

| Supplementary Table 4. Systemic Manipulation Models | | | | | | | | | |
|---|---|---|--|---|--------------------|--|--|---|---|
| Reference | | Luo et al., 2025 | Weiberg et al., 2018 | Liu et al., 2024 | Li et al., 2024c | Sun et al., 2023 | Patel et al., 2023 | Kuhbandner et al., 2019 | Huang et al., 2021 |
| Animal Model | | Allergen Challenged Models | | | | Autoimmune Model | Gene KO Models | | |
| Intervention | | a | b | c | d | e | f | g | h |
| Intervention | | Ceftriaxone administration + Ovalbumin injection | Resection of MLN + Ovalbumin administration | Injection of β -Lg allergen | Allergen per cutan | Myasthenia Gravis (AChR α -subunit syntetic peptide) | NOD - Gene KO | MAdCAM-1 - Gene KO | IL 10 - Gene KO |
| Gut Metrics | Dysbiosis | Yes | | Yes | Yes | Yes | No | No | No |
| | Structure Alteration ^{1,2} | Microscopic structural damage | | Microscopic structural damage | | | | | Increased gut permeability |
| | Immune Alteration ^{5,6,7,8,9} | | Increased adaptive pro-inflammatory response | Increased innate pro-inflammatory response; Decreased innate anti-inflammatory response | | | | Decreased innate and adaptive pro-inflammatory response; Decreased regulatory immune response | Decreased innate and adaptive pro-inflammatory response; Increased regulatory immune response |
| | Immunoglobulin expression ¹⁰ | Increased | Increased | | Increased | | | | |
| SCFAs ¹¹ | Decreased | | | | Decreased | | | | |
| Spleen Metrics | Structure Alteration ^{3,4} | | | Splenomegaly | Splenomegaly | | | | |
| | Immune Alteration ^{5,6,7,8,9} | Increased Innate pro-inflammatory and anti-inflammatory immune response | | Increased innate pro-inflammatory response | | Increased innate and adaptive pro-inflammatory response; Decreased innate anti-inflammatory response; Increased regulatory immune response | Increased adaptive pro-inflammatory response | Increased adaptive pro-inflammatory response; Increased regulatory immune response | Increased adaptive pro-inflammatory response |
| | Immunoglobulin expression ¹⁰ | Decreased | Increased | Increased | | Increased | | | |
| | Oxidative stress ¹² | | | | | | | | |

¹ Gut Macroscopic Measurement Alteration (Length, Weight) and Fecal Mass Alteration

² Gut Microscopic Structure Damage: Distrupted villi, Destroyed Mucosal Barrier, Depletion of Goblet cells, Infiltration of Inflammatory cells

³ Spleen Macroscopic Measurement Alteration: Spleen weight, Spleen index (Spleen Weight / Body Weight)

⁴ Spleen Microscopic Measurement: diffuse white pulp, smaller follicles, diffuse white-red pulp border, infiltration of inflammatory cells, vascularization

⁵ Innate Immunity Pro-Inflammatory Cells or Cytokines Expression (Macrophage, Neutrophils, NK Cells, IFN- γ , TNF- α , IL-6)

⁶ Innate Immunity Anti-Inflammatory Immune cells or Cytokine Expression (IL-10)

⁷ Adaptive Immunity Pro-Inflammatory Immune cells (CD3 T Lymphocyte, CD4 T Lymphocyte, CD8 T Lymphocyte; Th1 T Lymphocyte, Th2 T Lymphocyte; IgM B Lymphocyte)

⁸ Adaptive Immunity Anti-Inflammatory Immune cells or Cytokine Expression

⁹ Adaptive Immunity Regulatory Immune cells or Cytokines (Th17 Lymphocyte, IL-17 Cytokines, Foxp3 / Treg Lymphocyte)

¹⁰ Immunoglobulin Expression: sIgA, IgM, IgG, IgA

¹¹ SCFAs: butyrate, acetate, propionate

¹² Oxidative Stress: Increased Free Radical Markers (MDA), Decreased Anti-Oxidant Markers (SOD, CAT, GSH)