

Immune modulation by complement receptor 3-dependent human monocyte TGF- β 1-transporting vesicles.

Halder LD, Jo EAH, Hasan MZ, Ferreira-Gomes M, Krüger T, Westermann M, Palme DI, Rambach G, Beyersdorf N, Speth C, Jacobsen ID, Kniemeyer O, Jungnickel B, Zipfel PF, Skerka C (2020) Immune modulation by complement receptor 3-dependent human monocyte TGF- β 1-transporting vesicles. *Nat Commun* 11(1), 2331.

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Abstract

Extracellular vesicles have an important function in cellular communication. Here, we show that human and mouse monocytes release TGF- β 1-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- β 1-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- β 1 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- β 1 inhibition. Notably, human complement-opsonized apoptotic bodies induce production of similar TGF- β 1-transporting vesicles in monocytes, suggesting that the early immune response might be suppressed through this CR3-dependent anti-inflammatory vesicle pathway.

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