NEURONAL SURFACE ANTIBODIES (CELL MEMBRANE & SYNAPTIC)

	Antibody	Antigen	Cancer association	Clinical presentation	Sample
Autoimmune Channelopathies					
VGKC Complex	LGI1[1]	Leucine-rich, glioma Inactivated protein 1 Part of VGKC complex that interacts with other epilepsy-related proteins.	Thymoma in 10%	**Limbic encephalitis** (focal seizures followed by memory loss, disorientation and behavioral abnormalities) **Focal seizures** may be dyscognitive, dysautonomic or facio-brachial dystonic seizures (FBDS) **Facio-brachial dystonic seizures**: very brief repetitive dystonic contraction of the arm and face, refractory to AED treatment. **Insomnia and RBD** (REM behavior disorder) **Hyponatremia** in 60%. Ab positive in: serum > CSF CSF with lymphocytosis and OCB in 50% of patients MRI with T2 hippocampal hyperintensity in 74% of patients Response to immunomodulation: quick and marked response Residual deficits: amnesia for the disease period in 86% Relapses: third of patients develop relapses, can be as far as 8 years after initial episode. *N.B: mutation in LGI1 protein results in autosomal dominant lateral temporal lobe epilepsy*	**Serum**
	CASPR2	Contactin associated protein type 2 Part of VGKC complex, present in the brain & juxtaparanodal regions of myelinated axons and responsible for local differentiation of the axons at node of Ranvier.	Thymoma (10:30%)	**Neuromyotonia (Isaac Syndrome):** **Morvan syndrome:** more in patients with thymoma. Presents with diffuse hyperexcitability involving autonomic (hyperhidrosis & dysautonomia), peripheral (neuromyotonia, hyperexcitability) and central nervous systems (limbic encephalitis) **Limbic encephalitis** (focal seizures followed by memory loss, disorientation and behavioral abnormalities) in few cases. *N.B: CASPR2 mutation is seen in patients with autism*	**Serum**
	DPPX	Dipeptidyl-peptidase–like protein 6 Part of VGKC complex, responsible for blocking of back-propagation of action potentials. Present in the brain and myenteric plexus.	Lymphoma	**Triad of GI symptoms (diarrhea-weight loss), cognitive dysfunction, CNS hyperexcitability** Starts with diarrhea, weight loss (average 20Kg) followed by CNS hyperexcitability (myoclonus, seizures, hyperekplexia) and cognitive dysfunction (memory loss, hallucinations, agitation) over a few months period.	**CSF & Serum**
	Contactin2	Contactin2 protein Part of VGKC complex that interacts with CASPR2 and form bridges between the axon surface and myelin.	None	Although Contactin2 Ab were detected in a small number of patients with multiple sclerosis, it is not associated with disease activity and not associated with specific set of symptoms.	
	LGI1/CASPR2/DPPX negative VGKC	Antibodies against other parts of the VGKC complex.		Uncertain significance.	
	VGCC P/Q & N	P/Q & N type VGCC	SCLC	**Lambert Eaton Myasthenic Syndrome** (proximal weakness, dry mouth, constipation) Patients with LEMS should be screened with CXR every 6 months for lung cancer.	**Serum**

				Cerebellar ataxia	
	NMO-IgG	Aquaporin-4	None	NMO Spectrum Disorders (NMOSD)	**Serum**
Autoimmune Receptoropathies					
	NMDA	GluN1 receptor	Fertile women: Ovarian teratoma in 50%. Elderly: cancer in 25% Children: no cancer	Sometimes symptoms are preceded by headache and flu like symptoms that can persist for weeks/months then patients developed psychiatric symptoms (agitation, paranoia, psychosis), later on confusion, memory impairment and seizures proceed. Ab positive in: CSF > Serum MRI with variable T2 hyperintensities (percent) Response to immunomodulation: responsive but may take 1-2 years for full recovery – very sensitive to neuroleptics (may develop NMS) Residual deficits: 20% may attain residual deficits Relapses:	**CSF**
	AMPA	GluR1,2 receptor	SCLC, breast, thymus cancer in 70%	Varies from a single symptom (Confusion, disorientation – memory impairment – seizures) to multi-symptoms (similar to limbic encephalitis) to fulminant encephalitis.	**CSF**
	Metabotropic glutamate 1	mGluR1	Hodgkin lymphoma	Cerebellar ataxia (idiopathic or paraneoplastic)	
	Metabotopic glutamate 5	mGlur5	Hodgkin lymphoma	**Ophelia Syndrome** (Limbic encephalitis in patients with Hodgkin lymphoma)	
GABA Receptor	GABA-B	GABA-B receptor	SCLC in 50%	**Limbic encephalitis with marked refractory seizures**	
	GABA-A	GABA-A receptor	None	**Limbic encephalitis with marked refractory seizures**	
	Dopamine-2	Dopamine-2 receptor	None	**Sydenham chorea** **Basal ganglia encephalitis (parkinsonism, chorea, dystonia)**	
	Muscle AChR	Muscle AChR			
	Ganglionic AChR	Ganglionic AChR			
	Glycine	α1 subunit of GlyR (Present in brainstem & Spinal cord)	Cancer in 10%	**Stiff person syndrome** **PERM**: progressive encephalopathy, rigidity and myoclonus – more severe form of stiff person syndrome **Hyperekplexia**	
Cell Adhesion Proteinopathies					
	IgLON-5	Cell adhesion protein IgLON (LAMP, OBCAM, Ntm)	None	**Parasomnias – REB and non-REM behavior disorder – Chorea – Dementia – Ataxia – Vertical gaze palsy**	
	Neurexin-3 α	Cell adhesion protein	None	Prodrome of headache, fever, GI upset followed by seizures and altered mental status.	
	DNER (previously known as Anti-Tr)	Delta/notch-like epidermal growth factor-related receptor	Hodgkin lymphoma in 90%	Paraneoplastic cerebellar degeneration -> nystagmus, dysarthria, limb ataxia and gait ataxia **History**: Hodgkin disease patients with cerebellar degeneration were found to have their sera react against Purkinje cells in a specific pattern, named "Anti-Tr Ab pattern". In 2015, the target of Anti-Tr was found to be DNER. **Protein**: transmembrane protein carrying extracellular EGF-like repeats, DNER is upregulated in various cancers and knocking this protein down decreased cell proliferation and invasion.	