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Title: Structural pulmonary abnormalities on HRCT are early features of ACPA- positive rheumatoid arthritis

Mr. Reza 32378 Karimi reza.karimi@ki.se MD ¹, Ms. Gudrun 32379 Reynisdottir gudrun.reynisdottir@karolinska.se MD ², Ms. Helga 32380 Olsen helga.olsen@gmail.com MD ², Mr. Vijay 32381 Joshua vijay.joshua.balasingh@ki.se ², Ms. Aase 32382 Haj Hensvold aase.hensvold@ki.se ², Mr. Anders 32385 Harju anders.harju@karolinska.se MD ², Ms. Marianne 32393 Engström marianne.engstrom@ki.se ², Prof. Johan 32399 Grunewald johan.grunewald@ki.se MD ¹, Dr. Sven 32400 Nyren sven.nyren@karolinska.se MD ³, Prof. Anders 32401 Eklund anders.eklund@ki.se MD ¹, Prof. Lars 32402 Klareskog lars.klareskog@ki.se MD ², Dr. Anca Irinel 32403 Catarina anca.catarina@ki.se MD ² and Prof. Magnus 32409 Sköld magnus.skold@ki.se MD ¹. ¹ Karolinska University Hospital, Div Respir Med, Dept Medicine, Karolinska Institutet, Stockholm, Sweden ; ² Karolinska University Hospital, Rheumatology Unit, Karolinska Institutet, Stockholm, Sweden and ³ Karolinska University Hospital, Department of Molecular Medicine, Karolinska Institutet, Stockholm, Sweden .

Body: Background The epidemiologic association between exposure to smoking and ACPA (anti citrullinated proteins antibodies)-positive rheumatoid arthritis (RA) suggests that the immunologic process in RA might start in the lungs. To test this we investigated structural changes in the lungs in a cohort of RA patients with early disease. Material and methods A total number of 105 patients with early, untreated RA, median diseases onset 6 months, and 43 healthy non-RA individuals were performed inspiratory and expiratory scans by high resolution computer tomography (HRCT). Bronchoscopy and bronchoalveolar lavage were performed in 21 out of 105 RA patients. Presence of ACPA and total levels of IgG were detected in serum and BAL fluide by anti-CCP2 ELISA and radial immunodiffusion assays with rate nephelometry respectively. Results 51% (54/105) of the RA patients and only 28% (12/43) of the controls had any lung structural abnormalities (fibrosis, ground glass opacities, bronchioectasis, Nodules larger than 5 mm, emphysema) identifiable on HRCT (p<0.05). Fibrosis of any grade 11% (12/105) and ground glass opacities 4% (4/105) were found only in RA patients. Air trapping was found in 51% (52/105) of RA patients compared to 28% (12/43) in control, (p<0.05). ACPA presence rather than smoking status associated with the presence of lung abnormalities on HRCT. IgG ACPA values corrected for total amount of IgG were higher in BAL as compared to blood compartment. Conclusion Presence of ACPA associates with early pulmonary changes on HRCT. Smoking may promote citrullination in the lungs leading to generation of ACPA immunity.