Response to: 'Similarities and differences between severe COVID-19 pneumonia and anti-MDA-5 positive dermatomyositis associated rapidly progressive interstitial lung diseases: a challenge for the future' by Wang *et al*

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We thank Wang *et al* for their interest in our letter. In this study, we investigated pre-COVID-19 adult-onset anti-TIF1 autoantibody positive dermatomyositis (DM) patients, and identified antibodies against immunogenic epitopes with high sequence identity to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] We speculated that latent lifetime microbial exposure to the Coronaviridae family might contribute to future musculoskeletal autoimmune disease development.

In their correspondence,[2] Wang *et al* review the features of severe COVID-19 pneumonia and anti-MDA-5 (melanoma differentiation-associated gene 5) autoantibody positive DM presenting with rapidly progressive interstitial lung disease (RP-ILD). The authors compare the clinical signs and symptoms, demographics, likely pathogenesis, cytokine and chemokine profiles and pharmacological treatment of these two clinical presentations. Based on the clinical similarities identified, Wang *et al* suggest 'SARS-CoV-2 infection might mimic myositis and could also lead to catastrophic results in DM patients with prior ILD'. Therefore, it is important to be able to separate the muscle inflammation with interstitial pneumonia encountered in COVID-19 from that of autoimmune myositis.

We concur with the authors' suggestions to be able to distinguish between COVID-19 and autoimmune myositis and the need for clinicians to be vigilant to ensure differential diagnosis and treatment. Tests for myositis-specific autoantibodies should be carried out where clinically indicated, for example, in the presence of a DM rash. It is intriguing that the cytokine storm reaction bears similarities between the two conditions, where aggressive anti-cytokine treatment regimens have been suggested for both. At the same time, we note that autoimmune myositis is a rare disorder, with an incidence of up to 20 per million per year,[3] of whom only a proportion are MDA-5 autoantibody positive. However, as Wang *et al* observe, intriguing geographical differences exist in the prevalence of anti-MDA-5 autoantibodies and RP-ILD in individuals with DM of different ethnicity, particularly in the Japanese population, suggesting that genetic and/or environmental (eg, viruses) factors might play a role. Our experimental approach[1] might therefore be informative in anti-MDA-5 positive DM. Lung disease is also a well-established extra-muscular symptom of other autoimmune myositis subgroups, such as anti-synthetase syndrome.[4] Data on COVID-19 in myositis-specific autoantibody defined patient subgroups has not yet been reported. Notably, recent data from the COVID-19 Global Rheumatology Alliance physician-reported registry shows that the frequency of comorbid lung disease (chronic obstructive pulmonary disease, asthma, interstitial lung disease or other not specified) is higher in hospitalised than non-hospitalised COVID-19 rheumatic disease patients.[5]

Molecular mimicry of SARS-CoV-2 with epitopes of self-proteins is a possible scenario underlying COVID-19 heterogeneity,[6] but to our knowledge has not been experimentally explored. Several recent reports have suggested that SARS-CoV-2 infection could lead to various autoimmune and auto-inflammatory diseases in both children and adults.[6] In our opinion, there is a need to establish registries, epidemiological and molecular studies within both rheumatic disease cohorts and at the population level to explore the long-term sequelae of SARS-CoV-2 infection.

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