Isoform localization of Dectin-1 regulates the signaling quality of anti-fungal immunity.

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Abstract

Dectin-1 is recognized as a major receptor for fungal ß-glucans and contributes to anti-fungal immunity. Human monocyte populations express Dectin-1 isoforms A and B, which differ by the presence of a stalk region and its N-linked glycosylation site. Here, we analyzed the expression of both isoforms in human monocyte-derived cells. The cellular localization on cell lines stably expressing either Dectin-1 isoform A or B was studied by flow cytometry and confocal laser scanning microscopy. Intracellular protein signaling and cytokine production were analyzed by immunoblotting and cytometric bead array, respectively. Monocyte-derived cells showed cell type-specific expression of the two isoforms. Glycosylated Dectin-1 isoform A was predominantly localized at the cell surface, non-glycosylated isoform B was retained intracellularly. Inhibition of glycosylation resulted in efficient abrogation of cell surface expression of isoform A. Signaling quality following Dectin-1 stimulation was reduced in isoform B cells. Differential isoform specific cytokine secretion was observed by cytometric bead array. We show here that n-glycosylation of Dectin-1 is crucial for its cell surface expression and consequently signal transduction. Taken

together, unique cytokine secretion and varying expression levels of human Dectin-1 isoforms on monocyte-derived cells may indicate distinct isoform usage as a cell type-specific mechanism of regulating anti-fungal immunity.

Beteiligte Forschungseinheiten

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