学位論文審査結果の要旨

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（学位論文審査結果の要旨）

Intestinal Epithelium-Derived Luminally Released Extracellular Vesicles in Sepsis Exhibit the Ability to Suppress TNF-α and IL-17A Expression in Mucosal Inflammation

【主論文審査結果の要旨】

著者らは論文において下記の内容を述べている。

Sepsis is a systemic inflammatory disorder induced by a dysregulated immune response to infection resulting in dysfunction of multiple critical organs, including the intestines. Previous studies have reported contrasting results regarding the abilities of exosomes circulating in the blood of sepsis mice and patients to either promote or suppress inflammation. Little is known about how the gut epithelial cell-derived exosomes released in the intestinal luminal space during sepsis affect mucosal inflammation. To study this question, we isolated extracellular vesicles (EVs) from intestinal lavage of septic mice. The EVs expressed typical exosomal (CD63 and CD9) and epithelial (EpCAM) markers, which were further increased by sepsis. Moreover, septic-EV injection into inflamed gut induced a significant reduction in the messaging of pro-inflammatory cytokines TNF-α and IL-17A. MicroRNA (miRNA) profiling and reverse transcription and quantitative polymerase chain reaction (RT-qPCR) revealed a sepsis-induced exosomal increase in multiple miRNAs, which putatively target *TNF*-α and *IL-17A*. These results imply that intestinal epithelial cell (IEC)-derived luminal EVs carry miRNAs that mitigate pro-inflammatory responses. Taken together, our study

proposes a novel mechanism by which IEC EVs released during sepsis transfer regulatory miRNAs to cells, possibly contributing to the amelioration of gut inflammation.

敗血症における腸管上皮細胞由来の細胞外小胞は、炎症性サイトカイン TNF-α および IL-17Aの産生を阻害し粘膜炎症を抑制する能力を示すことを明らかにした論文であり、学術上極めて有益であり、学位論文として価値あるものと認めた。

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