

excessive and uncontrolled production of proinflammatory cytokines can be responsible for the onset and maintenance of chronic inflammatory diseases like systemic lupus erythematosus (SLE). The cytokine production that accompanies pathophysiological processes of chronic inflammation is reflected within the monocyte transcriptome. The present study was designed to define stimulus-specific expression patterns in tumour necrosis factor α (TNF α), interferon type I (IFN α) and IFN type II (IFN γ)-stimulated monocytes in vitro, and to use those cytokine signatures to unravel monocyte transcriptome from patients with SLE.

Methods Following in vitro stimulation of whole blood with TNF α , IFN α 2a and IFN γ for 1.5 h at 37°C, monocytes were isolated and analysed for gene expression profiles by microarray technology. These global in vitro expression profiles were compared with transcriptome of SLE monocytes.

Results In vitro stimulation of whole blood samples with TNF α , IFN α and IFN γ resulted in 7874, 8100 and 7132 differentially expressed probe sets, respectively (corresponding to about 3150, 3240 and 2850 genes). IFN α and IFN γ had very similar profiles in monocytes, but more than half of the IFN profile is shared with TNF α . Besides those shared inflammatory profiles, each stimulus was also able to depict the monocyte response in a specific manner. Compared with 1614 differentially expressed probe sets in SLE, cytokine-specific gene signatures could be identified for TNF α , IFN α and IFN γ , reflecting in part the complexity of the pathophysiology of SLE. 41.5% of differentially expressed genes in SLE overlapped with in vitro induced IFN α signature, 33.3% of SLE with IFN γ , while 22.5% of disease genes were contributed to TNF α signature. Although the IFN α imprint within SLE is predominant, it is also shared not only with IFN γ but also with TNF α (namely, 25.8% of the IFN α signature is shared with TNF α). On the other hand, the TNF α signature in SLE is identified not just as shared with IFNs but also as TNF α -specific.

Conclusion Our findings indicate that defining in vitro induced TNF α , IFN α and IFN γ gene expression profiles is able to decipher disease-specific profiles of SLE. These imprints could provide an overview into stimulus-specific genes that are associated with the pathogenesis and maintenance of chronic inflammation. In addition, they could be used as biomarkers for understanding the pathological mechanisms underlying diseases and for monitoring and predicting drug responsiveness.

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DEFINING TNF α -, IFN α - AND IFN γ -INDUCED GENE EXPRESSION PROFILES IN HUMAN MONOCYTES TO ESTIMATE THEIR CYTOKINE-SPECIFIC IMPACT IN INFLAMMATORY DISEASES

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Background Cytokines contribute to the host defence by an overall tuning of the immune system. Nevertheless, an