

Supplementary Table 2. Splenic Manipulation Models

Supplementary Table 2. Splenic Manipulation Models						
Reference		Thim-Uam et al., 2022; Wei et al., 2021	Jiang et al., 2025	Yang et al., 2024	Fang et al., 2022	Ali et al., 2024; Chen et al., 2021; Han et al., 2022; Khan et al., 2022; Li et al., 2024a; Li et al., 2024d; Liu et al., 2023a; Ma et al., 2023; Ning et al., 2024; Shen et al., 2025; Song et al., 2024; Yan et al., 2024; Zeng et al., 2023
Animal Model		Splenic Manipulation			Immunosuppressant Administration	
		a	b	c	d	e
Intervention		Splenectomy	Splenic Denervation	B-cell-specific TLR9 Gene KO	Busulfan Injection	Cyclophosphamide injection
Gut Metrics	Dysbiosis	Yes	No	No	Yes	Yes
	Structure Alteration ^{1,2}	Increased gut permeability	Microscopic structural damage; Increased gut Permeability	Macroscopic measurement alteration; Increased gut permeability		Microscopic structural damage; Increased gut Permeability
	Immune Alteration ^{5,6,7,8,9}					Reduced innate and adaptive pro-inflammatory response
	Immunoglobulin expression ¹⁰			Decreased		Decreased
	SCFAs ¹¹	Increased				Reduced
Spleen Metrics	Structure Alteration ^{3,4}		Disrupted splenic cellular organization		Disrupted splenic cellular organization	Splenic atrophy; Disrupted splenic cellular organization
	Immune Alteration ^{5,6,7,8,9}		Increased adaptive pro-inflammatory response	Increased adaptive pro-inflammatory response	Decreased innate and adaptive pro-inflammatory response	Complete immune dysruption
	Immunoglobulin expression ¹⁰			Decreased		Decreased
	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)

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, proprionate

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

(B Lymphocyte)