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INFLAMMATORY MYOPATHIES

NK cell function linked to antisynthetase syndrome

> "…tissue-infiltrating NK cells could be important in initiating and sustaining disease processes…"

A novel role has been proposed for NK cells in the pathogenesis of antisynthetase syndrome, according to new research by Baptiste Hervier and colleagues, published in *The Journal of Immunology*. NK cells from patients with active antisynthetase syndrome have reduced levels of the cell-surface receptor NKp30 (also known as natural cytotoxicity triggering receptor 3) and lack the ability to produce IFNγ, both spontaneously and when stimulated. This altered phenotype is coupled with a strong capacity to produce granzymes A and B, proteolytic enzymes that might contribute to the progression of interstitial lung disease.

Although already known to be involved in the pathogenesis of autoimmune diseases such as systemic lupus erythematosus and systemic sclerosis, the role of NK cells in antisynthetase syndrome has yet to be fully determined. Hervier and colleagues found higher numbers of NK cells in lung tissue from patients with antisynthetase syndrome-related interstitial pneumonia than in lung tissue from healthy individuals (148 cells/mm^2 versus 11 cells/mm^2). In these patients, NK cells were located in fibrotic areas of the lung rather than in tertiary lymphoid structures, and showed increased expression of granzymes A and B.

Extensive phenotypic analysis showed little difference between NK cells from patients with inactive disease and those from healthy individuals. However, NK cells from patients with active disease (defined as having active myositis, arthritis or interstitial lung disease) had significantly increased expression of CD57 and CD85j, and significantly decreased expression of NKp30. When combined, these three markers could be used to accurately predict the level of disease activity in patients with antisynthetase syndrome.

According to the authors, the decrease in NKp30 expression correlated strongly with alterations in NK-cell function, indicating a potential role for peripheral blood NK cells in antisynthetase syndrome. They suggest that the regulatory-like phenotype of peripheral blood NK cells in these patients is shared by lung-infiltrating NK cells. The high expression of granzyme B by these tissue-infiltrating NK cells could be important in initiating and sustaining disease processes, as granzyme B cleaves Jo-1, the antigen against which autoantibodies are directed in antisynthetase syndrome, thus stimulating immune cells and recruiting them to the lungs.

The low expression of NKp30 is thought to be caused by its down-regulation during NK-cell differentiation, rather than by an intrinsic abnormality in NK cells from patients with antisynthetase syndrome. Hervier and colleagues speculate that the decrease in NKp30 occurs before autoantibodies are produced, but the exact mechanisms involved are unclear. They conclude that further work is needed to determine the exact role of NK cells in the tissue.

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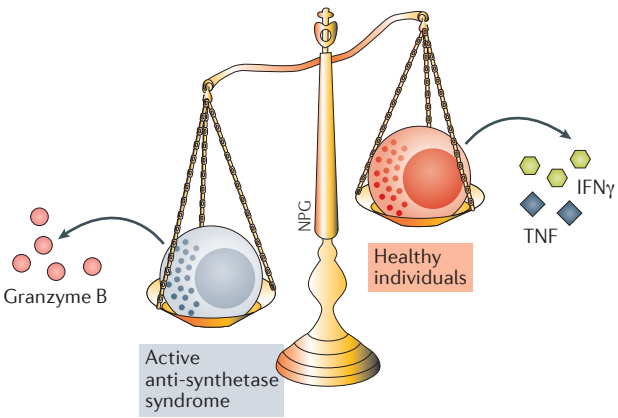

ORIGINAL ARTICLE Hervier, B. *et al.* Involvement of NK cells and NKp30 pathway in antisynthetase syndrome. *J. Immunol.* http://dx.doi.org/10.4049/jimmunol.1501902 (2016)