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INPLASY

Gut Microbiota–Derived Bacterial Extracellular Vesicles: Emerging Drivers of Immune Regulation and Autoimmunity

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Corresponding author:
Rahul Mittal

r.mittal11@med.miami.edu

Author Affiliation:
University of Miami.

Mittal, R; Mutha, V; Hirani, K.

ADMINISTRATIVE INFORMATION

Support - Not Applicable.

Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202630118

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 31 March 2026 and was last updated on 31 March 2026.

INTRODUCTION

Review question / Objective To systematically evaluate and synthesize experimental evidence on how gut microbiota–derived bacterial extracellular vesicles influence immune regulation, including effects on epithelial barrier integrity, innate and adaptive immune responses, and inflammatory signaling pathways, with relevance to autoimmune and inflammatory diseases.

Condition being studied Autoimmune and inflammatory diseases, with a primary focus on intestinal inflammation and inflammatory bowel disease (IBD), in the context of immune dysregulation mediated by gut microbiota–derived bacterial extracellular vesicles (BEVs). The review also considers broader systemic immune-mediated conditions influenced by microbiome-derived vesicle signaling.

METHODS

Participant or population Experimental models examining host–microbiome interactions, including in vitro cell culture systems (e.g., epithelial cells, macrophages, dendritic cells), animal models of intestinal inflammation and autoimmune disease (primarily murine models), and relevant translational studies involving human-derived biological samples where applicable.

Intervention Exposure to or administration of gut microbiota–derived bacterial extracellular vesicles (BEVs), including vesicles isolated from commensal, probiotic, or pathogenic bacterial species, used to evaluate their effects on host immune responses, epithelial barrier function, and inflammatory signaling pathways.

Comparator Control conditions including untreated or vehicle-treated models, baseline conditions without exposure to bacterial

extracellular vesicles, or comparisons with vesicles derived from different bacterial species (e.g., commensal/probiotic vs pathogenic), where applicable.

Study designs to be included Experimental mechanistic studies, including in vitro cell-based studies, in vivo animal studies, and translational studies using human-derived biological samples, that evaluate the effects of gut microbiota–derived bacterial extracellular vesicles on immune regulation, epithelial barrier function, or inflammatory signaling.

Eligibility criteria Studies will be included if they investigate extracellular vesicles produced by bacterial species associated with the gut microbiome and evaluate their effects on host inflammatory responses, epithelial barrier function, immune cell activation, or inflammatory disease models. Eligible studies will include mechanistic experimental investigations using in vitro systems, animal models of intestinal inflammation, or translational studies examining vesicle-mediated host signaling pathways. Studies will be excluded if they focus exclusively on mammalian extracellular vesicles, non-gut bacterial vesicles unrelated to the gastrointestinal microbiota, review articles, editorials, conference abstracts, or publications without experimental evaluation of vesicle-mediated host responses.

Information sources A comprehensive literature search will be conducted in the following electronic databases: PubMed/MEDLINE, Scopus, Web of Science, and EMBASE, from database inception to the date of search. Reference lists of included studies will also be screened to identify additional relevant articles.

Main outcome(s) Primary outcomes include measures of immune regulation and inflammatory responses induced by gut microbiota–derived bacterial extracellular vesicles (BEVs), including cytokine production, activation of innate and adaptive immune signaling pathways, and modulation of macrophage and dendritic cell function.

Additional outcome(s) Additional outcomes include effects on intestinal inflammation severity and epithelial barrier integrity (e.g., tight junction expression and permeability).

Quality assessment / Risk of bias analysis Risk of bias will be assessed using a combination of tools appropriate to study design. For animal studies, the SYRCLE (Systematic Review Centre for Laboratory Animal Experimentation) risk-of-bias tool will be applied. For in vitro, quasi-experimental, and laboratory-based studies, the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Quasi-Experimental Studies (non-randomized experimental studies) will be used.

Strategy of data synthesis Data will be synthesized qualitatively using a thematic approach due to heterogeneity across study designs and outcomes. Studies will be grouped by key mechanistic domains (e.g., inflammation, epithelial barrier function, immune cell responses, and systemic effects), and findings will be narratively summarized. Risk-of-bias assessments will be considered in interpreting the evidence.

Subgroup analysis Not applicable.

Sensitivity analysis Not applicable.

Country(ies) involved United States.

Keywords Bacterial extracellular vesicles; gut microbiota; microbiome; immune regulation; inflammation; autoimmune diseases; inflammatory bowel disease; epithelial barrier; host–microbiome interactions; immune signaling.

Contributions of each author
Author 1 - Rahul Mittal.
Author 2 - Vedaant Mutha.
Author 3 - Khemraj Hirani.