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The Differential Expression of CLEC12A on Neutrophils of Rheumatoid arthritis Patients Correlates with Clinical Parameters.

Introduction: CLEC12A is an inhibitory receptor predominantly expressed in myeloid cells. Several lines of evidence indicate that CLEC12A contributes to the pathogenesis of rheumatoid arthritis (RA). CLEC12A polymorphisms are associated with RA and CLEC12A knock-out mice suffer from exacerbated inflammation in response to collagen-induced arthritis. Moreover, CLEC12A negatively regulates the activation of the most abundant cell in the synovial fluid of RA patients, the neutrophil. A diminution in the expression of CLEC12A enhances neutrophil activation. Together, these observations suggest that CLEC12A expression is most likely decreased in myeloid cells of RA patients consequently lowering the threshold of activation of these leukocytes. Whether this decrease in CLEC12A expression occurs in circulation or in the inflamed joint, remains unknown.
Aim: To determine the level of expression of CLEC12A in circulating neutrophils of RA patients and identify potential correlations with clinical parameters.
Methods: CLEC12A expression was determined in neutrophils in whole blood of RA patients (from baseline to 18 months) and healthy donors (negative control) by flow cytometry. SAS 9.4 software was used to identify correlations between the level of CLEC12A expression and clinical parameters.
Results and Discussion: The cell-surface expression of CLEC12A is significantly higher on neutrophils of RA donors compared to healthy donors at baseline, 3 and 6 months. By 12 and 18 months, when the symptoms subside, the level of expression of CLEC12A drops to levels of healthy donors. Moreover, CLEC12A expression on human neutrophils negatively correlates with the SDAI score. This observation suggests that the increased CLEC12A expression on neutrophils increases the threshold of activation of neutrophils to counteract the subclinical inflammatory environment in the blood. Negative regulatory mechanisms are known to play a key role in avoiding neutrophil activation in circulation. In support of the presence of inflammation in the RA patients studied, ESR positively correlates with CLEC12A expression. Moreover, CLEC12A expression at baseline of RA patients is predictive of the SDAI score at three and six months.
Conclusions: We identified the CLEC12A inhibitory pathway as a potential, key regulator of neutrophil priming in the circulation of RA patients. This underscores the role of CLEC12A and potentially other myeloid inhibitory receptors in the early phases of RA. The delineation of the molecular mechanisms underlying the role of CLEC12A in priming will shed light onto why the level of expression of CLEC12A is predictive of disease activity in RA and also potentially identify novel therapeutic targets and/or modalities.