Identification of the inositol 1,4,5-trisphosphate receptor type 1 as a new autoantigen of Purkinje cells


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Introduction

Several neuronal autoantibodies target Purkinje cell antigens and can be determined by indirect immunofluorescence (IIF) using cryosections of rat, porcine, and primate cerebellum. They are generally associated with cerebellar ataxia and accompanied by an underlying tumour. Here we report on a new autoantibody directed against inositol 1,4,5-trisphosphate receptor type 1 (IP3R1).

Methods

Sera with antibodies against Purkinje cells which did not react with known target antigens such as Yo/CDR2, CDR2L, DNER, and Rho GTPase activating protein 26 (ARHGAP26) were collected after routine work-up. The antigen was identified by histo-immunoprecipitation (Histo-IP) with cryosections of rat cerebellum followed by SDS-PAGE and mass spectrometry and confirmed by IIF using HEK293 cells expressing IP3R1 as substrate.

Results

Three sera showed a strong staining of somata, axons, and dendrites of the Purkinje cells very similar to that of anti-ARHGAP26. SDS-PAGE following Histo-IP with rat and porcine cerebellum revealed a protein band at ~300 kDa that was identified as IP3R1. Double labelling of cerebellum with patient serum and an anti-IP3R1 antibody (ab) revealed a perfect overlay of the staining patterns. The patient sera also stained HEK293 cells expressing IP3R1 whereas controls were negative. Preadsorption of patient sera with HEK293 extracts containing IP3R1 neutralized the reaction on rat cerebellum whereas control HEK293 extracts had no effect.

Conclusion

IP3R1 is a new target of autoantibodies against Purkinje cells and complements the growing list of neuronal autoantibodies. Interestingly, IP3R1 interacts with CARP VIII and HOMER3, targets of autoantibodies that were recently identified in patients with paraneoplastic cerebellar ataxia.