

Piezo1 Activation Reduces Coronary Flow in ex vivo Perfused Mouse Hearts

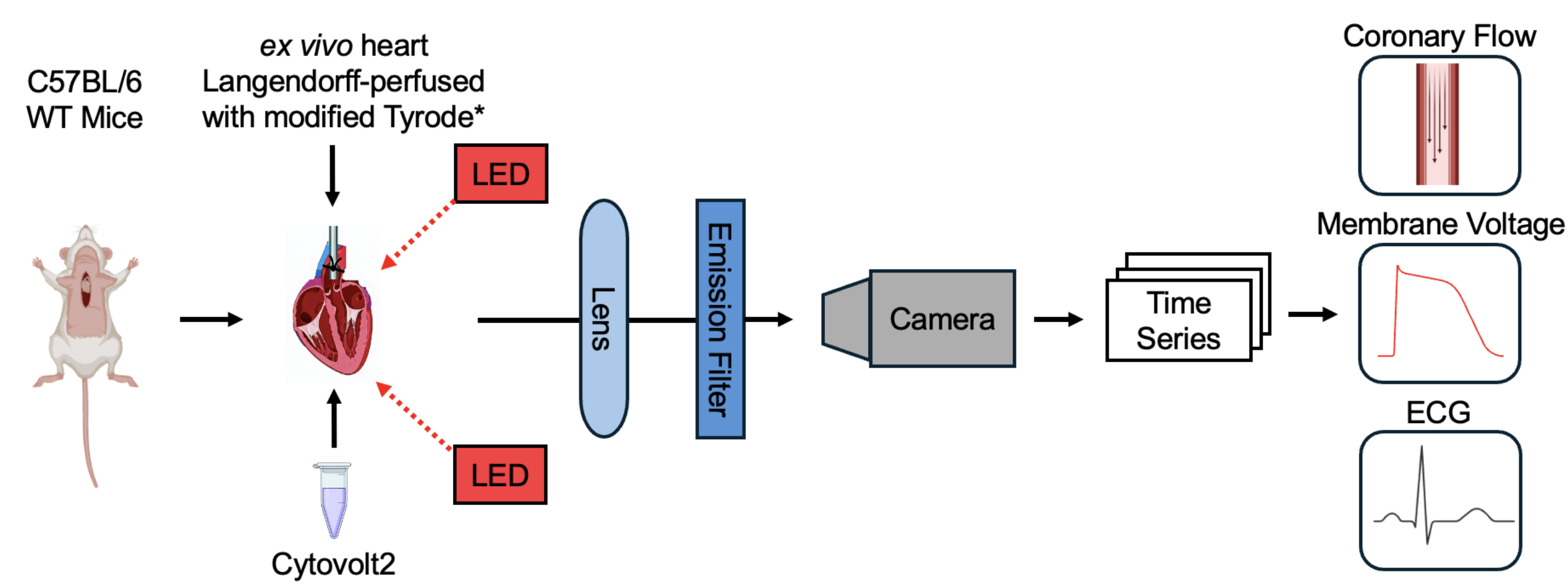
Introduction

- Normal myocardial function relies on adequate blood supply by the coronary vessels, compromised coronary flow underlies major cardiac pathologies.
- Piezo1 is expressed in vascular endothelial cells and smooth muscle cells and contributes to the regulation of vascular tone, primarily through nitric oxide-mediated vasodilation [1].
- Piezo1's role in the coronary microcirculation remains unclear.

Hypothesis: Piezo1 activation leads to dilation of coronary vessels, consistent with its established role in larger vessels.

Methods

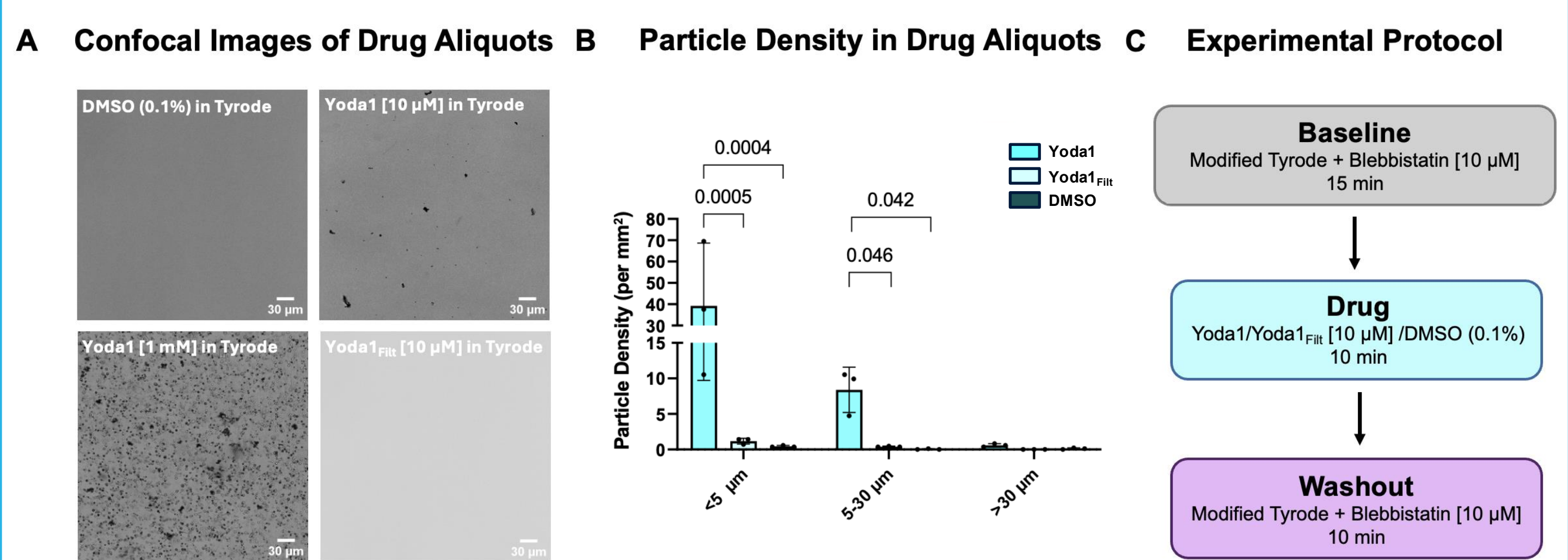
- Optical mapping: fluorescence imaging of membrane voltage



*Modified Tyrode in mmol/L: 140 NaCl; 5.4 KCl; 10 HEPES; 10 Glucose; 1.0 MgCl₂; 1.8 CaCl₂
 WT: Wild type; LED: Light Emitting Diode; ECG: Electrocardiogram

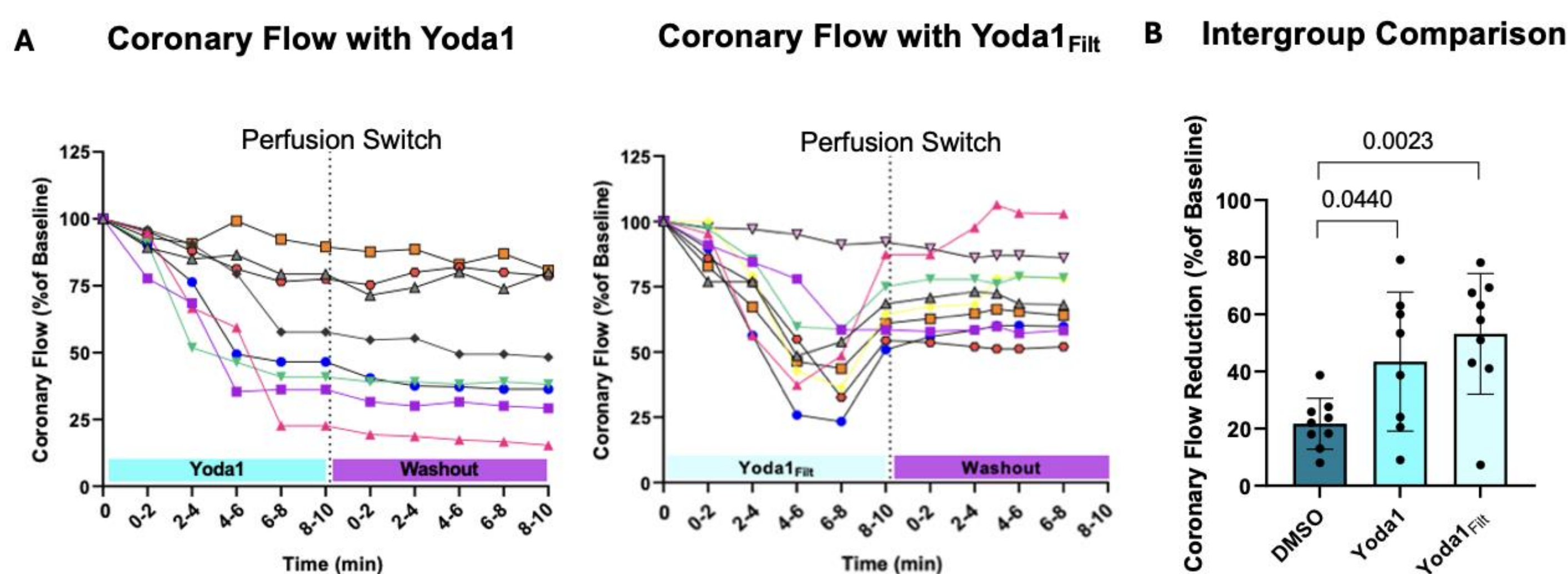
Experimental Optimisation

- Yoda1 precipitates in aqueous solutions



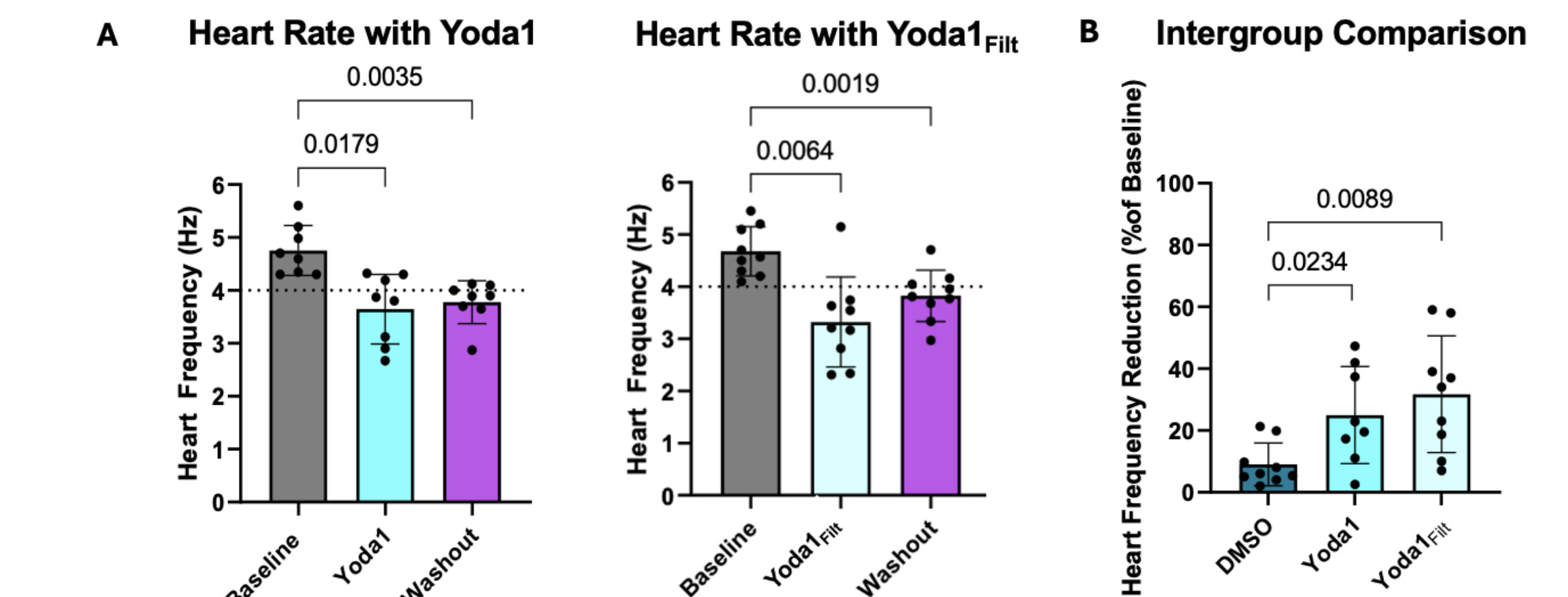
DMSO: Dimethyl sulfoxide; Yoda1_{Filt}: Yoda1 filtered through a 0.2 µm sterile filter

1. Piezo1 Activation Reduces Coronary Flow



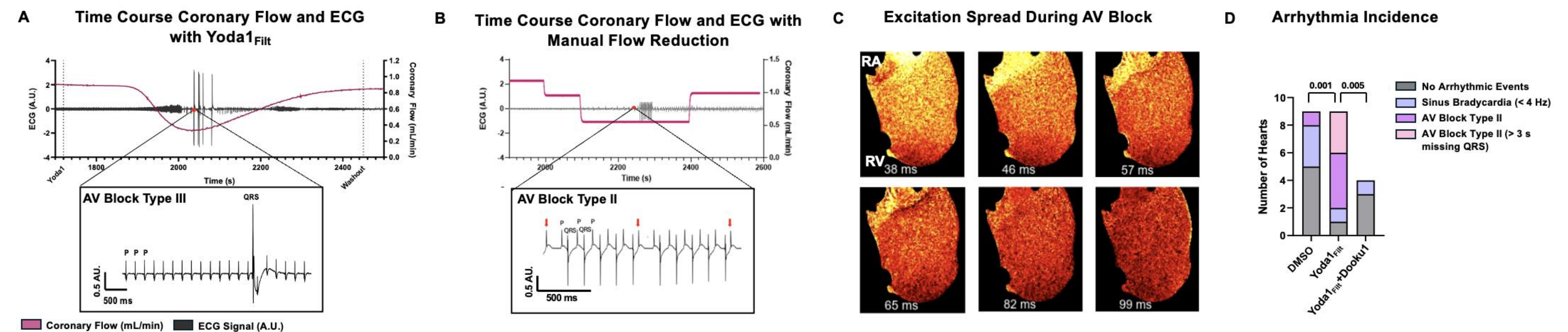
A: Mean flow averaged across 2 min intervals during perfusion with Yoda1 (n=8) and Yoda1_{Filt} (n=9) and washout.
 B: Relative flow reduction during 10 min drug perfusion. Statistical test: *Kruskal Willis with Dunn's post hoc*.

2. Piezo1 Activation Reduces Heart Rate



A: Mean heart rate averaged over 10 min throughout perfusion with Yoda1 (n=8) and Yoda1_{Filt} (n=9) and washout. Statistical test: *Friedman Anova with Dunn's post hoc*.
 B: Relative heart rate reduction during 10 min drug perfusion. Statistical test: *Friedman Anova*.

3. Piezo1 Activation Induces Arrhythmias

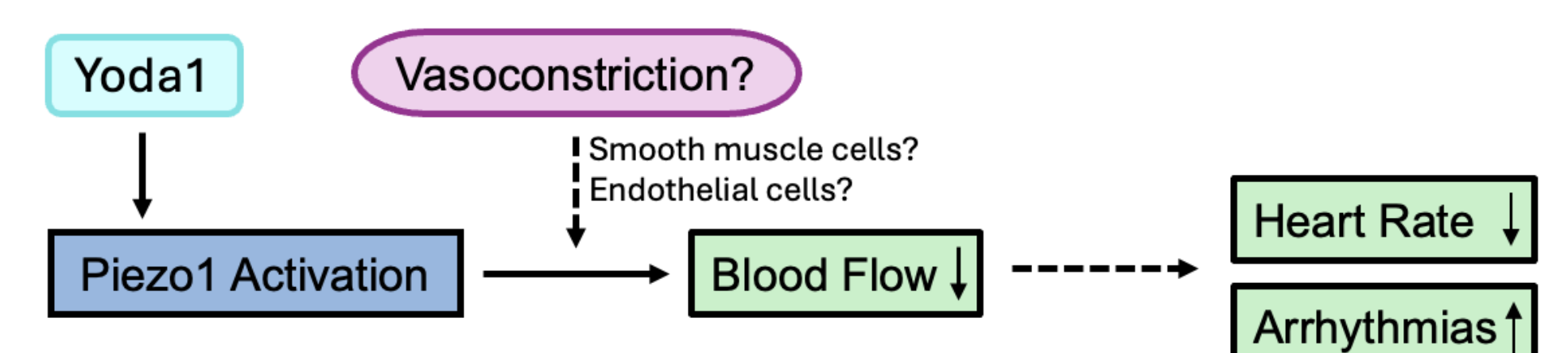


A: Coronary flow and ECG time course during Yoda1_{Filt} perfusion. AV: Atrioventricular.
 B: Coronary flow and ECG time course during manual flow reduction to ~ 50% of baseline flow.

C: Excitation wave across the myocardium during AV block. RA: Right atrium; RV: Right ventricle.
 D: Comparison of arrhythmia incidence across groups. Statistical test: *Boschloo's exact test*.

Conclusion and Outlook

- Piezo1 activation reduces coronary flow.
- **Piezo1 might induce coronary vasoconstriction?**
- Piezo1 activation induces arrhythmias, which might occur secondary to flow-induced ischaemia.
- Endothelial-specific Piezo1 knockout mice are needed to elucidate underlying mechanisms.



References

[1] Wang et al. *J Clin Invest*. 2016

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