6. SUMMARY

Monocytes play a pivotal role in the pathogenesis of the inflammation. In the acute phase of inflammation they obtain predominantly pro-inflammatory effects, which become visible in the expression of second messengers (cytokines, eicosanoids). During the inflammatory resolution phase the phenotype of the monocytes occurring in the inflammation area changes in such a way that they now synthesize predominantly anti-inflammatory mediators. Thus the acute inflammation reaction is terminated actively and the original structure of the inflammatory changed fabric is restored. In order to examine, whether Th2-cytokines (IL-4 and IL-13) can induce such a phenotype-switch, peripheral monocytes were cultivated in presence of IL-4 or IL-13 for 72 hours *in vitro* afterwards cellular expression profiles (more than 16,000 genes) were obtained by means of microarray analysis. The eight most strongly up-regulated (up to 290-fold up-regulation) genes were: 15-LOX-1, FN1, CD23, CD1C, MAO A, F13A1, MS4A4A and CCL22. In contrast, IFI44L, SN, CLGN, ORM1, C1S, INDO, ISG20 and KCNJ15 were the most strongly down-regulated (up to 100-fold down-regulation) genes. Under our experimental conditions classical pro-inflammatory cytokines (IL-1, IL-6, IL-8, IL 18, CCL2, TNFα) become down-regulated. And in addition we observed a reduction of the expression of enzymes (5-LOX, LTC4-Synthase, COX-2), which are involved in the synthesis of pro-inflammatory eicosanoids and of co-receptors (CD4, CXCR4, CCR5) for the human immunodeficiency virus-1 (HIV-1). In contrast, the expression of proteins with anti-inflammatory characteristics (TIMP, ANXA1, IL-10, HMOX1) are up-regulated. In addition to the up-regulation of the 15-LOX-1, which was the most strongly regulated gene in monocytes after IL-4 stimulation, we observed a 54-fold increase of MAO-A expression. This was particularly remarcable, as there was no experimental reference for a monocyte expression of this enzyme so far. However our data prove that the MAO-A in IL4-treated monocytes is expressed ad high level and that the enzyme could play a crucial role during the inflammatory resolution phase, as it is responsible for the degradation of some pro-inflammatory biogenic amines. Further experiments on the mechanisms of the expression regulation of the MAO-A and the HIV co-receptors indicated an important role of the cellular hydroperoxide tonus. So the IL-4-induced up-regulation of the MAO-A expression and the IL-4-dependent decrease of the cellular concentration of HIV-1 co-receptors could be induced by an increase of the cellular hydroperoxide tonus. This suggest, that at least a part of the IL-4-regulated genes is redox-dependent regulated. Since the enzymatic activity of the 15-LOX-1 can lead to an increase of the cellular oxidation status, the IL-4-induced up-regulation of the expression of this lipid-peroxiding enzyme by means of the IL-4-induced regulation cascade seems to be particularly important.