

# #150 Succinate Induces Relaxation of Murine

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## BACKGROUND

Succinate, an intermediate of glucose metabolism, and its GPR91 receptor have been implicated in different aspects of metabolic syndrome. In turn, metabolic syndrome is associated with impaired bladder function. We have previously shown that chronic administration of succinate to a rodent animal model compromises bladder morphology and function (Velasquez Flores, Mossa et al. 2018). Our aim is to investigate the role of succinate and its receptor in the bladder in acute settings.

## RESULTS

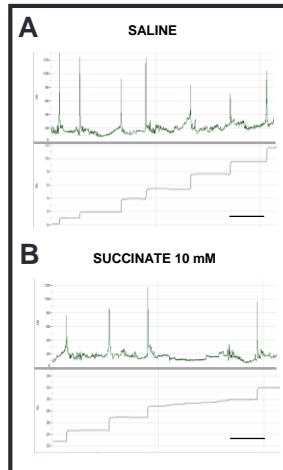
### Relaxation of rat bladder by succinate in cystometry

Table 1. Conscious cystometry performed in rats with saline followed by succinate 10 mM instillation.

Parameter	Saline	Succ 10 mM
ICI (s)	601.3 ± 77.8	829.0 ± 183.9
BCap (ml)	1.64 ± 0.21	2.16 ± 0.41
MV (ml)	1.74 ± 0.27	2.23 ± 0.46
BCom (ml cmH <sub>2</sub> O <sup>-1</sup> )	0.067 ± 0.0127	0.105 ± 0.009 *

Values expressed as mean ± SEM. \**P*<0.05. Paired *t*-tests comparing cystometry parameters between saline and succinate infusion.

Figure 1. Representative tracings of rat cystometry. Rat bladder infused with saline (A) followed by 10 mM succinate (B). Top panel shows bladder pressure. Bottom panel shows micturition volume. Scale bar = 10 min.



### Relaxation of bladder by succinate present in C57 mice, but not in GPR91 KO mice

Table 2. Conscious cystometry performed in C57 and GPR91 KO mice with saline followed by succinate 10 mM instillation.

Parameter	Strain	Saline	Succ 10 mM
ICI (s)	C57	453.8 ± 85.0	528.3 ± 88.7 **
	GPR91 -/-	277.5 ± 69.6	242.3 ± 58.0
BCap (ml)	C57	0.23 ± 0.04	0.26 ± 0.04 **
	GPR91 -/-	0.14 ± 0.03	0.12 ± 0.03
MV (ml)	C57	0.21 ± 0.05	0.27 ± 0.05 **
	GPR91 -/-	0.11 ± 0.02 #	0.10 ± 0.01
BCom (ml cmH <sub>2</sub> O <sup>-1</sup> )	C57	0.0084 ± 0.0009	0.0098 ± 0.0012
	GPR91 -/-	0.0052 ± 0.0008	0.0054 ± 0.0009

Values expressed as mean ± SEM. \**P*<0.05, \*\**P*<0.01; Paired *t*-test comparing cystometry parameters between saline and succinate infusion. #*P*<0.05; unpaired *t*-test comparing C57 and KO mice.

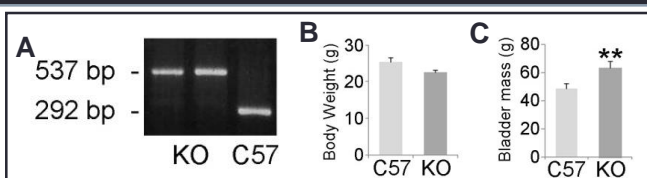


Figure 2. (A) RT-PCR confirms expression of the GPR91 in bladders of C57 mice, but not in KO mice. (B) Body and (C) bladder weight of C57 and KO mice. \*\**P*<0.01; unpaired *t*-test.

## METHODS

Conscious cystometry performed on Sprague-Dawley (SD) rats. ICI = intercontraction interval; BCap = bladder capacity; MV = micturition volume; BCom = bladder compliance.

- 1-hour infusion of saline followed by a 1-hour infusion of succinate (10 mM).

Bladders were collected from other SD rats and used for contractility assessment

- Kept intact or urothelium-stripped.

Stimulated with 1 μM carbachol and tested with increasing concentrations of succinate (1 – 100 mM).

- Repeated on C57BL/6 mice and GPR91 knockout (KO) mice.

Mice bladders were examined using the Masson's trichrome stain.

## RESULTS

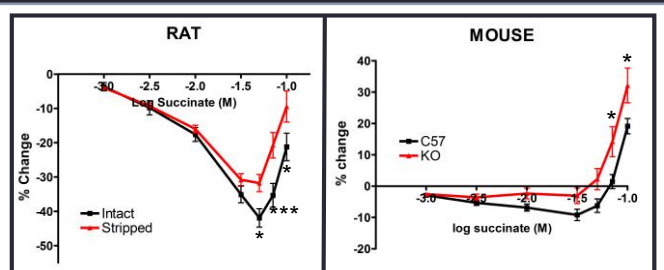


Figure 3. Succinate relaxation of bladder strips in SD rats and C57 and GPR91 KO after stimulation with 1 μM succinate. \**P*<0.05, \*\*\**P*<0.001; two-way ANOVA with Bonferroni post-hoc test to compare the differences in detrusor strips at each succinate concentration.

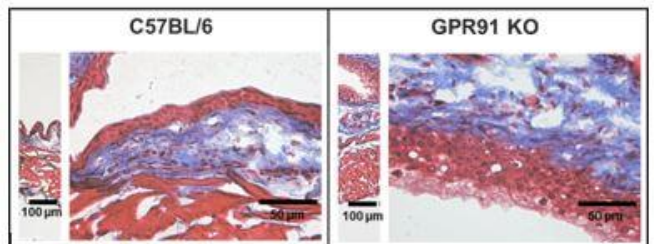


Figure 4. Masson's trichrome stain of C57 and KO mice. Quantitative analysis showed a relatively thicker urothelium and lamina propria in KO bladders compared to C57 bladders.

## CONCLUSIONS

- Direct instillation of succinate to the bladder leads to a relaxation of bladder that is mediated by the GPR91 receptor.

- Isolated detrusor strips from rats relax in the presence of succinate; this relaxation is weaker in the absence of the urothelium.

- In mice detrusor strips, the presence of the succinate receptor allows for a slight relaxation response to succinate.

- GPR91 is not only involved in relaxation response to succinate but also in the normal development of the mouse bladder.

## REFERENCES

Velasquez Flores, M., Mossa, A. H., Cammisotto, P., & Campeau, L. (2018). Succinate decreases bladder function in a rat model associated with metabolic syndrome. *Neurourology and urodynamics*.