Table 1: Antibodies included in diagnostic criteria for paraneoplastic neurologic syndrome (PNS)

This table accompanies the article, “The evolving landscape of autoantibody testing for autoimmune neurological diseases,” by Jack L. Wu, PhD, MLS(ASCP)^{CM} and John R. Mills, PhD, DABCC, FADLM, published the July-August 2024 issue of *Clinical Laboratory News.*

For a full list of references, see this article online at www.myadlm.org/cln.

Antigen target	Antigen location/ PNS risk classification	Recommended test	Specimen Type	Limitation	Prominent clinical presentation and phenotype	Associated cancer
ANNA-1 (Hu)	Intracellular, PNS high-risk	TIIF/IHC with confirmatory by Western blot/line blot	Serum/CSF	High sensitivity and specificity when detected and confirmed	Polyradiculoneuropathy, sensory neuronopathy, cerebellar ataxia, limbic encephalitis, gastrointestinal dysmotility [1-3]	SCLC, neuroendocrine tumors, neuroblastoma in children [1]
ANNA-2 (Ri)	Intracellular, PNS high-risk	TIIF/IHC with confirmatory by Western blot/line blot	Serum/CSF	High sensitivity and specificity when detected and confirmed	Brainstem syndrome, cerebellar ataxia, myelopathy, peripheral neuropathy, encephalitis [4]	SCLC in males, breast cancer in females [5]
PCA-1 (Yo)	Intracellular, PNS high-risk	TIIF/IHC with confirmatory by Western blot/line blot	Serum/CSF	High sensitivity and specificity when detected and confirmed	Rapidly progressive cerebellar syndrome, myelopathy, peripheral neuropathy [6]	Ovarian and breast cancer [6, 7]
PCA-2/MAP1B	Intracellular, PNS high-risk	TIIF/IHC	Serum/CSF	Lack of commercially available confirmatory methods	Encephalopathy, limbic encephalitis, cerebellar ataxia, peripheral neuropathy [8-10]	SCLC, breast cancer [9]

PCA-Tr/DNER	Cell Surface, PNS high-risk	TIIF/IHC with confirmatory by Western blot/line blot	Serum/CSF	High sensitivity and specificity when detected and confirmed	Rapidly progressive cerebellar syndrome [11]	Hodgkin lymphoma [11]
Amphiphysin	Intracellular, transiently on surface, PNS high-risk	TIIF/IHC with confirmatory by Western blot/line blot	Serum/CSF	Line blot not recommended as screening assay	Limbic encephalitis, stiff-person spectrum disorders, cerebellar ataxia, myelopathy, polyradiculoneuropathy [12-14]	SCLC and breast cancer [13]
CRMP5/CV2	Intracellular, PNS high-risk	TIIF/IHC with confirmatory by Western blot/line blot	Serum/CSF	Test performance affected by fixatives used in tissue-based tests. Some confirmatory immunoblots have poor diagnostic accuracy	Asymmetric polyradiculoneuropathy, gastroparesis, limbic encephalitis, cerebellar ataxia, chorea, olfactory/optic neuropathy, myelopathy, polyradiculopathy [10, 15]	SCLC, thymoma [15]
Ma2/Ta	Intracellular, PNS high-risk	TIIF/IHC with confirmatory western blot/line blot or ELISA	Serum/CSF	Test performance affected by tissue preservation method and fixatives used	Brainstem encephalitis, diencephalic encephalitis, limbic encephalitis, narcolepsy [16]	Testicular cancer in young males, SCLC [16]
SOX1/AGNA	Intracellular, PNS high-risk	TIIF/IHC, or line blot	Serum/CSF	Limited sensitivity for SOX1 detection. CBA maybe preferred	Lembert-Eaton myasthenic syndrome, cerebellar ataxia [17]	SCLC [17]

KLHL11	Intracellular, PNS high-risk	CBA with confirmatory by TIIF /ICH	Serum/CSF	CBA assays are useful as screening tests. Confirmatory testing with TIIF/ICH increases specificity	Brainstem and cerebellar syndrome, hearing loss [18]	Testicular cancer [19]
AMPAR	Cell Surface, PNS medium risk	TIIF/IHC and/or CBA	Serum/CSF	Optimal diagnostic accuracy when results from TIIF/IHC and CBA are concordant	Limbic encephalitis, seizures [20]	SCLC, thymoma [20, 21]
$GABA_BR$	Cell Surface, PNS medium risk	TIIF/IHC and/or CBA	Serum/CSF	Optimal diagnostic accuracy when results from TIIF/IHC and CBA are concordant	Limbic encephalitis, status epilepticus, rapidly progressing dementia, ataxia, opsoclonus myoclonus syndrome [22]	SCLC [22, 23]
NMDAR	Cell Surface, PNS medium risk	TIIF/IHC and/or CBA	CSF favored; serum available	CSF is preferred over serum. Optimal diagnostic accuracy when results from TIIF/IHC and CBA are concordant	Behavior/neuropsychiatric changes, speech disorders, seizures, dyskinesias, movement disorders, autonomic dysfunction [24]	Ovarian or extraovarian cancers [25]
CASPR2	Cell Surface, PNS medium risk	CBA	Serum favored; CSF available	Serum is preferred over CSF. Low sensitivity by TIIF/IHC	Morvan syndrome, limbic encephalitis, focal-onset seizures, neuromyotonia, neuropathy pain, sleep disturbance [26, 27]	Thymoma. Limited cancer association for non-Morvan syndrome [28]

mGluR5	Cell Surface, PNS medium risk	TIIF/IHC and/or CBA	Serum/CSF	Limited data comparing performance between methods	Ophelia syndrome, limbic/extra-limbic encephalitis, movement disorders, sleep disorders [29]	Hodgkin lymphoma, rare cases of SCLC
P/Q-type VGCC	Cell Surface, PNS medium risk	RIPA	Serum	High sensitivity. Low positive predictive value with lower titer results	Lambert-Eaton myasthenic syndrome, cerebellar syndrome [30, 31]	SCLC [31]
AQP4	Cell Surface, PNS low risk	Live cell-based assay (LCBA)	Serum favored; CSF available	LCBA is superior to fixed CBA in both sensitivity and specificity	Optic neuritis, myelitis, NMOSD [32]	Adenocarcinomas [33]
mGluR1	Cell Surface, PNS low risk	TIIF/IHC and/or CBA	Serum/CSF	Limited data comparing performance between methods	Cerebellar ataxia, cognitive deficits, seizures, psychiatric, dysgeusia [34-36]	Hematologic malignancy [35]
$GABA_AR$	Cell Surface, PNS low risk	TIIF/IHC and/or CBA	Serum/CSF	Commercial CBA recently made available	Encephalitis, focal-onset seizures, hyperkinetic movement disorders [37]	Thymoma [38]
GFAP	Intracellular, PNS low risk	TIIF/IHC and/or CBA	CSF favored; Serum available	Optimal diagnostic accuracy when results from TIIF/IHC and CBA are concordant. High specificity in CSF	Meningoencephalitis, isolated encephalitis [39]	Adenocarcinoma, ovarian teratomas, other diverse cancers [40]

GAD65	Intracellular, PNS low risk	RIPA or ELISA	Serum/CSF	Low titer by RIPA is not neurologic-specific. Neurologic-specific cut-offs are needed and are assay dependent	Limbic encephalitis, focal-onset seizures, stiff-person syndrome, cerebellar ataxia, cognitive deficits, myelopathy, brainstem disorders [41]	SCLC, neuroendocrine tumors, thymoma. Cancer more likely in patients in with cerebellar ataxia, but less likely in those with SPS [42]
LGI1	Cell Surface, PNS low risk	CBA	Serum favored; CSF available	Higher clinical sensitivity in serum. Lower sensitivity by TIIF	Limbic encephalitis, memory deficits, faciobrachial dystonic seizures, sleep disorders [43]	Thymoma [44]
DPPX	Cell Surface, PNS low risk	TIIF/IHC and/or CBA	Serum/CSF	Optimal diagnostic accuracy when results from TIIF/IHC and CBA are concordant	Encephalitis with central hyperexcitability, progressive encephalomyelitis with rigidity and myoclonus (PERM), gastrointestinal dysmotility [45, 46]	B-cell lymphoma [47]
Glycine Receptor	Cell Surface, PNS low risk	CBA	Serum/CSF	Limited data on alternative methodology	PERM, seizures, limbic encephalitis, stiff-person spectrum disorders. [48, 49]	Thymoma, Hodgkin lymphoma [49]
MOG	Cell Surface, PNS low risk	LCBA	Serum favored; CSF available		Acute-disseminated encephalomyelitis, unilateral cortical encephalitis, optic neuritis, myelitis. [50]	Ovarian teratomas [51]
NIF (αIN, NF-H, NF-L)	Intracellular, not classified	TIIF/IHC with confirmatory by CBA	CSF favored; Serum available		Encephalopathy, cerebellar ataxia, myeloradiculoneuropathies [56]	Neuroendocrine tumors, pancreatic tumors, SCLC [56]

AChR	Surface Receptor, not classified	RIPA or CBA. Low specificity with low titer by RIPA, limited data on CBA	Serum		Myasthenia gravis (muscle), autonomic neuropathy (ganglionic)	Thymoma [52]
MuSK	Cell Surface, not classified	RIPA or CBA	Serum	Low specificity with low titer by RIPA, limited data on CBA	Myasthenia gravis	Rare
ANNA-3	Intracellular, not classified	TIIF/IHC	Serum	Lack of commercially available confirmatory methods	Limbic encephalitis, cerebellar ataxia, myelopathy, peripheral neuropathy [54]	SCLC [54]
IgLON5	Cell surface, not classified	TIIF/IHC and/or CBA	Serum/CSF	CBA may have superior sensitivity	Sleep disturbances, bulbar symptoms, cognitive decline, chorea, motor-neuron signs. [55]	Rare
GRAF1	Limited Cell surface, not classified	TIIF/IHC with confirmatory by CBA	Serum/CSF		Limb and gait ataxia, cerebellar ataxia [60, 61]	Squamous cell carcinoma [60]
ITPR	Intracellular, not classified	TIIF/IHC with confirmatory by CBA	Serum/CSF		Cerebellar ataxia, peripheral neuropathies, encephalitis with seizures, myelopathy [68]	Breast, lung, and renal cell carcinoma [68]
TRIM46	Intracellular, not classified	TIIF/IHC with confirmatory by CBA	Serum/CSF		Subacute cerebellar syndrome, limbic encephalitis, seizure, myelopathy [69]	Neuroendocrine carcinomas, lung cancers [69]
PDE10A	TIIF/IHC, not classified	TIIF/IHC	Serum/CSF		Movement disorders [70]	Carcinomas, ICI therapy [70]