

Potential Role of Cannabinoid Receptors in Protecting Against *Salmonella* Infection: Insights from a Mouse Model Study

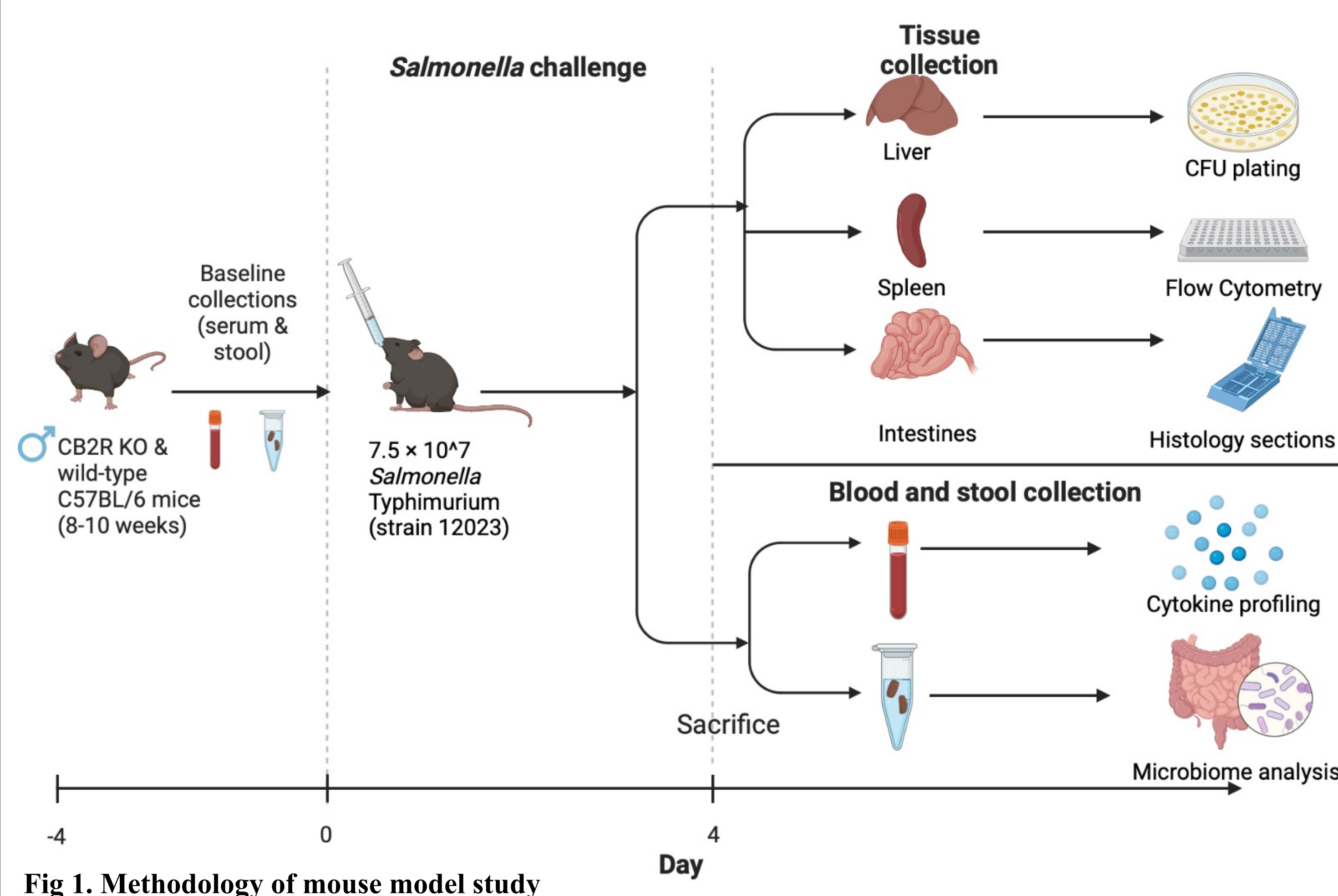
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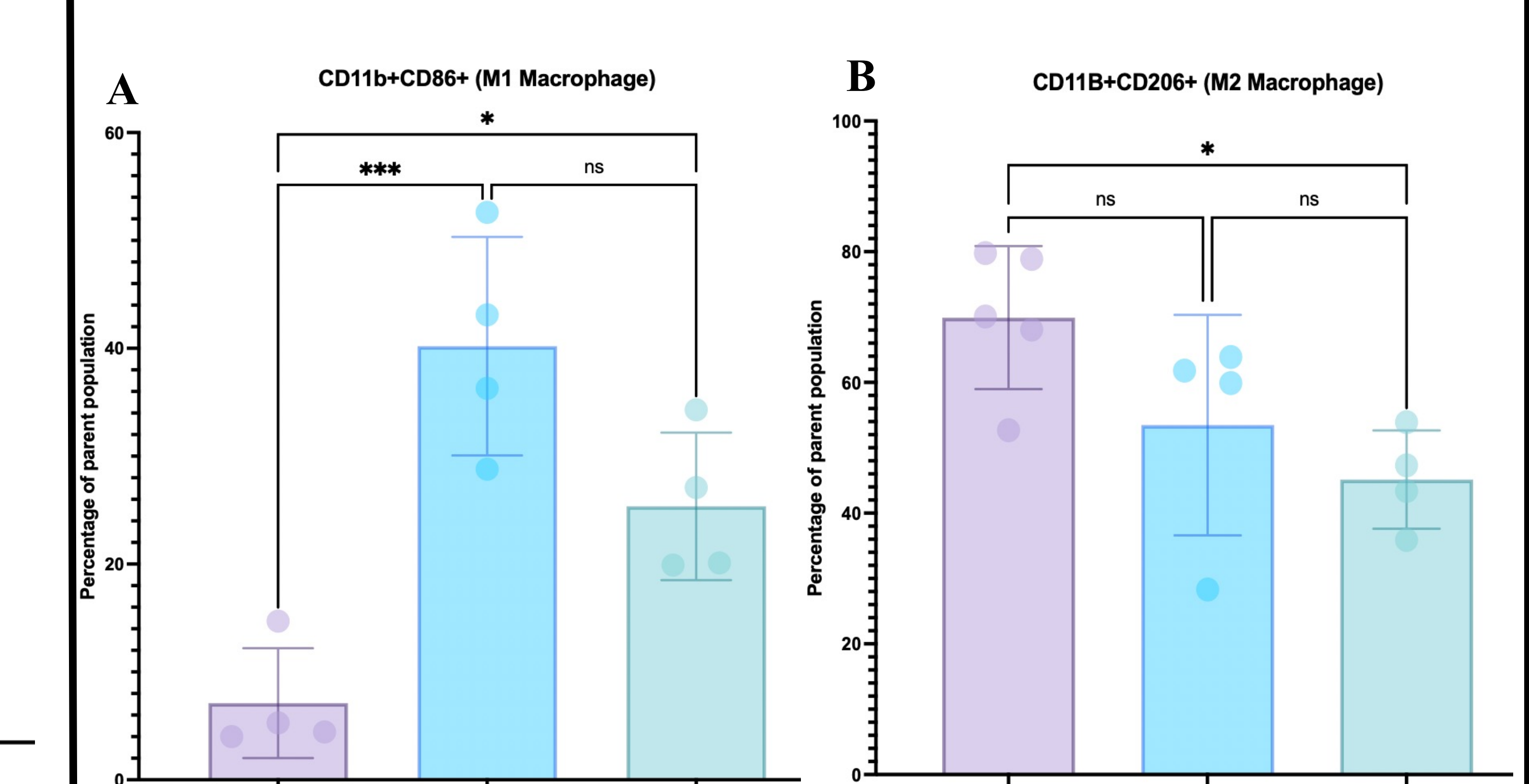
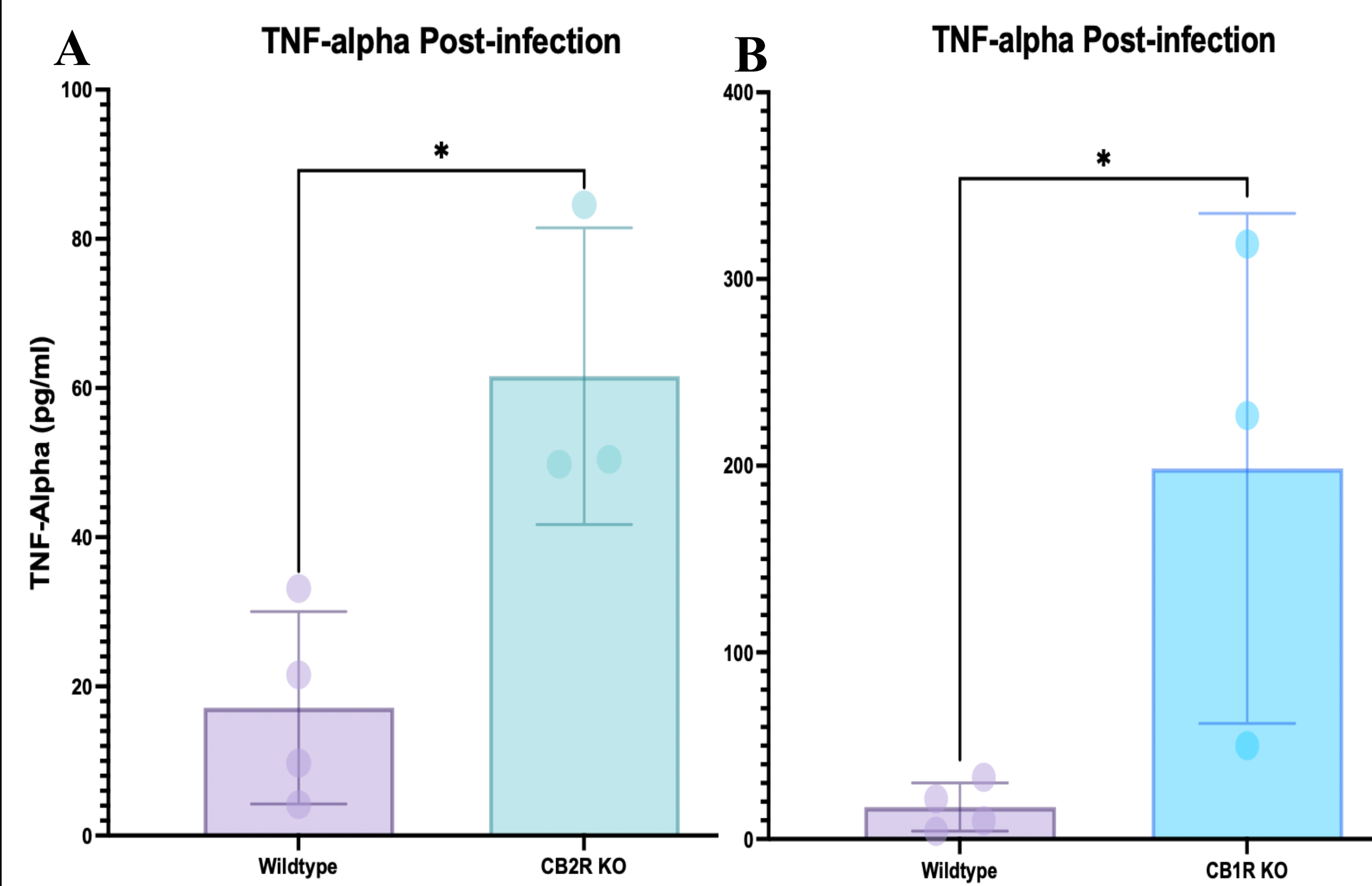
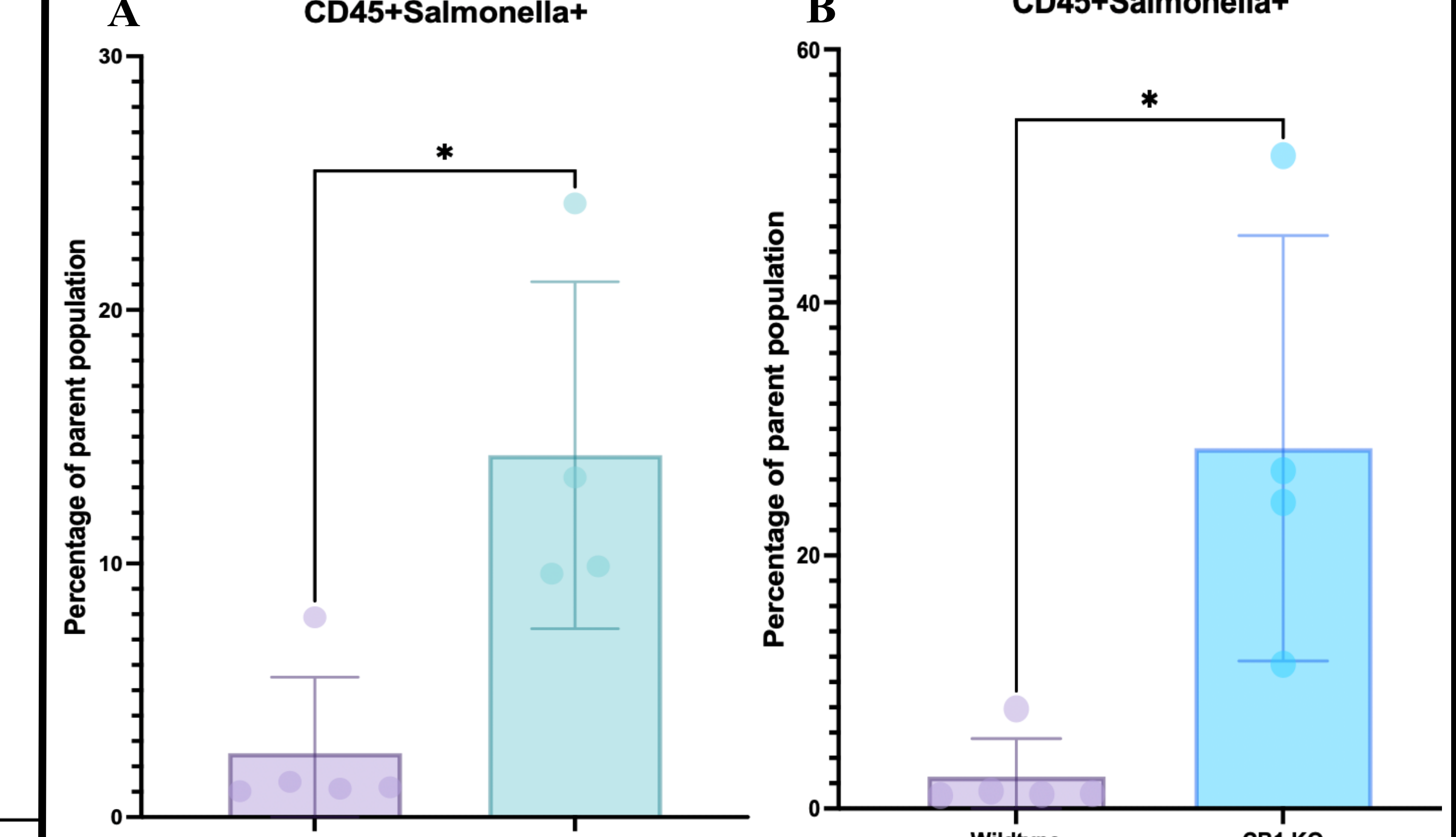
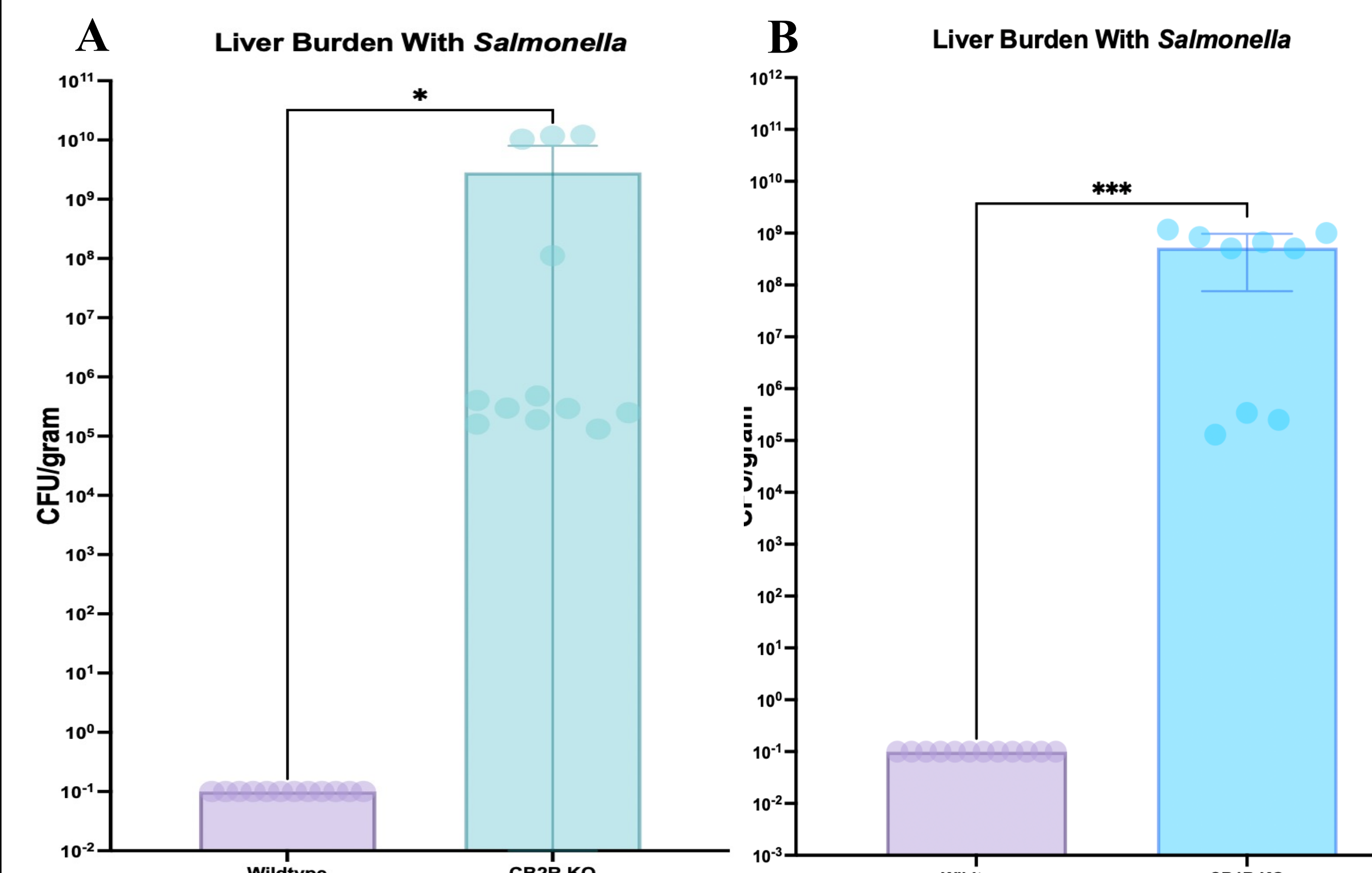
Introduction:

- Due to the rise of multi-drug resistant strains of disease-causing microbes from the overuse of treatments such as antibiotics, there is a need for a shift toward alternative therapies which target the host immune system
- Salmonella* Typhimurium is a Gram-negative intracellular bacterium that relies on the ability to infect a variety of cells, including antigen-presenting cells such as macrophages, to cause an infection
- The endocannabinoid (eCB) system is a pathway composed of bioactive lipids called endocannabinoids (eCBs), a set of receptors and associated biosynthesis/degradative proteins
- The cannabinoid receptors type 1 and 2 (CB1R and CB2R) are coupled to G-proteins widely expressed among many cell types
- CB2 receptors are highly expressed on immune cells and are linked to signaling cascades such as adenylyl cyclase, cAMP, MAPK, and regulation of intracellular calcium
- Endocannabinoid and cannabinoid receptor activation have many roles in maintaining homeostasis, including cell proliferation, migration, cytokine production, and lipid metabolism
- Macrophages polarize into specific phenotypes to perform specific jobs;
 - M1 phenotype is associated with a pro-inflammatory response against pathogens
 - M2 phenotype is associated with resolving inflammation and improvement in tissue healing
- TNF-alpha is a pro-inflammatory cytokine produced by immune cells and can be used to evaluate the state of the immune system and host
- By further understanding the role of cannabinoid receptors in bacterial infections, cannabinoid receptors could provide a novel target for therapies against *Salmonella*
- Our study aimed to characterize the role of cannabinoid receptors 1 and 2 (CB1R and CB2R) in activating the immune system and preventing the colonization of *Salmonella*

Methods:



Results:



Conclusions:

By challenging wild-type, CB1R knockout, and CB2R knockout mice with *Salmonella* Typhimurium, we were able to evaluate the role of cannabinoid receptors in preventing severe infection. Four days post-infection, mice lacking the CB1R or CB2R showed increased colonization of *Salmonella* in the liver and spleen as well as increased pro-inflammatory responses. Post-infection, macrophages lacking CB1R and CB2R primarily polarized towards an M1 phenotype characterized by increased pro-inflammatory response compared to macrophages derived from wild-type mice. Overall, our results indicate the potential role of CB1R and CB2R to play a protective role in vivo against *Salmonella* infection. Future directions will include using select cannabinoids as treatments for mice challenged against *Salmonella*.

Acknowledgements:

This study was funded by MMJ Clinical Outcomes Research Grant