Human MAIT cells are rapidly activated by *Aspergillus* spp. in an APC-dependent manner.

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Abstract

Mucosal associated invariant T cells (MAIT cells) are innate-like T cells (TC) which are known to be activated by several bacteria and viruses. However, activation of MAIT cells by moulds, such as the opportunistic human pathogen Aspergillus, is not well described. Stimulation of human PBMC with A. fumigatus, A. flavus, or A. terreus conidia revealed that in contrast to conventional CD4+ and CD8+ TC, MAIT cells responded already after 4 h of coincubation with upregulation of CD69. Furthermore, concurrent increase of CD107a expression and reduced intracellular expression of cytolytic proteins like perforin and granzyme indicated degranulation of intracellular vesicles. MAIT cell activation only occurred in the presence of APC and was dependent on cell-cell contact as separation of TC and APC abrogated MAIT cell activation. Furthermore, we observed that MAIT cell activation by moulds requires presentation of riboflavin metabolites and depends on TCR engagement as antibody blocking of MR1, the antigen presenting molecule for MAIT cells, prevented upregulation of CD69 and CD107a. In summary, we could demonstrate that MAIT cells

are activated by Aspergillus conidia in a TCR-dependent manner by APC. These findings reveal MAIT cells as an interesting new target in antifungal defense.

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