

# miR-511-3p, embedded in the macrophage CD206 gene, contributes to experimental colitis

Sigrid E.M. Heinsbroek, Mario Leonardo Squadrito, Ronald Schilderink, Francisca W. Hilbers, Marie Hofmann, Alexandra Helmke, Louis Boon, Manon E. Wildenberg, Joris J.T.H Roelofs, Cyriel Y. Ponsioen, Charlotte P. Peters, Anje A. te Velde, Siamon Gordon, Michele De Palma, Wouter J. de Jonge

## Introduction

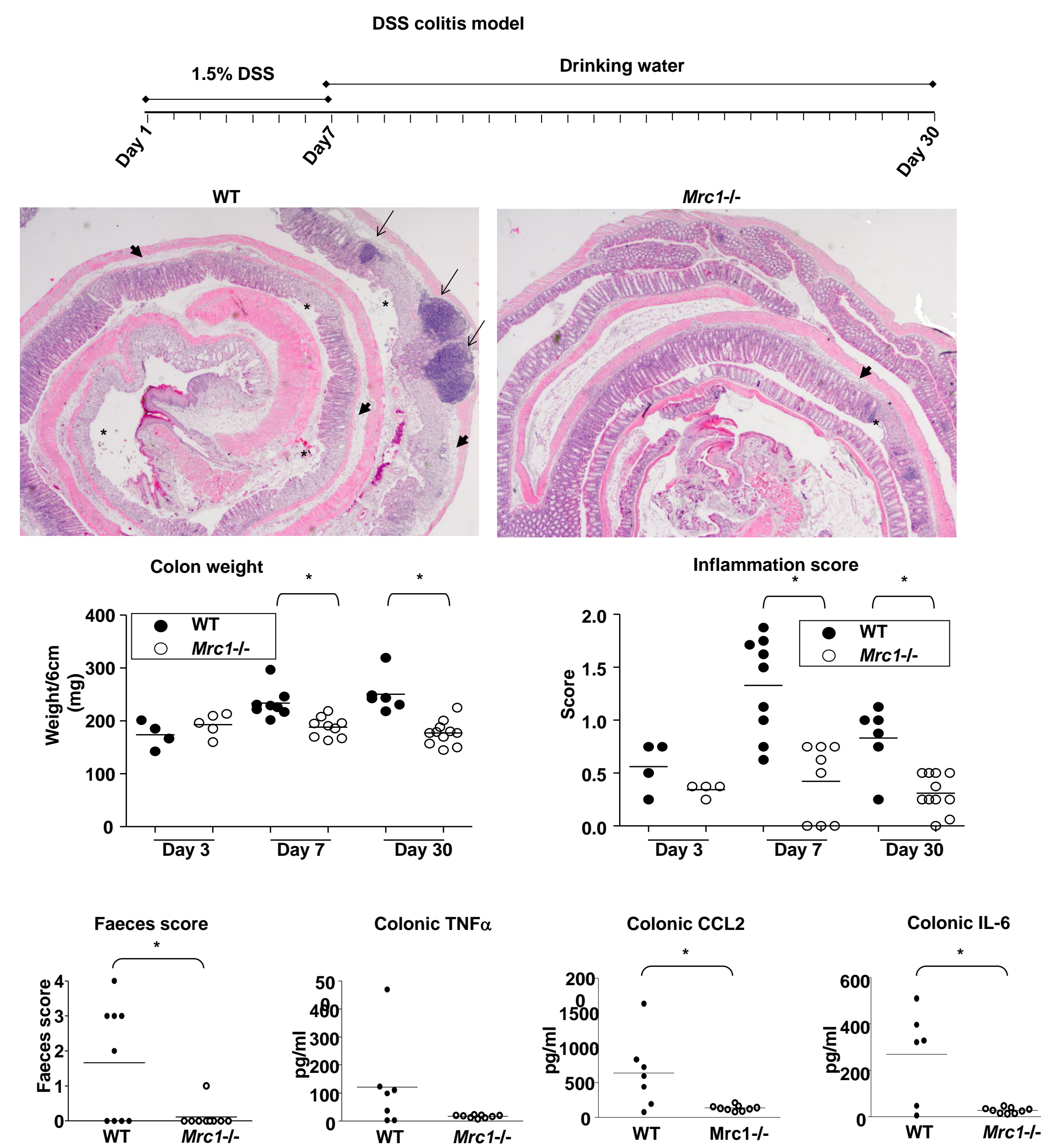
miR-511-3p is embedded in intron 5 of the macrophage mannose receptor (CD206) gene *Mrc1*, that is expressed by M2 macrophages. Expression of CD206 and miRNA511-3p is co-regulated. CD206 is a pattern recognition receptor which recognises a broad range of microbes. The contribution of both CD206 and miRNA511-3p to colitis is unclear. We examined the role of CD206 and miR-511-3p in intestinal inflammation in both mouse and human systems.

## Methods

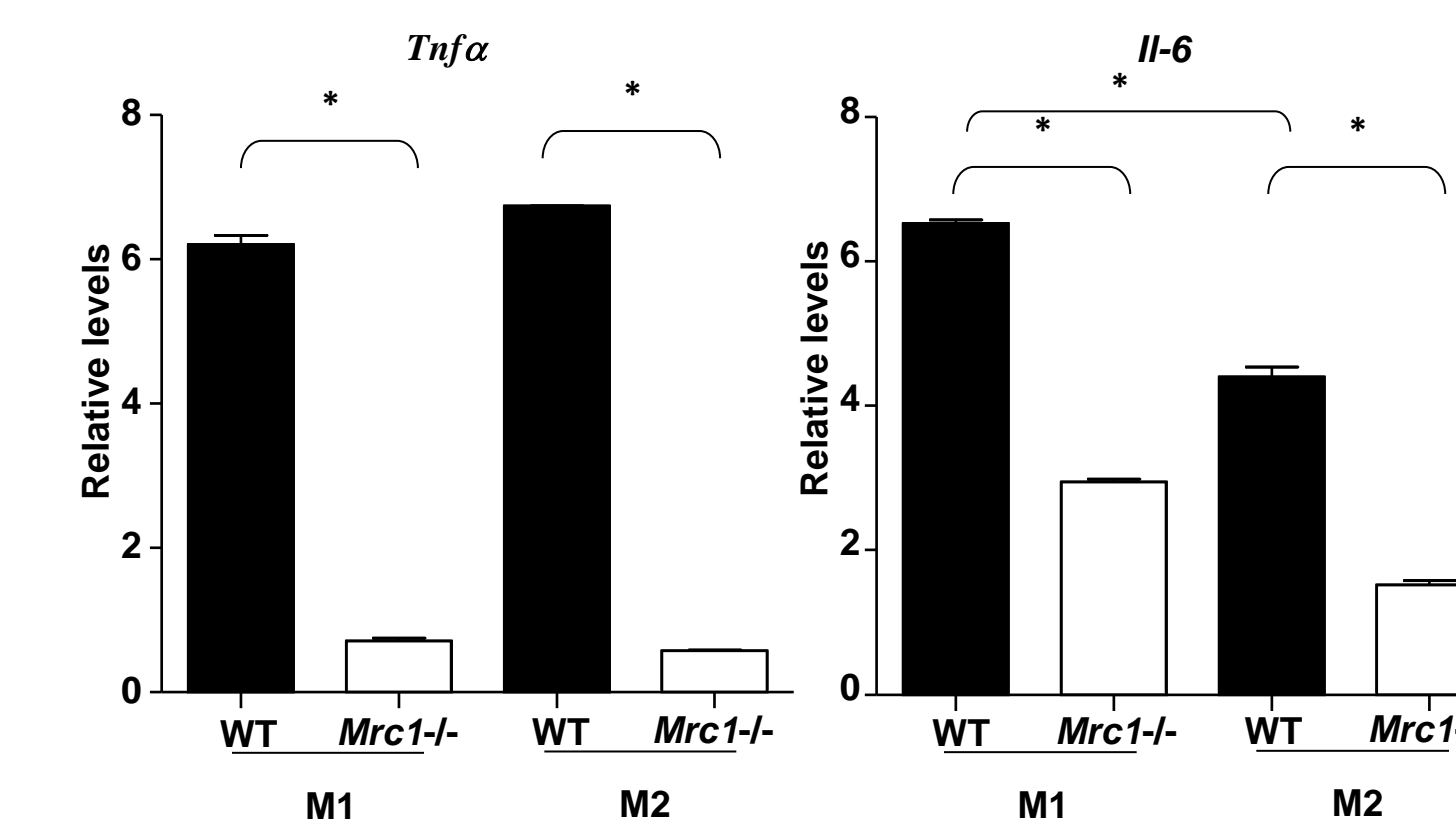
Colonic inflammation was induced by dextran sodium sulphate in CD206-deficient and WT mice, as well as mice in which the CD206 was blocked using a blocking antibody. Both M1 and M2 macrophages were stimulated with LPS, and cytokine responses measured. Expression levels of miR-511-3p were measured in macrophages from CD206-deficient mice using qPCR. Macrophages transduced to either overexpress or knock-down miR-511-3p were characterized.

## Results

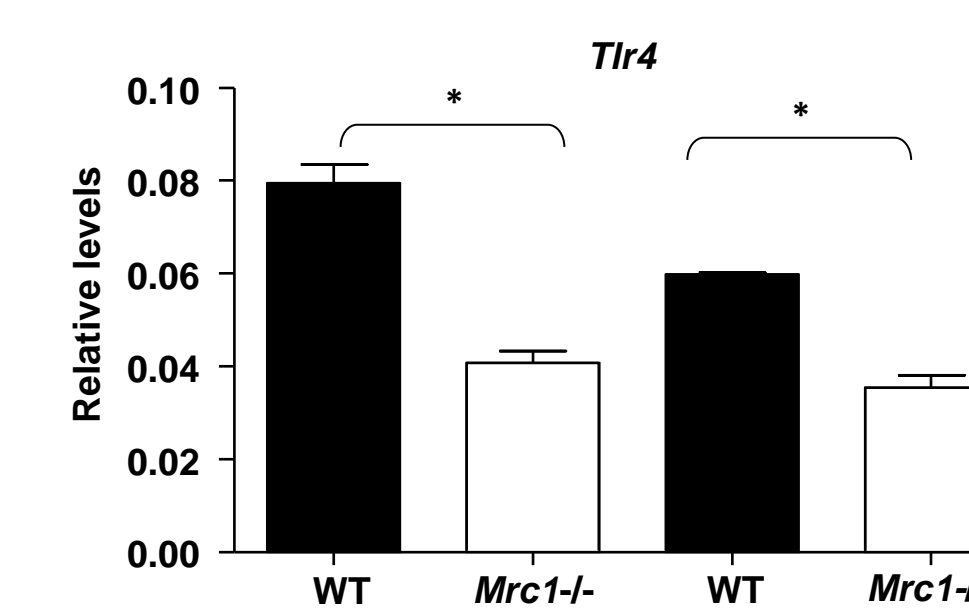
### Less inflammation in CD206<sup>-/-</sup> mice



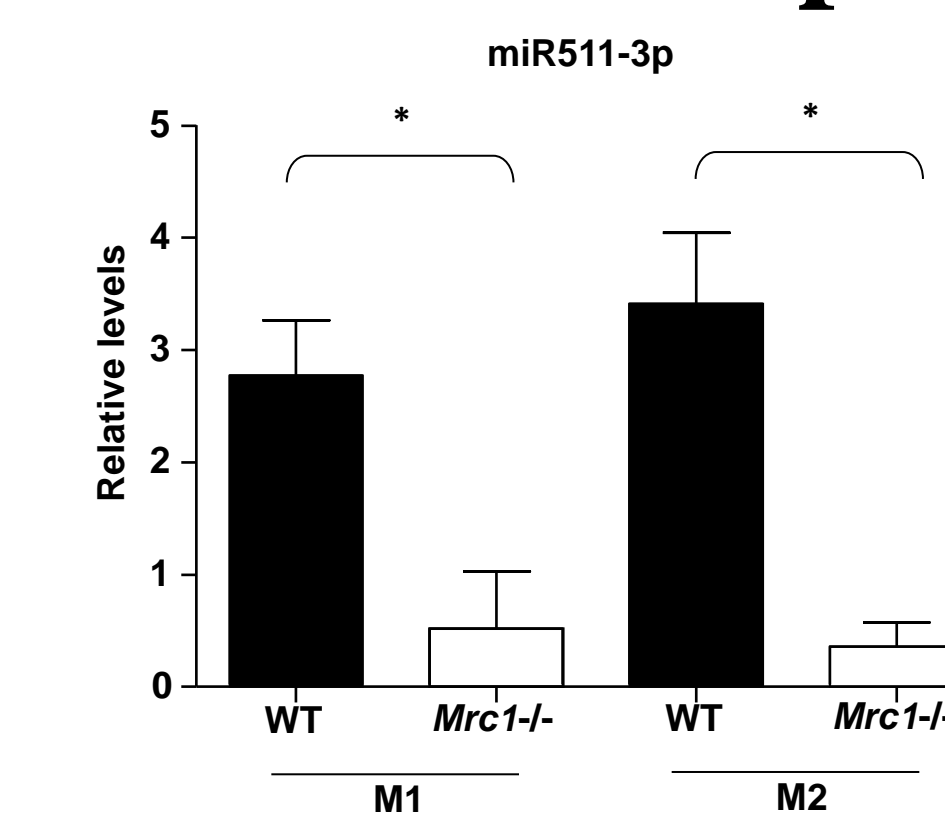
### CD206<sup>-/-</sup> macrophages have reduced LPS responses



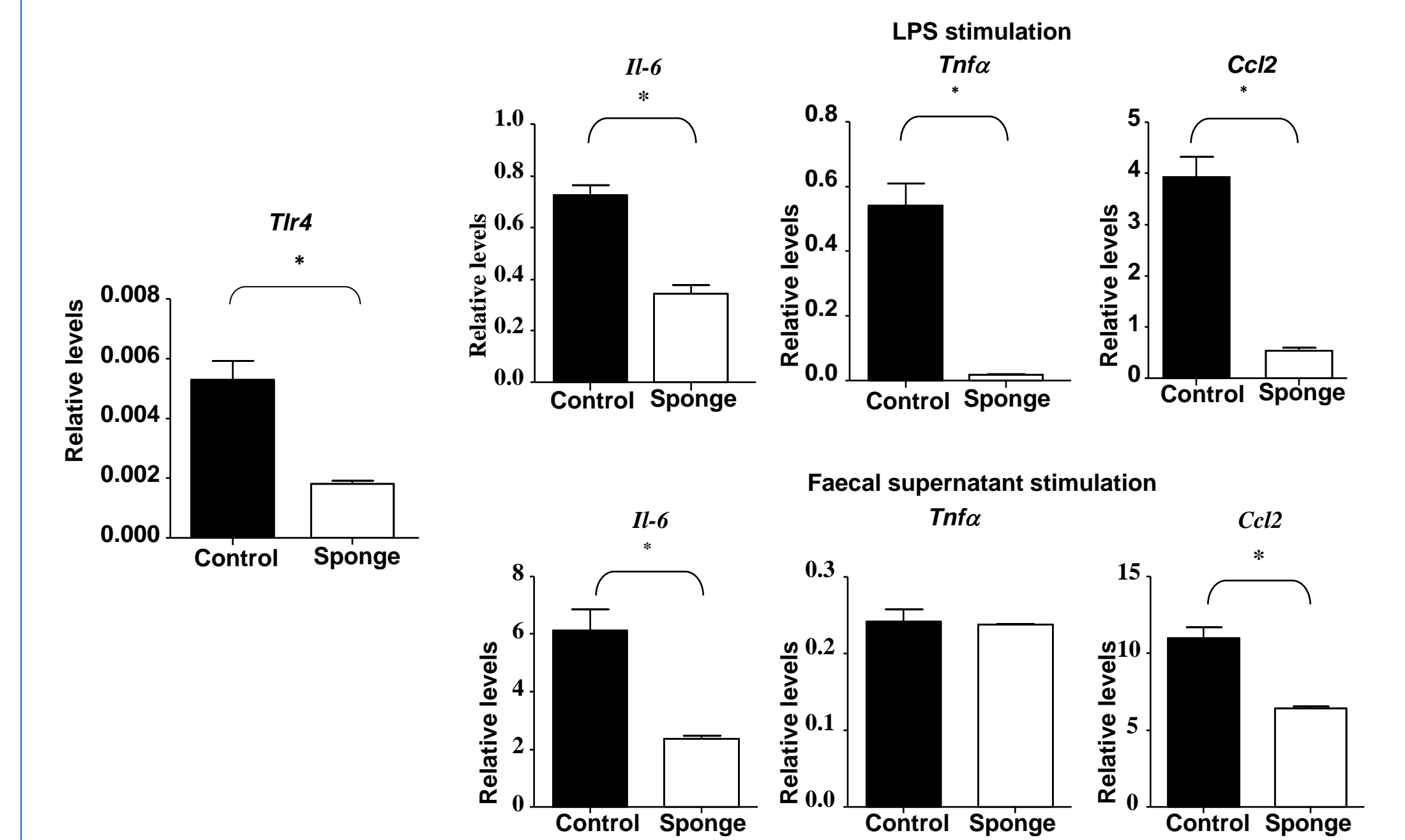
### CD206<sup>-/-</sup> macrophages have reduced TLR4 levels



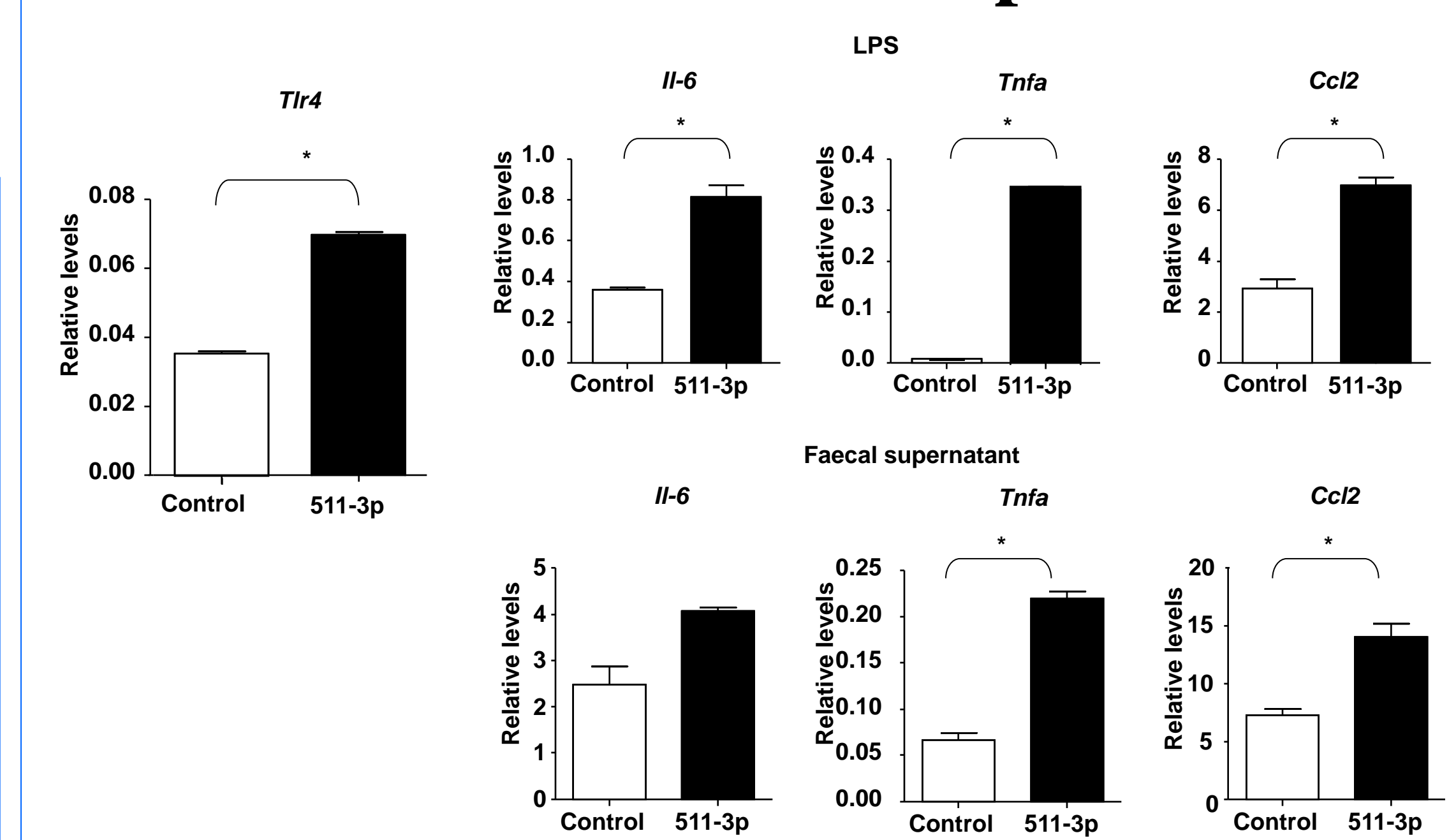
### CD206<sup>-/-</sup> macrophages have reduced miR-511-3p levels



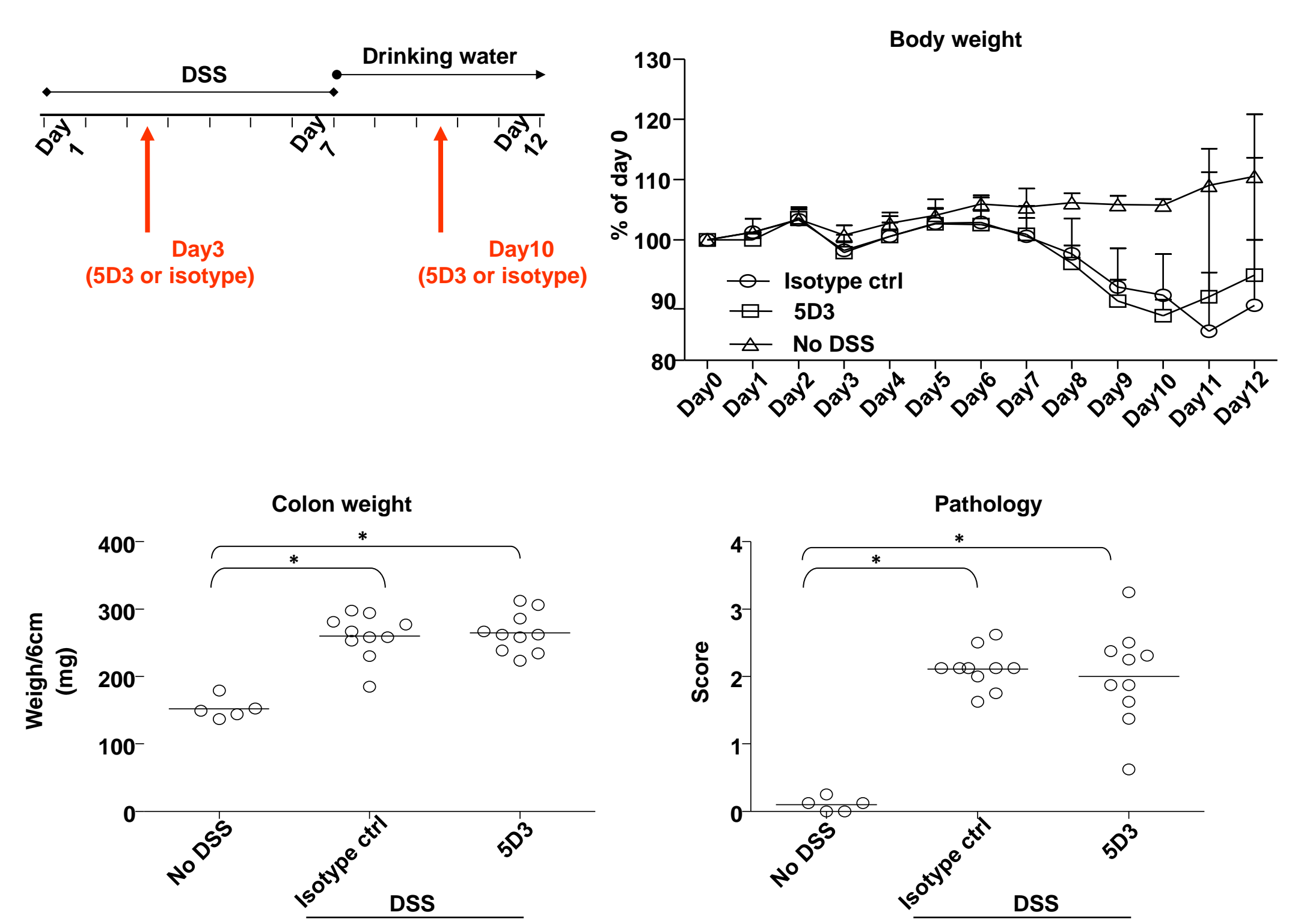
### miR-511-3p knockdown reduces TLR4 levels and responses



### miR-511-3p overexpression increases TLR4 levels and responses



### Blocking CD206 function does not affect colon inflammation



## Conclusion

We demonstrate that miR-511-3p plays a role in mouse colitis. Likely due to regulation of TLR4 expression levels.