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Preventing Sepsis by Preemptive Restoration of "Leaky Gut" with an Advanced Probiotic Platform

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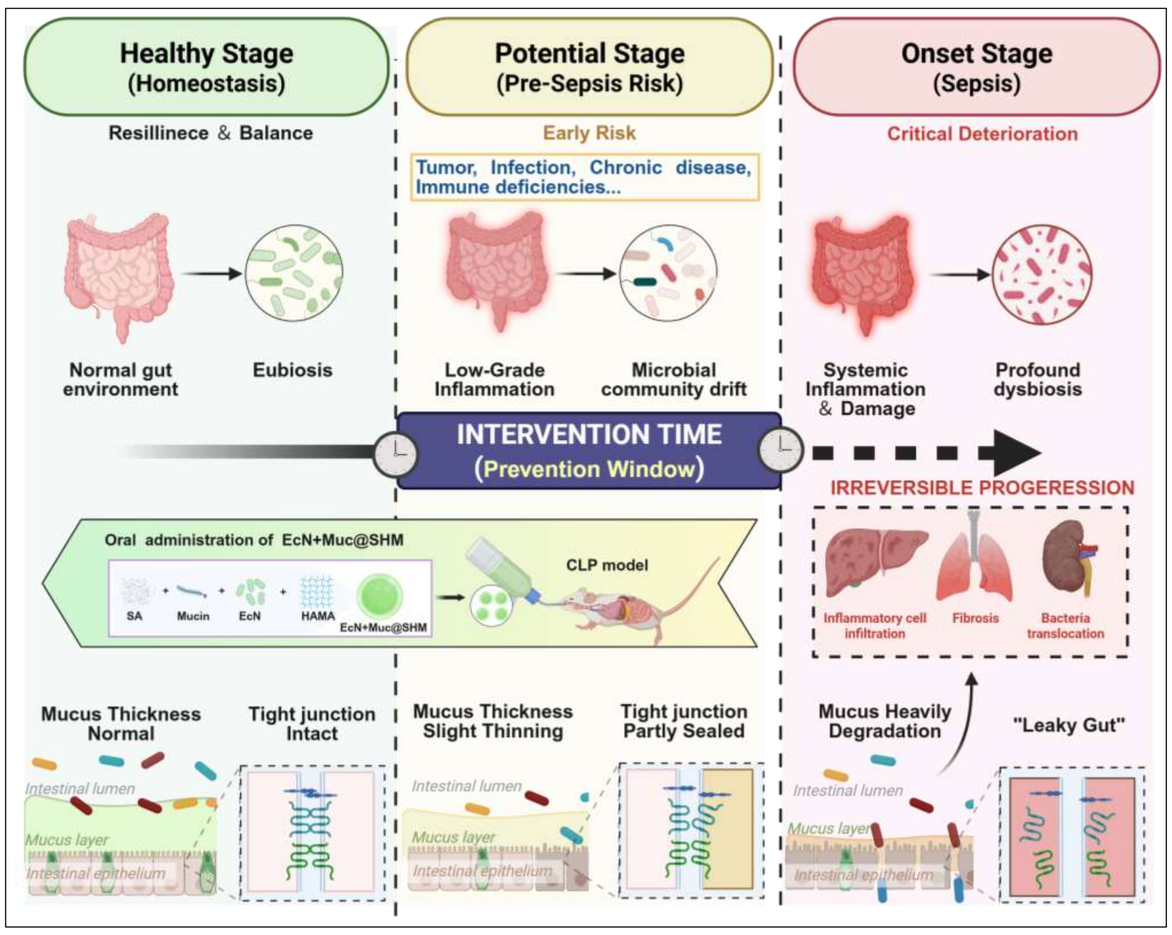
INTRODUCTION & AIM

Sepsis is a life-threatening condition driven by dysregulated host responses to infection, with high mortality among immunocompromised patients. **Emerging evidence links early intestinal barrier dysfunction and microbial dysbiosis to the onset of sepsis, suggesting that these pre-septic changes are targetable for prevention.** Current strategies focus mainly on infection control after sepsis onset, but proactive interventions are rare. This study aims to develop an engineered symbiotic platform capable of **simultaneously repairing gut barrier integrity, restoring microbial balance before septic progression**. By targeting pre-septic dysbiosis, we seek to establish a novel preventive paradigm that reduces sepsis incidence and mortality, particularly in high-risk and immunocompromised populations.



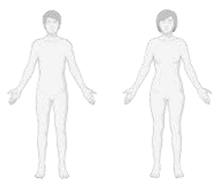
METHOD

In this study, **we designed and fabricated an advanced probiotic delivery platform based on ternary hydrogel microspheres,** designated EcN+Muc@SHM. These microspheres were constructed by first encapsulating *E. coli Nissle 1917* (EcN) and mucin within a methacrylated hyaluronic acid (HAMA) core via a **photopolymerization-coupled emulsification method**. Subsequently, a protective alginate shell was coated onto the surface through **ion polymerization** to enhance stability and targeted delivery.

RESULTS & DISCUSSION

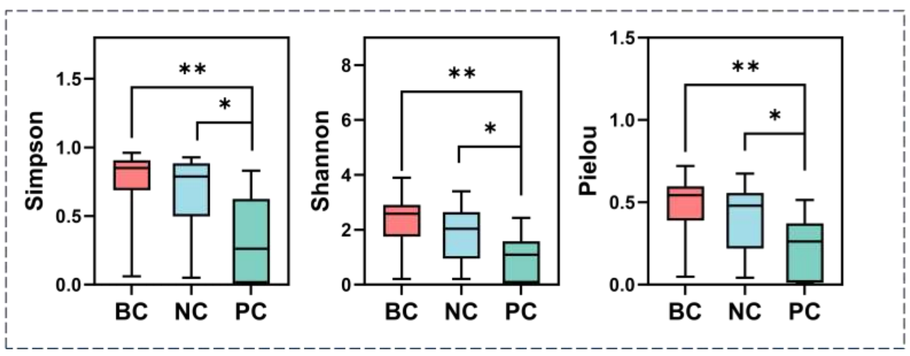
Sepsis progression correlates with reduced gut microbial diversity and compositional shifts, notably increased Firmicutes and decreased Bacteroidota, beginning prior to clinical diagnosis and potentially serving as early predictive biomarkers.

Fecal 16S rRNA sequencing

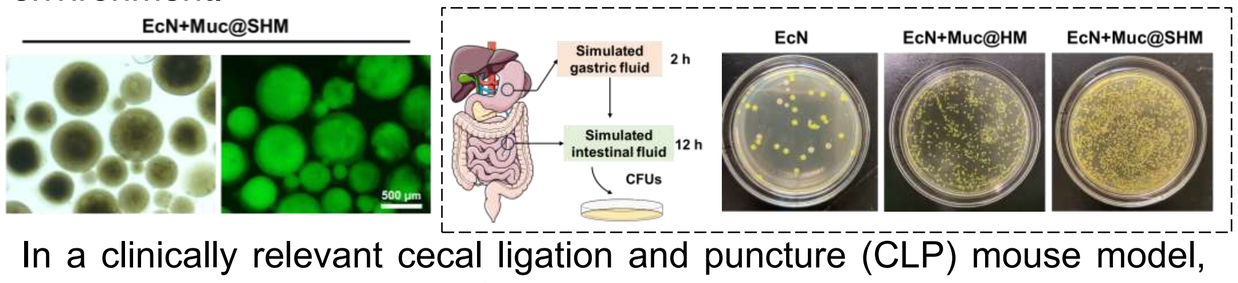


Human cohort

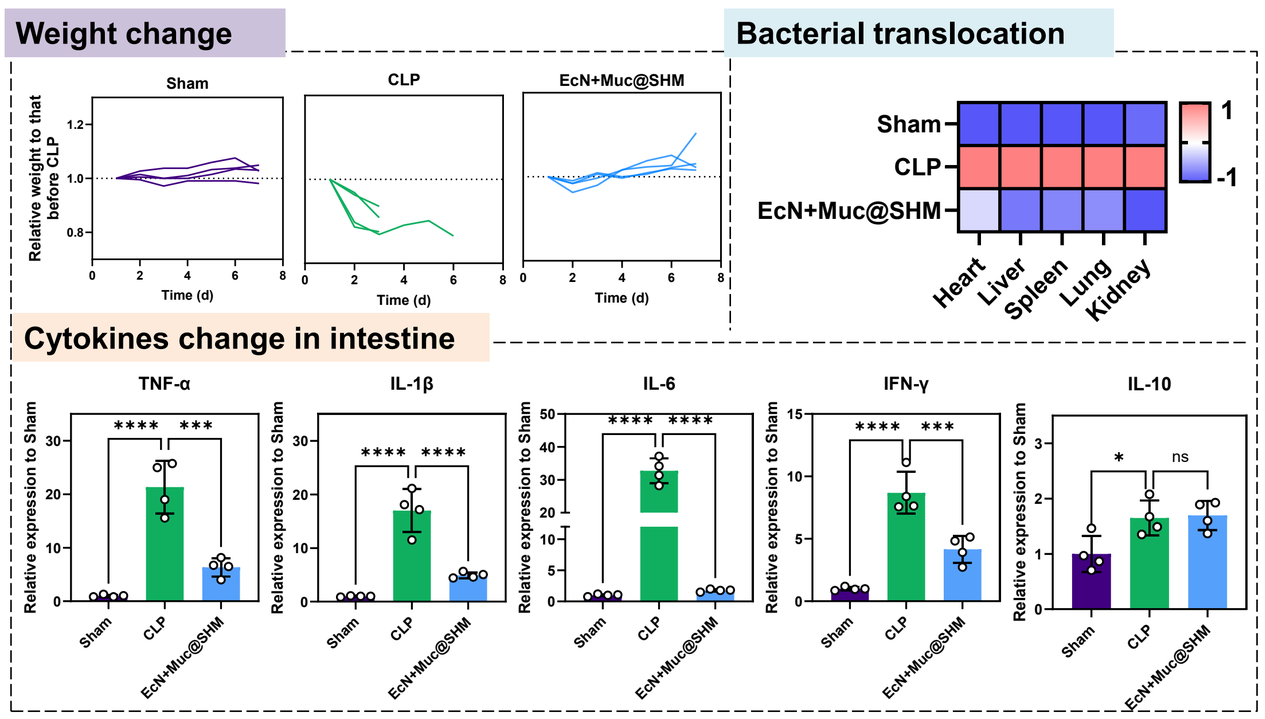
BC	NC	PC
10	16	11



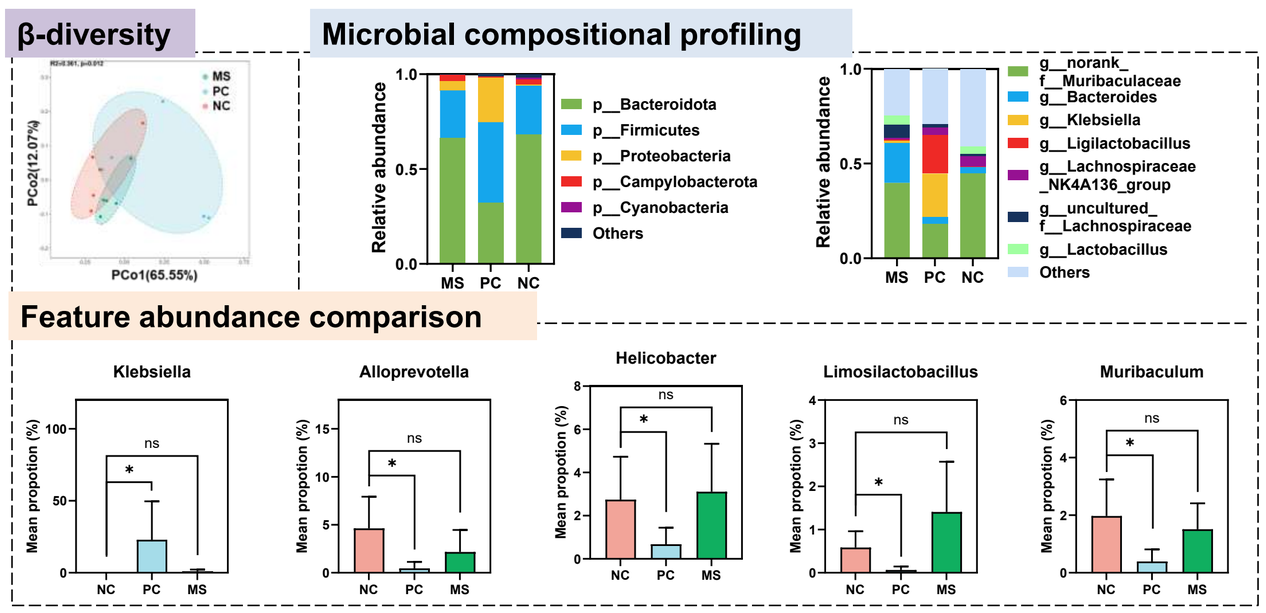
The integrated EcN+Muc@SHM microsphere structure conferred **robust protection to the probiotic EcN** payload against the harsh gastric environment.



In a clinically relevant cecal ligation and puncture (CLP) mouse model, this advanced probiotic platform exhibited remarkable prophylactic and therapeutic efficacy. Administration of the microspheres **significantly reduced bacterial translocation, resolved local inflammation, and alleviated intestinal injury.**



Fecal microbiome sequencing further revealed that **the treatment effectively corrected post-CLP dysbiosis,** thereby restoring microbial homeostasis and promoting the recovery of a healthy gut flora.



CONCLUSION

The EcN+Muc@SHM effectively restores gut barrier integrity, rebalances microbiota and inflammation in septic models. Functional analyses reveal enhanced glycosaminoglycan and bile acid metabolism, supporting intestinal homeostasis. **This preemptive strategy offers a promising approach for sepsis prevention, particularly in high-risk populations.**

FUTURE WORK / REFERENCES

Future studies will focus on optimizing formulation stability and evaluating long-term safety. Translation into clinical trials will assess preventive efficacy in immunocompromised patients.