

Supplementary Table 1. Microbial Disruption Models

Reference	Hu et al., 2016	Rosado et al., 2018	Liu et al., 2023a; Taitz et al., 2025; Wan et al., 2022	Wu et al., 2024	Abou Diwan et al., 2024	Zhang et al., 2023a	Chen et al., 2016; Liu et al., 2020, Liu et al., 2021; Ye et al., 2025	
Animal Model	Antibiotic Treatments			Toxic Substance Ingestion				
Intervention	a	b	c	d	e	f	g	
	Vancomycin administration during pregnancy	Birth from microbial sterile mothers, breastmilk from microbial sterile mothers (lack SIgA)	Broad spectrum antibiotics mixture administration	Lead administration	Organophosphate administration to dams	Lipophilic compound for industry administration	Colitis Ulcerative (DSS, CCL4)	
Gut Metrics	Dysbiosis	Yes	Yes	Yes	Yes	Yes	No	Yes
	Structure Alteration ^{1,2}	Macroscopic measurement alteration; Increased gut permeability		Macroscopic and Microscopic structural damage				Macroscopic and Microscopic structural damage
	Immune Alteration ^{5, 6, 7, 8, 9}	Increased innate pro-inflammatory response; Reduced adaptive pro-inflammatory response		Increased innate pro-inflammatory response			Increased innate pro-inflammatory response	Increased innate and adaptive pro-inflammatory response; Reduced innate and adaptive anti-inflammatory response
	Immunoglobulin expression ¹⁰			Increased				
	SCFAs ¹¹			Reduced		Increased	Increased	
Spleen Metrics	Structure Alteration ^{3,4}	Disrupted splenic cellular organization	Disrupted splenic cellular organization	Splenic atrophy; Disrupted splenic cellular organization	Splenomegaly; Disrupted splenic cellular organization	Bacterial translocation	Splenomegaly; Disrupted splenic cellular organization	Splenomegaly; Disrupted splenic cellular organization; Bacterial translocation
	Immune Alteration ^{5, 6, 7, 8, 9}	Reduced innate and adaptive pro-inflammatory response	Delayed innate pro-inflammatory response; Reduced adaptive pro-inflammatory response	Reduced innate pro-inflammatory response; Increased adaptive pro-inflammatory response	Reduced innate and adaptive pro-inflammatory response			
	Immunoglobulin expression ¹⁰		Reduced					
	Oxidative stress ¹²				Increased			

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)