BEACON IN VIVO A Eurofins Discovery Partner Lab

ANTI-CD40-INDUCED COLITIS IN MICE

Anti-CD40 Antibody (Agonist) Administered IP to Male RAGN12 KO (T- and B-cell Deficient) Mice[1]

CD40 is expressed in lamina propria cells of the proximal colon. When activated by anti-CD40 antibody, colitis develops in response to excess cytokine production (IL-23, IL-22, IL-1beta and IL-12)[2] driven by gut resident CX3CR1+ macrophages and IL-22-producing group 3 innate lymphoid cells (ILC3)[3]. Day 7 intestinal histopathological alterations include infiltration of innate immune cells and goblet cell atrophy.

DOSING PARADIGM

- Daily dosing on Study Days 0-7
- Possible routes of administration: PO, IV, IP, SC

HISTOPATHOLOGICAL ASSESSMENT

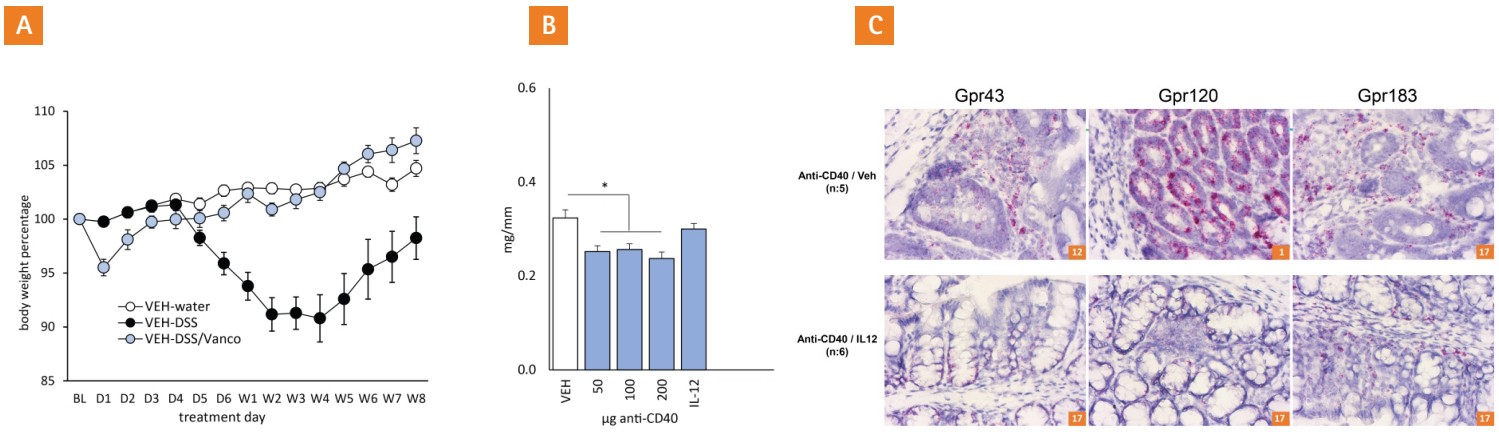
Colon is harvested, weighed, measured and further processed for RNA, MPO and histological analysis.

CLINICAL ASSESSMENT

- Body weight is collected on Study Days 0-7
- Day 6: Stool test

0 - Normal stool consistency with negative hemoccult
1 - Soft stools with positive hemoccult
2 - Very soft stools with traces of blood
3 - Watery stools with visible rectal bleeding

Sample data



A) Suppression of body weight percentage by anti-CD-40 is reversed by IL-12p40 MAb. B) Colon density (mg colon tissue/mm colon tissue) is significantly decreased by anti-CD-40 but protected by IL-12p40 MAb. C) In situ hybridization reveals that mRNA expression of colonic GPCRs involved in the inflammatory response are upregulated in the presence of the CD-40 antibody relative to IL-12p40 MAb treated controls.

OPTIONAL ENDPOINTS

- Body weight
- Body weight percentage
- Stool observations
- Colon length
- Colon weight (distal 4cm, proximal)
- Colon density (distal 4cm, proximal)
- Plasma cytokines (TNF, IL-6, IL12p40, IL-12p70, INFg, IL-10, IL-18)
- Plasma MPO
- qPCR (distal 4 cm, proximal)
- In situ hybridization
- H&E staining

REFERENCES

1. Joyce-Shaikh, B., Cua, D. J. and Bauché, D. (2019). Induction and analysis of anti-CD40-induced colitis in mice *Bio-protocol* 9(3): e3153. DOI: 10.21769/BioProtoc.3153.

2. Uhlig, H. H., McKenzie, B. S., Hue, S., Thompson, C., Joyce-Shaikh, B., Stepankova, R., et al. (2006). Differential activity of IL-12 and IL-23 in mucosal and systemic innate immune pathology. *Immunity* 25(2): 309-318.

3. Bauché, D., Joyce-Shaikh, B., Jain, R., Grein, J., Ku, K. S., et al. (2018). LAG3+ regulatory T cells restrain interleukin- 23-producing CX3CR1+ gut-resident macrophages during group 3 innate lymphoid cell-driven colitis. *Immunity* 49(2): 342-352: e345.

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