ISCHEMIC PRECONDITIONING REDUCES ENDOPLASMIC RETICULUM STRESS AFTER RENAL ISCHEMIA REPERFUSION INSULTS

Mahfoudh-Boussaid A [1]; Zaouali MA [2]; *Rosello-Catafau J* [2]; Saidane-Mosbahi D [1]; Miled AH [1]., Ben Abdennebi H [1].

1:Laboratory of Human Physiology ,Faculty of pharmacy Monastir/TUNISIA, 2 : Experimental Hepatic Ischemia-Reperfusion Unit, Institut d' Investigacions Biome`diques de Barcelona (IIBB), CSIC-IDIBAPS.

Supported by the international cooperation Tunisia-Spain (A/020255/08)

Renal ischemia-reperfusion (RIR) : Main cause of acute kidney injury

mortality and morbidity in a variety of clinical contexts.

Several pathogenic mechanisms have been identified:

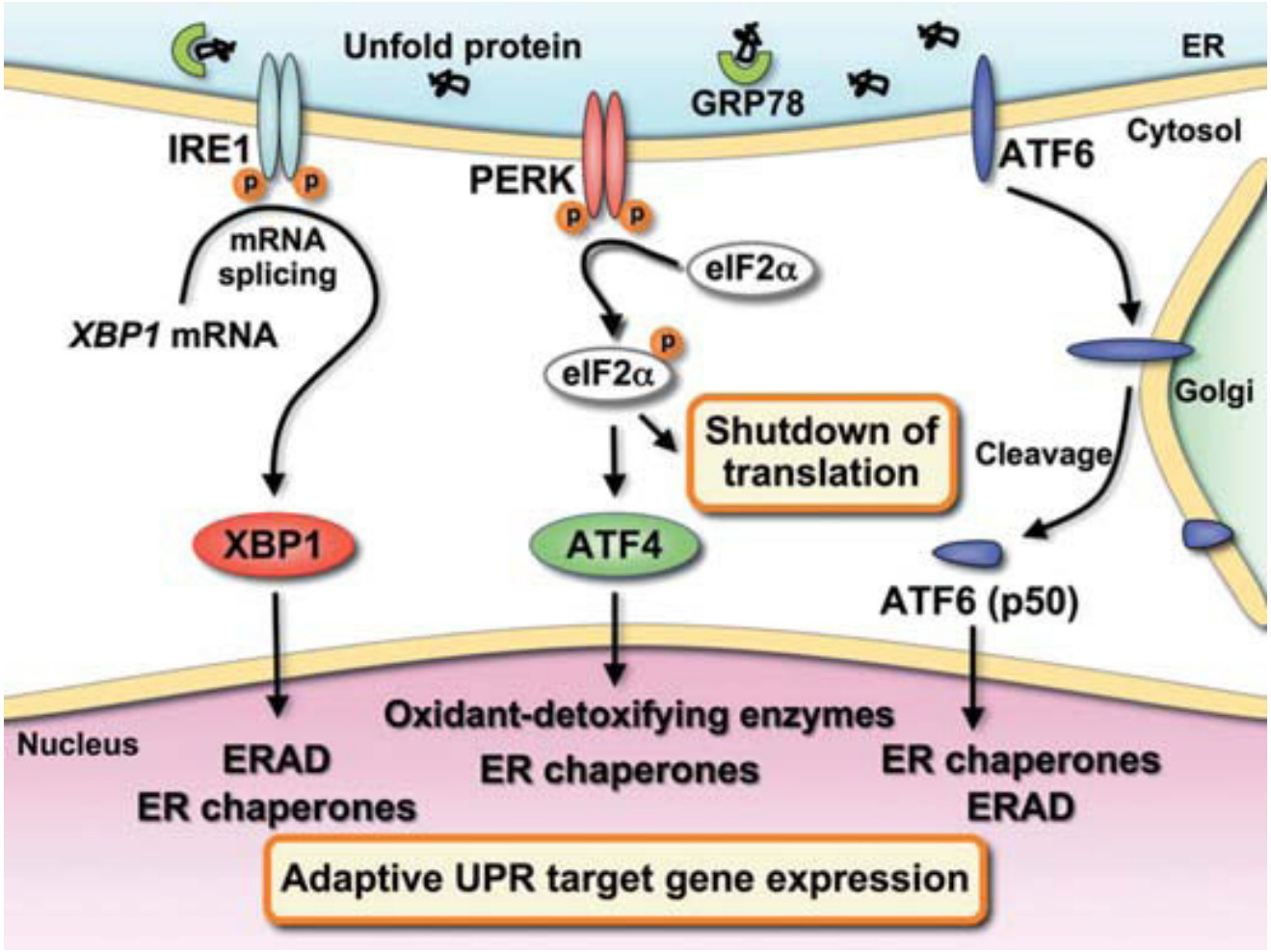
- inflammation, oxidative stress, apoptosis, necrosis….

-Disruption of **endoplasmic reticulum (ER)** homeostasis

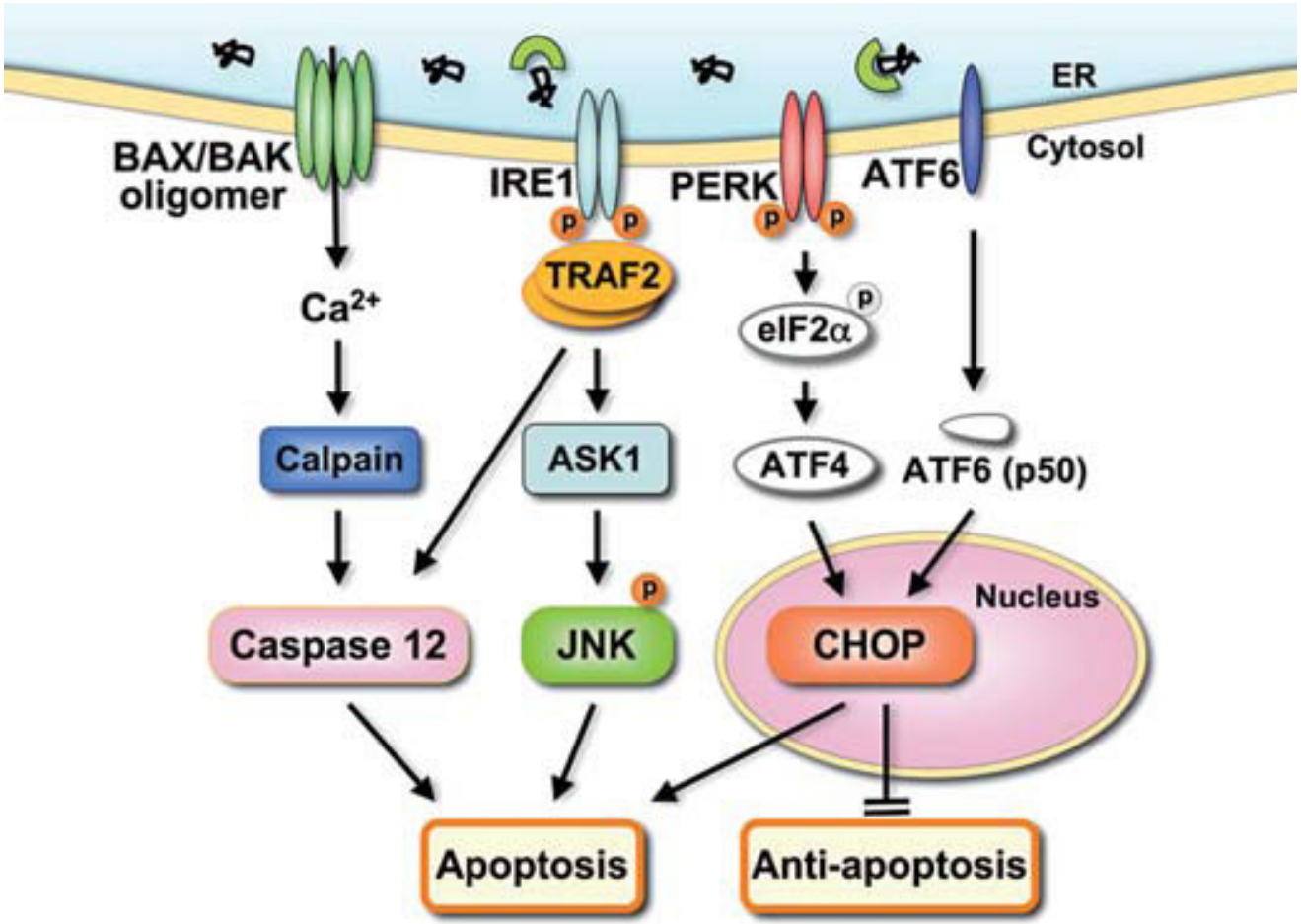
:

ER Stress

ADAPTATIVE PATHWAY : *(Unfolded Protein Response)*



APOPTIC PATHWAY



Ischemic Preconditioning (IPC) : consists of a short period of I/R.

- It renders an organ more tolerant to subsequent prolonged I/R .
- It's precise mechanisms remain undefined

In this study, we investigated whether the renoprotective effect of IPC was associated with modulation of ER Stress.

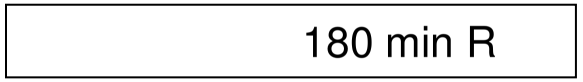
ANIMALS :

- Adult male Wistar rats (160-230).
- Anesthetized with ketamine intraperitoneally (50 mg/Kg body weight).

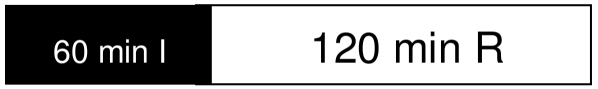
.

Experimental groups

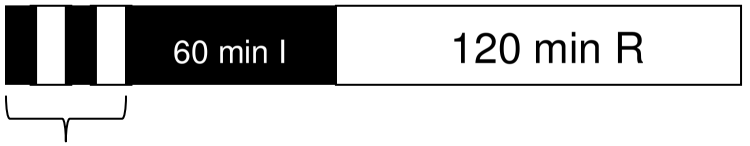
1) SHAM group (n=5)



2) I/R group (n=6)



3) IPC group (n=6)



1) Sodium concentration in urine and plasma → **Sodium reabsorption rate (NaRR)**

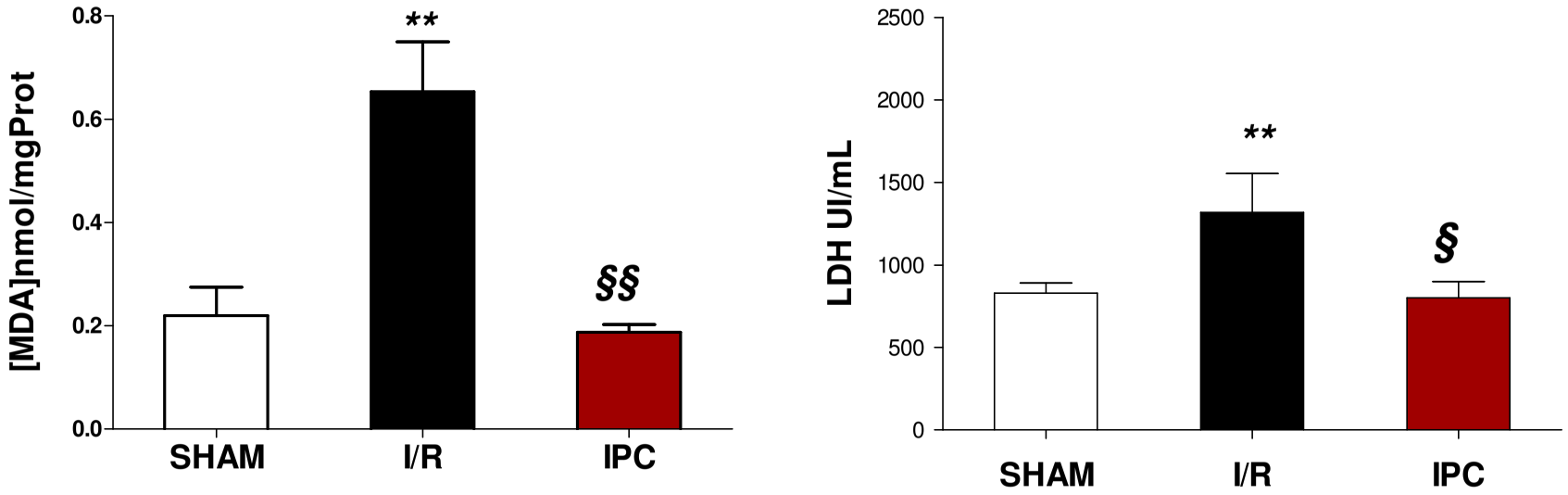
2) Creatinine concentration in plasma and urine → **Creatinine clearance (GFR)**

*3)*Plasmatic Lactate dehydrogenase (LDH) activity → **Cellular lysis**

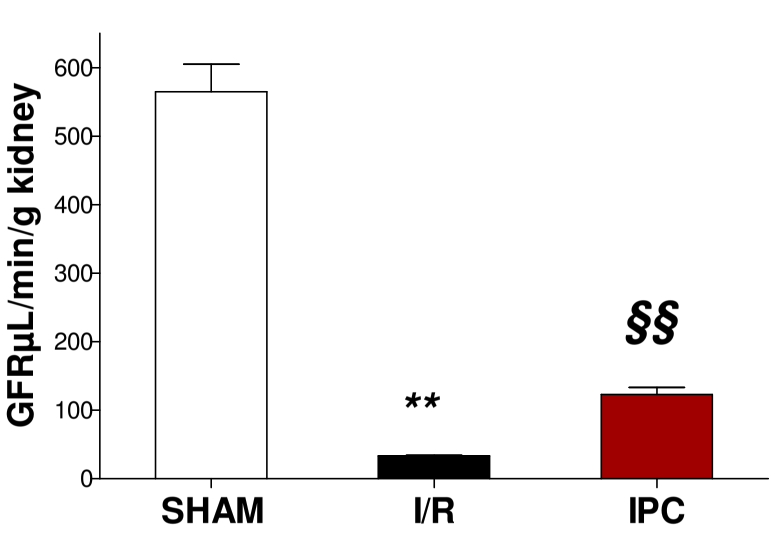
*4)*Tissue maondialehyde (MDA-tbar) concentration → **Lipid peroxydation**

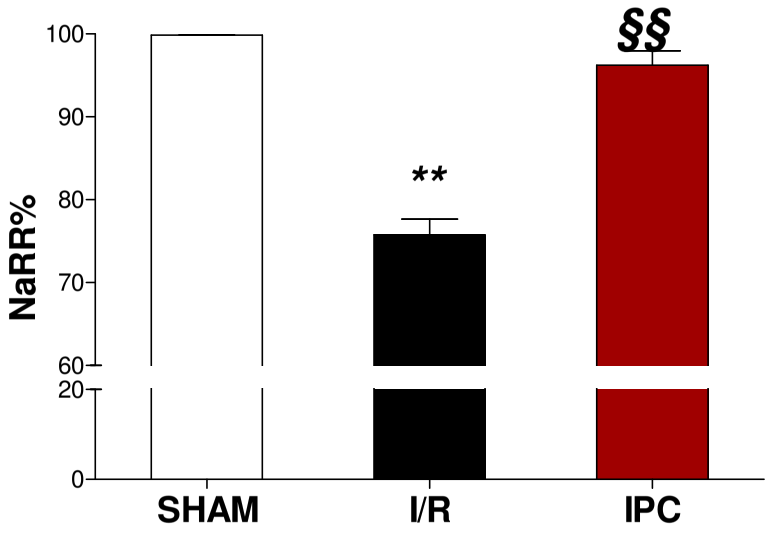
5) Western blot analysis of ER Stress parameters:

- **GRP78** : Glucose Regulated Protein 78
- **eiF2α** : eukaryotic initiation Factor 2
- **ATF4** : Activating Transcription Factor 6
- **TRAF2**: Tumor necrosis Receptor Activator Factor
- **XBP-1** : X-box Protein 1



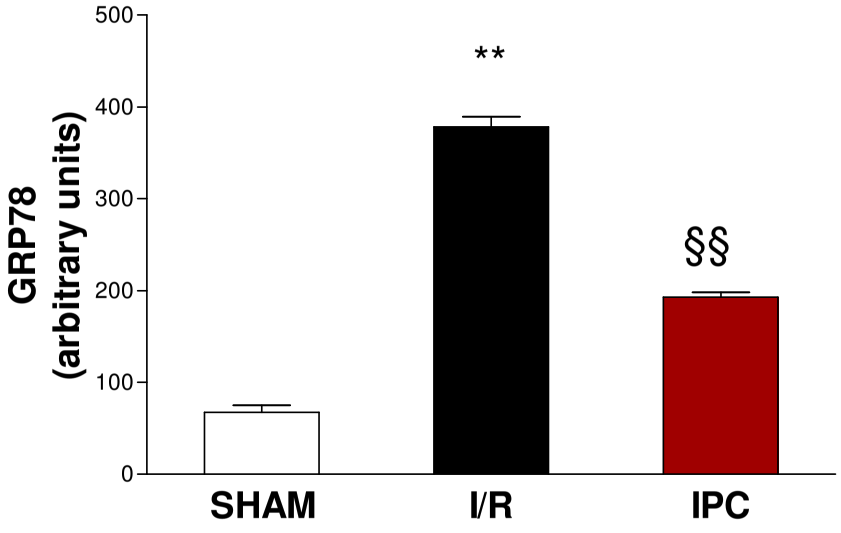
**: p<0.01 vs SHAM; §: p<0.05 vs I/R ;§§: < 0;01 versus I/R

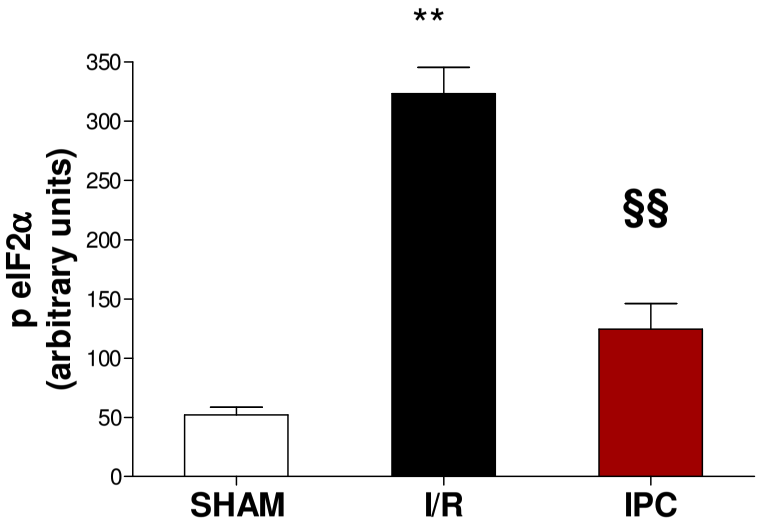




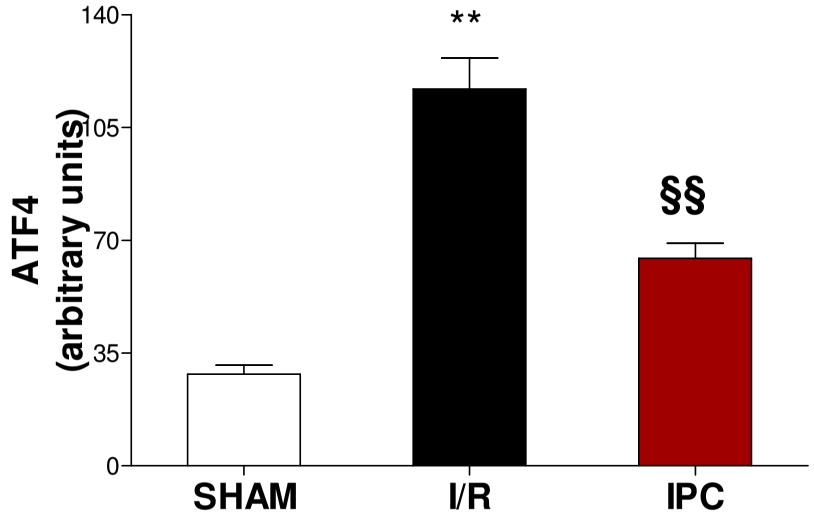
**: p < 0.01 vs SHAM, §§: < 0;01 versus I/R

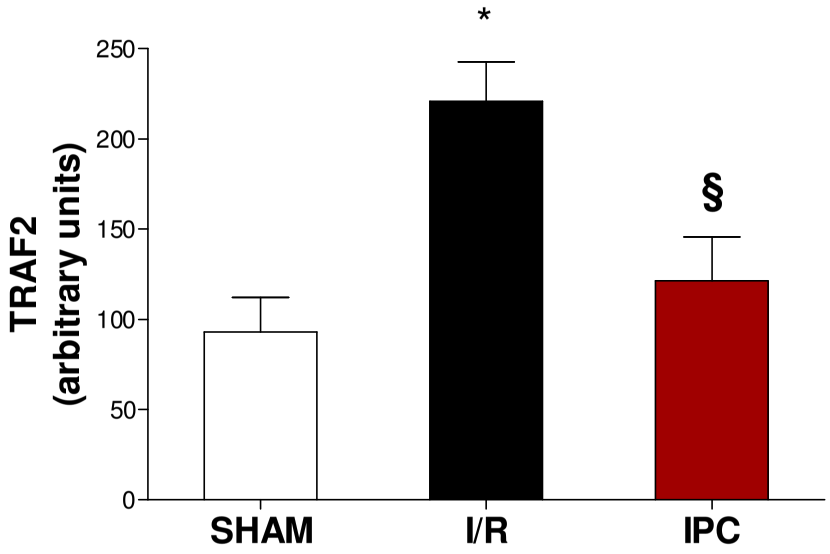
Effect of IPC on ER stress parameters:



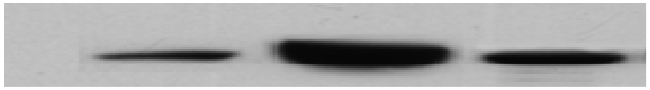


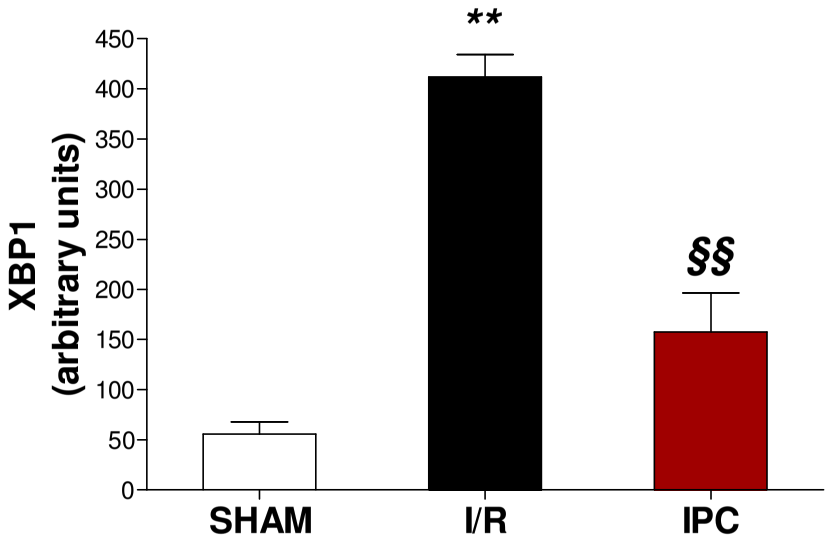
**: p < 0.01 vs SHAM, §§: < 0;01 versus I/R





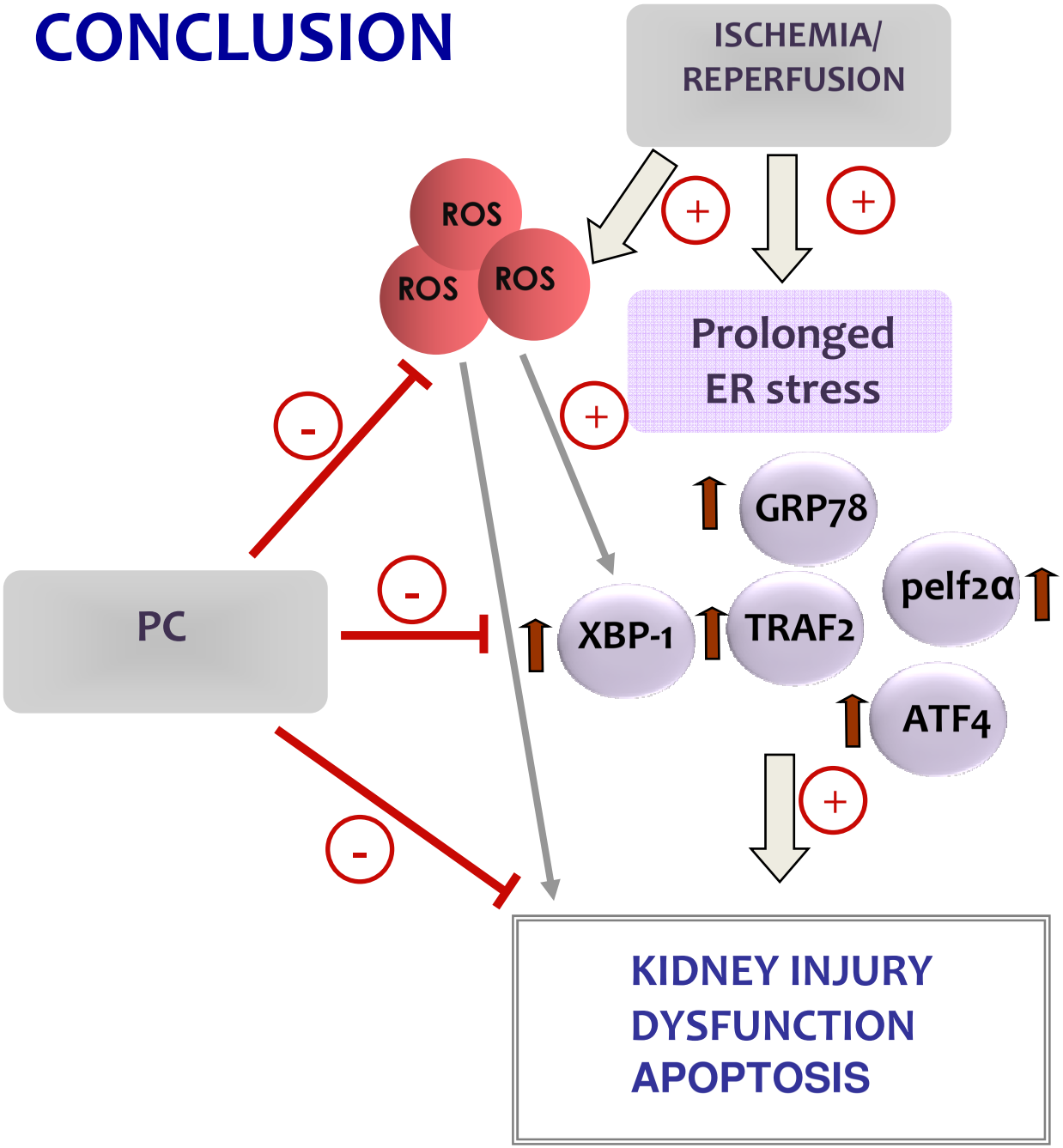
*: p<0.05 vs SHAM; ** : p<0.01 vs SHAM; §: p<0.05 vs I/R; §§: p < 0;01 vs I/R





** : p < 0.01 vs SHAM, §§: < 0;01 versus I/R

CONCLUSION


ISCHEMIA/
REPERFUSION
ROS
ROS
ROS
+
+
Prolonged
ER stress
+
-
GRP78
PC
-
XBP-1
TRAF2
pelf2α
ATF4
+
-
KIDNEY INJURY
DYSFUNCTION
APOPTOSIS