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Functional analysis of invariant Natural Killer T cells in human paracoccidioidomycosis

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Invariant Natural Killer T (iNKT) cells represent a particular T cell population that recognizes lipids in the context of CD1d molecules. Upon TCR activation, iNKT cells release both Th1 (IFN-γ and TNF-α) and Th2 (IL-4, IL-10 and IL-13) cytokines. Currently, it is accepted that these cells are an important link between innate and adaptative immunity. However, their implication in human pathology, mainly in granulomatous infectious diseases, remains to be determined. Few studies reported reduced levels of circulating iNKT cells in patients with pulmonary tuberculosis. After treatment, iNKT cell number returned to normal levels in some but not in all patients. This disturbance was pointed as a possible mechanism contributing to tuberculosis susceptibility. Thus, the aim of our study was to analyze iNKT cell number and function in another granulomatous disease, paracoccidioidomycosis, the most prevalent deep fungal infection endemic in South America. Study groups were: healthy individuals previously exposed (PCC+, n=5) or not (PCC-, n=5) to the fungus and individuals cured of paracoccidioidomycosis (CUR, n=7). We quantified by flow cytometry, using CD1d-tetramers, the number, the cytokine-producing capacities and the ratio of expansion induced by the following iNKT cell agonists: alpha-galactosyl-ceramide (α-GalCer), iGb3 and OCH. The number of circulating iNKT cells were similar between cured and control groups, varying from 0.01 to 0.46% of PBMCs and all groups had a ~200 fold expansion rate after ~12 days of culture with α-GalCer. The main cytokine produced was IFN-γ, between 17-91% and 37-94% of positive cells among gated iNKT cells observed ex-vivo or after α-GalCer expansion; no significant differences were observed between the groups. CD1d expression in monocytes and monocyte-derived dendritic cells in presence of α-GalCer was also comparable. In conclusion, we suggest that susceptibility to paracoccidioidomicosys is not associated with impairment in iNKT functions, number or expansion capacity.

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