# A Monoclonal Antibody Blocking Interleukin-1 Receptor Accessory Protein Reduces Acute Viral Myocarditis Severity

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## Introduction

- Canakinumab (anti-IL-1β) reduces recurrence of cardiovascular events in MI patients with elevated inflammatory markers.
- Evidence shows that complementary IL-1, IL-33 and IL-36 have pro-inflammatory roles in myocarditis.
- We hypothesized that blockade of shared co-receptor for IL-1, IL-33 and IL-36, IL-1 receptor accessory protein (IL1RAP; Cantargia AB), would reduce Coxsackievirus B3 (CVB3) myocarditis severity and preserve cardiac function.

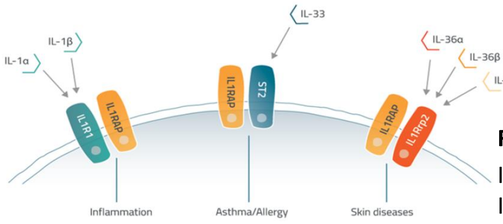


**Figure 1.**
IL1RAP is involved in IL-1/33/36 signaling

## Objectives

To study the effect of an IL1RAP-blocking antibody on severity of acute CVB3 myocarditis.

## Materials and Methods

We induced CVB3 myocarditis in 10 week-old Balb/c male mice. Animals were treated with mCAN10 (anti-IL1RAP, Cantargia) or controls according to the schedule in Table 1.

Echocardiography was performed at 9 d.p.i and mice were sacrificed and organs harvested 10 d.p.i.

**Table 1.**

| Group | Dose | Schedule |
|---|---|---|
| mCAN10 | 10 mg/Kg (i.p) | Biweekly |
| Isotype | | |
| PBS | 100 ul (i.p) | |
| IL1Ra | 25 mg/Kg (s.c) | Daily |

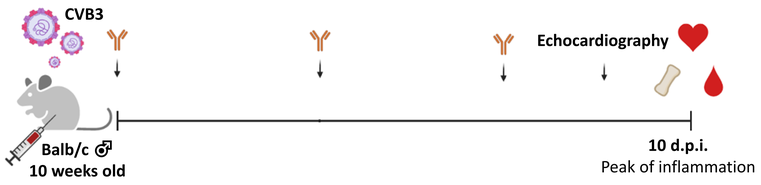


**Figure 2-** CVB3 myocarditis experimental design

## Results

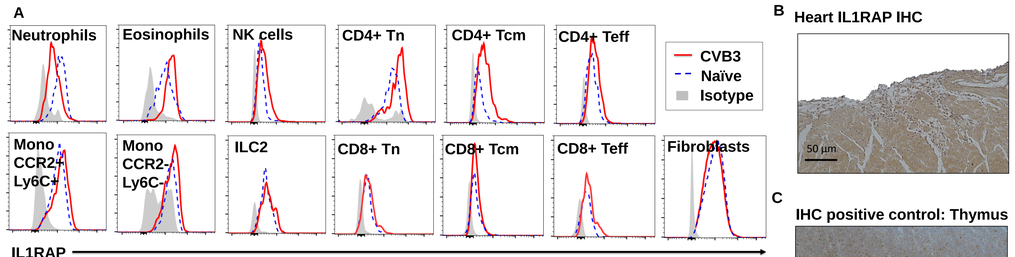


**Figure 3 – IL1RAP is widely expressed in murine heart immune and stromal cells at day 10 of CVB3 myocarditis**
**a)** Flow cytometry determination of IL1RAP expression in select cardiac populations **b,c)** Representative examples of IL1RAP IHC-stained slides in heart (b, 40x) and thymus (c, 10x). Scale bars= b: 50 µm; c: 200 µm

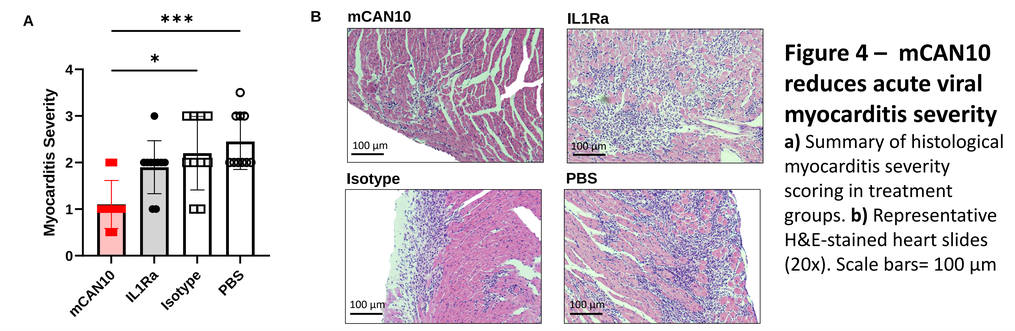


**Figure 4 – mCAN10 reduces acute viral myocarditis severity**
**a)** Summary of histological myocarditis severity scoring in treatment groups. **b)** Representative H&E-stained heart slides (20x). Scale bars= 100 µm

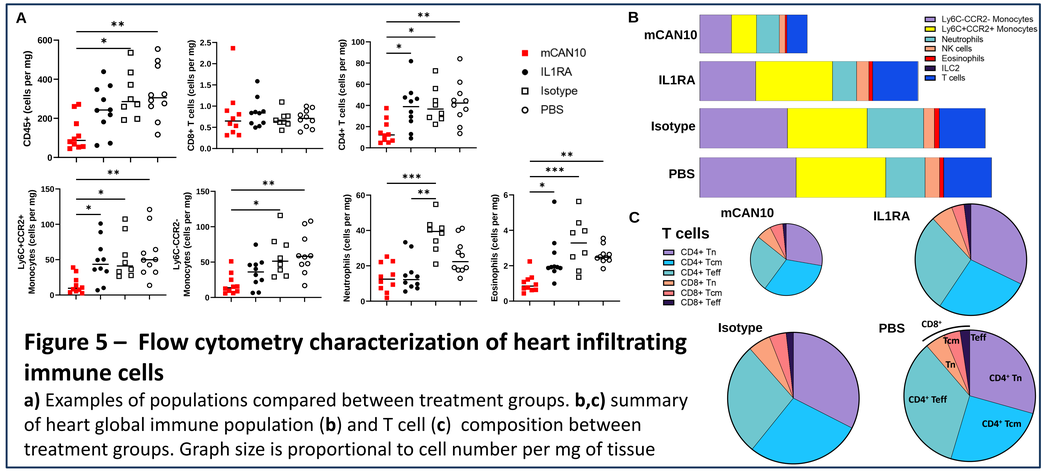


**Figure 5 – Flow cytometry characterization of heart infiltrating immune cells**
**a)** Examples of populations compared between treatment groups. **b,c)** summary of heart global immune population (**b**) and T cell (**c**) composition between treatment groups. Graph size is proportional to cell number per mg of tissue

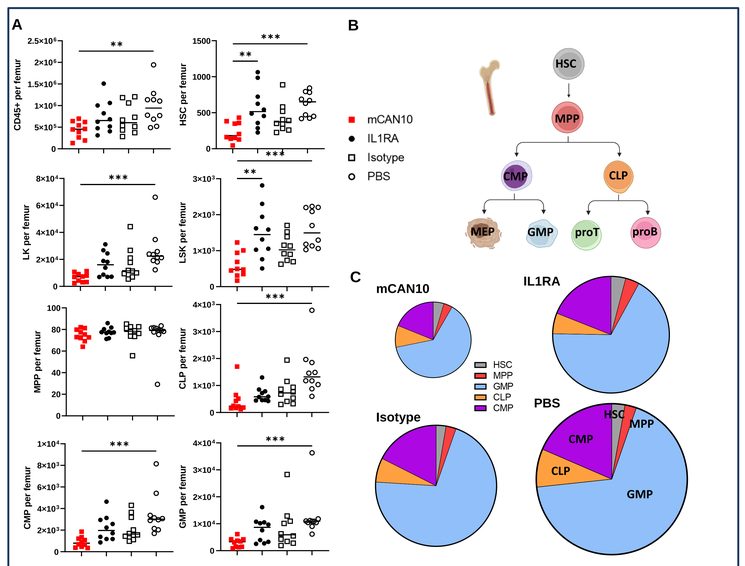


**Figure 6 – mCAN10 reduces increased bone marrow leukocyte precursors**
**a)** Graphs comparing bone marrow population between treatment groups. **b)** Schematic diagram of bone marrow differentiation lineages. **c)** Summary of **(a)**, where graph size is proportional to number of cells per femur

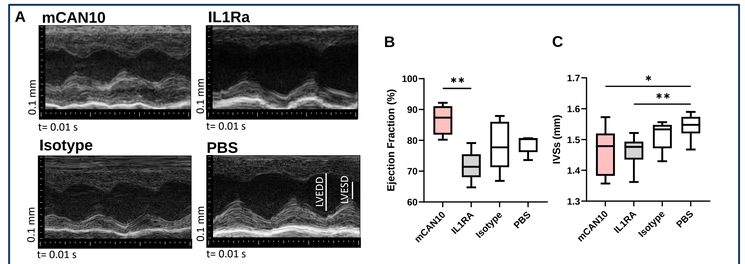


**Figure 7 – mCAN10 preserves heart function in CVB3 myocarditis**
**a)** Representative m Mode echocardiography strips. x-axis: time, ticks= 0.01 seconds; y-axis: diameter, ticks= 0.1 mm. **b)** ejection fraction, **c)** interventricular septum diameter

## Conclusions

mCAN10 reduced the severity of acute CVB3-myocarditis by decreasing inflammatory leukocyte populations in the heart and bone marrow. This resulted in preserved cardiac function.

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