Development of new pre-clinical model of pulmonary hypertension associated with left heart disease

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Introduction

**Heart failure (HF) and pulmonary hypertension (PH)**
- Heart failure with preserved ejection fraction (HFrEF) affects over than 50% of all patients with HF
- 50% of HFrEF culminates to pulmonary hypertension (PH) associated with poor prognosis

**Metabolic syndrome (MS) and PH**
- MS affects more than 34% of adults in the world
- Strongly associated with HFrEF (prevalence of 35%)
- Associated with PH (prevalence of 34.3%)

**MS and PH may predispose to PH**

**Lack of good preclinical model that preclude extensive investigation**
Objective

Develop a new animal model for WHO2 PH associating HFpEF and MS
Induction of HFpEF

SAB: supracoronary aortic banding
Induction of HFpEF

SAB induces HFpEF
Induction of MS

- **High fat diet (HF)**
  - Ad libidum; 9 weeks

- **Olanzapine**
  - 4mg/Kg/2 weeks; 9 weeks

- **High fat diet + olanzapine**

*References*

Panchal SK et al; *J Cardiovasc Pharmacol*, 2009

Vance L Albaugh; *Obesity*, 2009
Induction of MS

Fat accumulation

Visceral Fat

Mediastinal Fat

**Ctrl** Sham Sab+HF+Olan

- Ctrl
- Sham
- Sab+HF+Olan

- Sham + HF
- SAB + HF
- Sham + SAB + Olan
- SAB + Olan

- Sham + HF + Olan

![Image of a rat](image-url)
Induction of MS

Fat accumulation

Dyslipidaemia

Systemic hypertension

Fat/Lean (U.A.)

Visc Fat/Femur (U.A.)

Mediastinal Fat/Femur (U.A.)

TG (µg/ml)

Systolic pressure (mmHg)

- Ctrl
- Sham
- SAB
- Sham + Olan
- SAB + Olan
- Sham + HF
- SAB + HF
- Sham + HF + Olan
- SAB + HF + Olan

Values are expressed as mean ± S.E.M. *p < 0.05; **p < 0.01; ***p < 0.001; ****p < 0.0001.
Induction of MS

Fat accumulation

Dyslipidaemia

Systemic hypertension

HF + Olanzapine induces MS
MS increases incidence of PH due to left heart disease
PH severity correlate with ectopic fat accumulation
Conclusion

- We developed a new model of group 2 PH
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- We demonstrated that MS worsen PH associated with HFpEF

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- We developed a new model of group 2 PH
- We demonstrated that MS worsen PH associated with HFpEF
- We displayed that PH severity correlates with ectopic fat accumulation
Thank you