Unveiling the muco-microbiotic layer: a three-component framework for mucosal health and disease

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Dear Editor,

We wish to bring attention to the critical role of the muco-microbiotic layer,[1,2] a dynamic and integrated system located at mucosal surfaces. This layer represents a cornerstone of host-microbe interactions, composed of three key components: the mucus, the microbiota, and extracellular nanovesicles (commonly referred to as exosomes).

The mucus layer acts as a viscoelastic physical barrier, preventing pathogens from directly accessing epithelial cells.[1,2] Composed primarily of mucins secreted by goblet cells, it also provides a structured habitat for commensal microorganisms while supporting nutrient and metabolite exchange essential for maintaining mucosal health.

The diverse microbial communities residing in the mucus include bacteria, fungi, archaea, and viruses. These microorganisms play essential roles in modulating the host immune response, competing with pathogens for resources, and producing metabolites that regulate epithelial homeostasis.[1–3] A balanced microbiota supports intestinal barrier integrity and systemic health, while dysbiosis has been linked to inflammatory disorders and metabolic diseases.

Exosomes are lipid bilayer vesicles ranging from 30 to 150 nm, produced by host epithelial cells and commensal microorganisms. These vesicles are central to intercellular communication, transferring proteins, lipids, and nucleic acids that influence immune regulation and microbiota composition.[1–3] Recent evidence highlights their involvement in maintaining mucosal immune tolerance, modulating inflammation, and serving as decoys to neutralize pathogenic factors.[1–4]

Disruption in any component of the muco-microbiotic layer can lead to a cascade of detrimental effects, including chronic inflammation, impaired immune responses, and increased susceptibility to infections. Novel therapeutic strategies targeting this layer, such as engineered exosomes or interventions designed to restore mucus integrity and microbiota balance, hold promise for a range of conditions from inflammatory bowel disease to metabolic syndromes.

We would like to encourage further investigation into the muco-microbiotic layer as a unified morphofunctional structure. Understanding the synergies and communication pathways among its three components could reveal novel biomarkers and therapeutic targets for mucosal and systemic diseases.

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