GALA-based SOM (Somah) Protects Coronary Endothelial and Vasomotor Function following Ex Vivo Heart Perfusion

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BACKGROUND

- **Ex Vivo Heart Perfusion (EVHP)** has been developed to address paucity of donor hearts for transplantation and **enables use of organs donated after circulatory death.**
- **Endothelial dysfunction remains the hallmark of transplantation injury**, increasing the risk of Primary Graft Failure and Cardiac Allograft Vasculopathy.
- EVHP provides a platform to **mitigate coronary ischemia-reperfusion injury** (IRI); however, optimal perfusate composition has yet to be determined.
- We investigated the effects of **Somah**, a solution designed to meet energy requirements of coronary endothelium, and **STEEN**, a primary perfusate component for ex-vivo perfusion, on **coronary artery reperfusion injury.**

METHODS

In vitro:

- HCAEC were exposed to 24 hours of hypoxia (0.1% O_2) in culture medium followed by 24 hours of reoxygenation (21% O_2) in either culture medium, STEEN or Somah solutions to simulate the *ex vivo* reperfusion setting;
- ICAM-1 cellular surface expression was analyzed by flow cytometry and leukocyte adhesion by a dynamic leukocyte adhesion assay;

Ex vivo:

- Nine porcine hearts were submitted to 4 hours of EVHP on a custom-made system;
- Hearts were divided into 3 groups according to perfusate composition: Saline, STEEN, or Somah added to whole blood;
- Following EVHP, endothelial-dependent (Edep) and independent (Eind) vasorelaxation were assessed on segments of Left Anterior Descending artery using a vessel myograph.

RESULTS

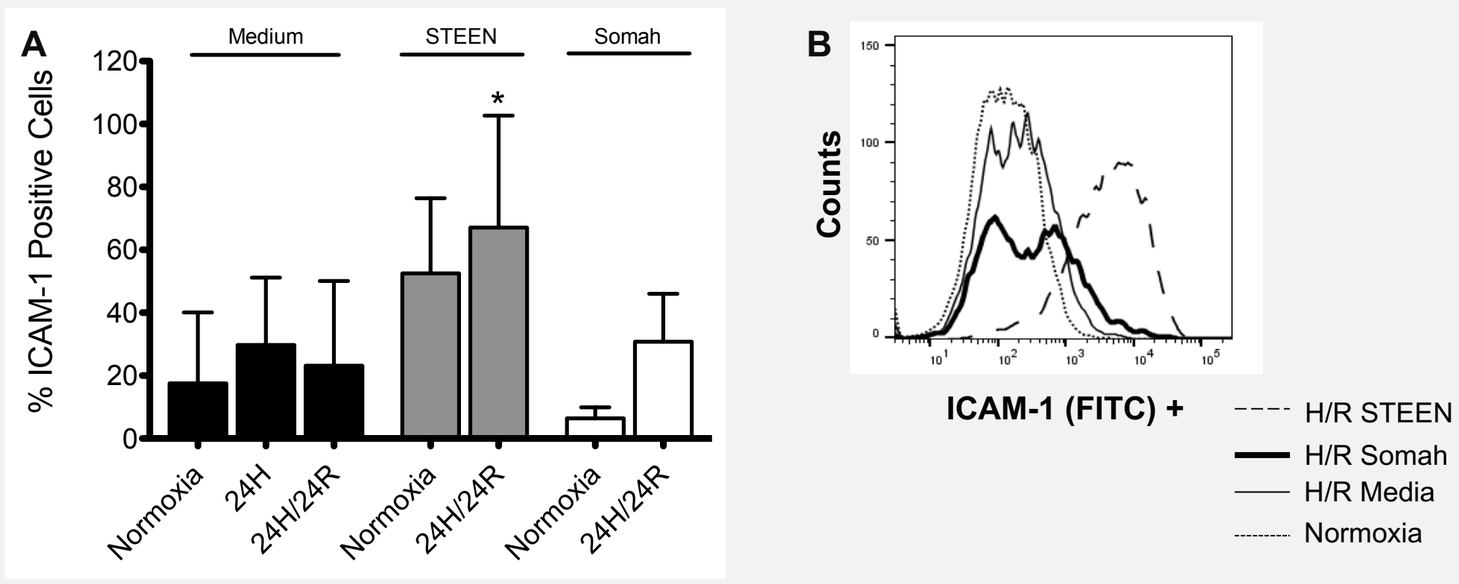


Figure 1. ICAM-1 cell surface expression. A: Surface expression of ICAM-1 was significantly increased in the STEEN group, while reoxygenation in Somah demonstrated similar levels to normoxic cells (Control: 16.6, EC Medium: 20, STEEN: 69.1, Somah: 29.6% of ICAM-1 positive cells; p<0.05; n=4/group). B: Histogram of ICAM-1 positive HCAEC.

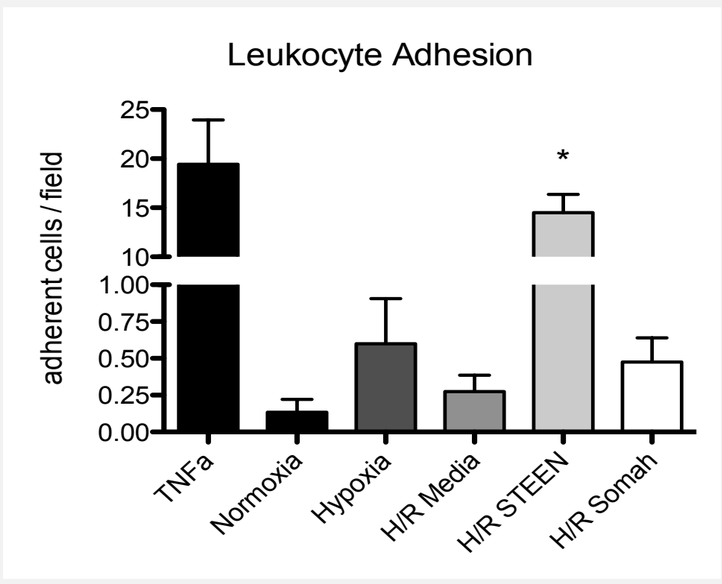
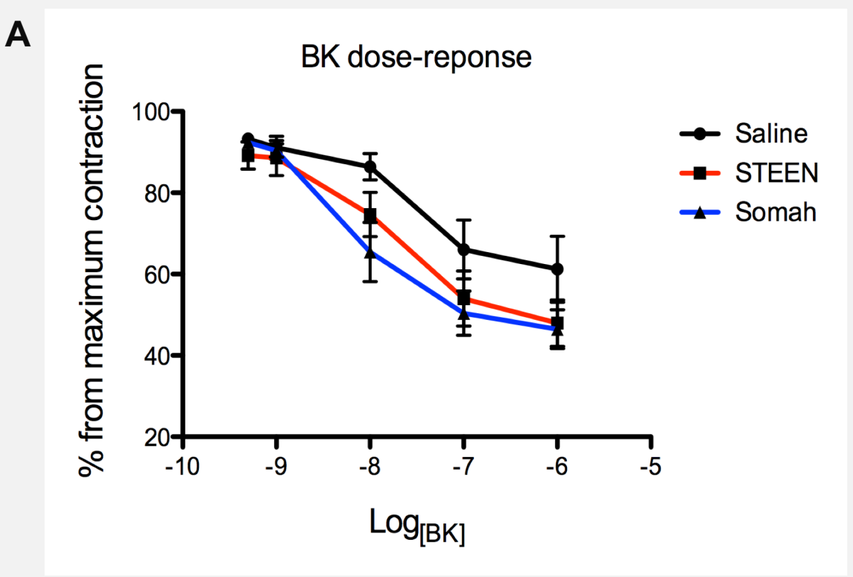
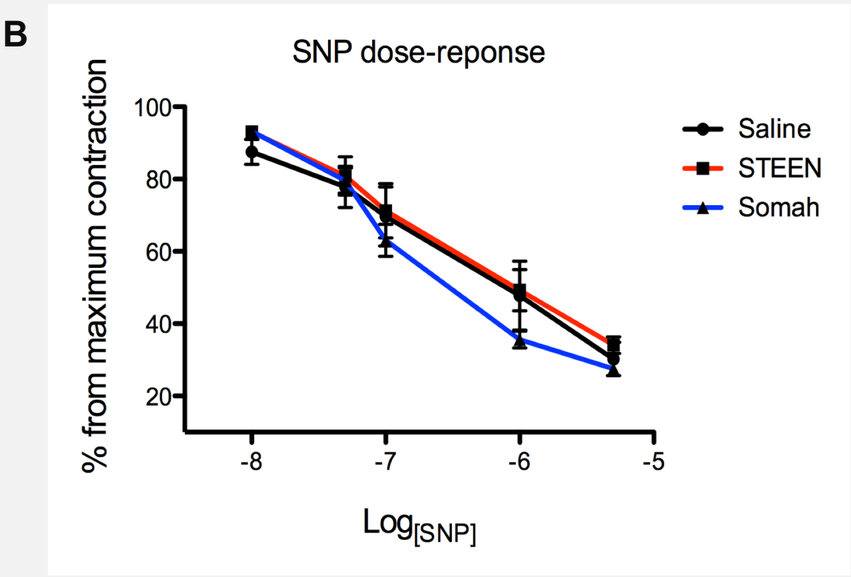


Figure 2. Leukocyte adhesion. STEEN demonstrated significant increase in leukocyte adhesion compared to Somah and culture media (Normoxia: 0.13, H/R EC Medium: 0.27, H/R STEEN: 14.5, H/R Somah: 0.47 cells/field; p<0.001; n=4/group).



	Saline	STEEN	Somah	p
$LogIC_{50}$	-5.48 ± 0.38*#	-6.38 ± 0.23#	-6.6 ± 0.19*	0.011
Emax%	40.1 ± 8	52.3 ± 6	55.1 ± 5	0.242



	Saline	STEEN	Somah	p
$LogIC_{50}$	-6.11 ± 0.15	-5.99 ± 0.11*	-6.35 ± 0.06*	0.034
Emax%	70 ± 4	65.9 ± 2*	72.6 ± 2*	0.192

Figure 3. Coronary vasomotor function. A: Endothelial-dependent (E_{dep}) vasorelaxation. B: Endothelial-independent (E_{ind}) vasorelaxation. Coronary segments from both Somah and STEEN hearts demonstrated significantly improved E_{dep} vasorelaxation compared to Saline ($LogIC_{50}$ Saline -5.5, STEEN -6.4, Somah -6.6; p=0.01). Somah group showed a significantly greater E_{ind} vasorelaxation compared to STEEN group ($LogIC_{50}$ STEEN -6, Somah -6.4; p=0.03) and a non-significant trend towards improved vasorelaxation compared to Saline group ($LogIC_{50}$ -6.1). *p<0.05; #p<0.05; n=3/group. BK: Bradykinin. SNP: Sodium Nitroprusside. Emax: maximum vasorelaxation from baseline (%). $LogIC_{50}$: dose to achieve 50% of Emax.

CONCLUSIONS

- STEEN **increased cellular adhesion molecule** expression, leading to **increased leukocyte adhesion** to endothelial cell surface**,** while Somah demonstrated **similar levels to normoxic controls;**
- Coronary segments from both Somah and STEEN hearts demonstrated **improved E_{dep} vasorelaxation** compared to Saline; Somah also showed **improved E_{ind} vasorelaxation** compared to STEEN group;
- Overall, Somah **better preserved coronary vasomotor function** following EVHP, while STEEN solution increased endothelial injury;
- While the role of STEEN solution during EVHP remains to be further investigated, the **addition of Somah** to the perfusate can **improve cardiac preservation** and limit reperfusion injury.

REFERENCES

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DISCLOSURE

I **will** discuss the off label and/or investigational use of STEEN Solution™ and GALA-based SOM (Somah).

STEEN was provided by XVIVO.

Somah was provided by Somahlution.