

Monoclonal Antibodies Against Mature Interleukin-18 Ameliorate Colitis and Repair Goblet Cell Function

Supplementary Information

Jingxi Mu, MD, ^a, Keiko Maeda, MD, PhD, ^{a*}, Ayako Ohashi, MD, PhD, ^a, Takeshi

Urano, MD, PhD, ^{b,c,d}, Yuko Nariai, PhD, ^d, Hiroki Kamino, PhD, ^d, Masanao

Nakamura, MD, PhD, ^e, Takeshi Yamamura, MD, PhD, ^a, Tsunaki Sawada, MD, PhD, ^e,

Eri Ishikawa, MD, PhD, ^a, Kentaro Murate, MD, PhD, ^a, Kenta Yamamoto, MD, PhD,

^e, Takashi Hirose, MD, PhD, ^a, Kazuhiro Furukawa, MD, PhD, ^a Mitsuhiro Fujishiro,

MD, PhD, ^f, Hiroki Kawashima, MD, PhD, ^a

^aDepartment of Gastroenterology and Hepatology, Nagoya University Graduate School of Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya 466-8550, Japan

^bDepartment of Biochemistry, Shimane University School of Medicine, Izumo 693-8501, Japan

^cmAbProtein Co. Ltd., Izumo 693-8501, Japan

^dCenter for Vaccines and Therapeutic Antibodies for Emerging Infectious Diseases, Shimane University, Izumo, Japan

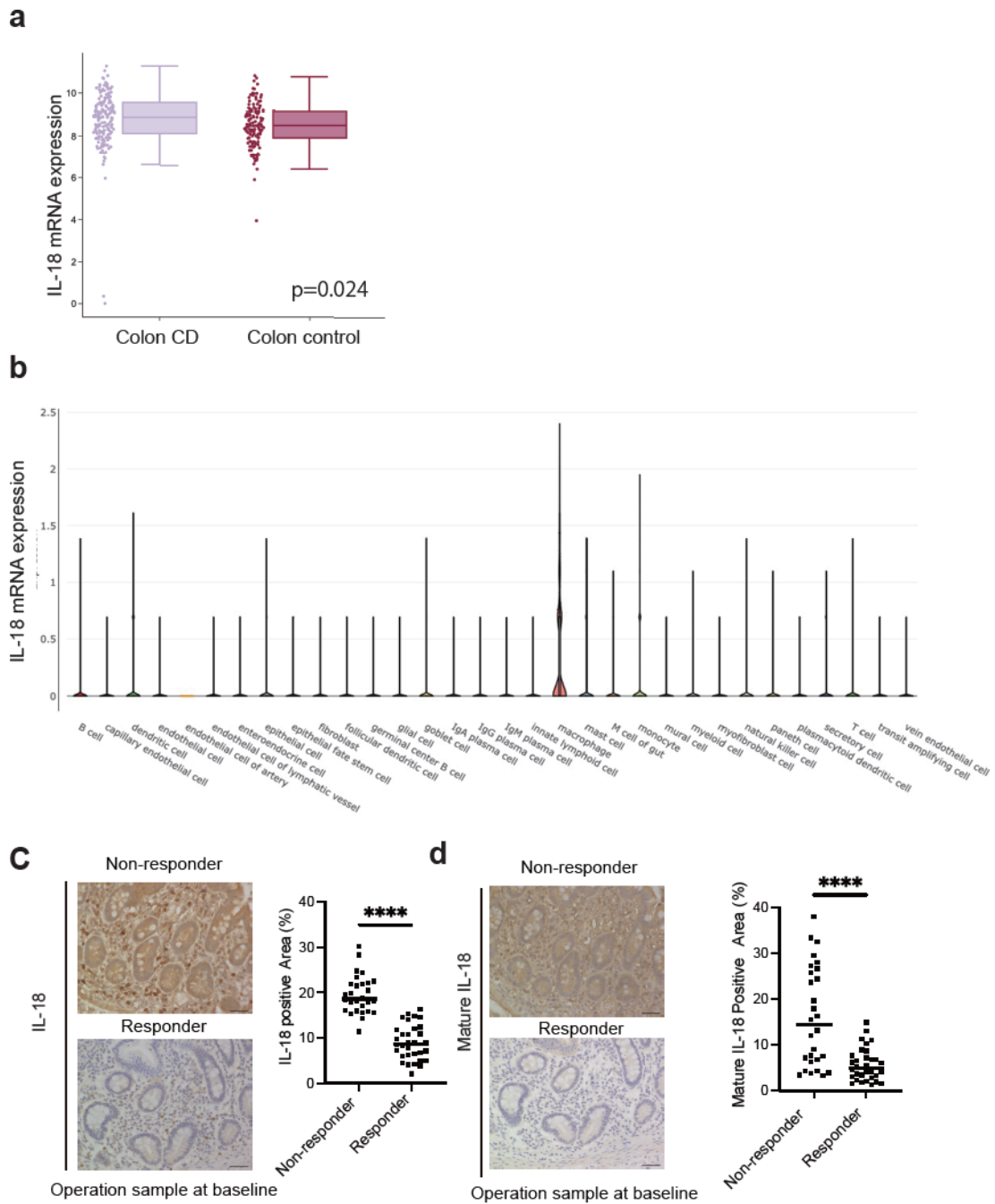
^eDepartment of Endoscopy, Nagoya University Graduate School of Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya 466-8550, Japan

^fDepartment of Gastroenterology, Graduate School of Medicine, The University of Tokyo, 7-3-1, Hongo, Bunkyo-ku, Tokyo, 113-8655, Japan

***Corresponding author**

Keiko Maeda, Email address: kmaeda@med.nagoya-u.ac.jp

Department of Gastroenterology and Hepatology, Nagoya University Graduate School of
Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya 466-8550, Japan.

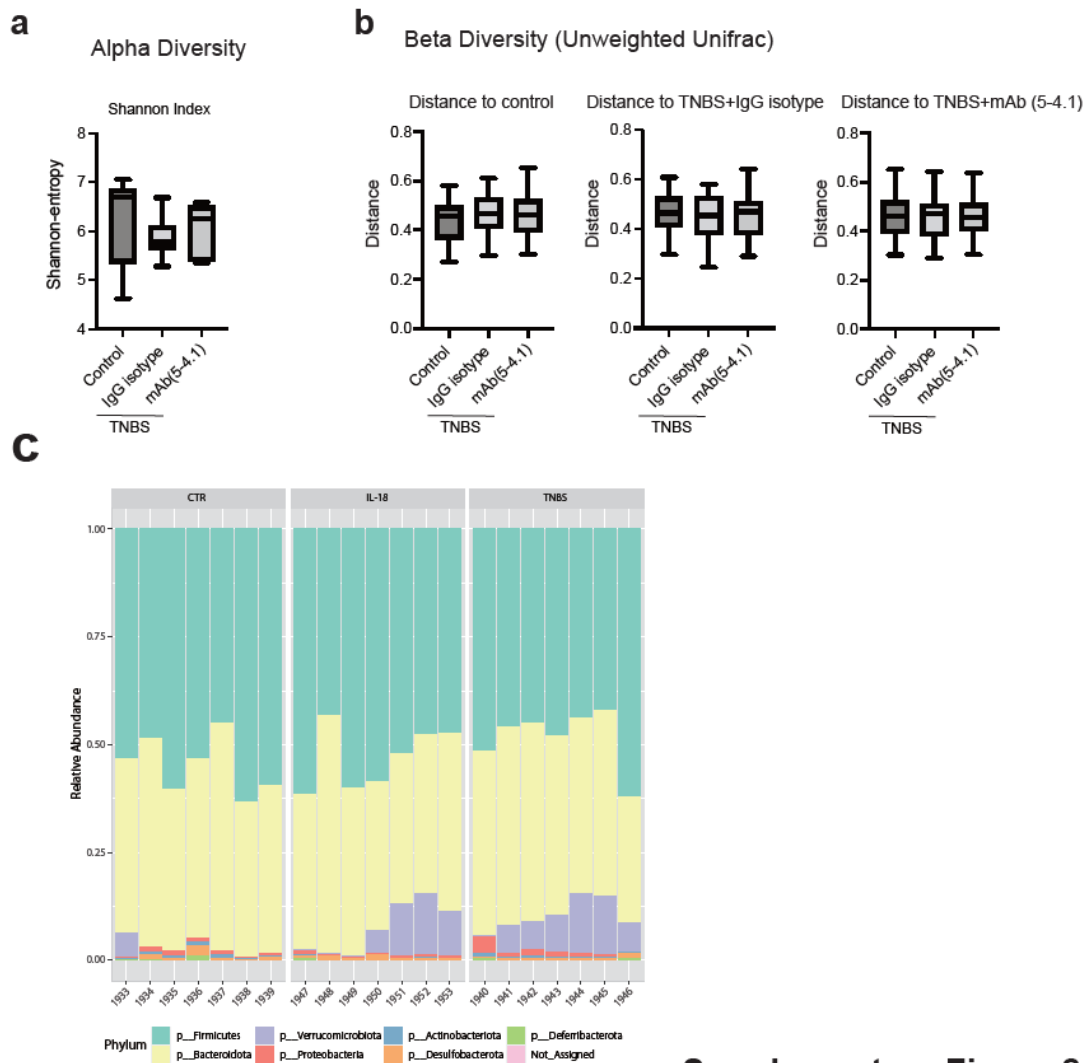


Supplementary Figure 1

Supplementary Figure 1: IL-18 and mature IL-18 expression is upregulated in patients with CD.

(a) IL-18 expression in patients with CD using bulk RNA-seq database IBD

Transcriptome and Metatranscriptome Meta-Analysis, IBD TaMMA; <https://ibd-meta-analysis.herokuapp.com>). (b) Cell type expressing IL-18 using scRNA-seq databases derived from the Single Cell Portal (SCP1423, https://singlecell.broadinstitute.org/single_cell). (c) Anti-IL-18 mAb (11-4.1) recognition of precursor and mature IL-18 in surgical samples and quantification of IL-18-positive areas. (d) Immunohistochemistry with anti-IL-18 mAb (9-10.2) showing mature IL-18 in surgical samples and quantification of the mature IL-18-positive areas. Non-responder n=14, responder n=17, Scale bar: 40 μ m. Data are presented as the means \pm SD. Statistical comparisons were performed using an unpaired *t*-test. **P* < 0.05, ***P* < 0.01, ****P* < 0.001, *****P* < 0.0001.



Supplementary Figure 2

Supplementary Figure 2: Gut microbiota analysis after administration of anti-IL-18 mAb (5-4.1).

(a and b) Comparison of alpha-diversity and β -diversity at day 5 after TNBS administration. (c) Comparison of the intestinal microbiota at the phylum level, $n=7$ for each group. Data are presented as the means; $*P < 0.05$ by one-way ANOVA, followed by Tukey's post-hoc test.