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Letter to the Editor


Letter to the Editor: Comment on Mulder J et al. (2021) indirect immunofluorescence for detecting anti-neuronal autoimmunity in CSF after COVID-19 – possibilities and pitfalls

To the Editor,

We read the letter by Mulder et al. with great interest (Mulder et al., 2021). It supports the notion that optimized indirect immunofluorescence stainings of murine brain tissue can be a valuable tool to increase the yield when searching for antibody-mediated neurological and psychiatric conditions (Franke et al., 2020). We share the authors' enthusiasm regarding the obvious additional value for clinical routine, the potential re-classification of unresolved immunotherapy-responsive cases, the increased understanding of underlying autoimmune mechanisms and the emerging techniques of antibody target identification – clearly reaching beyond the current COVID-19 pandemic.

We advocate the use of brain tissue-based immunofluorescence assays for many years (Endres et al., 2020; Kreye et al., 2020; Schumacher et al., 2019), given that the technique allowed the identification of numerous treatment-responsive autoantibody-positive cases in the past and facilitated the clinical decision for successful initiation of immunotherapy. The complex methodology and availability limited to research laboratories prevented the widespread use until now. Also, different techniques of tissue fixation reduce comparability, such as the commonly used fixation with paraformaldehyde (as performed in Mulder et al.), methanol or acetone. We recommend the (additional) use of unfixed tissue, which is even more challenging technically, but provides the chance to detect antibody binding to the native conformation of some membrane proteins (Kreye et al., 2020).

It is tempting to speculate that many more case series which reported similar clinical presentations of COVID-19 but did not identify anti-neuronal autoantibodies in routine assays, might show autoantibodies when being re-assed using optimized tissue-based assays. Neuropsychiatric symptoms due to or post COVID-19 might be a chance to raise awareness for the unused potential of tissue-based screening in clinical routine settings. We therefore suggest initiating the development, standardization, harmonization and quality control of indirect immunofluorescence protocols across different centers.

Along these lines, we invite Mulder et al. and all interested colleagues to initiate a collaborative international network for the implementation of standard operating procedures, surveillance and continuous improvement of diagnostic protocols, and reporting of

clinical correlations and outcomes, collectively aiming for earlier diagnosis and treatment of antibody-mediated neurological and psychiatric diseases.

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Christiana Franke^a, Harald Prüss^{a,b,*}

^a Department of Neurology and Experimental Neurology, Charité – Universitätsmedizin Berlin, Berlin, Germany

^b German Center for Neurodegenerative Diseases (DZNE) Berlin, Berlin, Germany

* Address: Department of Neurology, Charité – Universitätsmedizin Berlin, Charitéplatz 1, 10117 Berlin, Germany.
E-mail address: harald.pruess@charite.de (H. Prüss).

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