LETTER TO THE EDITOR

Reply: PRKAR1B mutations are a rare cause of FUS negative neuronal intermediate filament inclusion disease

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Sir,
We thank Pottier et al., 2015 for their interest in our recent study, reporting the identification of a novel mutation in the PRKAR1B gene in a family with cases of FUS-negative neuronal intermediate filament inclusion disease (NIFID) (Wong et al., 2014). Mutations in this gene seem to be rare in most neurodegenerative disorders as no additional pathogenic mutations have been found to date in patients with Parkinson’s disease, frontotemporal dementia and Alzheimer’s disease (Cohn-Hokke et al., 2014; Wong et al., 2014).

In their letter, Pottier et al., 2015 report the absence of mutations in the PRKAR1B gene in a small series of three pathologically confirmed NIFID cases who were FUS negative. This observation in NIFID cases with strong accumulation of neurofilament proteins is especially important, as the protein kinase A (PKA) holoenzyme has a strong effect on phosphorylation of neurofilament proteins. Therefore, we agree with their suggestion that genetic screening in the PRKAR1B pathway may identify new genetic defects in the aetiology of FUS-negative NIFID. Finally, screening in the PRKAR1B gene is still indicated in patients with frontotemporal dementia and parkinsonism, especially in those with positive family history.

References
Pottier C, Baker M, Dickson D, Rademakers R. PRKAR1B mutations are a rare cause of FUS negative neuronal intermediate filament inclusion disease. Brain 2015; 138: e357.

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