Supporting Information for

Cross-reactivity of a pathogenic autoantibody to a tumor antigen in $GABA_A$ receptor encephalitis

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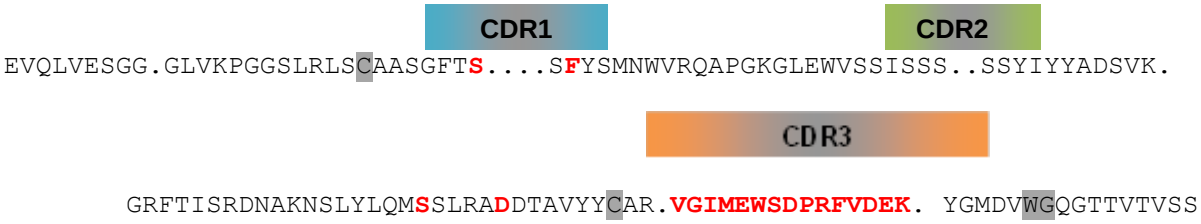
SI References

Heavy chain: IGHV3-21*01



Light chain: IGKV3-20*01

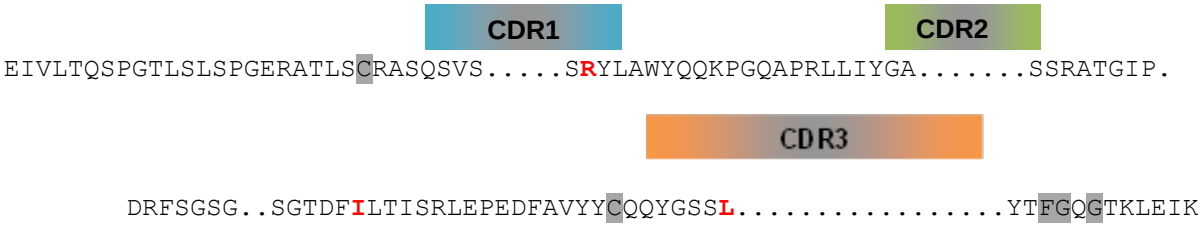


Figure S1: Sequence of the expanded antibody Ab-IP2 from patient IP2.

Amino acid sequences of the dominant H- and κ-chains of antibody Ab-IP2 are shown. Amino acid mutations introduced by somatic hypermutation and recombination are printed in red letters. The canonical cystein (C) residues and the conserved sequences in the J-regions (WGXG and FGXG) are highlighted in grey. The complementarity determining regions (CDR) 1 to 3 are indicated.

Figure S1

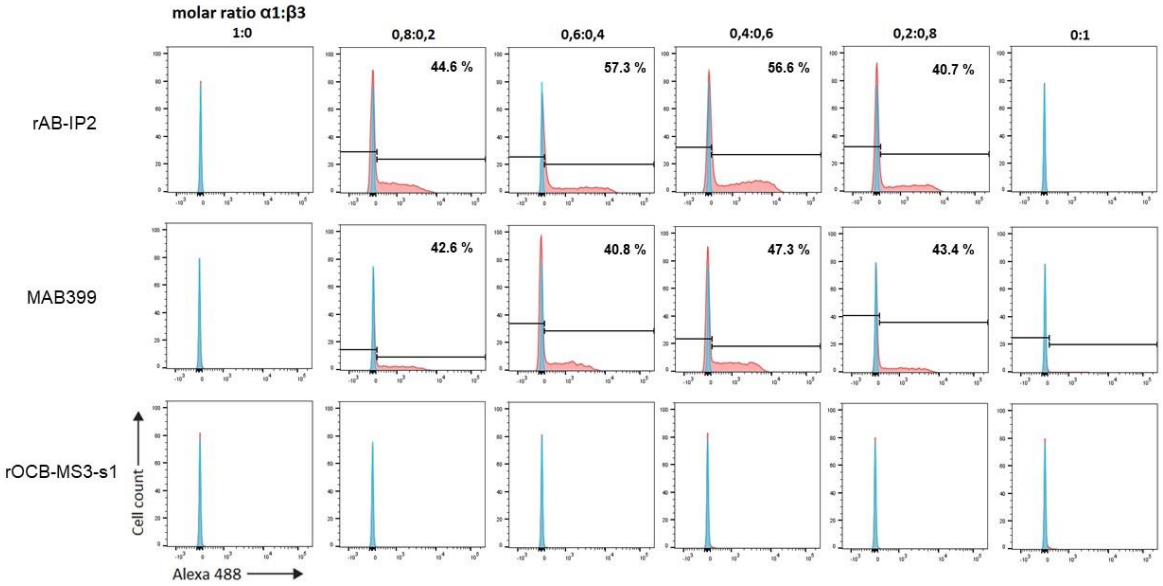


Figure S2: rAB-IP2 recognizes GABA$_A$-R

HEK293Expi cells, which grow in suspension, were transiently transfected with expression plasmids encoding the α1- and β3-subunits of GABA$_A$-R at different molar ratios shown in the uppermost lane. Cells were analyzed by flow cytometry for binding of rAb-IP2 (upper panel), the commercial anti-GABA$_A$-α1 antibody MAB399 (middle panel), and the negative control antibody rOCB-MS3-s1 (lowest panel). The percentages of positive cells are indicated in the plots. Binding of rAb-IP2 and MAB399 to transfected HEK293Expi cells was observed at different molar ratios of the α1- and β3-subunits, while no binding was observed, when only one subunit was transfected.

Figure S2

Subject	Disease type	Age	Sex	OCBs	Disease-specific antibody titers (CBA) at diagnosis	Immunotherapy preceding biosampling	Further clinical remarks
IP2	$GABA_A$-R Enc.	51	m	yes	Serum: $GABA_A$-R > 1:1280; CSF: $GABA_A$-R > 1:320	IVIG, PLEX, Cyclophosphamide, Rituximab	ITP, AT (1)
$GABA_A$-R-1	$GABA_A$-R Enc.	34	m	no	Serum: $GABA_A$-R 1:100; CSF: $GABA_A$-R 1:10	none	
$GABA_A$-R-2	$GABA_A$-R Enc.	47	f	no	Serum: $GABA_A$-R 1:320; CSF: $GABA_A$-R 1:10	none	
MS-1	RRMS	38	f	yes	none	none	anti-phospholipid antibody syndrome
MS-2	RRMS	21	f	yes*	none	none	
MS-3	RRMS	23	f	yes	none	none	
MS-4	PPMS	43	m	yes*	none	none	
MS-5	PPMS	45	m	yes	none	none	
Enc-1	NMDAR Enc.	20	f	yes*	Serum: NMDA-R 1:3.2; CSF: NMDA-R negative	Rituximab	3 cycles, 13 6, and 0.5 months before sampling
Enc-2	LGI-1 Enc.	62	m	yes*	Serum: LGI-1 1:800; CSF: LGI-1 positive	PLEX, Prednisolone	Both 2 months before sampling
Enc-3	GAD Enc.	49	f	no	Serum: GAD65 78 U/ml; CSF: GAD65 139 U/ml	Rituximab Azathioprin	5 cycles ~every 6 months, starting 28 month before sampling. starting 13 months before sampling, ongoing
NIC-1	IIH	43	f	no	none	none	
NIC-2	IIH	57	f	no	none	none	
NIC-3	IIH	58	m	no	none	none	

Table S1: Clinical characteristics of all subjects. Columns 1 and 2 list the subjects and their disease types. We analyzed CSF samples from patient IP2, three other cases with idiopathic anti-GABAA-R encephalitis ($GABA_A$-R-1 and -2), five cases with MS (MS-1 to -5), three cases with other forms of antibody associated CNS diseases (AACNSD-1 to -3), and three non-inflammatory disease controls (NID-1 to -3). Abbreviations are: RRMS = relapsing-remitting

MS; PPMS = primary progressive MS; NMDAR Enc = anti-N-Methyl-D-Aspartate-receptor encephalitis; LGI-1 Enc. = anti-leucine-rich-glioma-inactivated-1 associated encephalitis; GAD Enc. = anti-glutamic acid decarboxylase encephalitis; IIH = idiopathic intracranial hypertension. Column 3 lists the ages of the subjects, column 4 their sex, column 5 presence or absence of CSF-specific OCBs, column 6 the disease-specific antibody titers determined by cell-based-assays at diagnosis, column 7 the immunotherapies at the time point of lumbar puncture (LP), and column 8 further clinical remarks. Further abbreviations are: AT = autoimmune thyreoditis; CBA = cell-based-assay; ITP = idiopathic thromocyopenic purpura; IVIG = intravenous immunoglobulines; PLEX = plasma exchange; OCB = oligoclonal bands: * = in these subjects, OCBs were detected in CSF and in serum, indicating non-intrathecal OCB production.

Table S1

SI Reference

1. M. Petit-Pedrol et al., Encephalitis with refractory seizures, status epilepticus, and antibodies to the GABAA receptor: a case series, characterisation of the antigen, and analysis of the effects of antibodies. Lancet Neurol 13:276-286 (2014).