Sir, The letter by Prüss and colleagues on the detection antibodies to neurofascin in Guillain–Barré syndrome raises a number of important questions and highlights exciting recent developments in the field of novel autoantibodies in both peripheral and central nervous system disorders. As such, there is a compelling case for investigating this area in much more detail. Neurofascin is one of a large number of potential nodal complex protein candidates to be explored, as Prüss et al. point out. While in principle this sounds straightforward, in practice it is complicated in terms of technical issues and experimental design. In particular, there would be a preference to screen extracellular domains of conformationally intact proteins that would presumably be the best target for pathogenic autoantibodies; this requires target protein expression and screening in appropriate cell lines, which is not a trivial task.

The enzyme-linked immunosorbent assay data presented are tantalizing, but fall short of proof of involvement for these antibodies as primary mediators of disease, as is acknowledged. Here, Prüss et al. are careful to state that neurofascin antibodies might be relevant to development, augmentation or perpetuation of nerve injury in Guillain–Barré syndrome, or indeed might represent a bystander effect. Macrophage ingestion of myelin and axonal debris at nodes of Ranvier, with subsequent antigen presentation would be a mechanism by which this might occur in Guillain–Barré syndrome. Since Guillain–Barré syndrome is a transient, post-infectious disorder with onset at ~10 days and resolution within 30 days, it would be important to consider immunologically how anti-neurofascin antibodies might arise and decay in this infectious context. This has been well documented for ganglioside antigens including GD1a in relation to Campylobacter jejuni infection, in which molecular mimicry is the paramount pathway. One interesting approach to this would be to also examine the Prüss et al. serum cohort for such anti-glycolipid antibodies, and determine whether anti-neurofascin antibodies segregated with the anti-ganglioside antibody C. jejuni cases, or not. If the former was observed, it might suggest that the anti-neurofascin antibodies were pathophysiologically redundant in terms of disease initiation, but may alternatively play other roles such as disease perpetuation, or a bystander effect.

One of the key messages highlighted here is the need to cooperate in such comparative studies using large, well-defined clinical and serological databases, in which the antibody repertoires in individual patients and sera can be mapped in their entirety, and in relation to other clinical factors. A move in this direction is ongoing in the Guillain–Barré syndrome field with the recent establishment of the International Guillain–Barré Syndrome Outcomes Study (IGOS), run by Dr Jacobs of the Rotterdam Guillain–Barré Syndrome Group and managed through the Inflammatory Neuropathy Consortium (INC). This aims to capture clinical, genetic and serological data on 1000 Guillain–Barré syndrome cases worldwide and will thereby act as an invaluable resource for wide-ranging collaborative studies such as those considered here.