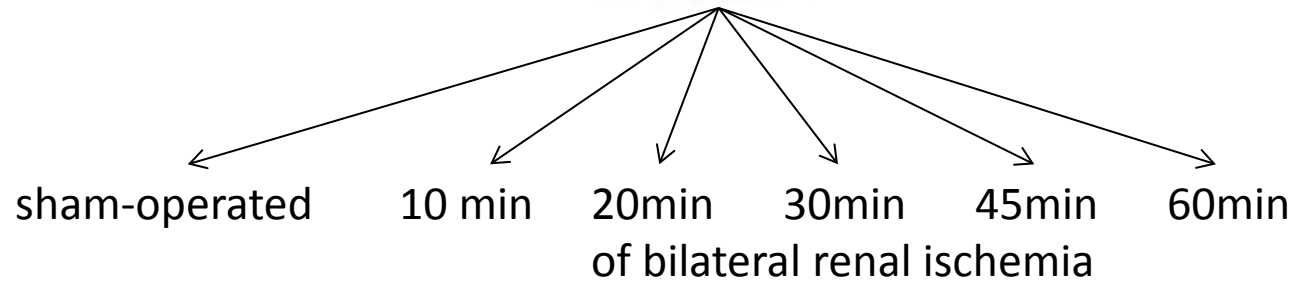
Hsp72 is an early and sensitive biomarker to detect acute kidney injury

- HSP72 biomarker for AKI?
- as biomarker to monitor a renoprotective strategy?

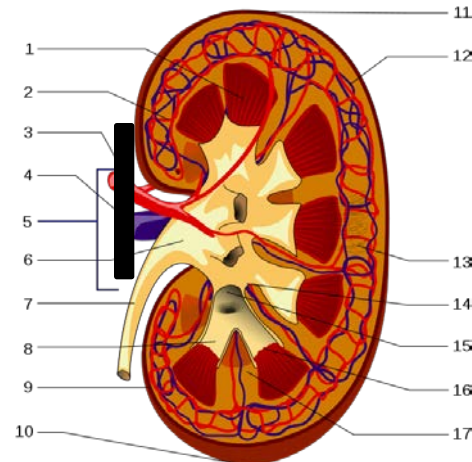


criver.com, oct. 2012

72 Wistar rats
270 – 300 g



24 h reperfusion





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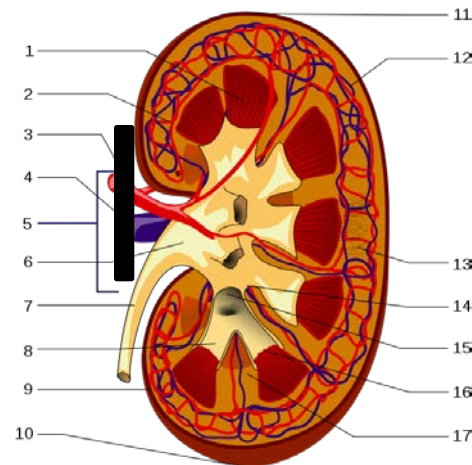
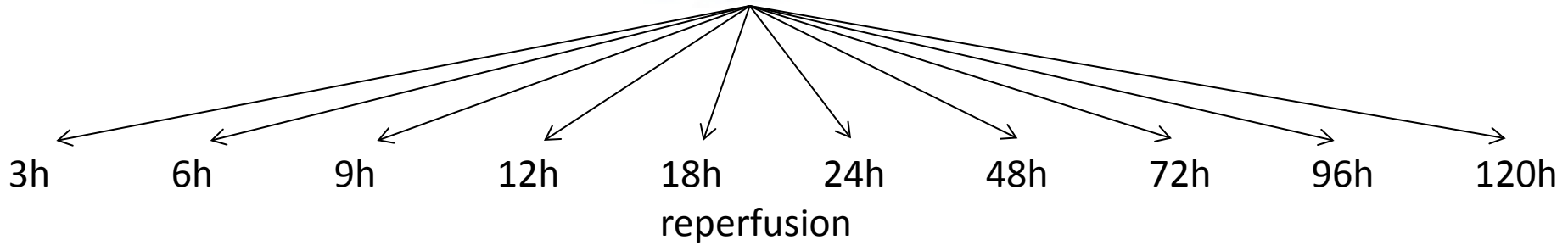
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30 Wistar rats
270 – 300 g
30 min ischemia



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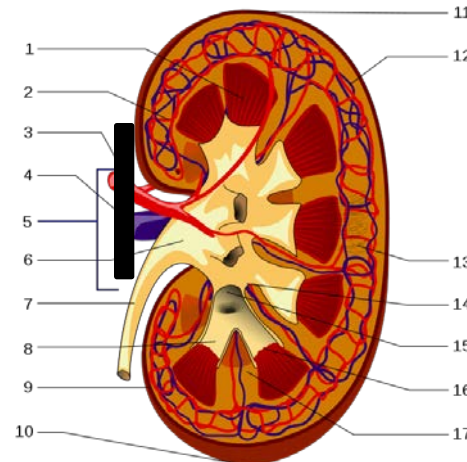
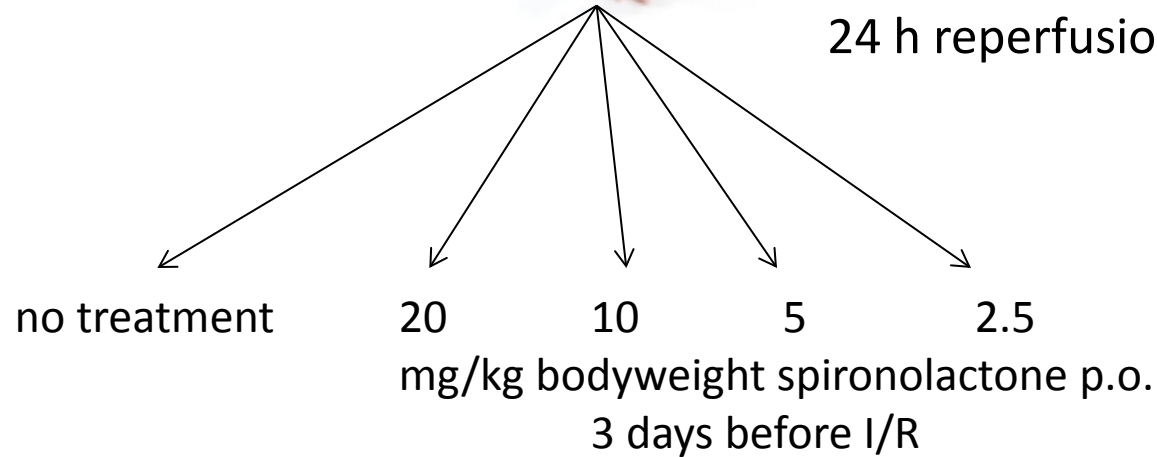
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25 Wistar rats
270 – 300 g
30 min of ischemia
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Research Article

Hsp72 as a novel biomarker to detect AKI



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us.vwr.com, oct. 2012



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healthland.time.com, oct. 2012



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urine protein excretion
N-acetyl- β -D-glucosaminidase

- increased lysosomal activity in renal tubular cells
- a measure of altered function in the renal tubules

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Research Article

Hsp72 as a novel biomarker to detect AKI



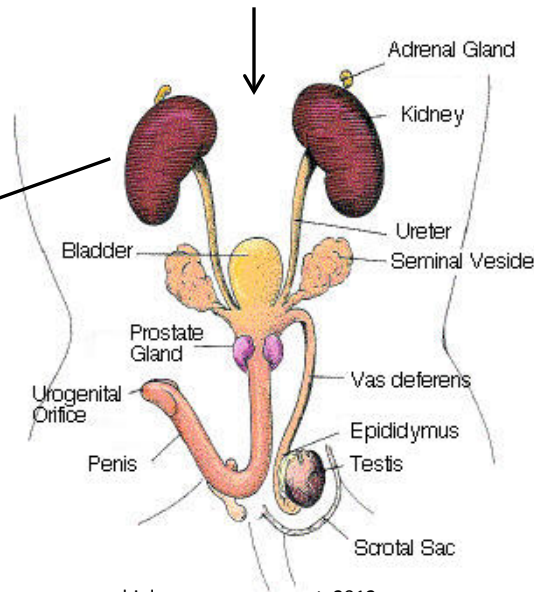
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urine protein excretion
N-acetyl- β -D-glucosaminidase



www.flickr.com/photos/doctorow/2288526230/,
oct. 2012



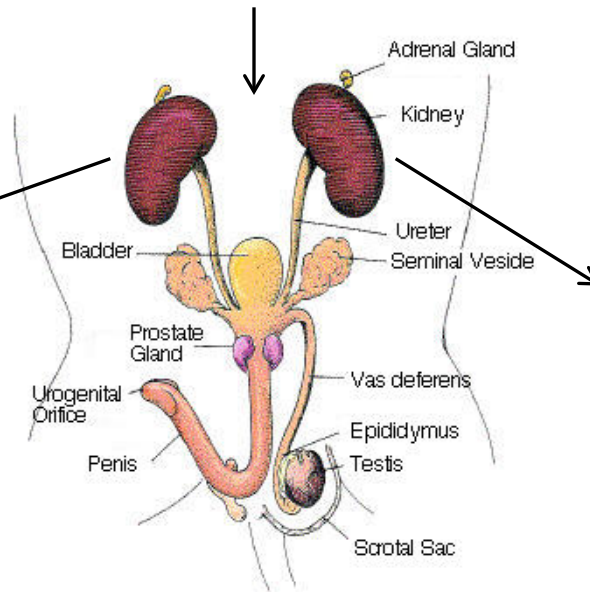
biologycorner.com, oct. 2012



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urine protein excretion
N-acetyl- β -D-glucosaminidase



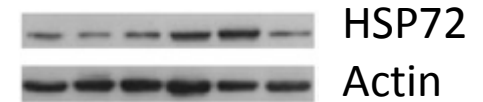
suesse.de, oct. 2012

Periodic acid-Schiff

- glycogen
- glycoproteins
- glycolipids
- cellulosis



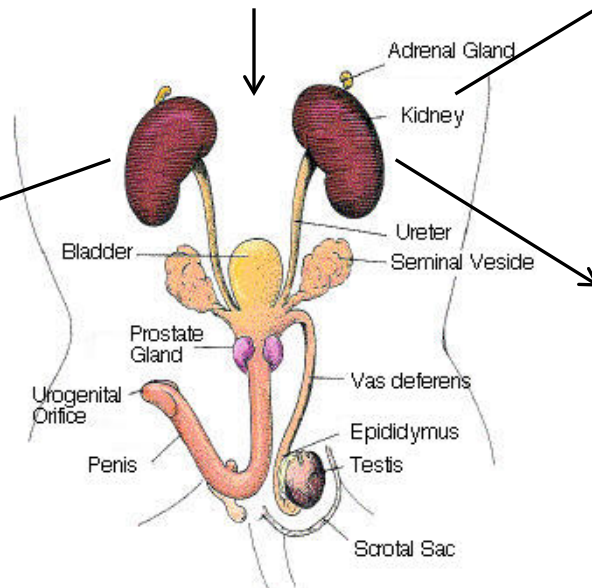
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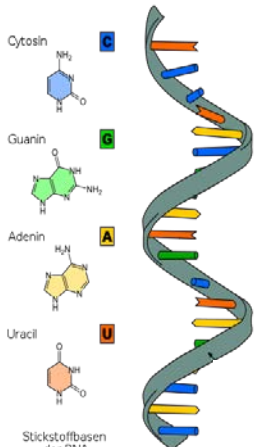
different ischemia
6 rats each group

Periodic acid-Schiff

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urine protein excretion
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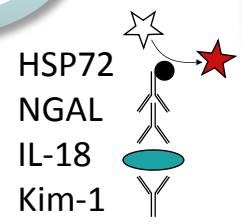


HSP72

wikipedia.de, Spnck, oct. 2012



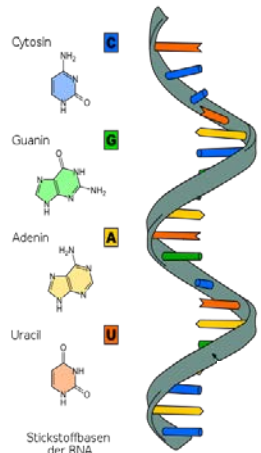
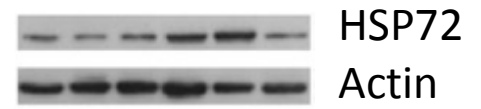
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urine protein excretion
N-acetyl-β-D-glucosaminidase



WB
HSP72

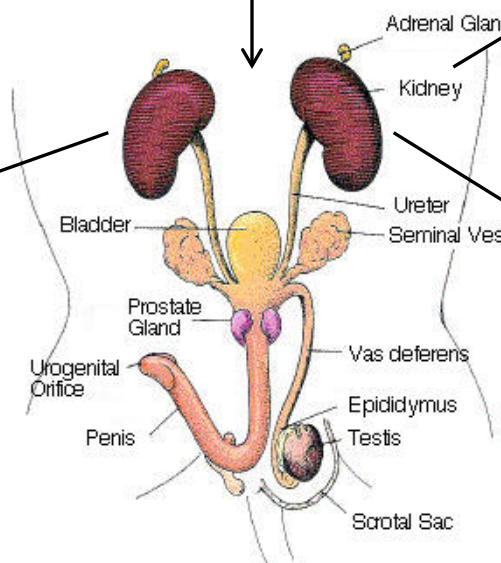


RNA
Ribonukleinsäure

HSP72



different ischemia
6 rats each group



Periodic acid-Schiff



- glycogen
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- cellulosis



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5 healthy kidney donors

9 patients with septic AKI

patients with respiratory
and organ failure

5 patients without AKI

5 patients with AKI

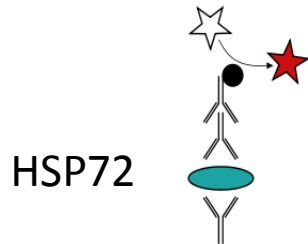
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HSP72

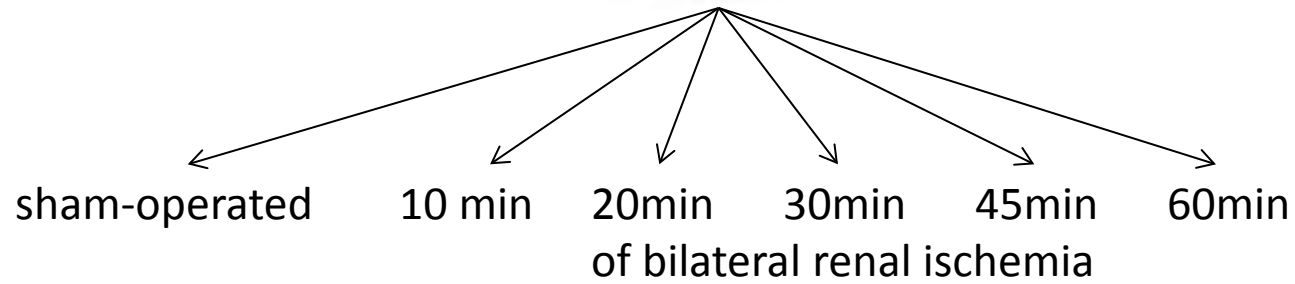


HSP72

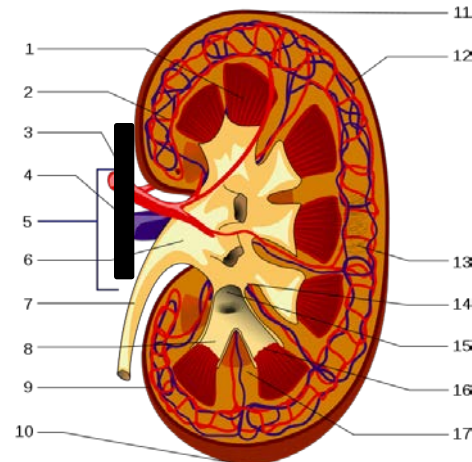


criver.com, oct. 2012

72 Wistar rats
270 – 300 g

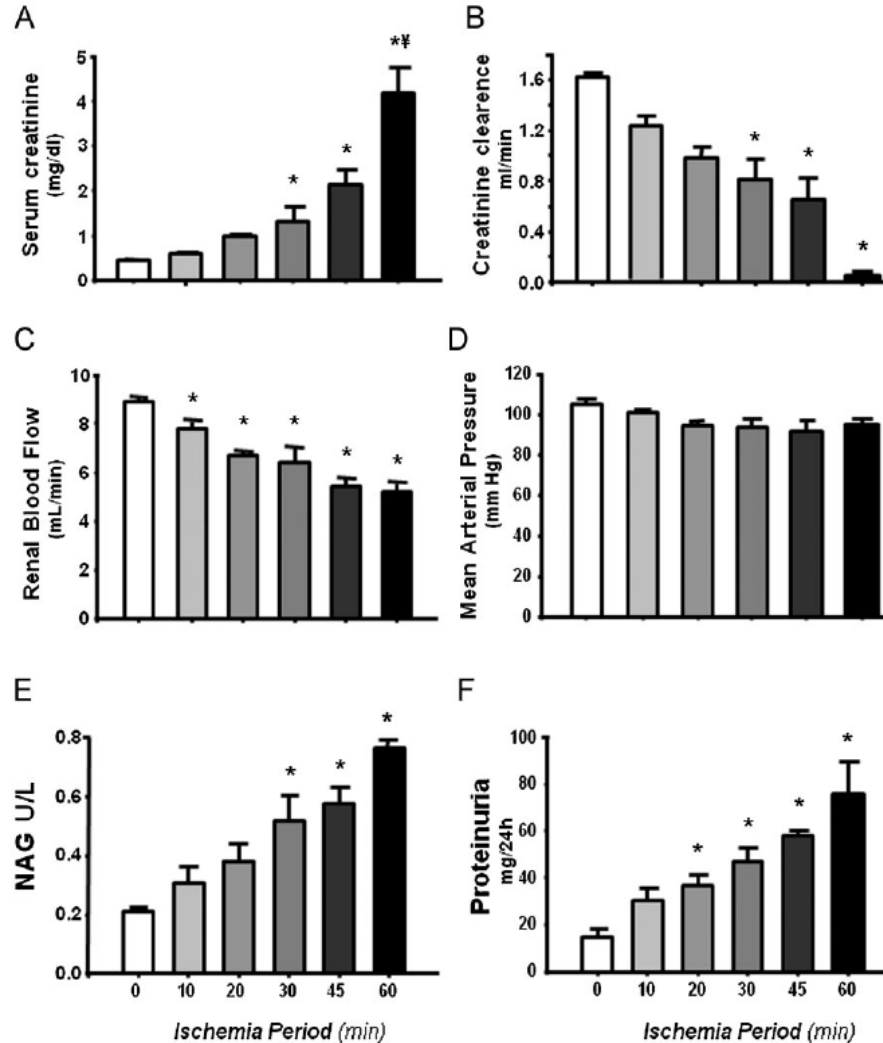


24 h reperfusion



Different ischemia period

Result I

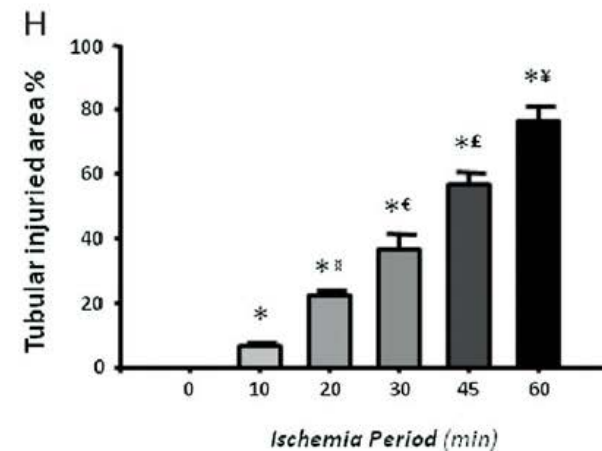
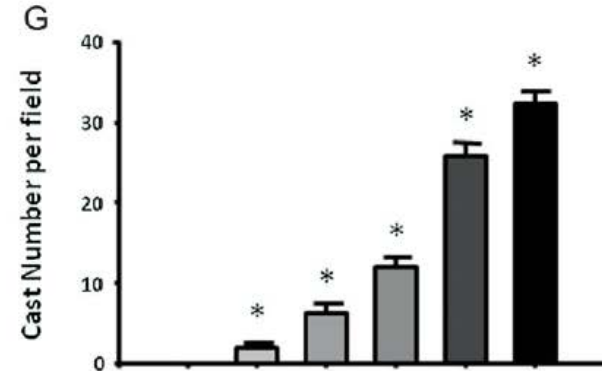
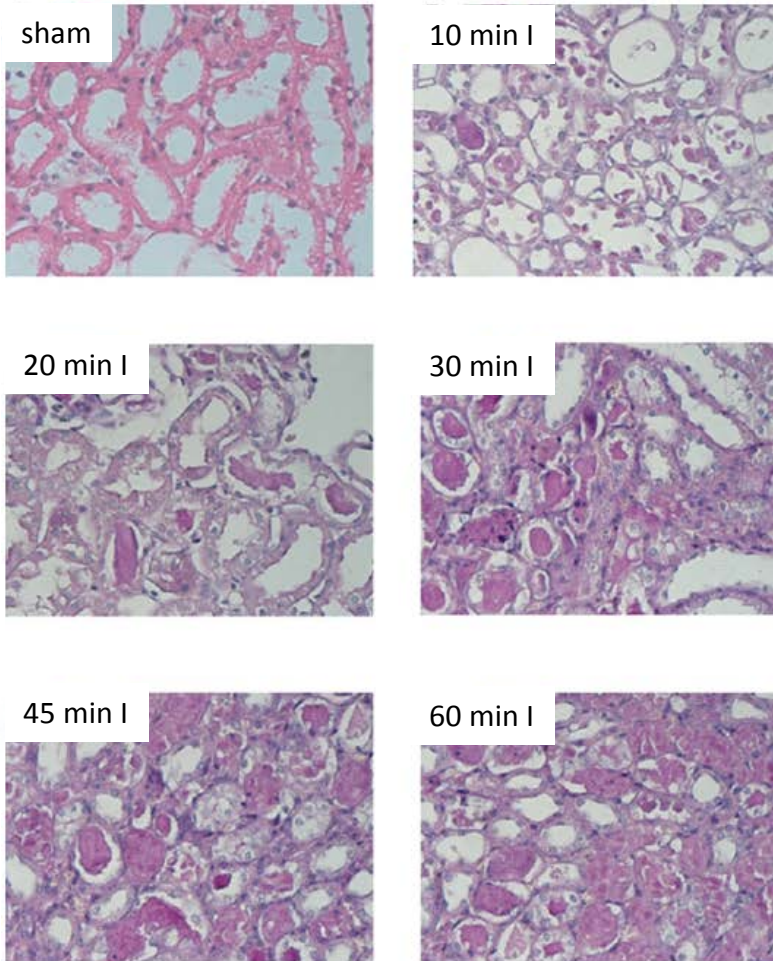


N-acetyl-β-D-glucosaminidase

- increased lysosomal activity in renal tubular cells
- a measure of altered function in the renal tubules

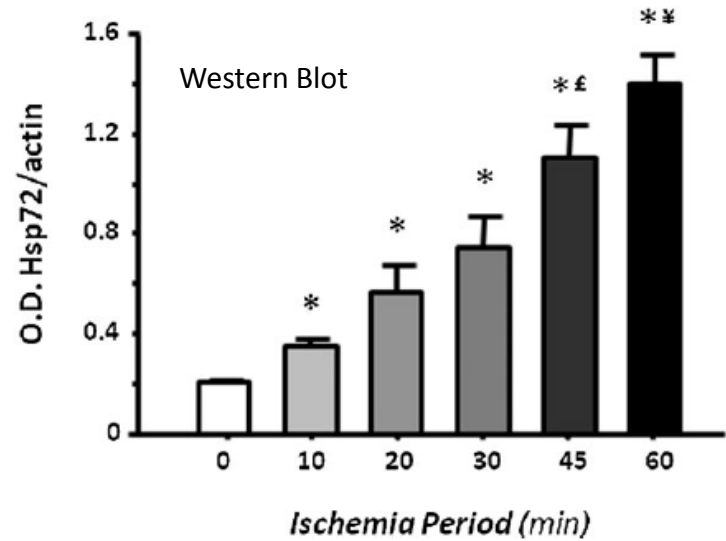
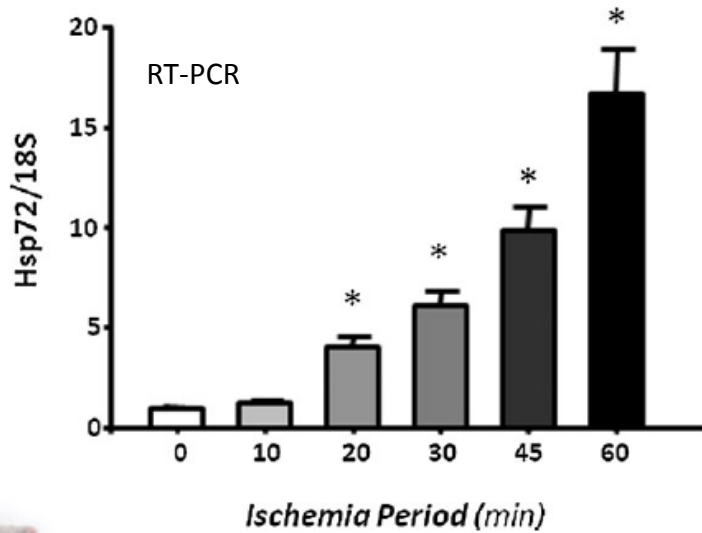
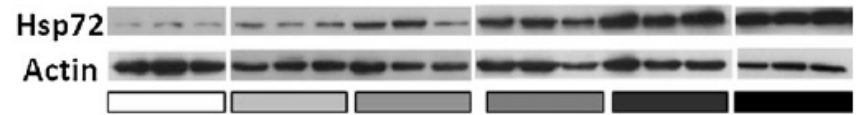
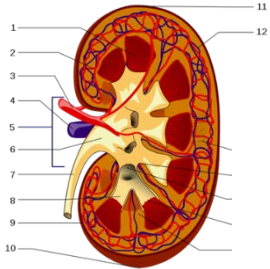
Different ischemia period

Result II



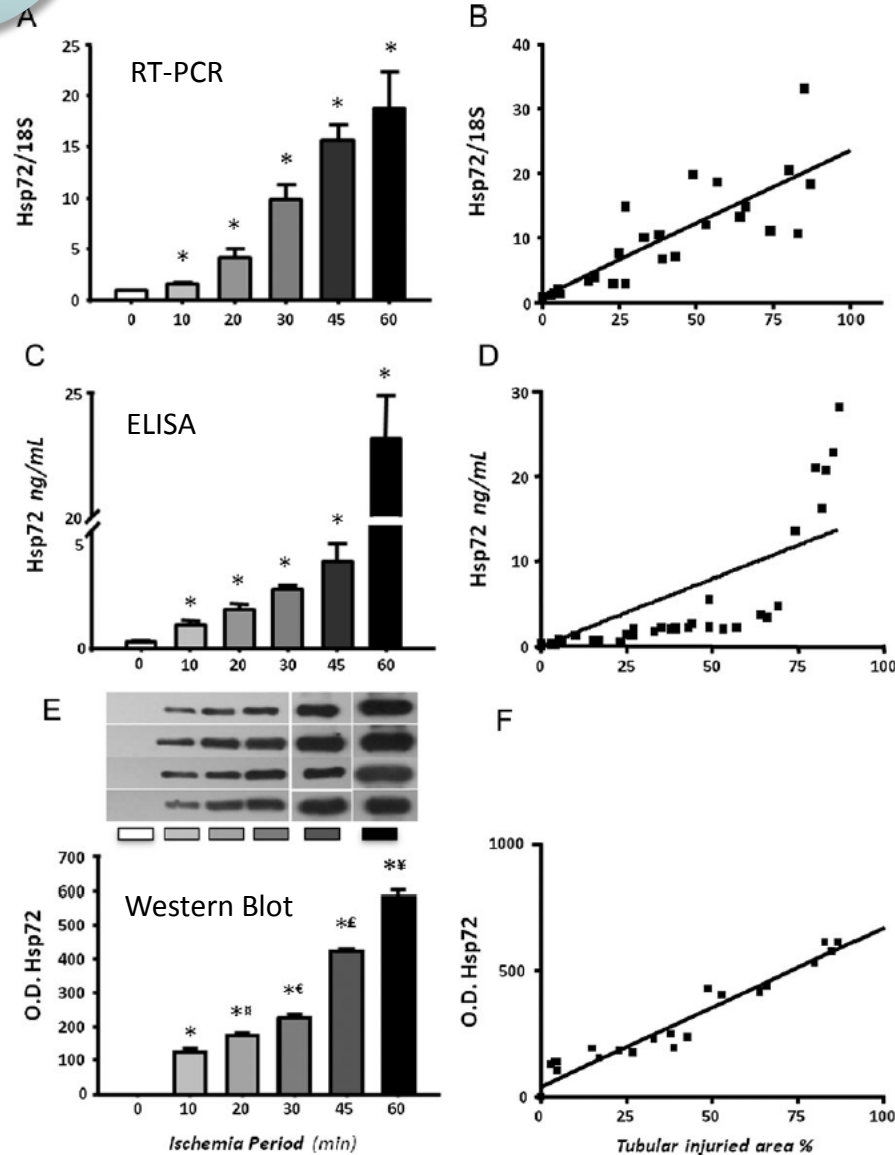
Different ischemia period

Result III



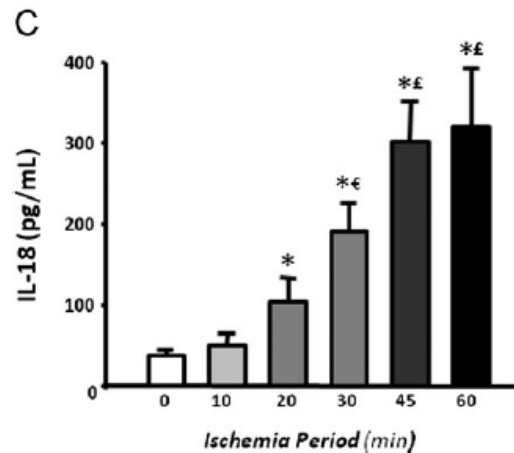
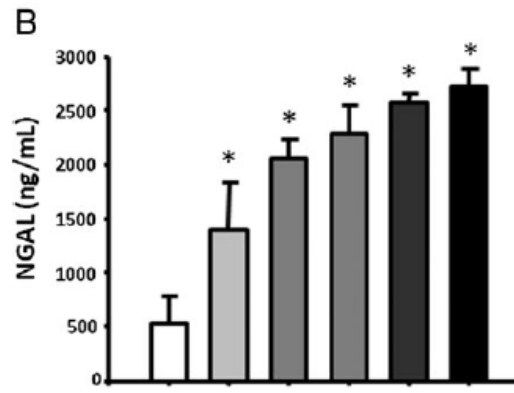
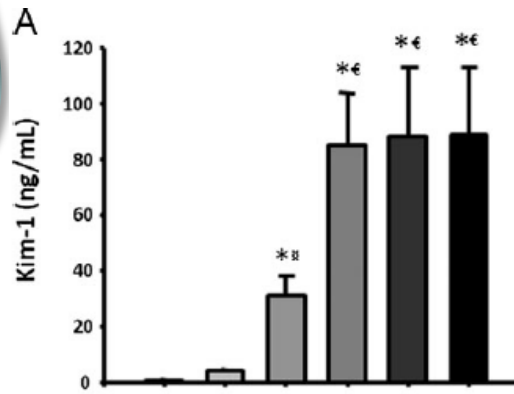
Different ischemia period

Result IV

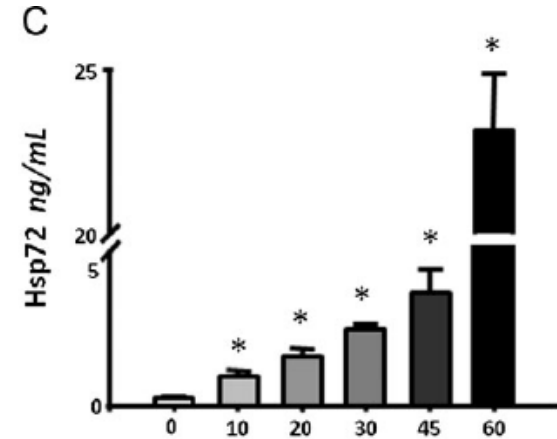


Different ischemia period

Result V

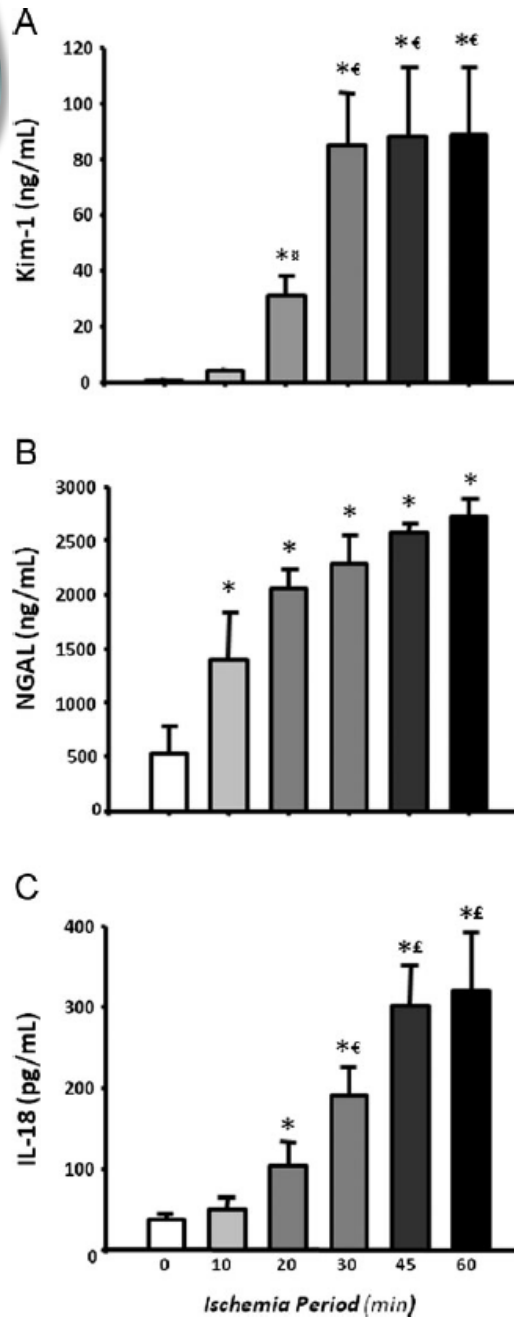


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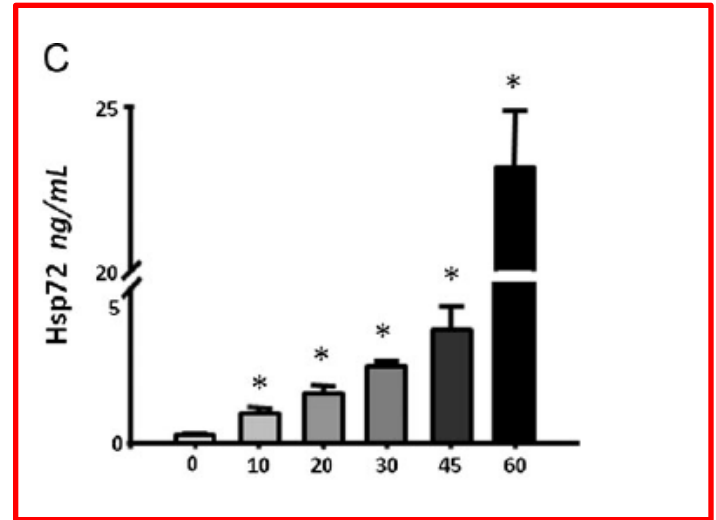


Different ischemia period

Result V



ELISA



highest correlation with tubular injury



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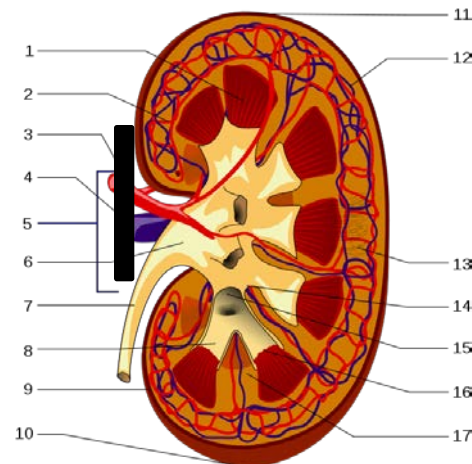
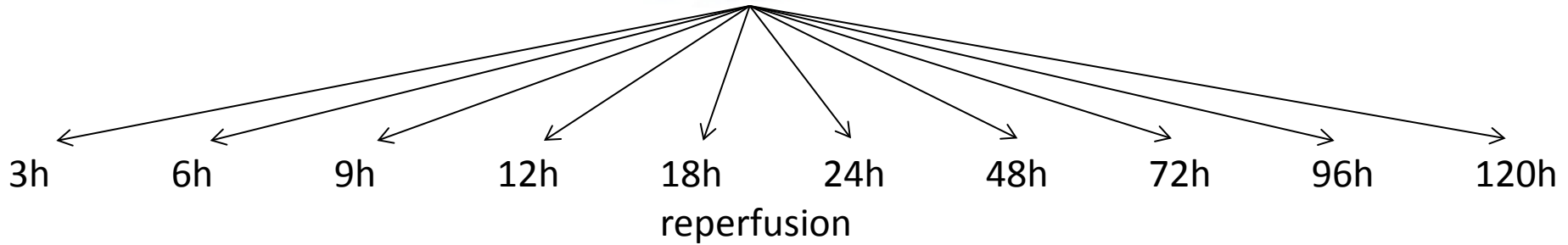
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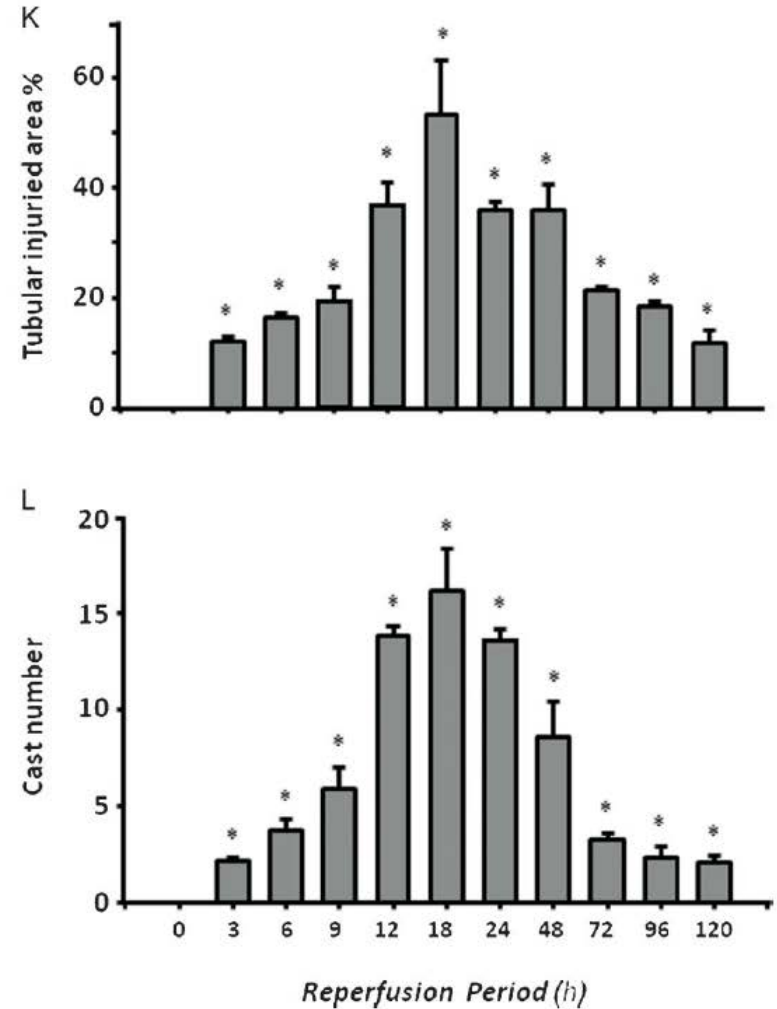
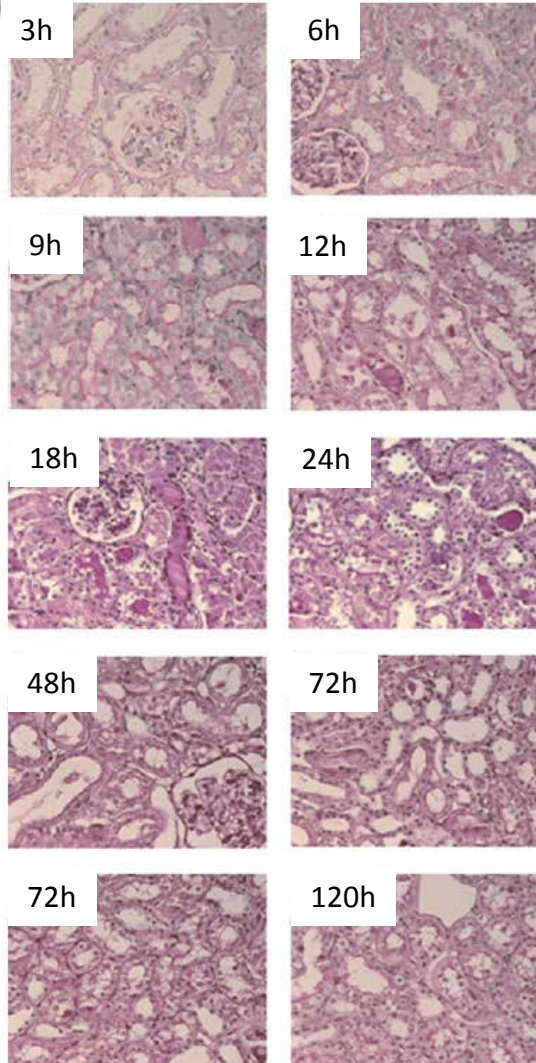
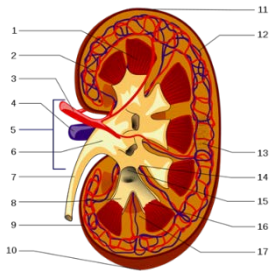
30 Wistar rats
270 – 300 g
30 min ischemia



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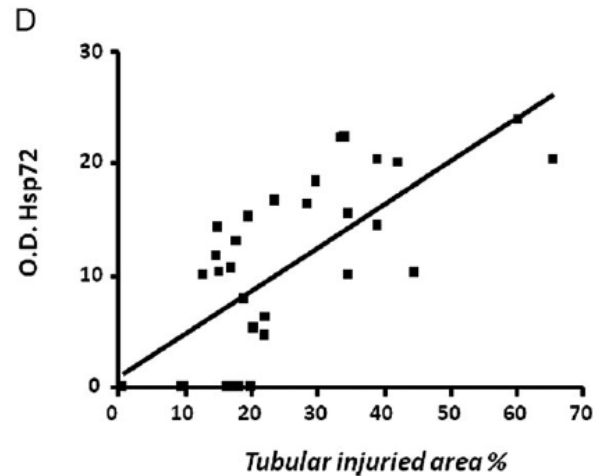
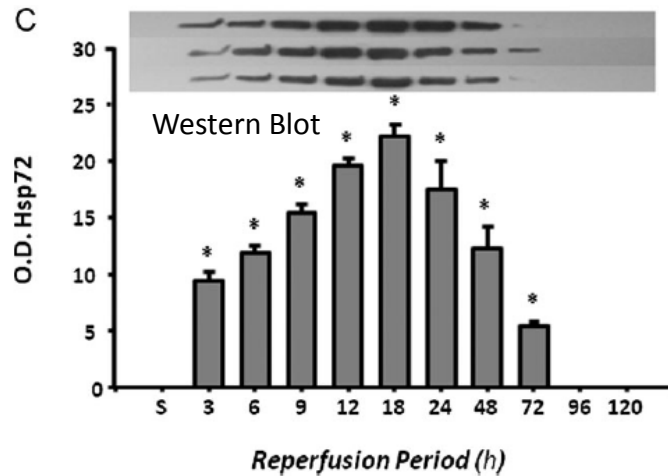
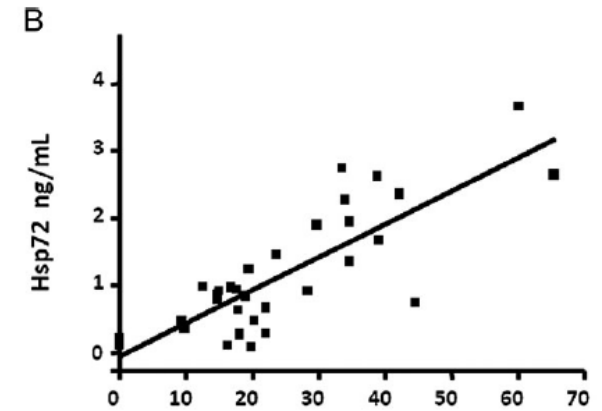
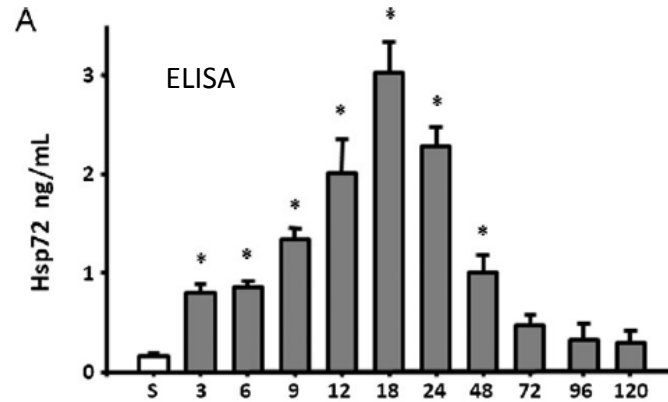
Different reperfusion period

Result I



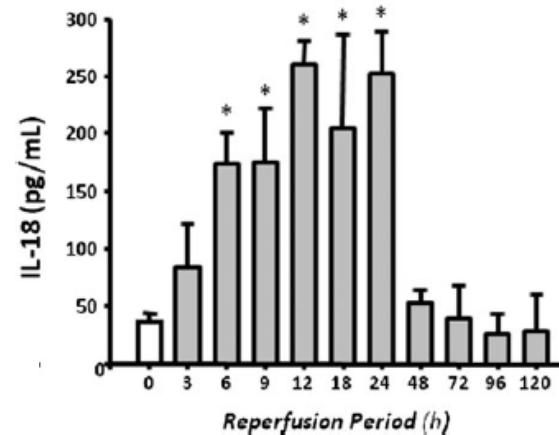
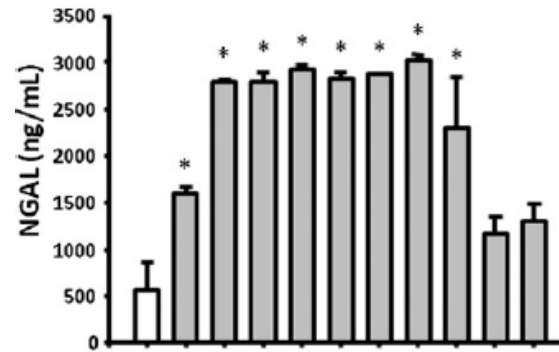
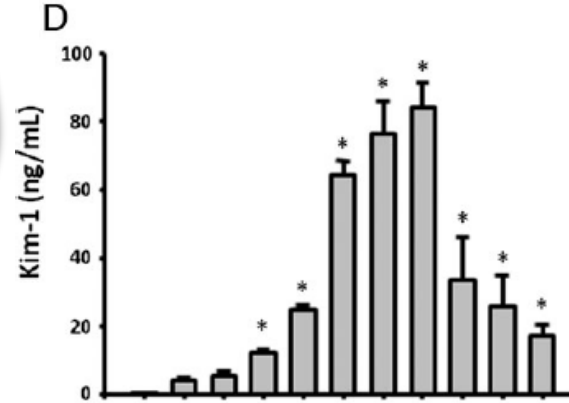
Different reperfusion period

Result II

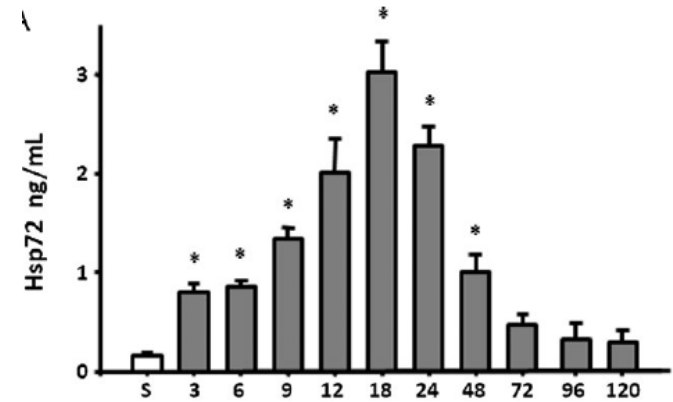


Different reperfusion period

Result III

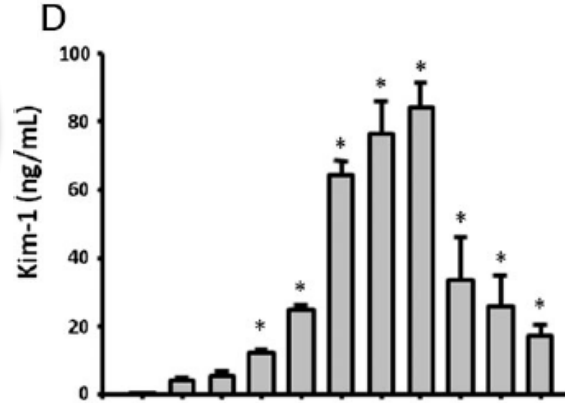


ELISA

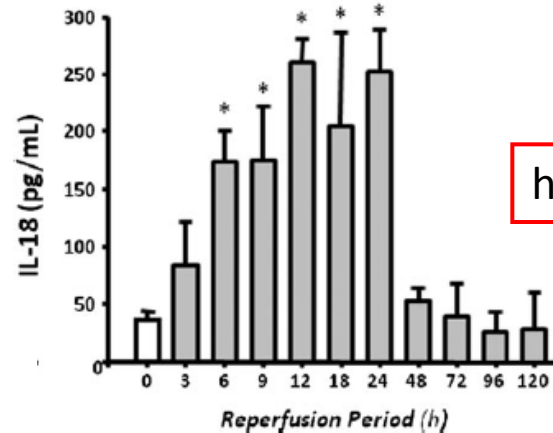
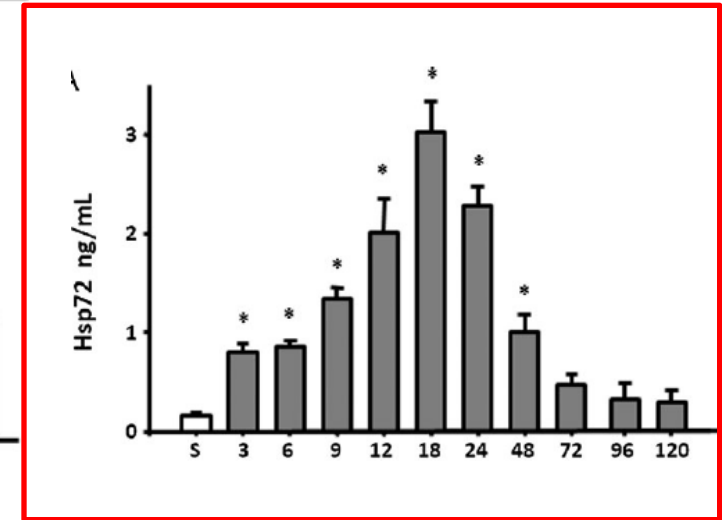
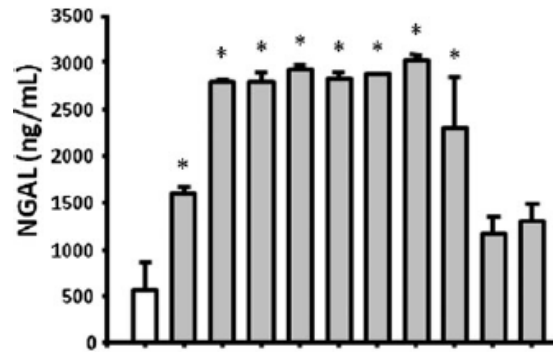


Different reperfusion period

Result III



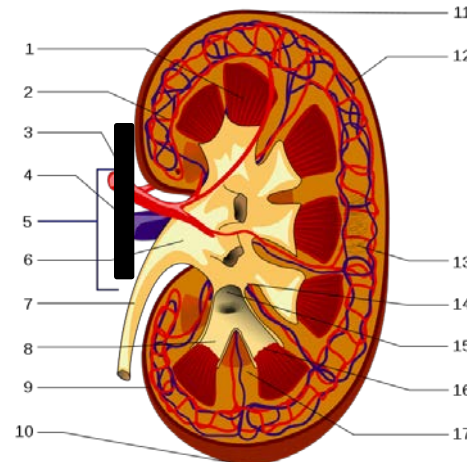
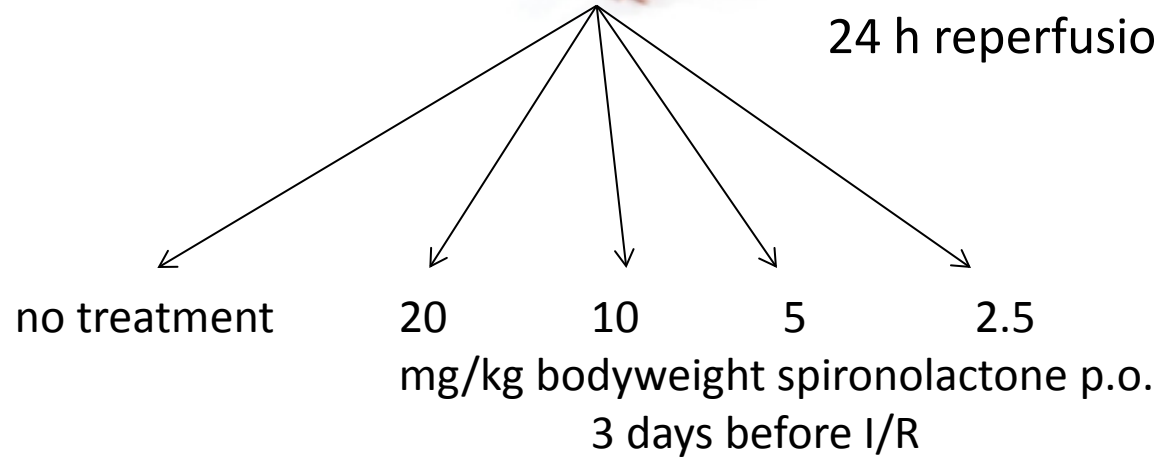
ELISA



highest correlation with tubular injury

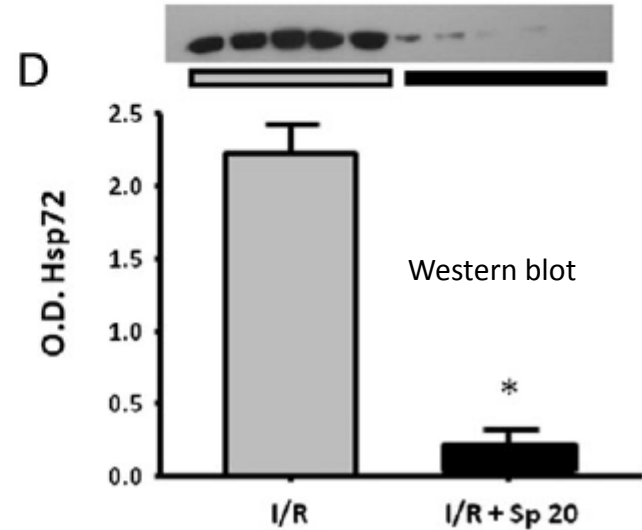
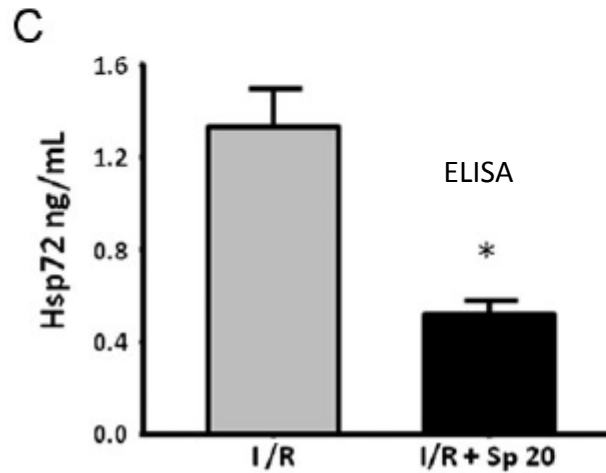
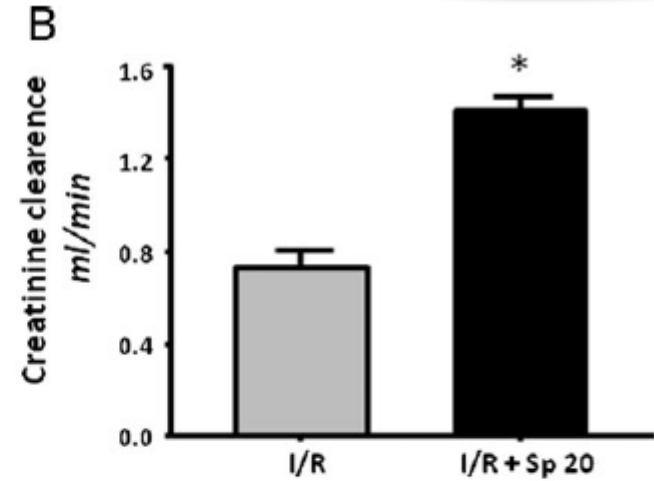
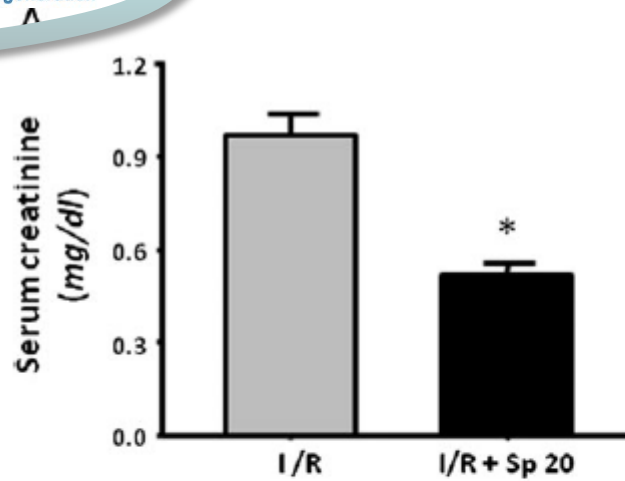


25 Wistar rats
270 – 300 g
30 min of ischemia
24 h reperfusion



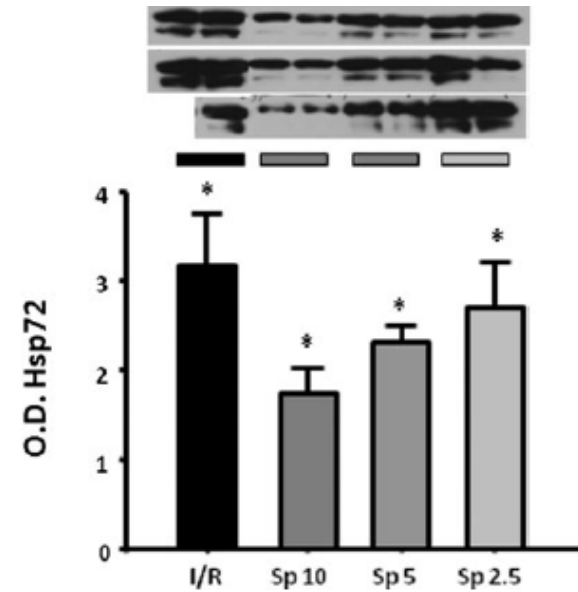
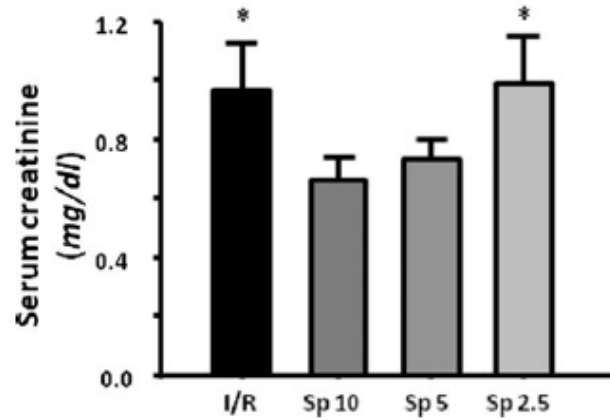
Spironolactone

Result I



Spironolactone

Result II

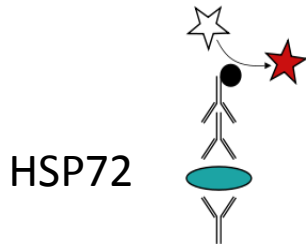




5 healthy kidney donors

9 patients with septic AKI

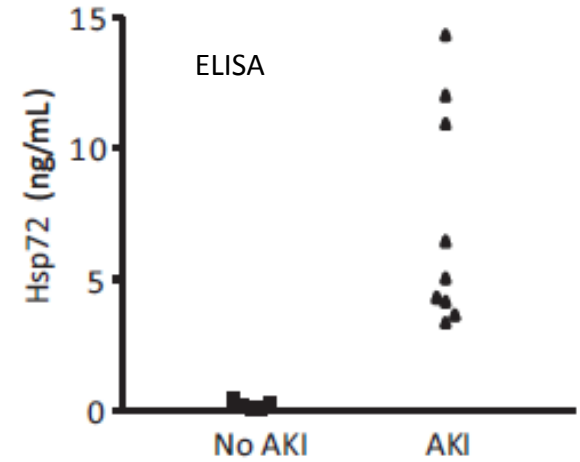
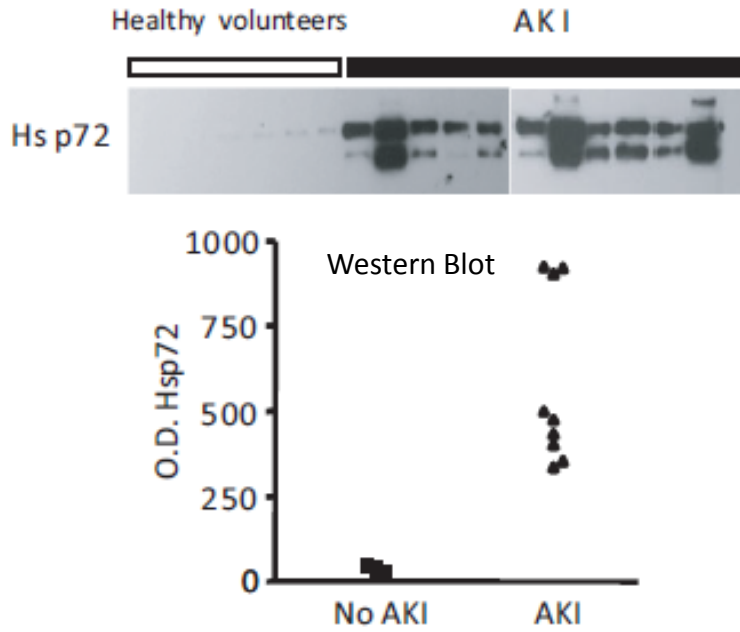
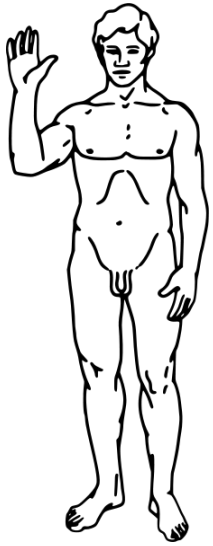
patients with respiratory
and organ failure



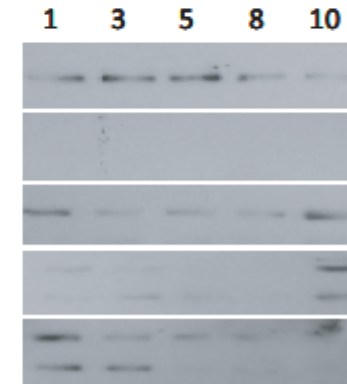
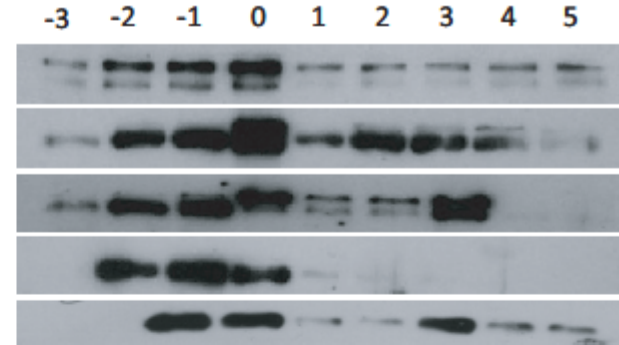
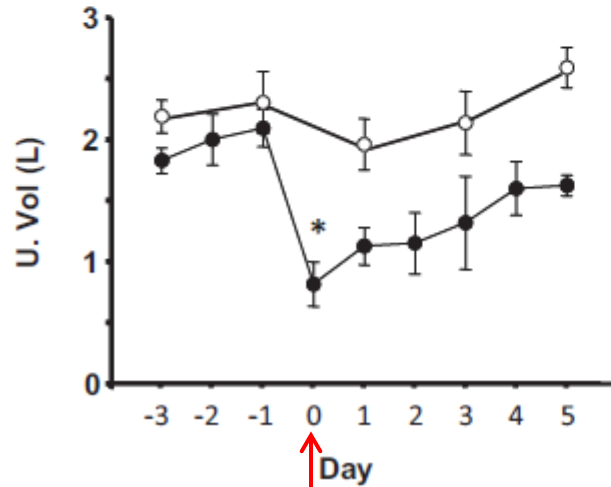
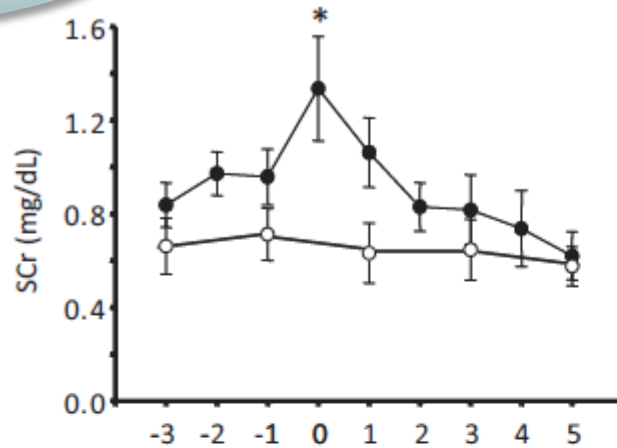
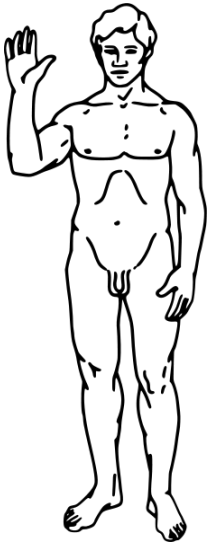
HSP72



HSP72



Patients with respiratory and organ failure



Conclusion

HSP72 as sensitive biomarker:

- stratify renal injury
- correlates with tubular injury
- correlates with tubular recovery
- tool to monitor effectiveness of a pharmacological intervention
- clinical setting

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Thank you for your attention

Hsp72 is an early and sensitive biomarker to detect acute kidney injury

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