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Role of Outer Membrane Vesicles (OMVS) in *Serratia grimesii* Interactions with CaCo-2 Cells

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Opportunistic bacteria *Serratia grimesii* are able to invade eukaryotic cells; however, the molecular mechanisms of their invasive activity remains unclear. Previously, we have shown that *in vitro* S. *grimesii* secrete membrane vesicles that penetrate cultured eukaryotic cells and promote invasion of *S. grimesii* into these cells (Bozhokina et al., 2020). Therefore, the aim of this work was to study the role of *S. grimesii* membrane vesicles in the process of interaction between bacteria and the host cell. The results of our experiments showed that exposure of *S. grimesii* to cold shock or oxidative stress induced by hydrogen peroxide increased the secretion of membrane vesicles, and the isolated vesicles enhanced the invasion of bacteria into CaCo-2 cells. Also, *S. grimesii* membrane vesicles induced the immune response of CaCo-2 cells, and demonstrated cytotoxic activity towards these cells, determined by the level of lactate dehydrogenase release. In the presence of vesicles obtained under the stress conditions, bacteria adhered to and penetrated into CaCo-2 cells more actively. Moreover, we have shown for the first time that the cell surface receptor E-cadherin is involved in the invasion of *S. grimes*ii membrane vesicles into CaCo-2 cells. Our results suggest that the vesicle-mediated delivery of virulence factors into eukaryotic cells can significantly contribute to the pathogenesis induced by *S. grimesii* infection.

Keywords*: S. grimesii*, membrane vesicles, grimelysin, invasion