ANTI-CITRULLINATED PROTEIN ANTIBODIES (ACPA) MODULATE CYTOKINE GENE EXPRESSION IN LYMPHOCYTES DERIVED FROM PATIENTS WITH ACPA POSITIVE RHEUMATOID ARTHRITIS AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE.

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Background: Rheumatoid arthritis (RA) is an autoimmune disease characterized by production of pathogenic autoantibodies leading to chronic inflammation of the joint. RA patients' sera contain autoantibodies to citrullinated proteins (ACPA). Although ACPA have diagnostic value in RA, their biological role in disease development and their involvement in other organ damage is still unclear. ACPA have been shown to be able to initiate arthritis in murine models of RA. Pulmonary disease is a well-recognized and important extra-articular manifestation of RA. Smoking is a strong environmental risk factor linked to RA, and a large data-based study found that RA is associated with chronic obstructive pulmonary disease (COPD). To study new pathways leading to ACPA pathogenicity in RA we first determined the modulatory effect of ACPA on immune cells.

Methods: ACPA were affinity purified from sera of RA patients. The ability of ACPA to modulate cytokine gene expression was studied in splenocytes derived from rats having adjuvant induced arthritis and in cells from ACPA positive COPD and RA patients. The presence of ACPA in the sera of COPD and RA patients was analysed by ELISA.

Results: ACPA significantly up-regulated mRNA of the inflammatory cytokines, TNFα and IL-6 in arthritic rats' lymphocytes compared to control cells. At the same time, we observed reduction of the anti-inflammatory cytokine TGFβ expression. Generally we observed similar tendencies in lymphocytes from ACPA positive COPD patients and RA controls.

Conclusions: Our *in vitro* study suggests that ACPA can modulate the immune response through enhancing the production of inflammatory cytokines.

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