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Poster presentation

Functional characterization of GM-CSF induced monocyte subsets

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Background

Monocytes and macrophages may either promote or down-regulate inflammatory reactions depending on their state of activation. The effects of Granulocyte Macrophage-Colony Stimulating Factor (GM-CSF), one of the most widely used growth factors for modulating immune responses, on monocytes are currently not well defined.

Materials and methods

We analyzed the GM-CSF-induced expression pattern in human monocytes by microarray technology. The results were independently confirmed by real-time polymerase chain reaction (PCR), flow cytometry and assessed by independent functional assays evaluating the influence of defined cytokine combinations (+GM-CSF, ± IL-4, ± Il-6, ± IL-8, ± TNFα, ± IFNγ).

Results

We identified GM-CSF-dependent regulation of 402 genes, including important immune-regulatory molecules. Functional clustering of GM-CSF-regulated genes indicated induction of monocytic properties such as lymphocyte activation and tumour necrosis factor (TNF) receptor binding as well as repression of apoptosis, oxidative burst, cell motility and migration. Expression data show an up-regulation of M2-phenotype genes (CCL 13, 23 and 17) and down-regulation of M1-phenotype genes (CXCL10, 11 and 13) indicating a GM-CSF induced alternative macrophage activation. Independent functional analysis revealed suppression of apoptosis by GM-CSF. However GM-CSF induces apoptosis in monocytes activated by TNFα which may contribute to anti-inflammatory actions of GM-CSF treatment in vivo.

Conclusion

GM-CSF treatment did not simply cause a transitory amplification of innate immunity but results in differentiation of a specific phenotype which may be actively involved in resolution of acute and possibly also chronic inflammatory reactions.