

The cGMP Pathway (III)

**Attenuation of
myocardial
ischemia-reperfusion
injury by modulation
of the pathway**

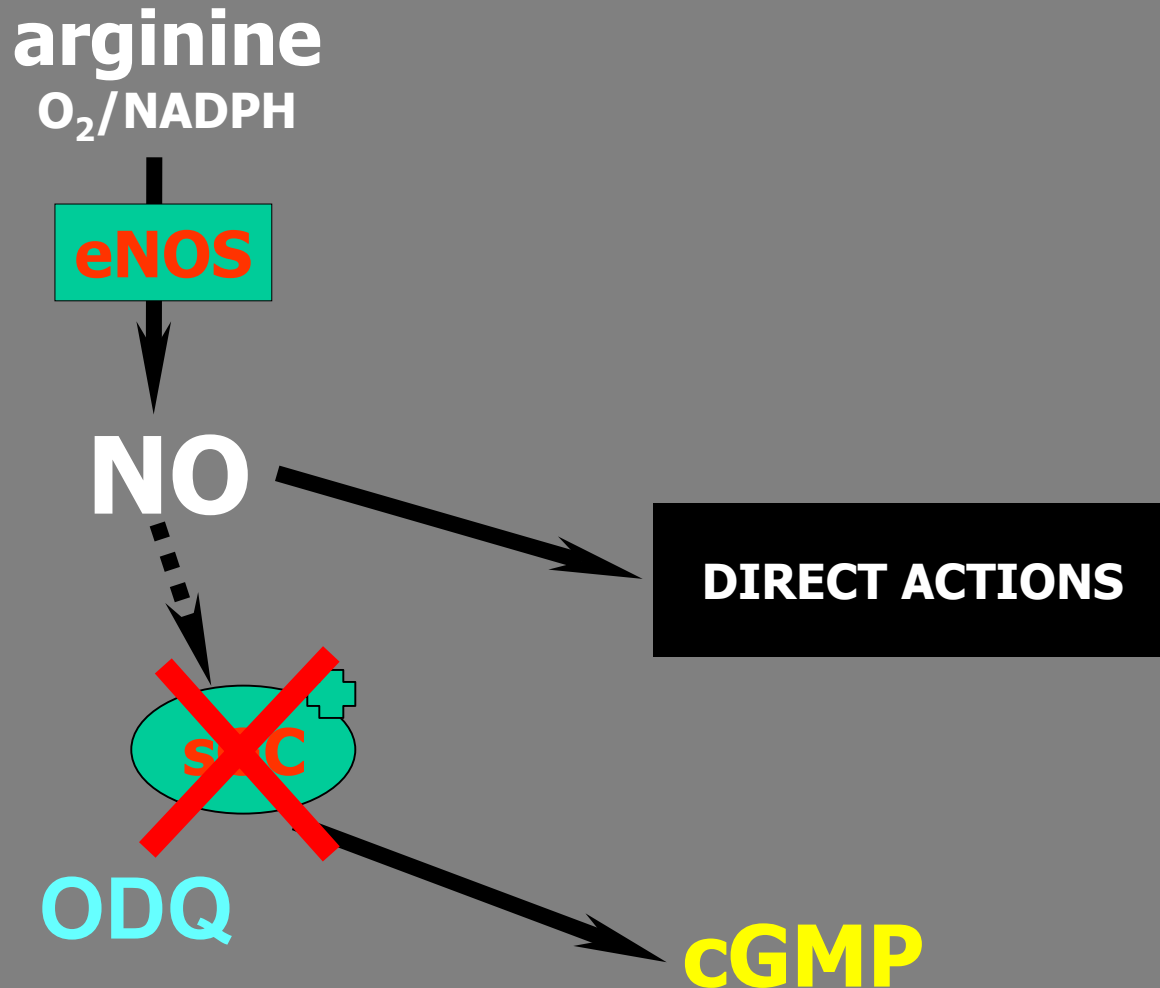
Ischemia-reperfusion protocol:

- 1) No-flow ischemia (60min) in isolated rat hearts**
- 2) LAD occlusion (48min) in *in situ* pig hearts**

Quantification of ischemia-reperfusion injury:

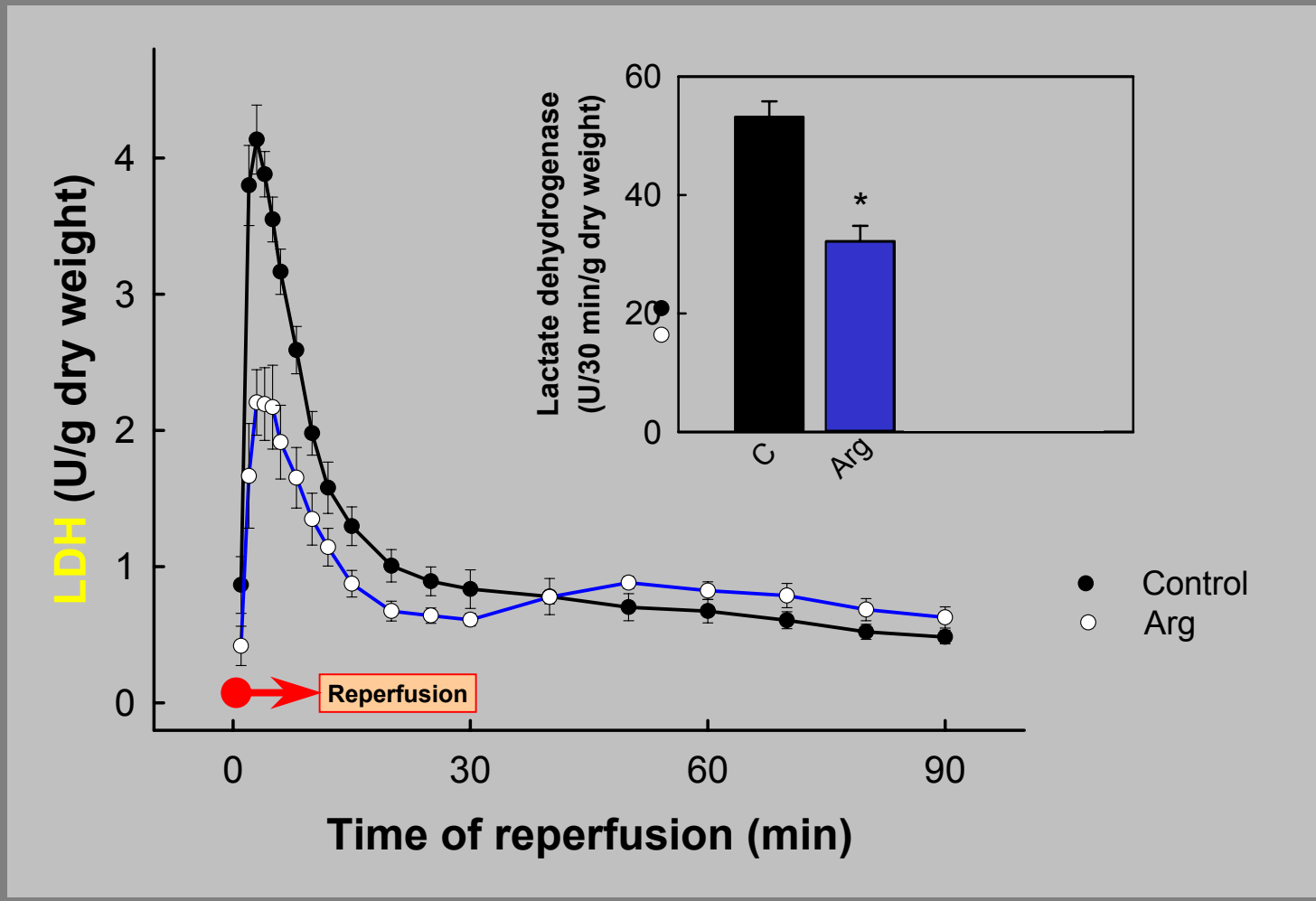
- 1) LDH release in the perfusion medium (isolated rat hearts)**
- 2) infarcted risk area (%) by TTC in *in situ* pig hearts**

Modulation of cGMP pathway: Increasing NO production



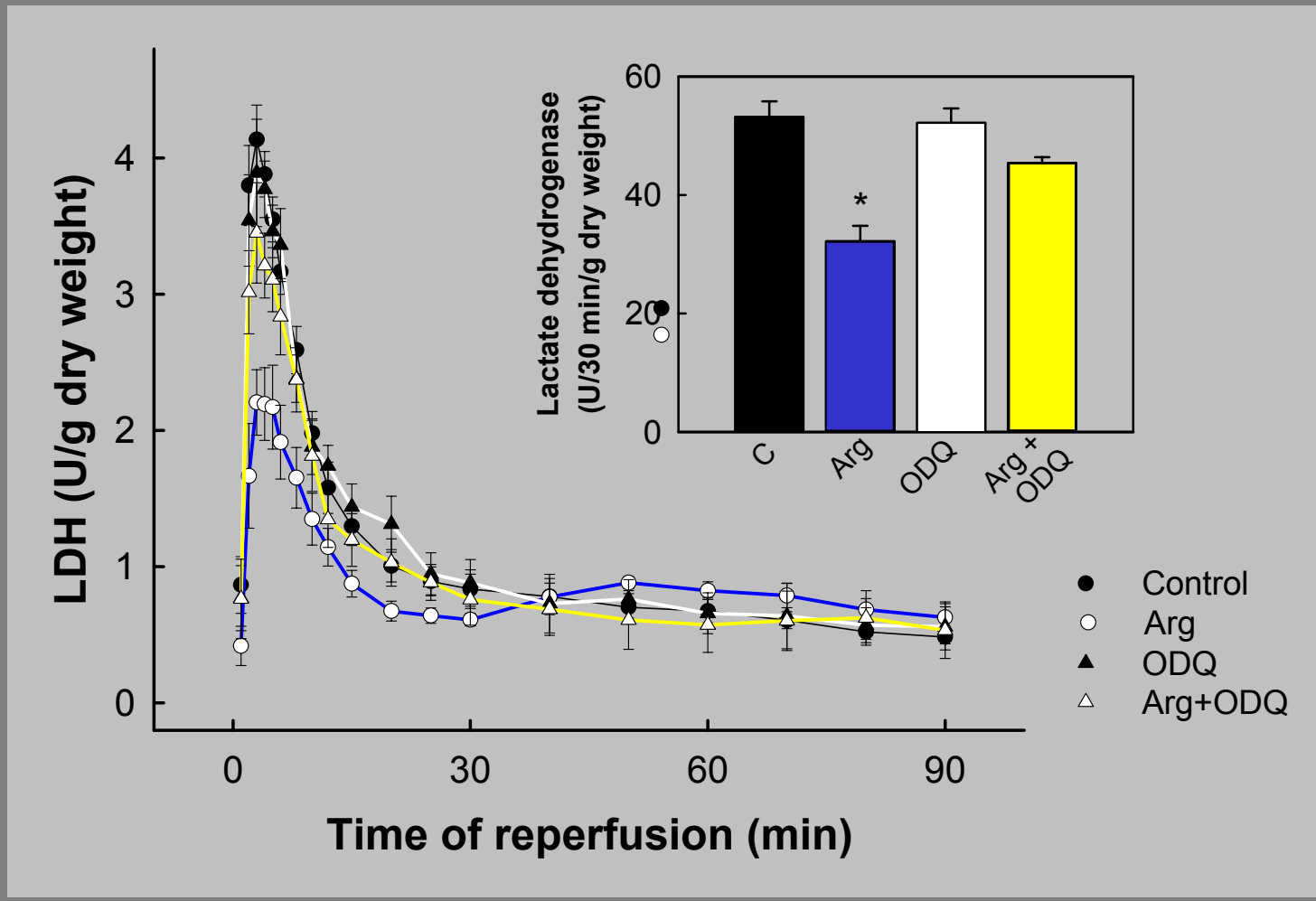


Modulation of cGMP pathway: Increasing NO production



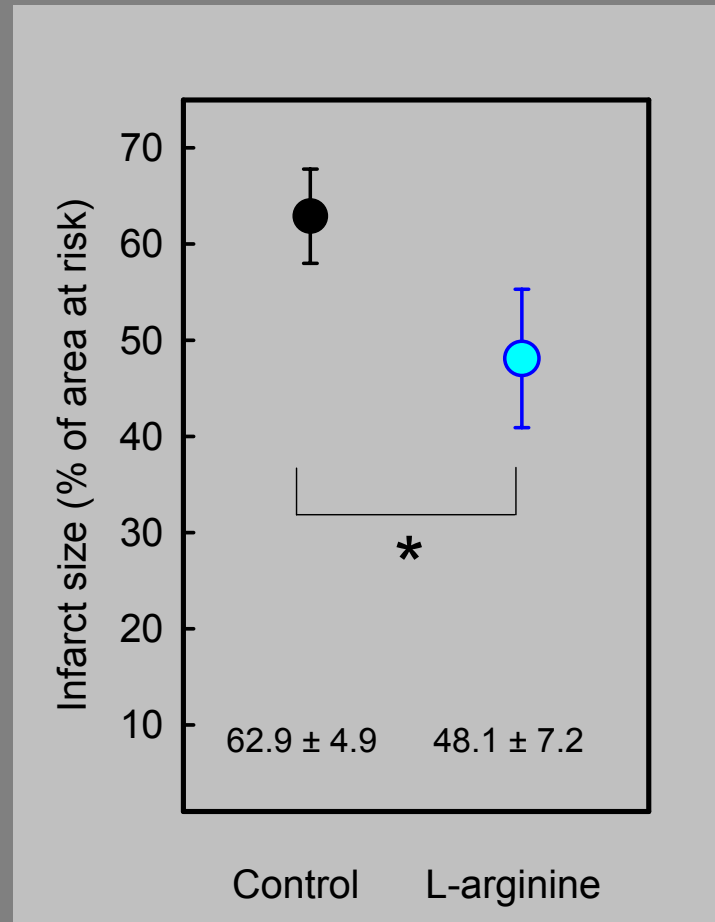


Modulation of cGMP pathway: Increasing NO production

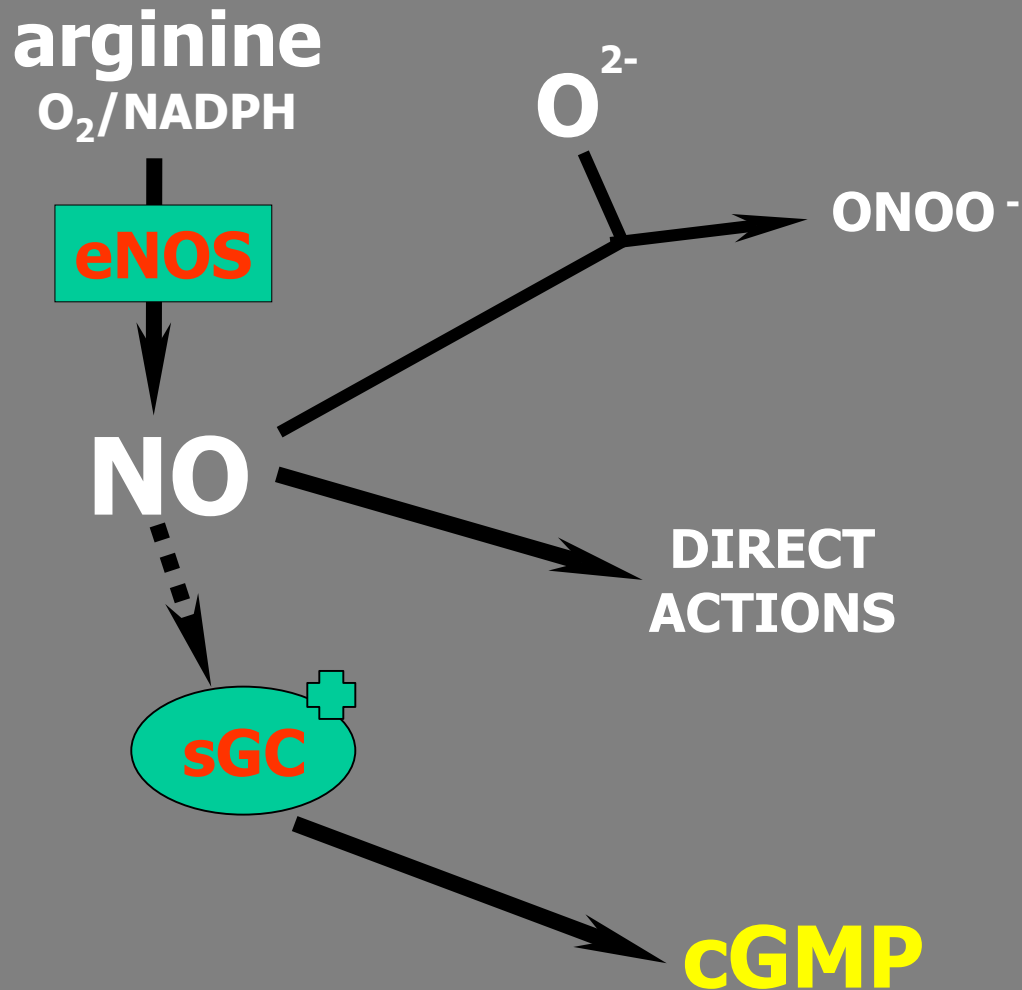




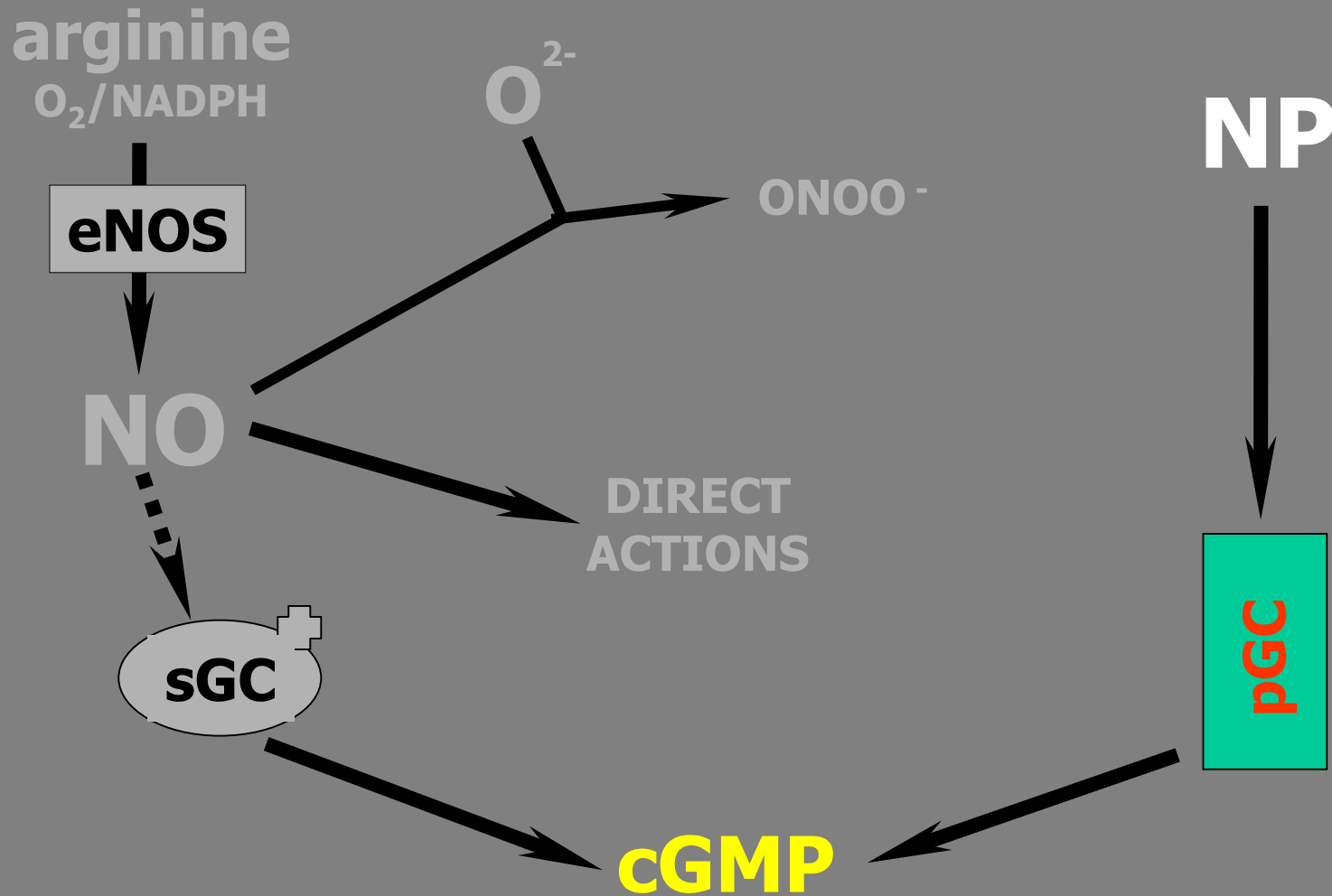
Modulation of cGMP pathway: Increasing NO production



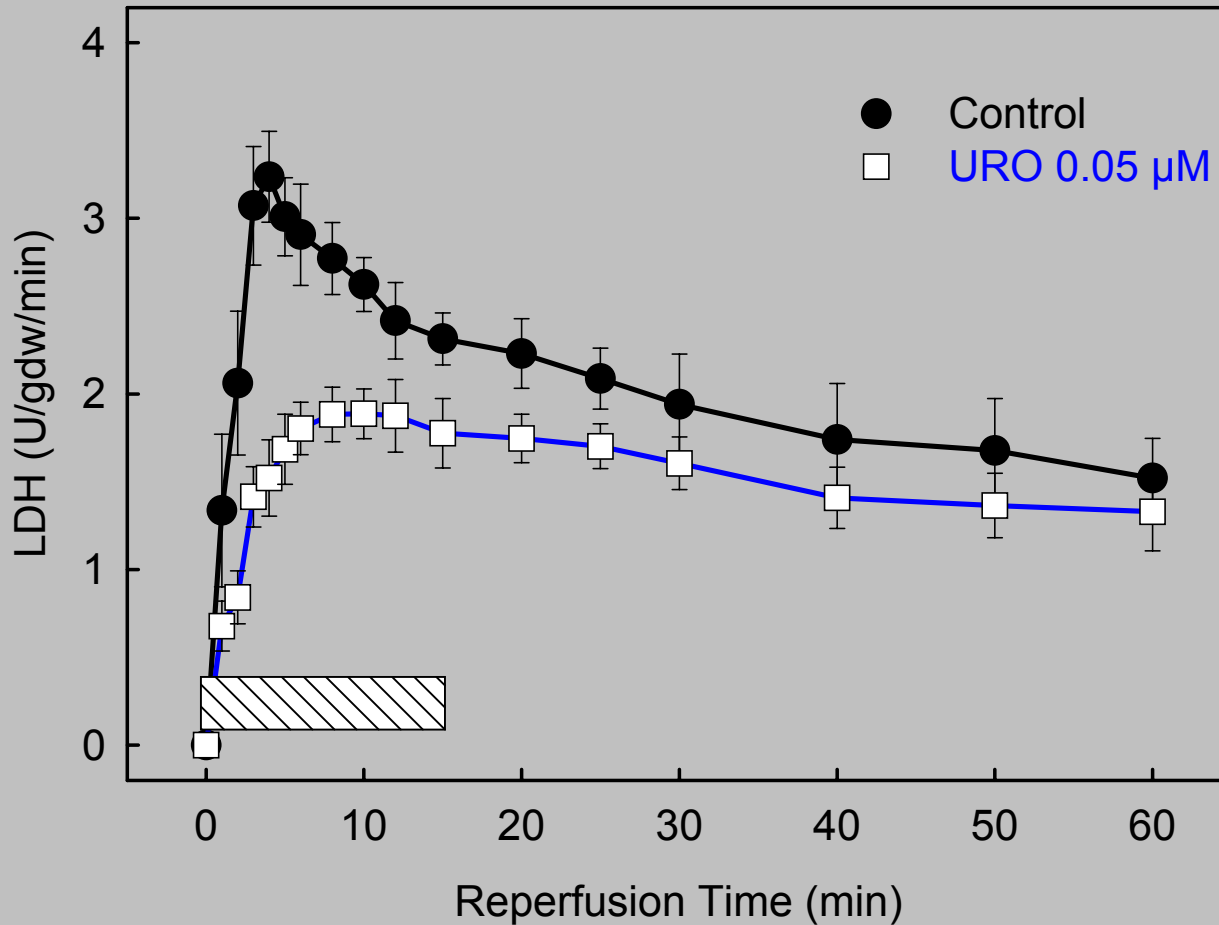
Modulation of cGMP pathway: Direct stimulation of pGC



Modulation of cGMP pathway: Direct stimulation of pGC

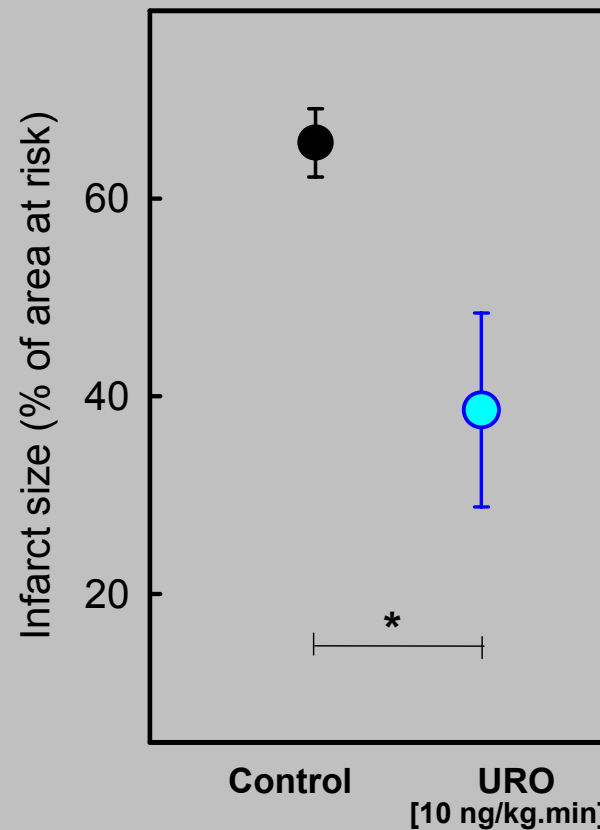


Modulation of cGMP pathway: Direct stimulation of pGC





Modulation of cGMP pathway: Direct stimulation of pGC



Padilla F et al. *Cardiovasc Res*
2001, 51: 592

Beneficial effect of cGMP: Conclusions

- **To normalize cGMP content is beneficial**
- **Excessive increase of cGMP can revert the beneficial effect**
- **Mechanism: Inhibition of hypercontracture**
- **Drugs without acute secondary effects**

cGMP pathway:

**A promising pharmacological
target to decrease
IR injury?**