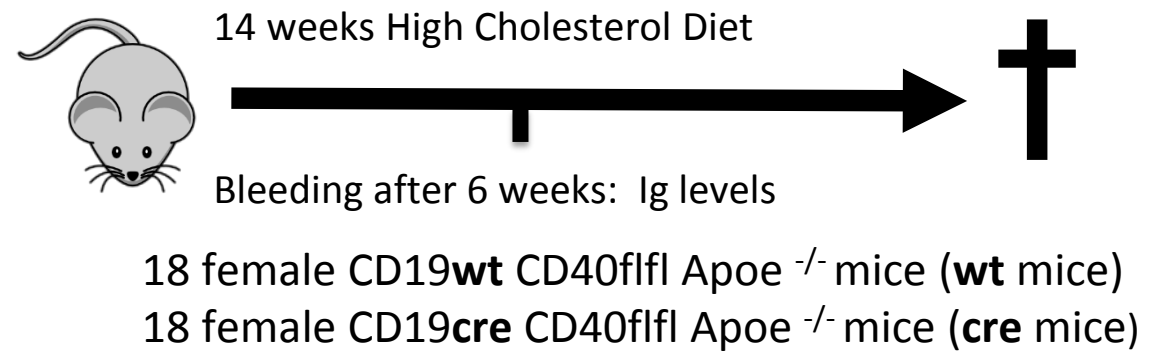


# B cell CD40 protects against atherosclerosis in hypercholesterolemic mice

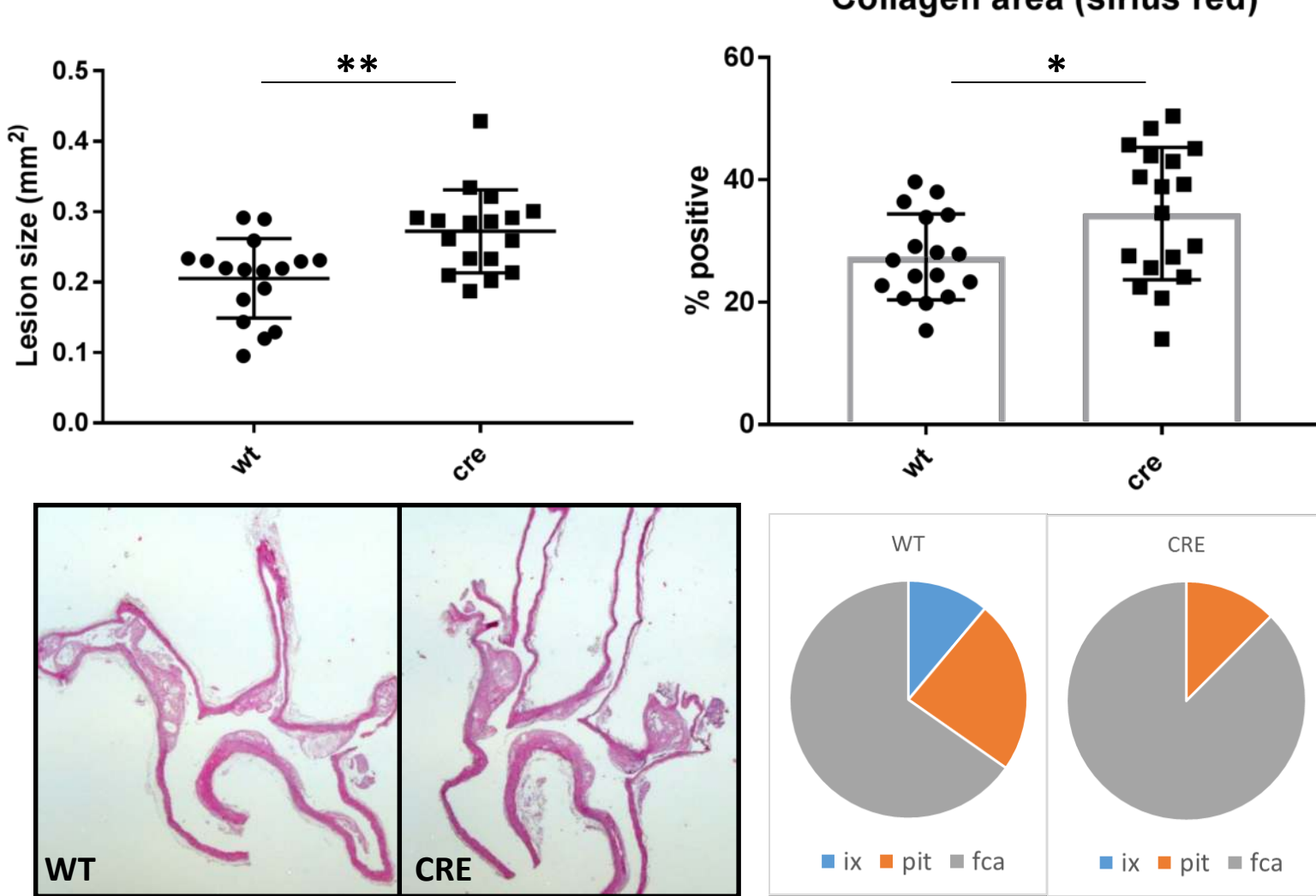
Myrthe Reiche<sup>1\*</sup>, Pascal Kusters<sup>1</sup>, Claudia van Tiel<sup>1</sup>, Tom Seijkens<sup>1</sup>, Kikkie Poels<sup>1</sup>, Hessel Poelman<sup>1</sup>, Gerry Nicolaes<sup>1</sup>, Stephen Malin<sup>2</sup>, Christoph Binder<sup>3</sup> & Esther Lutgens<sup>1,4</sup>

## Introduction

The co-stimulatory CD40L-CD40 dyad is a major driver of atherosclerosis. CD40-TRAF signaling on B cells is crucial for B cell function, including isotype switching and germinal center formation. Here we aim to unravel the function of B cell CD40 on atherosclerosis, as well as the different TRAF-signaling pathways involved.

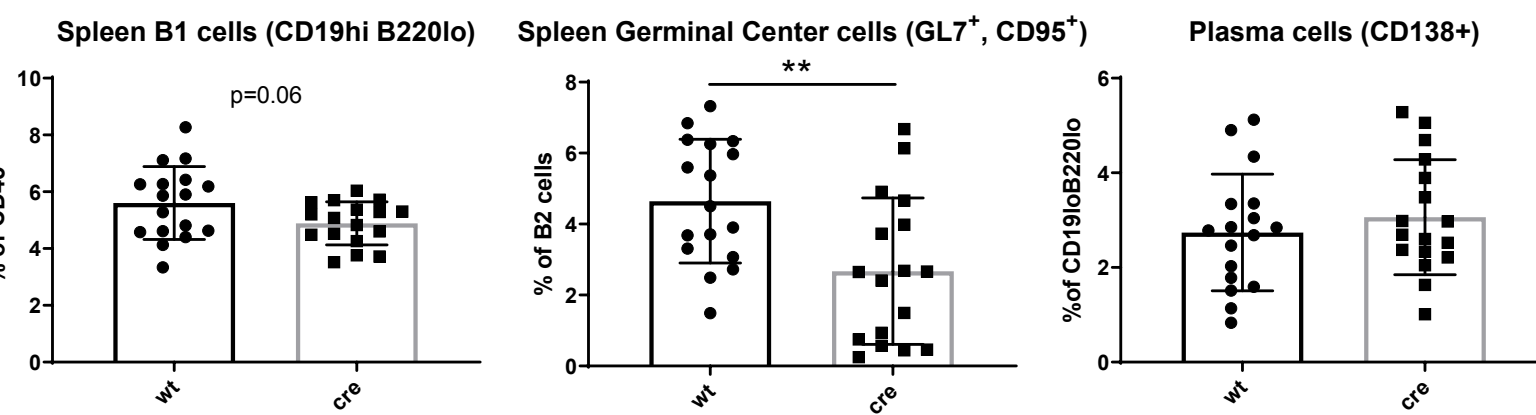


## Lesion size was significantly increased

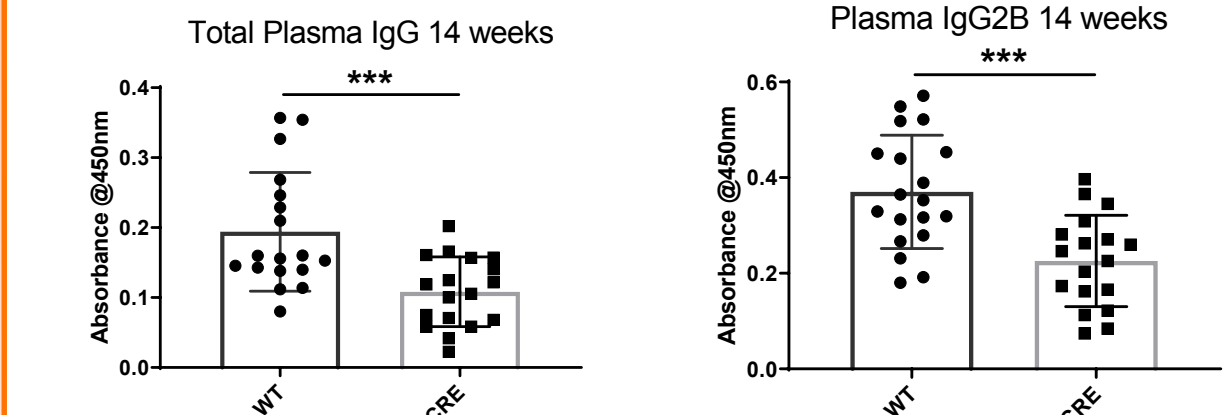
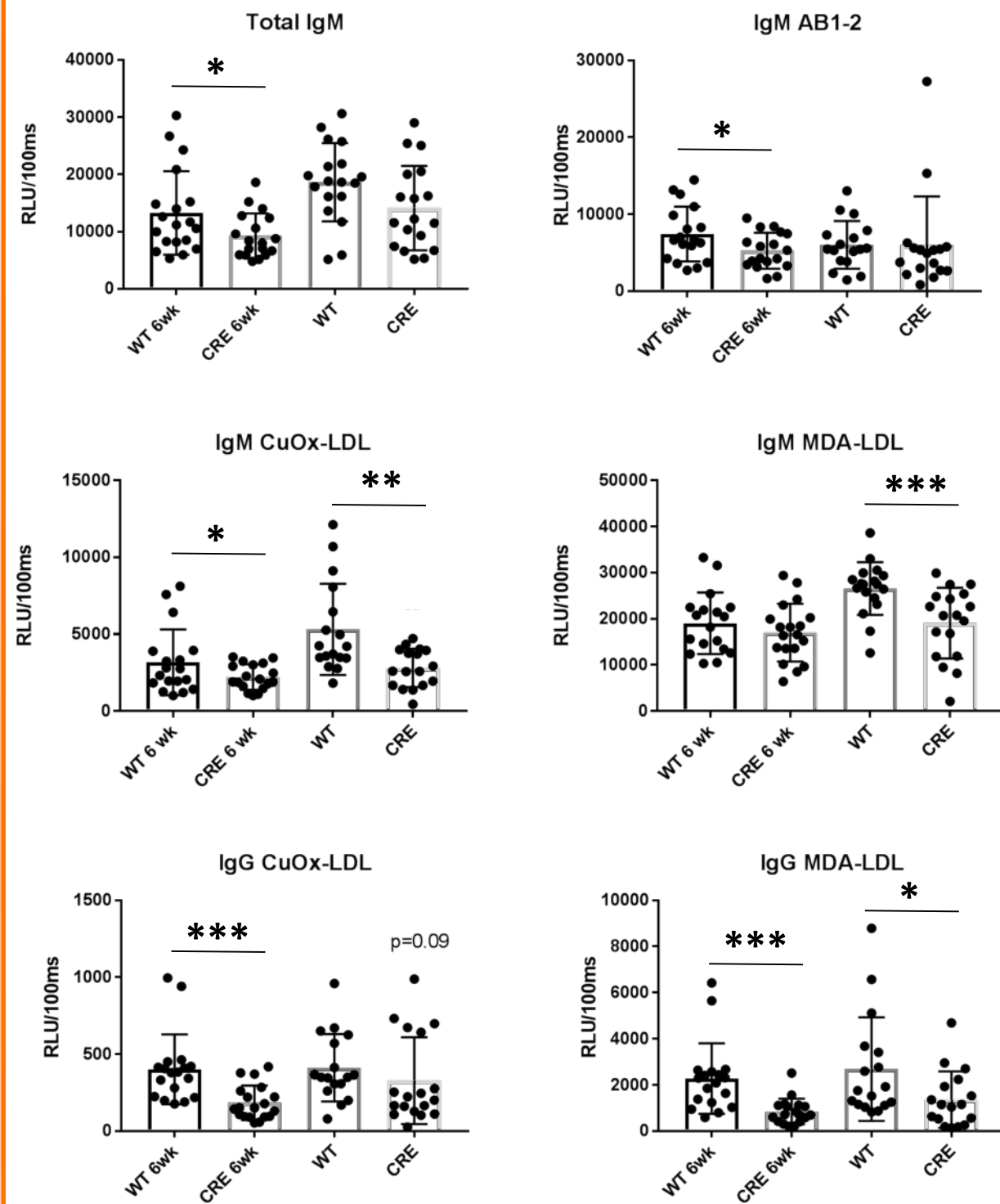


B cell deficiency of CD40 led to a significant increase in lesion size and collagen content after 14 weeks of diet. IX=intimal xanthoma, PIT=pathological intimal thickening, FCA=fibrous cap atheroma. \*= $p < 0.05$ , \*\*= $p < 0.01$ , \*\*\*= $p < 0.001$

## Germinal center cell count is decreased



Flow analysis of spleens of B cell CD40 deficient mice show decreases in B1 and germinal center cells, while plasma cells quantities are unchanged compared to WT.



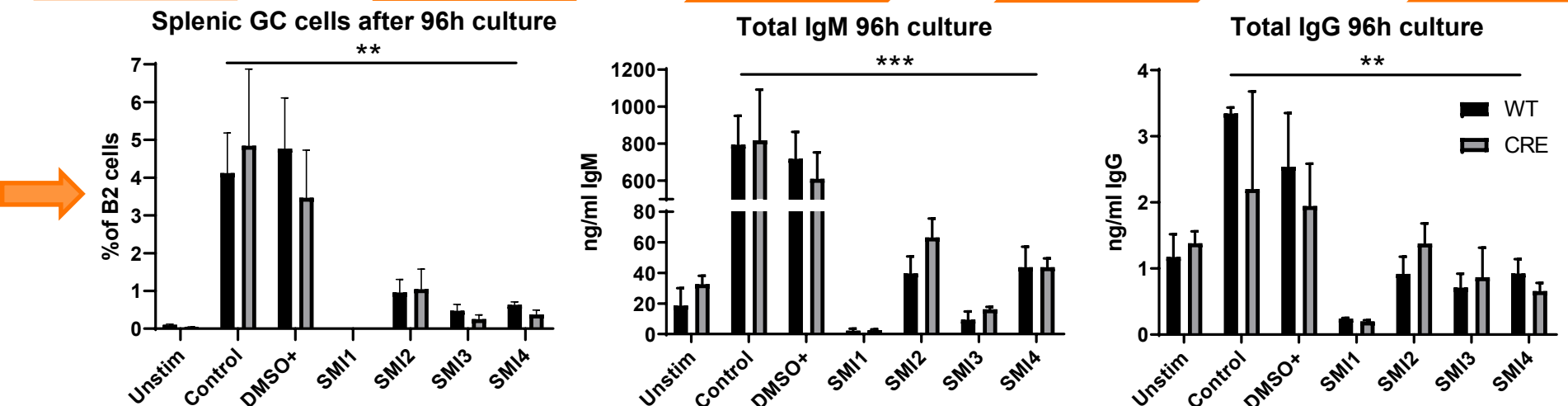
B cell CD40 deficient mice had decreased plasma total IgG and IgM levels, as well as reduced anti-MDA/oxLDL IgG and IgM levels.



**TRAF2 Small Molecule Inhibitors**

- Unstimulated B cells
- Control +LPS +IL4
- DMSO +LPS +IL4
- SMI1-4 +LPS +IL4

96h culture



**TRAF2 compounds inhibit B cell development to GC and plasma cells. IgM and IgG production is decreased**

## Conclusion

Our data indicate a protective role of global B cell CD40 in atherosclerosis most likely via boosting the B1-driven, protective anti-oxLDL IgM response. The newly developed TRAF2 inhibitors will help us unravel the effects of CD40-TRAF2 signaling in B cells.

## Acknowledgements

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