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 (TNFα), interferon type I (IFNα) and IFN type II (IFNγ)-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 TNFα, IFNα 2a and IFNγ 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 TNFα, IFNα and IFNγ resulted in 7874, 8100 and 7132 differentially expressed probe sets, respectively (corresponding to about 3150, 3240 and 2850 genes). IFNα and IFNγ had very similar profiles in monocytes, but more than half of the IFN profile is shared with TNFα. 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 TNFα, IFNα and IFNγ, reflecting in part the complexity of the pathophysiology of SLE. 41.5% of differentially expressed genes in SLE overlapped with in vitro induced IFNα signature, 33.3% of SLE with IFNγ, while 22.5% of disease genes were contributed to TNFα signature. Although the IFNα imprint within SLE is predominant, it is also shared not only with IFNγ but also with TNFα (namely, 25.8% of the IFNα signature is shared with TNFα). On the other hand, the TNFα signature in SLE is identified not just as shared with IFNs but also as TNFα-specific.

Conclusion Our findings indicate that defining in vitro induced TNFα, IFNα and IFNγ 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.

A79 DEFINING TNFα-, IFNα- AND IFNγ-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