activation, have been described in RA patients. It has been observed that the expression of the signaling chain subunit of the TCR/CD3 complex, the TCR ζ chain, is downregulated in T lymphocytes of RA patients. Chronic TNF-α treatment appears to reproduce many of the TCR signaling defects observed in T cells from RA patients, suppress a broad range of T cell responses and attenuates intracellular Ca2+ mobilization. Several studies carried out on patients with rheumatoid arthritis have documented increased endogenous NO synthesis, but its contribution to T cell dysregulation is not known. We investigated the possible role of NO in T cell dysfunction in RA.

Our present data indicate that T cells from RA patients produce >2.5 times more NO than control healthy donor T cells (p<0.001). Although NO is an important physiological mediator of mitochondrial biogenesis, mitochondrial mass is similar in RA and control T cells (p=0.65), whilst increased NO production is associated with increased cytoplasmic Ca2+ concentrations in RA T cells (p<0.001). We observed that T cell NO production decreased in most RA patients following anti-TNF treatment. TNF treatment of Jurkat cells (10-50ng/ml) induces dose dependent NO production (p<0.001). Furthermore, chronic NO treatment, like TNF, downregulates TCR ζ expression. Experiments also indicate that NO seems to regulate TNF induced apoptosis. These data suggest that TNF induced NO production in T lymphocytes is a key modulator of T cell responses, and its overproduction may contribute to perturbations of immune homeostasis in RA.

AB04

Function of human invariant NKT cells is regulated by the distinct binding kinetics of their TCRs to the CD1d/glycolipid complexes

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Background: Human invariant NKT cells (iNKT) are a unique subset of T cells that co-express an invariant V24 TCR and receptors from the NK lineage. iNKT cells recognize exogenous and yet unknown endogenous glycolipids presented by a non-classical Ag-presenting complex, the TCR αβ chain, is downregulated in T lymphocytes of Systemic Lupus Erythematosus patients.

Objective: To investigate whether human iNKT pool is heterogeneous with regard to their TCR binding kinetics to CD1d/glycolipid complexes. Differential responses induced by α-GalCer and OCH could thus be due to the different iNKT TCR binding characteristics to CD1d loaded with α-GalCer or OCH.

Methods: Peripheral blood mononuclear cells (PBMCs) from healthy donors were cultured in vitro in the presence of α-GalCer, OCH or control lipid β-GalCer and then analyzed with flow cytometer using fluorescent tetrameric CD1d/glycolipid (α-GalCer, OCH or β-GalCer) complexes. iNKT clones and lines were directly sorted by the same method. Preliminary results suggested that the expression level of p70S6 kinase was significantly increased in SLE T lymphocytes than in healthy donor T lymphocytes. As regard the activation state of these kinases experimental data suggested an enhanced phosphorylation of p70S6 kinase without significant phosphorylation of mTOR in SLE T lymphocytes when compared with healthy donor T lymphocytes.