Ruprecht-Karls-Universität Heidelberg
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Dissertations-Kurzfassung

Comparative analysis of macrophage differentiation using concurrent stimulation of monocytes with CSF1 and Th1 versus Th2 cytokines

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CSF1, which is present in many tissues under steady-state homeostasis, Here, we assessed how Th1 or Th2 signature cytokines (i.e. IFNγ, IL-4) affect monocyte phenotype and their interaction with lymphocytes when concurrently exposed to CSF1. The cells are hereafter defined as “M1” and “M2” macrophages. The results revealed that: 1) “M1” and “M2” have similar characteristics as classical M1 and M2 macrophages with respect to TNFα and IL-10 production, yet for cell surface markers, the expression of CD86 in M1 was higher as compared to M2, the reverse was found for “M1” and “M2”. Also, downregulation of CD14 expression was more pronounced in “M2” as compared to M2 macrophages. 2) COX1/2, 15-LO, IDO-1 and HO-1 were differently expressed in “M1” and “M2” macrophages (“M1”: COX-1^-, 15-LO^-, IDO-1^+, HO-1^+; “M2”: COX-1^+, 15-LO^+, IDO-1^-, HO-1^+). Differences between M1 and “M1” macrophages were only observed for COX-1 and HO-1. The latter macrophages expressed COX-2 upon LPS stimulation and produced significantly more PGE_2 than LPS stimulated “M2” macrophages. 3) Compared to LPS stimulated “M2” macrophages, “M1” cells were poorly stimulating T cells proliferation in allogeneic mixed leukocyte culture (MLC), despite upregulation of CD86 by LPS. Yet, IL-17A and IFNγ production in MLC was significantly higher when LPS-stimulated “M1” macrophages were used in MLC. For classical polarized macrophages, M1 cells were slightly superior to M2 cells in stimulating T cell proliferation in allogeneic MLC. 4) “M2” mediated T cell proliferation seemed to be COX-1 dependent since aspirin inhibited T cell proliferation through its action on “M2” macrophages. Thus, our results suggest that concurrent stimulation of monocytes with CSF1 and IFNγ or IL-4 leads to macrophage polarization that differs from that generated by classical protocols.