

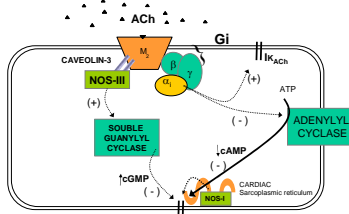


# Inhibition of Gi Causes NOS-III Dependent Attenuation of Inotropic and Chronotropic Responses to Beta-Adrenergic Stimulation in Murine Atria *In-Vitro*

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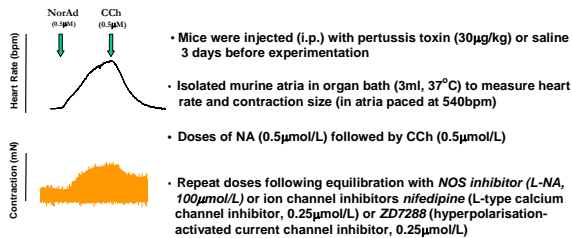
## Introduction: Role of Gi and NO In autonomic control

Inhibitory G proteins (Gi) and nitric oxide (NO) are both associated with the cardiac muscarinic receptor and implicated in the modulation of autonomic control of heart rate and contractility. We tested the hypothesis that NO inhibits  $\beta$ -adrenergic responses in the presence of Gi-blockade.



## Methods:

### Heart rate and contractile measurements in-vitro

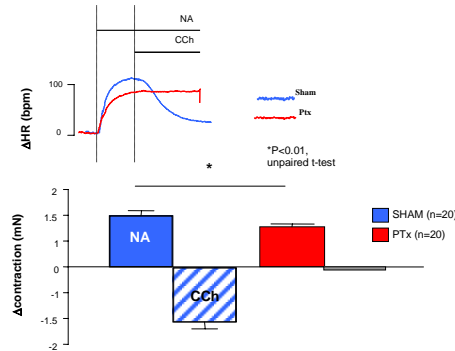


### Western Blot analysis

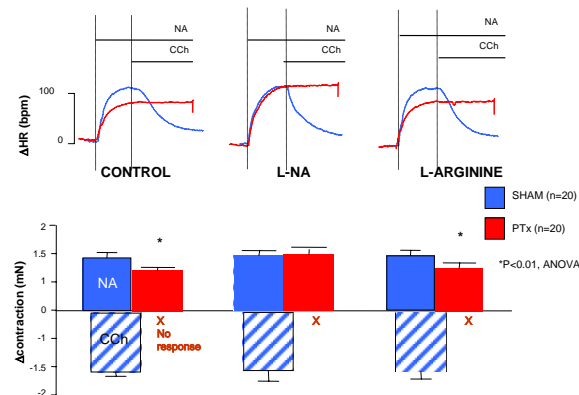
Western Blot analysis was performed using polyclonal rabbit antibodies against NOS-III, NOS-1 or  $\beta$ -actin (to control for protein loading).

## Results:

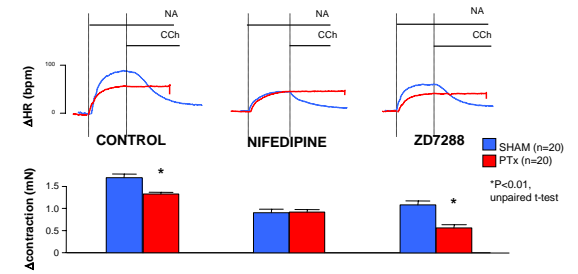
Heart rate and contractile responses to NA are attenuated in Ptx atria whilst CCh responses are abolished



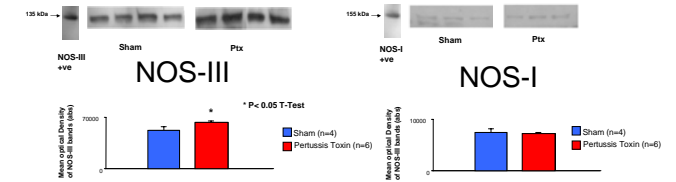
NOS inhibition normalizes responses to NA in PTx group with respect to sham, but does not affect CCh responses or sham responses



Nifedipine normalizes responses to NA in PTx group with respect to sham, but ZD7288 does not.



NOS-III expression increases in Ptx atria, but NOS-1 does not change



## CONCLUSION

- Cardiac muscarinic signalling requires intact Gi signalling for functional autonomic control (including signals mediated by NO)
- Inhibition of Gi increases atrial NOS-III expression and nifedipine-sensitivity and attenuates the response to noradrenaline by a NO-dependent mechanism

