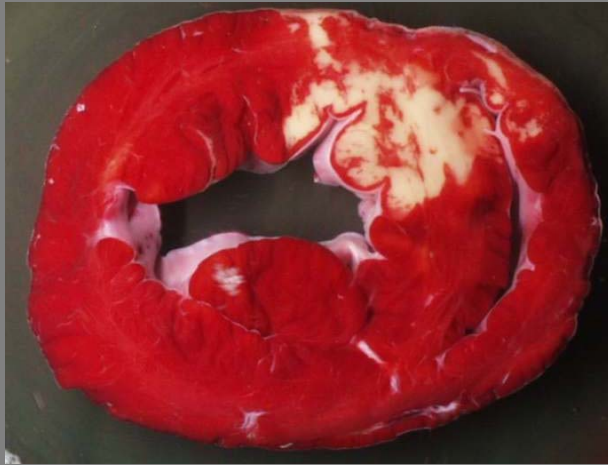


The cGMP Pathway (II)

**Changes in cGMP
signaling during
myocardial
ischemia-reperfusion**

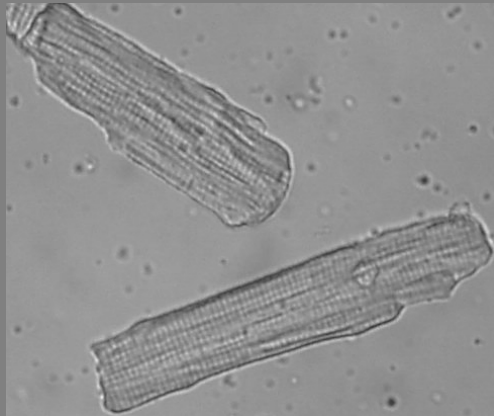
Experimental models used



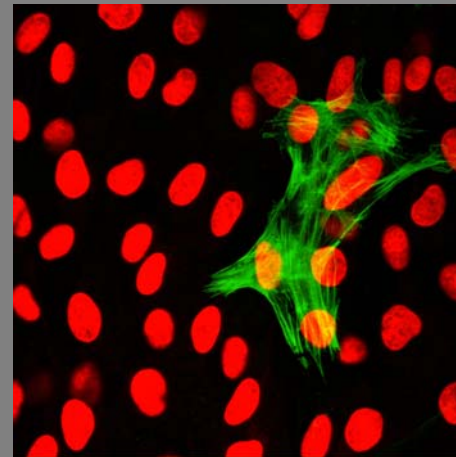
In situ pig heart



Isolated rat heart



Isolated
cardiomyocytes



Microvascular
endothelial cells

**Initial effects observed on
isolated rat heart and on
in situ pig heart**

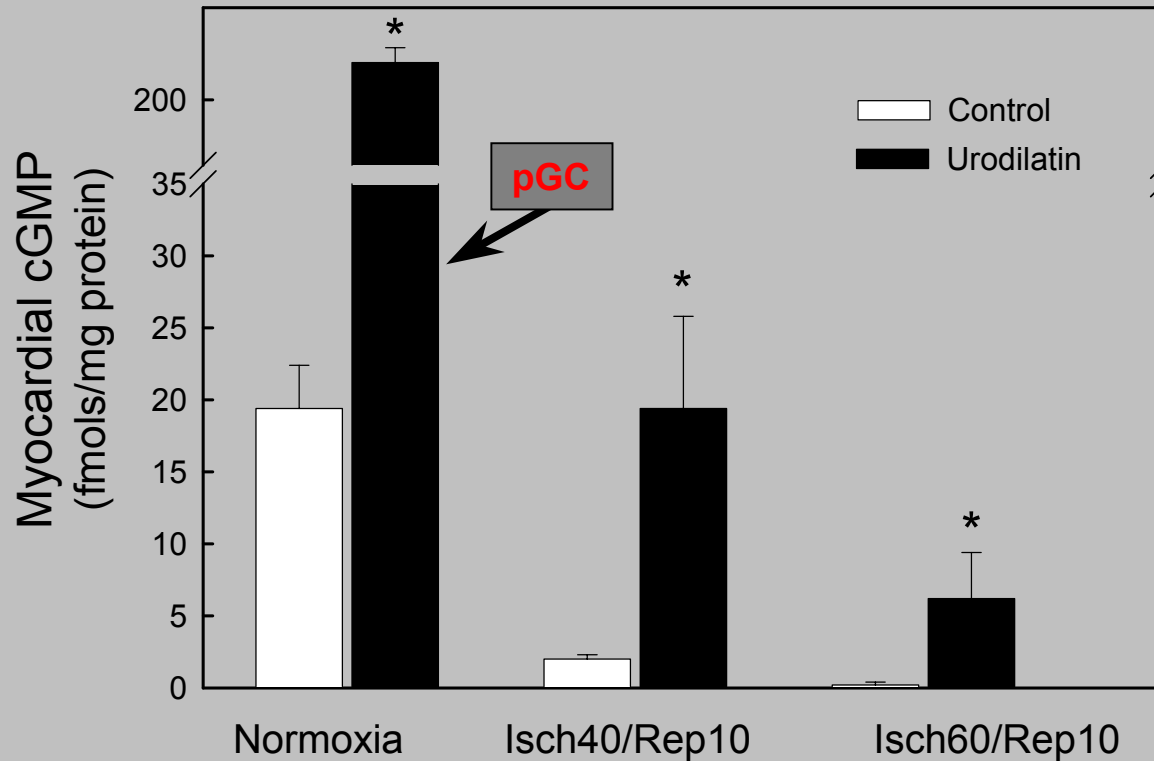
Ischemia-reperfusion protocol:

- 1) No-flow ischemia (60min) in isolated rat hearts**
- 2) LAD occlusion (48min) in *in situ* pig hearts**
- 3) Measurement of basal levels of cGMP or after heart stimulation with a natriuretic peptide (*urodilatin*)**

Decrease of cGMP concentration in reperfused myocardium



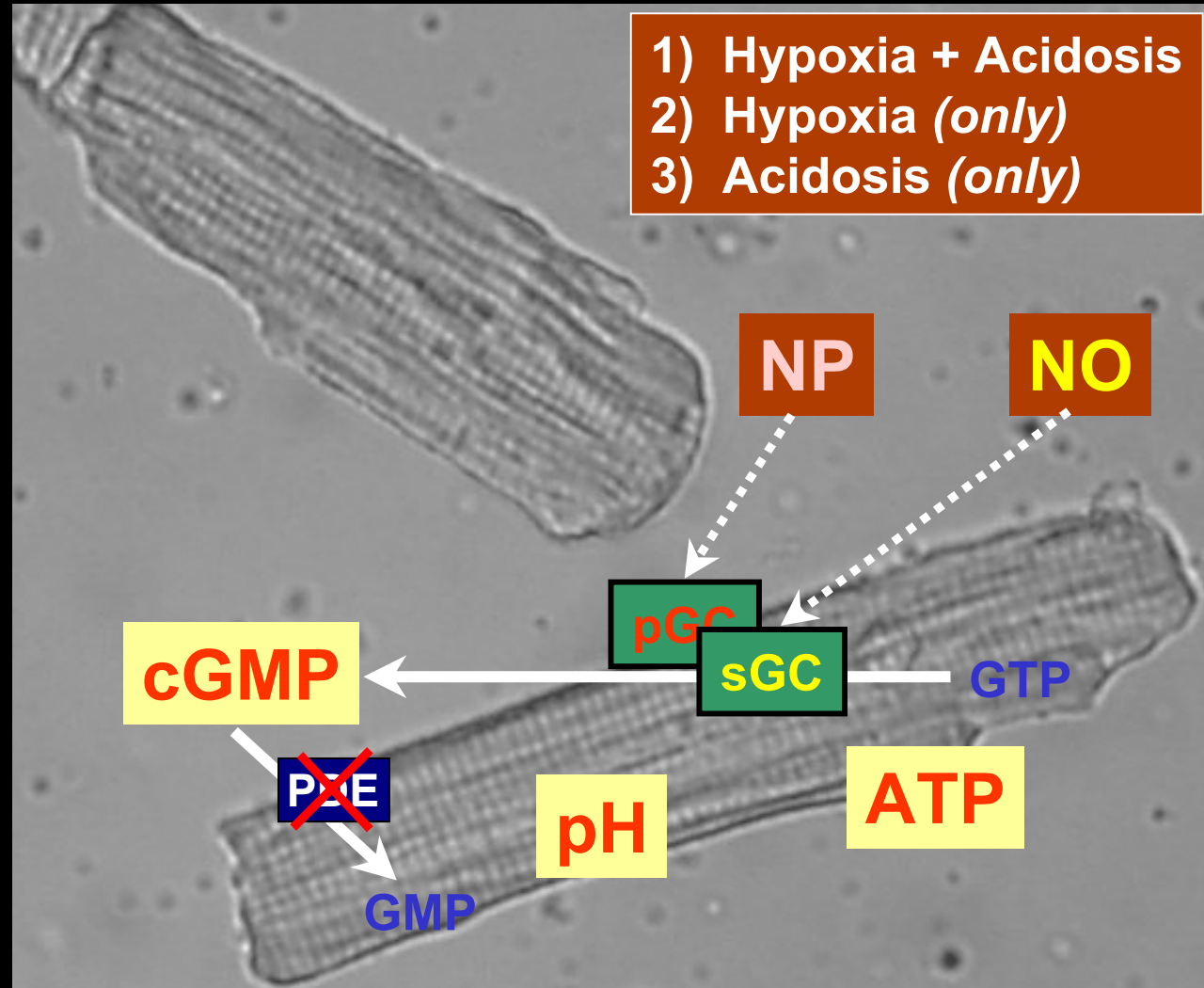
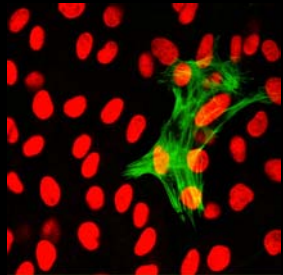
Inserte J et al. *Cardiovasc Res* 2000, 45:351



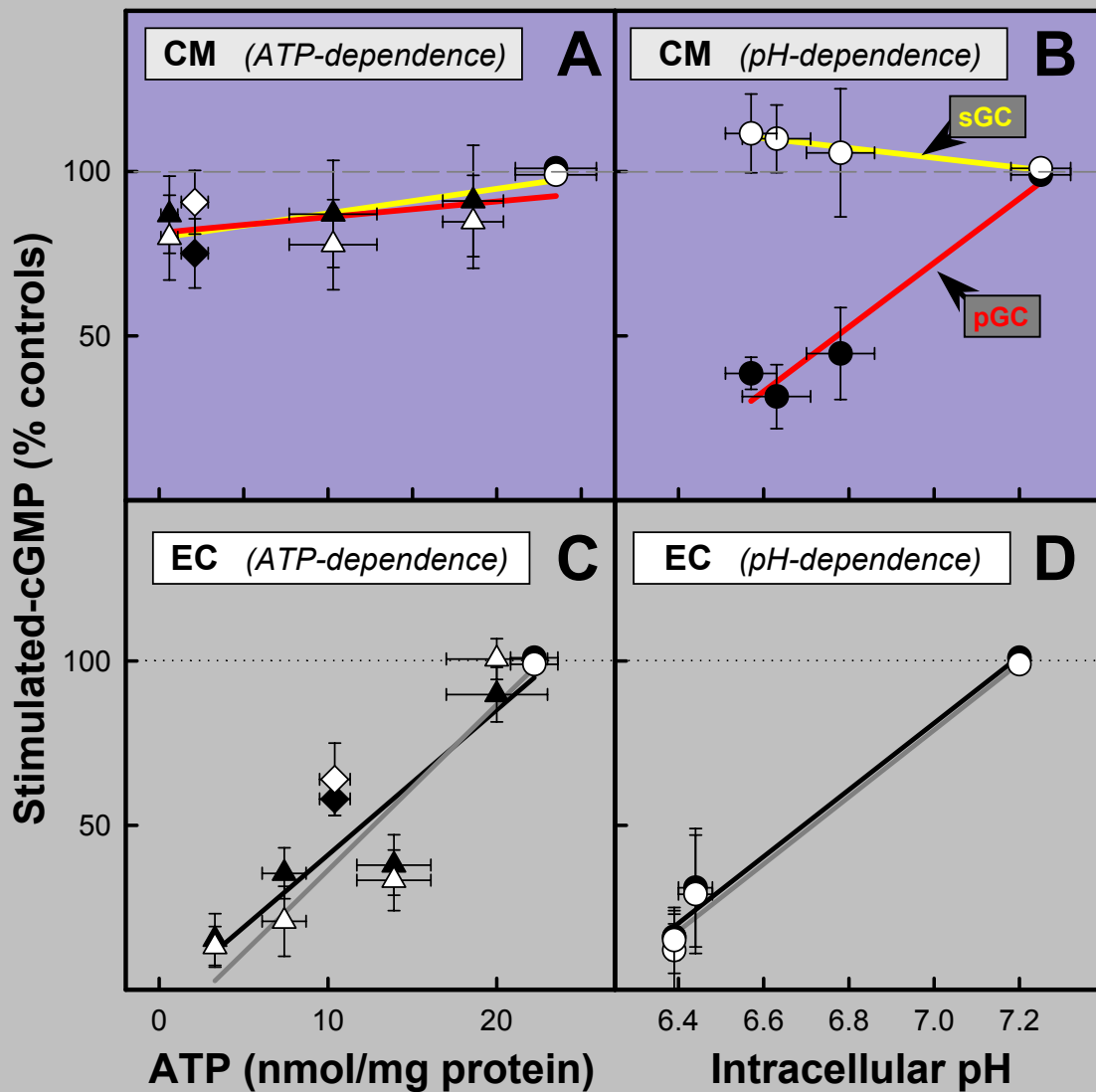
**Study of the mechanisms
responsible for this decrease:
studies on cell cultures**

We have studied:

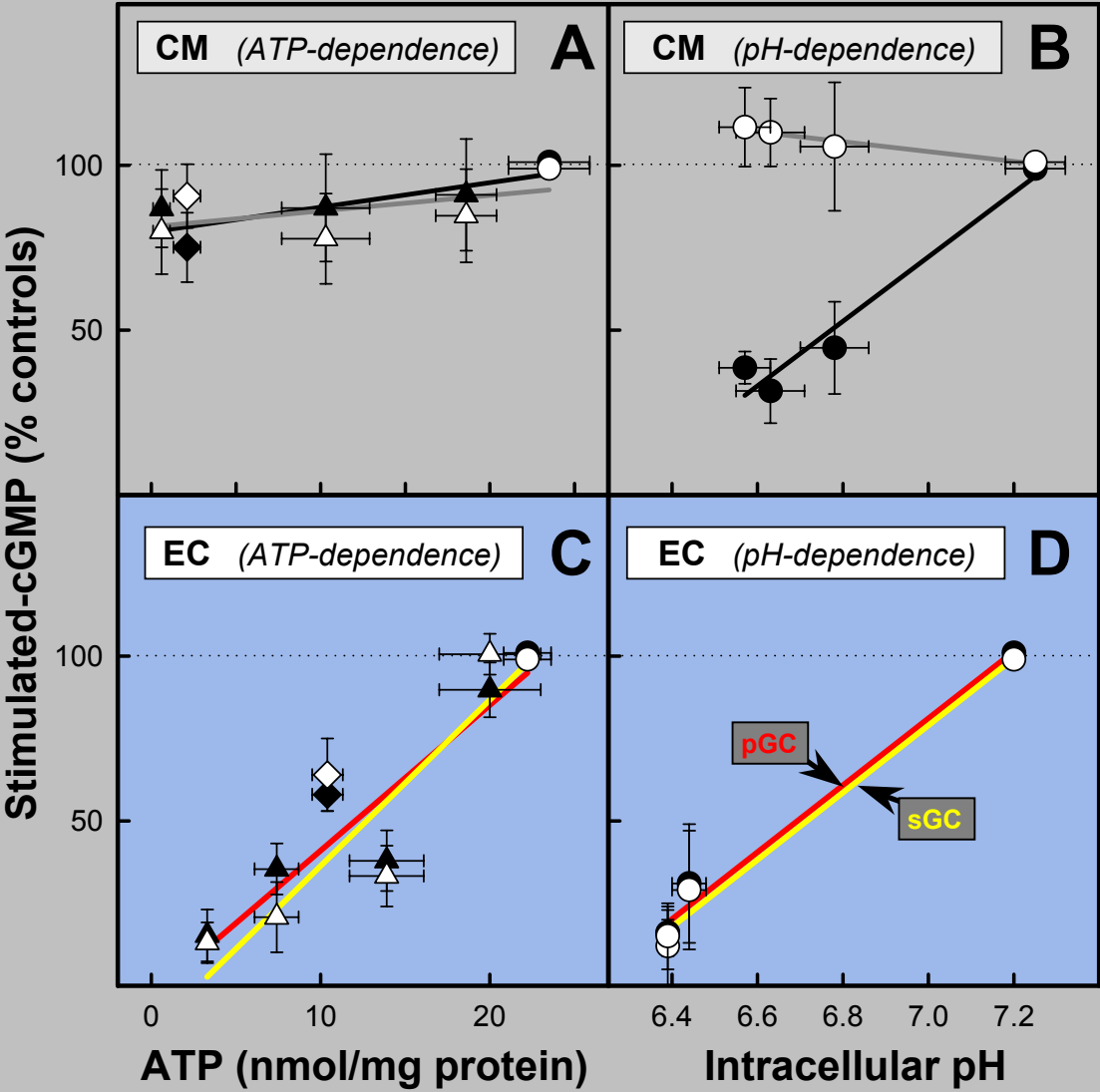
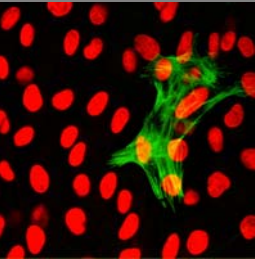
- A) Cells implicated (*cardiomyocytes/endothelial cells*)
- B) Role of ATP depletion (*hypoxia*) and acidosis
- C) Effects on both pathways of cGMP synthesis



Effect of ATP and acidosis on cGMP synthesis in cardiomyocytes



Effect of ATP and acidosis on cGMP synthesis in endothelial cells



Decrease of cGMP concentration: Conclusions

- cGMP synthesis is reduced during ischemia
- Crucial role of acidosis (*reversible effect*)
- Role of energy depletion (*partially reversible*)
- Dependence on the cell type