

Supplementary Information

Supplementary Data 1. Raw dataset presented in the study.

All data in the study are included in Supplementary Data 1.xlsx.

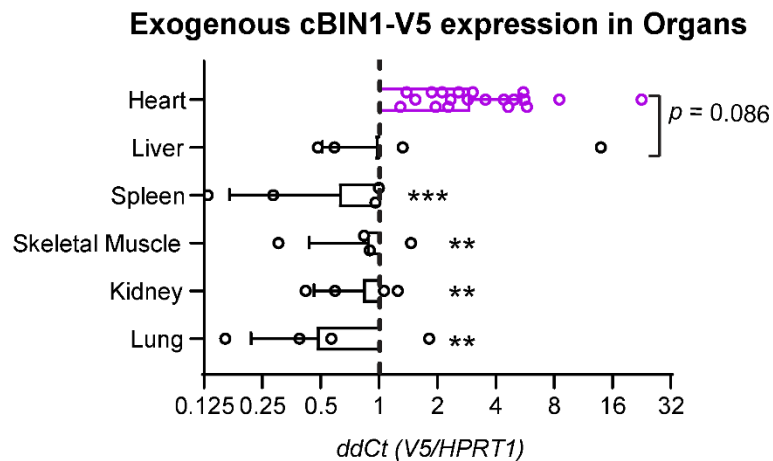
Supplementary Figure 1. AAV9 transduced exogenous cBIN1-V5 gene expression across different organ tissues.

Supplementary Figure 2. Histopathology analysis of other organ tissues in heart failure minipigs treated with AAV9-cBIN1.

Supplementary Figure 3. Full western blots for cBIN1 and GAPDH used in Figure 3b.

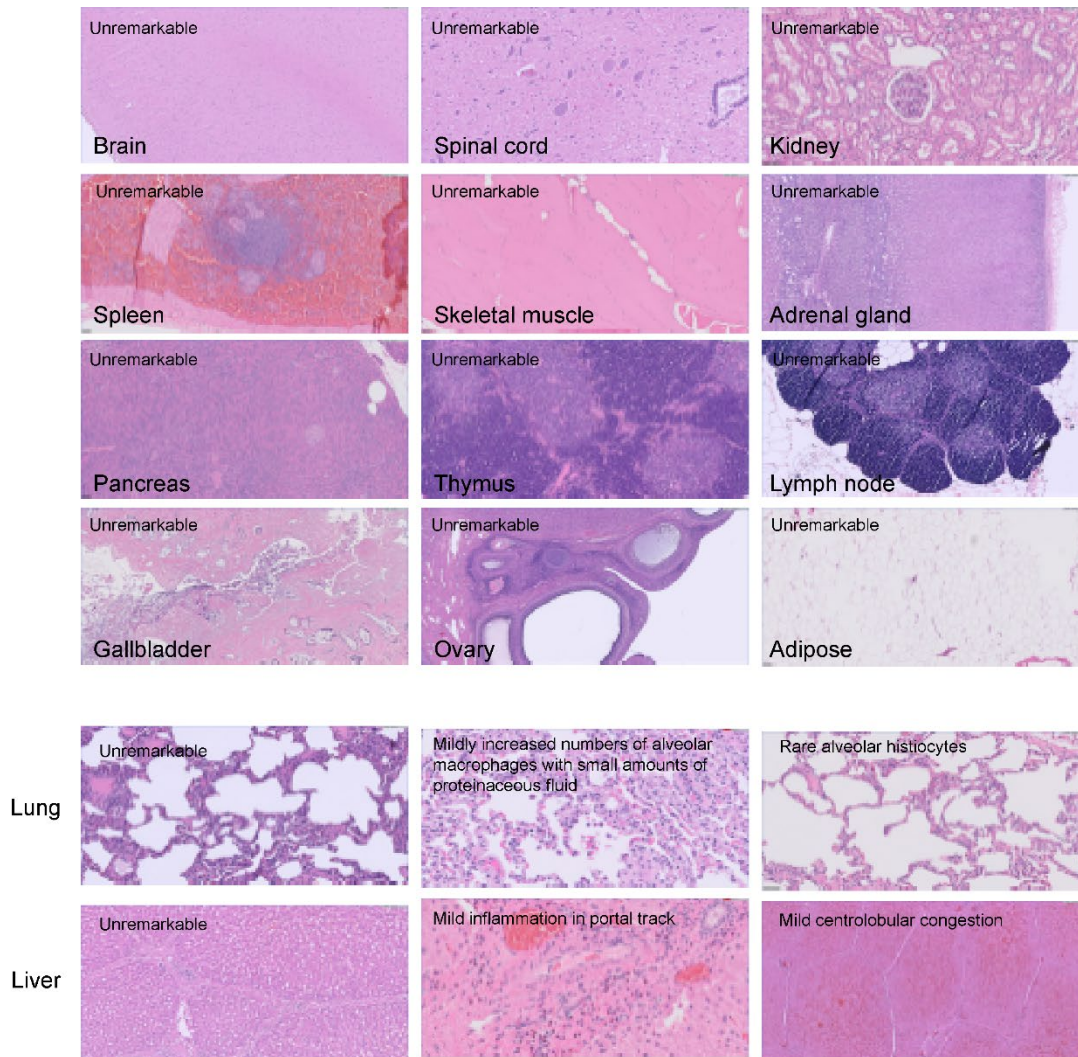
Supplementary Table 1. The ARRIVE Essential 10: Compliance Questionnaire.

Supplementary Figure 1. AAV9 transduced exogenous cBIN1-V5 gene expression across different organ tissues.



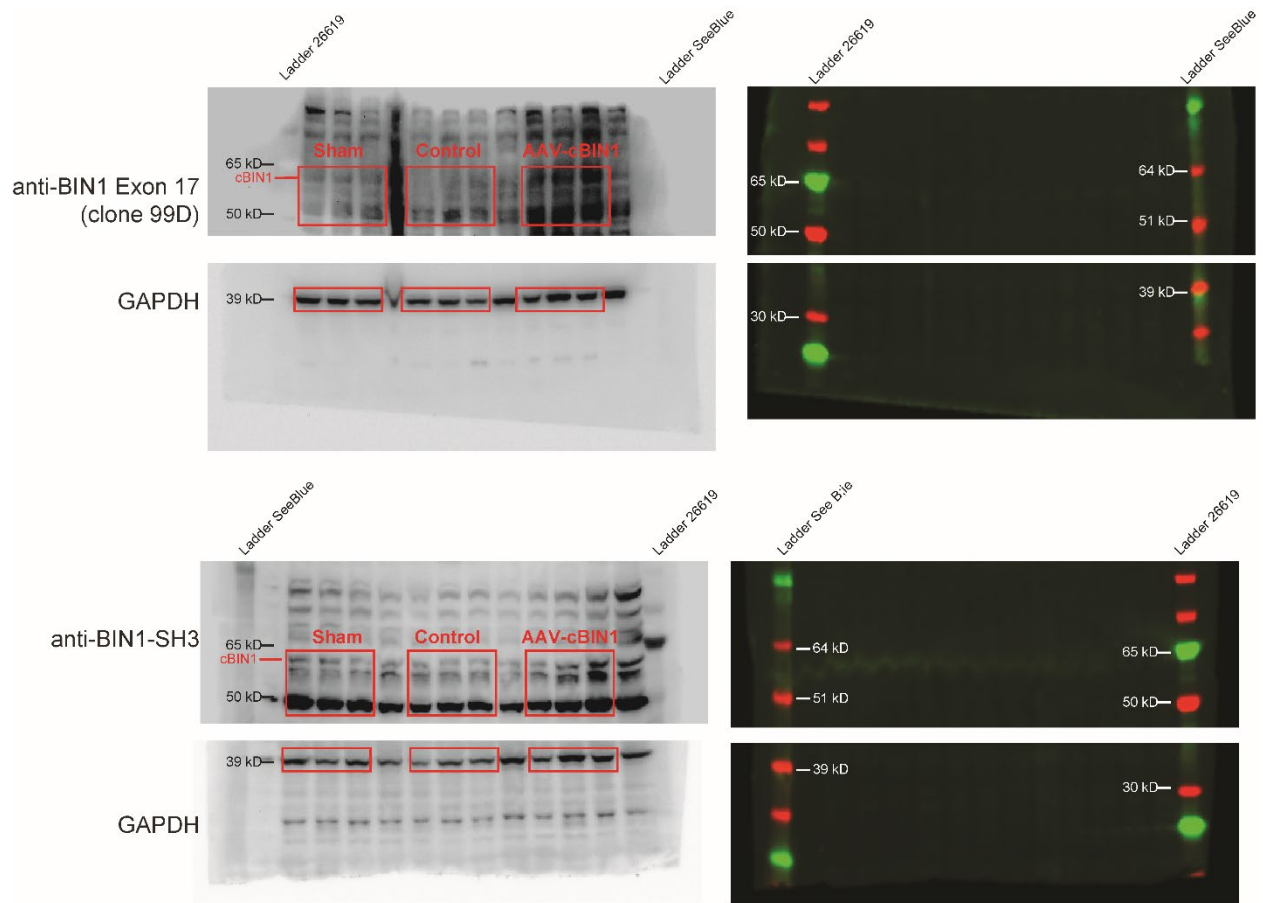
Supplementary Figure 1. AAV9 transduced exogenous cBIN1-V5 gene expression across different organ tissues. Exogenous cBIN1-V5 transgene expression (RT-qPCR detected *V5/HPRT1* and expressed as $ddCt$ from PBS controls, dotted line marks $ddCt=1$ of the PBS controls) in minipig tissues from heart, liver, spleen, skeletal muscle, kidney, and lung (N=4 animals). Data are presented as mean $\pm$ SEM. Kruskal-Wallis test followed by Fisher's LSD test was used for comparison between different organs and heart. **, *** indicates $p < 0.01$, 0.001 , respectively, for comparison vs. heart.

Supplementary Figure 2. Histopathology analysis of other organ tissues in heart failure minipigs treated with AAV9-cBIN1.



Supplementary Figure 2. Histopathology analysis of other organ tissues in heart failure minipigs treated with AAV9-cBIN1. Histopathology analysis by specialized veterinary pathologists identified no abnormality (unremarkable H&E images) in brain, spinal cord, kidney, spleen, skeletal muscle, adrenal gland, pancreas, thymus, lymph node, gallbladder, ovary, and adipose from minipigs at 6 months after AAV9-cBIN1 treatment. Liver and lung histopathology revealed no abnormality or mild inflammation / congestion related to improved heart failure in minipigs post AAV9-cBIN1 treatment.

Supplementary Figure 3. Full western blots for cBIN1 and GAPDH used in Figure 3b.



Supplementary Figure 3. Full western blots for cBIN1 and GAPDH used in Figure 3b.

Left top two blots: mouse anti-BIN1-exon 17 blot (clone 99D) with the corresponding GAPDH blot from the same gel; left bottom two blots: rabbit anti-BIN1-SH3 blot with the corresponding GAPDH blot from the same gel. Boxed areas: representative 3 lanes from each group included in Figure 3b. Right: corresponding fluorescent molecular markers of the loaded ladders.

Supplementary Table 1. The ARRIVE Essential 10: Compliance Questionnaire*

Item		Question(s)	Answers
1	Study Design	Are all experimental and control groups clearly identified?	☒ Yes, for at least one experiment ☐ No
		Is the experimental unit (e.g. an animal, litter or cage of animals) clearly identified?	☒ Yes, for at least one experiment ☐ No
2	Sample Size	Is the exact number of experimental units in each group at the start of the study provided (e.g. in the format 'n=')?	☒ Yes, for at least one experiment ☐ No
		Is the method by which the sample size was chosen explained?	☒ Yes, for at least one experiment ☐ No
3	Inclusion & Exclusion Criteria	Are the criteria used for including and excluding animal, experimental units, or data points provided?	☒ Yes, for at least one experiment ☐ No
		Are any exclusions of animals, experimental units, or data points reported, or is there a statement indicating that there were no exclusions?	☒ Yes, for at least one analysis ☐ No
4	Randomization	Is the method by which experimental units were allocated to control and treatment groups described?	☒ Yes, for at least one experiment ☐ No
5	Blinding	Is it clear whether researchers were aware of, or blinded to, the group allocation at any stage of the experiment or data analysis?	☐ Yes, for at least one experiment ☒ No
6	Outcome Measures	For all experimental outcomes presented, are details provided of exactly what parameters was measured?	☒ Yes, for at least one experiment ☐ No
7	Statistical Methods	Is there statistical approach used to analyze each outcome detailed?	☒ Yes, for at least one analysis ☐ No
		Is there a description of any methods used to assess whether data met statistical assumptions?	☒ Yes, for at least one analysis ☐ No ☐ Not applicable
8	Experimental Animals	Are all species of animal used specified?	☒ Yes, for at least one experiment ☐ No
		Is the sex of the animals specified?	☒ Yes, for at least one experiment ☐ No ☐ Not applicable to species
		Is at least one of age, weight, or developmental stage of the animals specified?	☒ Yes, for at least one experiment ☐ No

9	Experimental Procedures	Are both the timing and frequency with which procedures took place specified?	☒ Yes, for at least one experiment ☐ No
		Are details of acclimatization periods to experimental locations provided?	☒ Yes, for at least one experiment ☐ No
10	Results	Are descriptive statistics for each experimental group provided, with a measure of variability (e.g. mean and SD, or median and range)?	☒ Yes, for at least one experiment ☐ No ☐ Not applicable to the type of data collected
		Is the effect size and confidence interval provided?	☒ Yes, for at least one experiment ☐ No ☐ Not applicable to the type of analysis used

* Percie du Sert, N. et al. The ARRIVE guidelines 2.0: Updated guidelines for reporting animal research. PLoS Biol 18, e3000410 (2020).