Response to: 'Autoantibodies and interstitial lung disease in rheumatoid arthritis: towards a 'mix-and-match' approach' by Alunno *et al*

We welcome the comments by Alunno *et al* on our article about the association between anticarbamylated protein antibody (anti-CarP) specificities and rheumatoid arthritis-associated interstitial lung disease (RA-ILD).[1] The authors proposed a 'mix and match approach' consisting of the assessment of various antibody specificities at RA diagnosis with the aim of predicting the development of ILD.[2] We believe this hypothesis is reasonable, considering that different antimodified protein antibodies (AMPA) including anti-CarP, anticitrullinated and antiacetylated protein antibodies (ACPA and anti-AceP, respectively) have been associated with RA-ILD.[1 3 4] Furthermore, a greater number of coexisting specificities of a single AMPA have been found in patients with RA-ILD.[3 5]

The prevalence of ILD and its risk factors fluctuate between RA cohorts, partially due to differences in the screening methods, the population examined, and the defining criteria used. Although these factors were controlled in our study, there were differences in some baseline features between the main population and the replication sample, as pointed out by Alunno *et al*.[2] This may be due to the small sample size of the replication sample or because ILD screening and diagnosis was ultimately based on physician's criteria based on the ILD committee dictates from two hospitals. However, our final model was fitted after adjusting for these features and so they did not affect the results. Recently, Zhu *et al* reported a higher proportion of anti-CarP in Chinese patients diagnosed with RA-ILD compared to RA controls without ILD (53% vs 16%).[6] Their findings are consistent with and enhance the external validity of our observations. However, larger multiethnic studies are still required.

We consider the association between ILD and RA is a 'two-way street'. It should be considered that: (1) ILD may be present before or around RA onset in one in three patients[7] and (2) ACPA have been found in more than 20% of patients with idiopathic pulmonary fibrosis (IPF),[8] of whom approximately one-third subsequently may develop RA.[9] Thus, the 'mix and match approach' should be considered in RA and IPF. We believed a broader view (eg, multidisciplinary ILD committees) on the issues implied in the relation between ILD and RA should be considered in the design of future prospective collaborative studies.

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