Immune modulation by complement receptor 3-dependent human monocyte TGF-ß1-transporting vesicles.

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Abstract

Extracellular vesicles have an important function in cellular communication. Here, we show that human and mouse monocytes release TGF-β1-transporting vesicles in response to the pathogenic fungus *Candida albicans*. Soluble β-glucan from *C. albicans* binds to complement receptor 3 (CR3, also known as CD11b/CD18) on monocytes and induces the release of TGF-β1-transporting vesicles. CR3-dependence is demonstrated using CR3-deficient (CD11b knockout) monocytes generated by CRISPR-CAS9 genome editing and isolated from CR3-deficient (CD11b knockout) mice. These vesicles reduce the pro-inflammatory response in human M1-macrophages as well as in whole blood. Binding of the vesicle-transported TGF-β1 to the TGF-β receptor inhibits IL1B transcription via the SMAD7 pathway in whole blood and induces

TGFB1 transcription in endothelial cells, which is resolved upon TGF-β1 inhibition. Notably, human complement-opsonized apoptotic bodies induce production of similar TGF-β1-transporting vesicles in monocytes, suggesting that the early immune response might be suppressed through this CR3-dependent anti-inflammatory vesicle pathway.

Involved units

Infection Biology Peter F. Zipfel Read more

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Leibniz-HKI-Authors



Luke Donald Halder

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Md Zahidul Hasan

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Ilse Denise Jacobsen

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Emeraldo Jo

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Olaf Kniemeyer

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Thomas Krüger

Details



Diana Palme

Details



Christine Skerka

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Peter F. Zipfel

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