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BIOGENESIS OF OUTER MEMBRANE VESICLES IN HUMAN GUT BACTERIA

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Extracellular vesicles are produced in all three domains of life, and their biogenesis have common ancient origins in eukaryotes and archaea. Although bacterial vesicles were discovered several decades ago and multiple roles have been attributed to them, no mechanism has been established for vesicle biogenesis in bacteria. For this reason, there is a significant level of skepticism about the biological relevance of bacterial vesicles. In *Bacteroides thetaiotaomicron* (Bt), a prominent member of the human intestinal microbiota, outer membrane vesicles (OMV) have been proposed to play key physiological roles. By employing outer membrane-retained and OMV-specific markers fused to fluorescent proteins we visualized OMV biogenesis by live-cells. We performed comparative proteomic analyses to demonstrate that Bt actively tailors its vesicle cargo to optimize the breakdown of diet- and host-derived complex glycans. We also show that, in Bt, a negatively-charged N-terminal motif acts as a signal for protein sorting into OMVs irrespective of the nutrient availability. Furthermore, we identified a new family of sigma factors family (Dual membrane-spanning anti-sigma factors, "Dma", which controls OMV biogenesis. Dma1 has a previously uncharacterized domain organization that enables Dma1 to span both the inner and outer membrane of Bt. Our work provides mechanistic insights into the regulation of OMV biogenesis in human gut bacteria and lays the foundation for further investigations into the physiological relevance of OMVs and their roles in gut homeostasis.

Palabras clave: palabras_clave