that this has become so serious

Neuronal antibodies

The autoimmune disorder of the nervous system linked to an underlying tumour has been known since the 18th century. This is due to an attempt by the immune system to subjugate the growth of the tumour expressing neuronal antigens. The unfortunate consequence is a cross reaction by the immune components against the nervous tissue resulting in rapid onset of a variety of neurological deficits known as Paraneoplastic Neurological Syndrome. The resulting disability is considered irreversible because the nervous system lacks the capacity to regenerate following the immune onslaught. This phenomenon is rare, occurring at an approximate frequency of less than 1% and often accompanied by the presence of specific high-titre autoantibodies in both the cerebrospinal fluid and blood. These antibodies are non-pathogenic and are very useful early diagnostic markers of the brain disease and also, in some cases, underlying malignancy thus facilitating faster diagnosis and earlier treatment with better prognosis.

Summary of paraneoplastic neurological antibodies

Open all sections

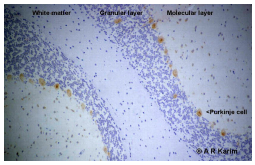
Antibody	MW (kDa)	Staining pattern	PND	Associated tumours
Recoverin	23, 65	Retinal photoreceptor	Retinopathy	SCLC
Yo (PCA-1)	34, 52, 62	Purkinje cell cytoplasm & axons	PCD	Ovary, breast
Ma (Ma1)	37, 40	Neuronal nuclei	PCD, BE	Various cancer
Ta (Ma2)	41.5	Neuronal nuclei, perikaryon	PCD, LE	Testicular cancer
Hu (ANNA1)	34-40	Nuclei of both central and peripheral neurones	PCD, PEM, SN	SCLC
Ri (ANNA2)	55, 80	Nuclei of central neurones	OM, PCD, BE	Breast, SCLC, gynaecological
GAD	65, 67	Islet cells & grey matter	SPS	Breast, colon, SCLC
CV2/CRMP5	66	Oligodendrocytes cytoplasm	PEM, SN	SCLC, thymoma
Amphiphysin	128	Central presynaptic terminals	SPS, SN	Breast cancer, SCLC
mGluR1	~140	Purkinje cell cytoplasm, climbing fibre	PCD	Hodgkin's lymphoma
ANNA-3	170	Purkinje cell cytoplasm & nucleus + glomerular podocytes	PCD, PEM, SN	SCLC
PCA-2	280	Purkinje cell cytoplasm and other neurones	PEM, PCD, LEMS	SCLC
AGNA	??	Nuclei of Bergmann glia of cerebellar Purkinje layer and glial in white matter	PND	SCLC
Tr	??	Purkinje cell cytoplasm with "dots" in molecular layer	PCD	Hodgkin's lymphoma

KEY: PND = paraneoplastic neurological disorder, PCD = paraneoplastic cerebellar degeneration, PEM = paraneoplastic encephalomyelitis, SN = sensory neuropathy, OM= opsoclonus/myclonus, BE = brainstem encephalomyelitis, LE = limbic encephalomyelitis, LEMS = Lambert-Eaton myasthenic syndrome, SPS = Stiff person syndrome, SCLC= small cell lung carcinoma. ?? = No common band has been identified by Western blot analysis

For the detection of paraneoplastic neurological antibodies, it is necessary to be familiar with cerebellar histology (see below).

Cerebellar architecture

The cerebellum consists of the white and the grey matter. The latter is subdivided into Molecular, Purkinje cell and Granular layer (contains densely packed granular cells|). The Purkinje cells can easily be identified due their large size (click on image). These are located on the border of granular and molecular layer.



(/Images/College-MDS-only/facilities/cis/neuroimmunology/HE(2).jpg)

The method of choice for detection of paraneoplastic antibodies is to screen the patient's serum on cerebellum and any positive reaction producing identifiable pattern is further confirmed by an alternative method such as line blot which consists of painted recombinant proteins.

Detection method for paraneoplastic antibodies

Antibodies produced in specific autoimmune diseases can be screened on an appropriate tissue using indirect immunofluorescence techniques.

PRINCIPLE: Autoantibodies, which attach to the appropriate antigen during an initial incubation with substrate tissue, can be detected by an immunoglobulin reagent (IgG, IgA or IgM), which has been conjugated with a fluorochrome for visualization under UV light following excitation.

ROUTINE SUBSTRATE SLIDES (commercially available)

Primate cerebellum can be used to detect the following antibodies:- GAD, PCA (Yo), ANNA1 (Hu), ANNA2 (Ri), Ma/Ta, amphiphysin, CV2/CRMP5, AGNA, and Tr.

METHOD:

- Diluted serum is incubated with tissue section in a moist chamber at room temperature.
- Then unbound antibodies are removed by washing the slides in PBS.
- Sections are incubated with diluted anti-human immunoglobulins (monkey adsorbed)-FITC at room temperature.
- The FITC conjugate is washed off as above.
- The sections are mounted under a glass cover slip using buffered glycerol +DABCO.
- The slides are ready for viewing under the fluorescence microscope.
- Pattern indicative of neuro-autoantibodies must be confirmed by other means (Western blot etc) and results disseminated to the appropriate physician as soon as

possible.

VK, Buffalo, NY, USA "I very much appreciate your contributions in the area of autoantibody detection specifically in the field of paraneoplastic antibody detection. We enjoy visiting your web site which is full of information..... "