Response to: 'Immune-mediated necrotizing myopathies and interstitial lung disease are predominant characteristics in anti-Ku positive patients with idiopathic inflammatory myopathies' by Yang *et al*

We would like to thank Yang *et al*[1] for their rewarding comment on our work, in which we report that patients harbouring anti-Ku autoantibodies with elevated serum levels of creatine kinase (elevated CK) are at risk of interstitial lung disease (ILD), whereas anti-Ku patients with anti-dsDNA are frequently affected by systemic lupus erythematosus and are at risk of glomerulonephritis.[2]

Yang *et al* retrospectively investigated 1214 patients with myositis (defined on Bohan and Peter criteria) in a single Chinese centre. Twenty-one patients (1.7%) had anti-Ku antibodies, defined as a fine speckled pattern seen at immunofluorescence, together with positive commercial assay results.

In accordance with our results, Yang *et al* found that ILD was a predominant characteristic of anti-Ku patients with myositis (76.2%).

Interestingly, using commercial assays, Yang *et al* also reported the frequent (48%) coexistence of anti-Ku with myositis-specific or myositis-associated autoantibodies (MSA/MAA). Moreover, as compared with patients with isolated anti-Ku antibodies, a skin rash was more frequent in these patients, as well as better pulmonary functional test results. In our cohort, anti-Ku antibodies were systematically confirmed using an in-house immunodiffusion technique. Apart from anti-Jo1 and anti-U1-RNP, MSA/MAA status was not available in all our anti-Ku patients. However, when searched for (using D-Tek line immunoassay, Mons, Belgium), the result was generally negative and only two anti-Ku patients with elevated CK tested positive for a coexisting MSA/MAA (table 1). None of them had a dermatomyositis rash. False positivity for MSA/MAA has recently been shown to be common when using commercial assays (14%), anti-Ku being the most frequent false positive specificity of the EuroImmun line immunoassay (3%).[3] Thus, the important report by Yang *et al* highlights the diagnostic challenge posed by the 'anti-Ku syndrome' in view of the limitations of currently available routine tests.

Table 1 Myositis-specific and associated autoantibodies in our 15 patients with anti-Ku autoantibodies and elevated CK

MSA and MAA	Anti-Ku patients with elevated CK n=15
Anti-Jo1	0/15
Anti-PL7	0/13
Anti-PL12	0/13
Anti-OJ	0/9
Anti-EJ	0/9
Anti-Ha	0/9
Anti-Zo	0/9
Anti-KS	0/9
Anti-U1-RNP	0/15
Anti-PM/Scl	1/14
Anti-Mi2	0/12
Anti-MDA5	1/9
Anti-TIF1γ	2/9
Anti-NXP2	0/9
Anti-SAE	0/9
Anti-SRP	0/11
Anti-HMGCR	0/9
Total	**2***

*One patient was positive for both anti-MDA5 and anti-TIF1γ; another had anti-PM/scl and anti-TIF1γ.
CK, creatine kinase; MAA, myositis-associated autoantibodies; MSA, myositis-specific autoantibodies.

In this regard, Yang *et al* additionally described the muscle biopsy findings available in 13 of their 21 anti-Ku patients. Noteworthily, the immune-mediated necrotising myopathy (IMNM) pattern, as defined by the 2017 ENMC criteria, was found in 6/7 (86%) of their patients with isolated anti-Ku versus 1/6 (17%) of their counterparts. Similarly, in our cohort, an IMNM pathological pattern was found in 7 of 8 anti-Ku patients who underwent a muscle biopsy (88%) . The sole muscle lesion found in our remaining patient was patchy (not perifascicular) sarcolemmal major histocompatibility complex class I expression.

Overall, these data emphasise that interstitial lung disease is a predominant feature in anti-Ku patients with myositis and, importantly, highlight that IMNM might be part of this anti-Ku syndrome.

Lionel Spielmann ,[1] **Benoit Nespola,**[2] **Alain Meyer**[3,4,5]

[1]Service de Rhumatologie, Hôpitaux civils de Colmar, Colmar, France
[2]Laboratoire d'immunologie, Hopitaux universitaires de Strasbourg, Strasbourg, France
[3]Exploration fonctionnelle musculaire, Service de physiologie, Hôpitaux Universitaires de Strasbourg, Strasbourg, France
[4]Centre National de Référence des Maladies Auto-Immunes Systémiques Rares de l'Est et du Sud-Ouest, Service de rhumatologie, Hôpitaux Universitaires de Strasbourg, Strasbourg, France
[5]Fédération de médecine translationnelle de Strasbourg, FRU 6702, Université de Strasbourg, Strasbourg, France

Correspondence to Dr Lionel Spielmann, Service de Rhumatologie, Hospices civils de Colmar, Colmar, Alsace 68024, France; lionel.spielmann@ch-colmar.fr

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ORCID iD
Lionel Spielmann http://orcid.org/0000-0003-1057-6890

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