Multi-Antigen Imaging Reveals Inflammatory DC, ADAM17 and Neprilysin as Effectors in Keloid Formation

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Running Title
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BACKGROUND
Keloid disorder is an aberrant scarring process of the skin, characterized by excessive extracellular matrix synthesis and deposition. The pathogenesis of this prevalent cutaneous disorder is not fully understood; however, a persistent inflammatory process is observed. To obtain more insight into this process, we analyzed lesional, perilesional and healthy tissue using multi-antigen-analysis (MAA) in conjunction with a data mining approach.

METHODS
To obtain more insight into this process, we analyzed lesional, perilesional and healthy tissue using multi-antigen-analysis (MAA) in conjunction with a data mining approach.

RESULTS
Here, we demonstrate that monocyte-derived inflammatory dendritic cells (CD1a+, CD11c+, CD14+) and activated CD4+ T lymphocytes (CD45 RO+) dominated the immune infiltration in keloids while associating with fibroblasts. In perilesional tissue, precursor immune cells were dominant in the perivascular area, suggesting that they were attracted by an immune process, potentially in the lesional area. Supporting this hypothesis, only in keloid lesions, high levels of ADAM10/17 and Neprilysin (CD10) were observed in both fibroblasts and leukocytes. The spatial proximity of these two cell types, which could be confirmed by image analysis only in lesional tissue, could be a potential factor leading to the activation of fibroblasts.

CONCLUSİON
Our findings provide new insight into the pathogenesis of keloid formation and reveal metalloproteinases as a target for therapeutical intervention.