

**The small molecule *Chicago Sky Blue* promotes heart repair following myocardial infarction in mice**

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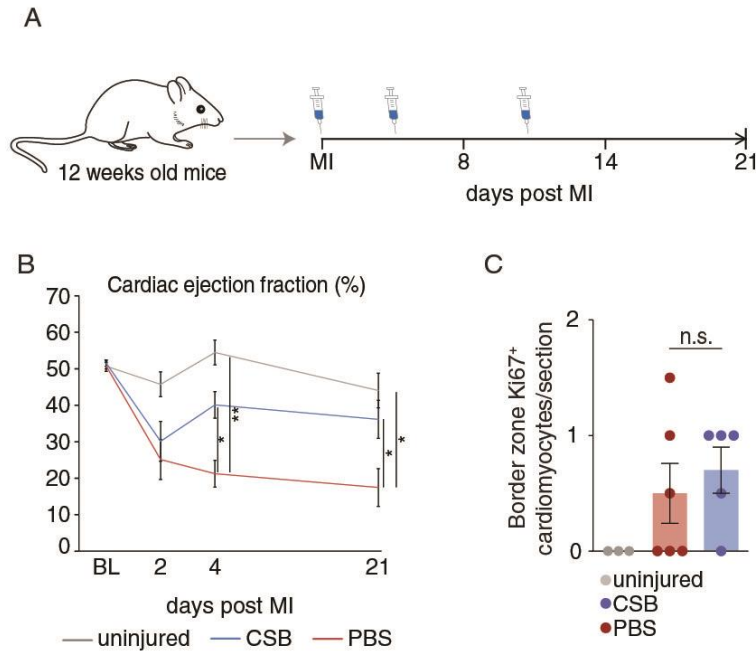
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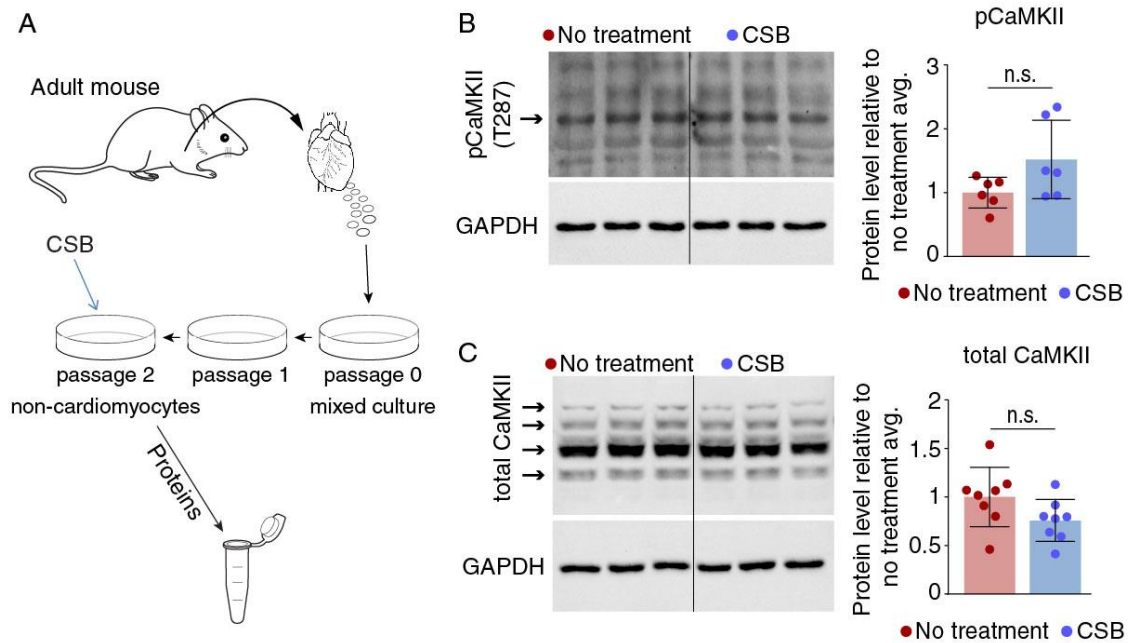
## Supplemental data

### Supplemental Figure 1.



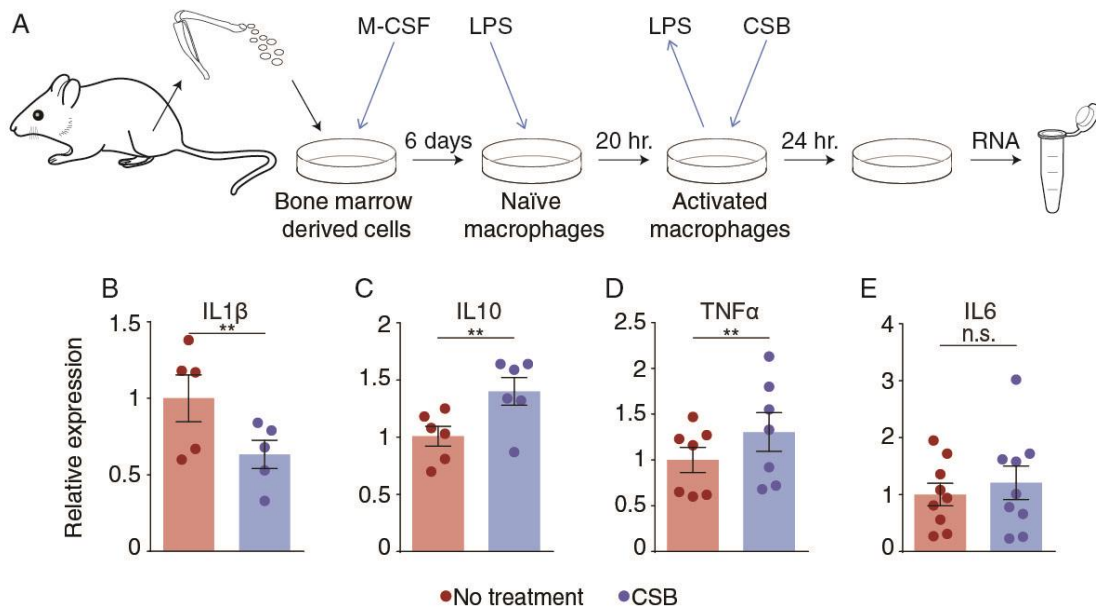
**Supplemental Figure 1. CSB improves cardiac function of adult mice following MI without inducing cardiomyocyte proliferation - additional validation.** (A) Schematic representation of the MI experiment timeline. (B) Cardiac ejection fraction of uninjured mice (n=4), PBS treated mice (n=5) and CSB treated mice (n=10) up to 21 days post MI measured by *Vevo 770* (*VisualSonics*) echocardiography system (mean  $\pm$  S.E.M, one-way ANOVA and Dunnett's post-hoc test). (C) Number of Ki67<sup>+</sup> cardiomyocytes per section in the heart of uninjured adult mice (n=3) or in the border zone of PBS treated (n=6) or CSB treated (n=5) adult mice 8 days post MI (mean  $\pm$  S.E.M, one-way ANOVA and Tukey's post-hoc test,). Hearts were sectioned transversely and border zone was defined as 0-400  $\mu$ m from injured zone. For all panels: \*p<0.05, \*\*p<0.01, n.s.- not significant.

**Supplemental Figure 2.**



**Supplemental Figure 2. CSB does not decrease total-CaMKII or phospho-CaMKII protein level in non-cardiomyocyte cells.** (A) Illustration of experimental scheme. Cardiac cells were isolated from adult mice and were plated *in vitro*. After two passages during 8 days the culture did not contain cardiomyocytes. The cells were incubated for 4 days with CSB 10  $\mu$ M and proteins were purified for analysis. (B and C) Western blot images and quantification of total-CaMKII (C) and phospho-CaMKII (pCaMKII) (B) protein level in non-cardiomyocyte cells that were incubated for 4 days with or without CSB. For quantification in panel B: n=6 from 2 separate isolations. For quantification in panel C: n=8 from 3 separate isolations. For all panels: mean  $\pm$  STDEV, unpaired two-tailed Student's *t*-test, n.s.-not significant.

### Supplemental Figure 3.



### Supplemental Figure 3. CSB modulates inflammatory gene expression in macrophage culture.

(A) Schematic representation of the experiment procedure. Bone marrow cells were differentiated to macrophages (BMDM) using macrophage colony-stimulating factor (M-CSF) and were activated with lipopolysaccharide (LPS). The activated macrophages were treated with CSB and RNA was purified. (B-E) Inflammatory and anti-inflammatory gene expression in BMDM. Expression is relative to no-treatment average. For each treatment: IL1 $\beta$ : n=5, IL10: n=6, TNF $\alpha$ : n=7, IL6: n=9, data are mean  $\pm$  S.E.M. All genes were tested on cells from 3 separate isolations. Statistical analysis was performed using paired two-tailed Student's *t*-test; \*\*p<0.01, n.s.-not significant.