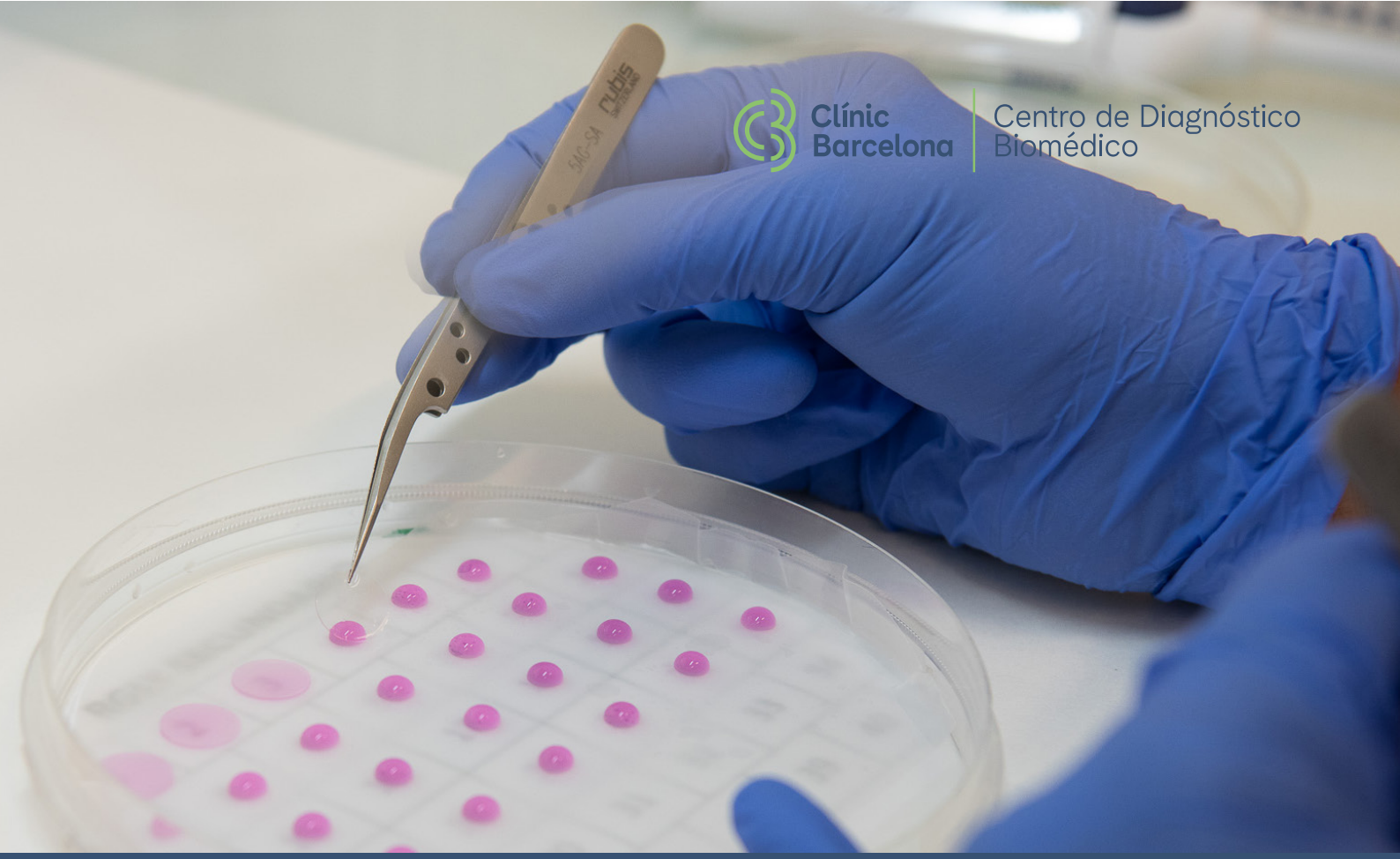


Clínic Barcelona | Centro de Diagnóstico Biomédico

Inmunoneurology

Get to know us

Immune Response and Hypersensitivity Section
Pathogenesis of Autoimmune Neurological Disorders

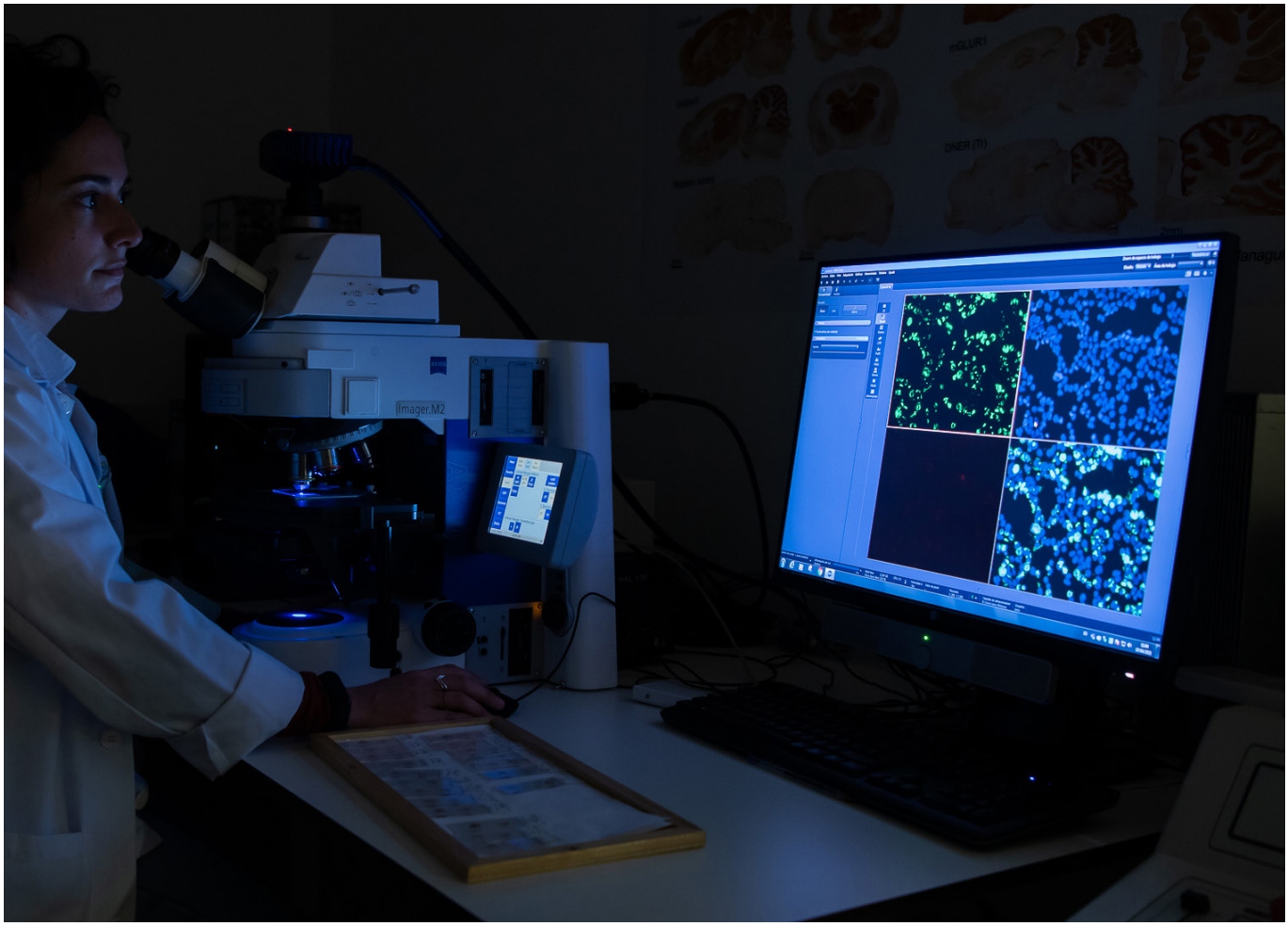
Hospital Clínic de Barcelona
Biomedical Diagnostic Centre

Generalitat de Catalunya
Departament de Salut

Who are we?

The Immunoneurology Unit is composed of professionals from the Immune Response and Hypersensitivity Section, part of the Immunology Service at the Biomedical Diagnostic Center (CDB) of Hospital Clínic. This area was created through knowledge transfer between the Neuroimmunology group at IDIBAPS, led by Dr. Graus, Dr. Dalmau and Dr. Saiz, and the Immune Response and Hypersensitivity Section (Immunology Service) at the CDB.

We are a highly specialized unit exclusively dedicated to the management of immune-mediated neurological diseases. We combine clinical care and research through projects aimed at expanding current knowledge about the etiopathogenesis of these diseases. To this end, we use the most advanced analytical techniques in the field of neurological disease diagnostics.



Area of excellence

Our team specializes in diagnosing **immune-mediated neurological diseases and identifying new biomarkers.**

These diseases belong to a heterogeneous group characterized by an inflammatory profile affecting the central and/or peripheral nervous system. Diagnosis is complex and must rely on **clinical criteria and laboratory data**.

At the CDB of Hospital Clínic de Barcelona, we offer a wide range of tests to support and confirm the diagnosis of these diseases. These techniques mainly involve the detection and characterization of autoantibodies that recognize neural antigens (neuronal and glial), which allows us to: 1. Confirm the diagnosis of neurological syndromes; 2. Guide the treatment with immunosuppressants or immunomodulators; 3. Interpret clinical manifestations when antibodies target antigens on the surface of neurons or glial cells.

Diagnostic approach for neurological diseases

At the Immunoneurology Unit we offer testing for the following antibodies and associated diseases:

Description	Technique	Disease
Onconeural and/or intracellular antibodies (Onco+GAD), serum/CSF. Hu, Ri, Yo, CV2 (CRMP5), Ma2/Ma1, Anfifisina, Tr (DNER), ZIC4, SOX1, GAD, GFAP, AK5 and others (less frequent)[¥].	Immunohistochemistry screening on tissue (cerebellum)[*].	• Paraneoplastic syndromes. • Autoimmune cerebellar ataxia. • Autoimmune encephalitis. • Stiff-Person syndrome.
Anti-**neuronal surface** antibodies, serum/CSF. NMDAR, AMPAR, GABABR, LGI1, CASPR2, GABAAR, mGluR1, mGluR2, mGluR5, DPPX, IgLON5, Neurexina-3a, SEZ6L2, GluK2, ynd others (less frequent).	Immunohistochemistry screening on tissue (brain)[*].	• Autoimmune encephalitis. • Cerebellar syndrome.
Anti-**Recoverin** antibodies, serum/CSF.	Inmunoblot.	• Cancer-associated retinopathy.
Anti-**Glycine receptor**, serum/CSF.	Live cell-based assay.	• Stiff-Person syndrome/PERM. • Autoimmune encephalitis.
Anti-**AQP4** (NMO) and anti-**MOG** antibodies profile, serum/CSF.	Live cell-based assay.	• Neuromyelitis optica spectrum disorder (NMOSD). • MOGAD.
Anti-**D2R** (dopamine receptor), serum/CSF.	Fixed cell-based assay.	• Basal ganglia encephalitis.
Anti-**MAG** antibodies(IgM), serum.	ELISA.	• IgM monoclonal gammopathy associated peripheral neuropathy.
Anti-**ganglioside** antibodies (IgG and IgM), serum. GM1, GM2, GM3, GM4, GD1a, GD1b, GD2, GD3, GT1a, GT1b, GQ1b, sulfatide.	Inmunoblot.	• Autoimmune neuropathies • (GBS, CIDP, MMN...).

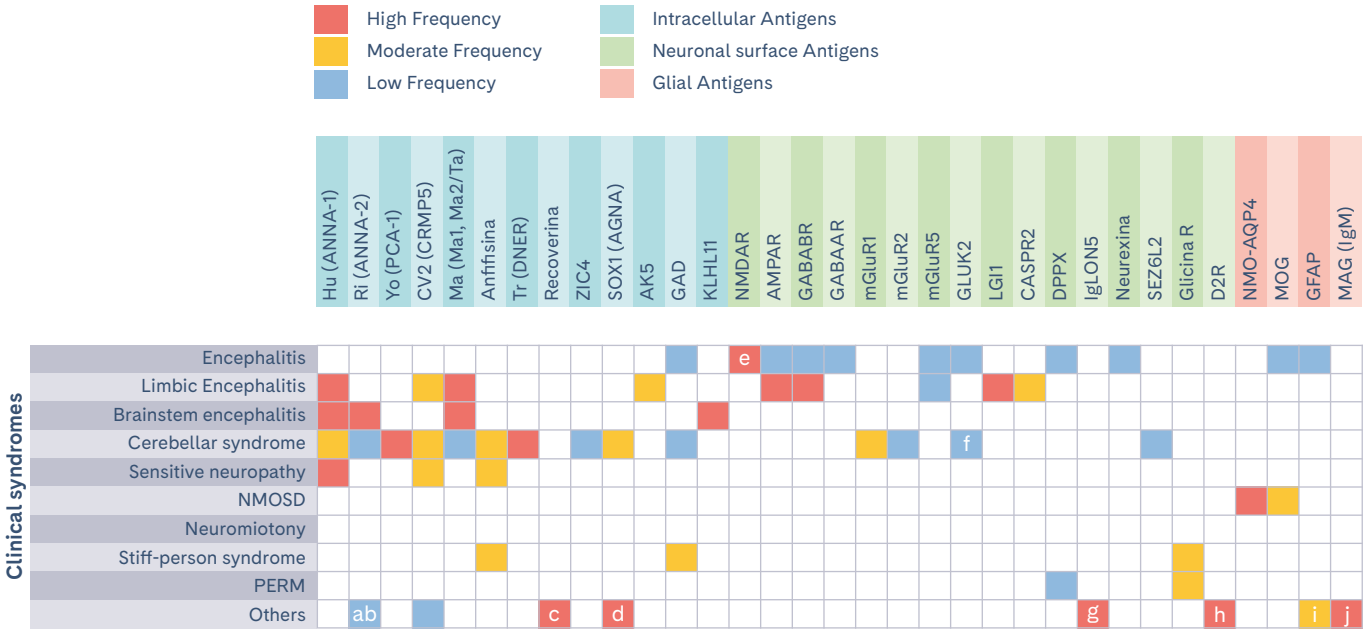
[*] In case of a positive result, the presence of antibodies will be confirmed by immunoblot or cellular assays, as appropriate.
[¥] After contact with the laboratory, other less frequent tests such as Septin-5, KLHL-11 and others associated with cerebellar ataxias can be performed.

Diagnostic approach for neurological diseases

At the Immunoneurology Unit we offer testing for the following antibodies and associated diseases:

Description	Technique	Disease
Oligoclonal IgG bands, CSF (serum required). **Oligoclonal IgM bands,** CSF (serum required).	Isoelectrofocusing.	• Multiple sclerosis. • Other CNS inflammatory disorders.
Prion protein detection for Creutzfeldt-Jakob disease (**PrP-RTQuIC**), CSF.	RT-QuIC (*Real-time quaking-induced conversion*) SAA.	• Prion diseases.
14-3-3 Protein, CSF.	ELISA.	
PRNP gene study, whole blood with EDTA.	Sanger.	
Alpha-synuclein detection by **aSyn-RT-QuIC, LCR**.	RT-QuIC (*Real-time quaking-induced conversion*) SAA.	• Alfa-sinucleinopathies (Parkinson, Lewy body dementia, Multiple System Atrophy).
Neurofilament light chain (**NfL**) quantification, serum/CSF.	Simoa.	• Neuronal damage biomarkers.

Diagnostic approach for neurological diseases



a: Adult opsoclonus mioclonus paraneoplasic; **b**: Corea; **c**: Cancer-associated retinopathy (CAR); **d**: Lambert-Eaton myasthenic syndrome; **e**: Psychosis, dyskinesias, dysautonomia-hypoventilation; **f**: Cerebellitis; **g**: Gait distorder, apnea, NREM sleep disorder; **h**: Basal ganglia encephalitis; **i**: Meningoencephalomyelitis; **j**: Peripheral neuropathy in the context of IgM monoclonal gammopathies (MGUS, Waldenström's macroglobulinemia); * Teratoma.

Abbreviations

AGNA: anti-glial nuclear antibody; AK5: Adenylate kinase 5; **AMPAR**: Alpha-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid receptor; **ANNA**: anti-neuronal nuclear antibodies; **AQP4**: aquaporin-4; **CASPR2**: contactin asociated protein 2; **CRMP5**: collapsin response-mediator protein; **D2R**: Dopamine-2 receptor; **DNER**: Delta-Notch like epidermal growh factor receptor; **DPPX**: Dipeptidil peptidase like protein 6; **GABA**: Gamma-aminobutiric acid; **GAD**: Glutamic acid descarboxilase; **GFAP**: Glial fibrilary acidic protein; **GLUK2**: Glutamate receptor ionotropic, kainate 2; **KLHL11**: Kelch-like protein 11; **MAG**: myelin associated glycoprotein; **mGluR**: metabotropic glutamate receptor; **MOG**: myelin oligodendrocyte glycoprotein; **NMDAR**: N-methyl-D-Aspartare receptor; **NMOSD**: neuromyelitis optica spectrum disorders; **LGI1**: Leucine-rich glioma inactivated 1; **PCA**: Purkinje cell cytoplasmic antibody; **SEZ6L2**: seizure 6 like protein 2; **ZIC4**: Zinc finger protein ZIC 4.

Recommendations/comments

1) a-Yo antibodies have to be confirmed by tissue-based techniques; **2)** a-Recoverin antibodies lack clinical value outside the context of retinopathy; **3)** a-ZIC4 antibodies have low specificity for paraneoplastic neurological syndromes; 4) sit is recommended to confirm alpha-GAD antibodies in CSF.

Physician staff

Dra. Raquel Ruiz

Degree in Pharmacy, University of Salamanca (2009) and PhD in Biomedical Research (Immunology), Complutense University of Madrid (2017).
Specialist in Immunology (2015), Hospital Universitario 12 de Octubre.

Research:
Pathogenesis of autoimmune neurological diseases.

Dra. Laura Naranjo

Degree in Biochemistry, University of Seville (2014) and PhD in Biomedical Research, Complutense University of Madrid (2022).
Specialist in Immunology (2015), Hospital Universitario 12 de Octubre.

Research:
Pathogenesis of autoimmune neurological diseases.

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Immunoneurology Request Form

Immune Response and Hypersensitivity Section
Pathogenesis of Autoimmune Neurological Diseases

Hospital Clínic de Barcelona
Centro de Diagnóstico Biomédico

Generalitat de Catalunya
Departament de Salut

Contact

Sample Submission Address:
Sample Reception
Hospital Clínic de Barcelona
C/ Villarroel, 170
Inter-pavilion 9–11, 1st floor
08036 – Barcelona
Hours: Monday to Friday, 08:00 to 19:00
Phone: +34 93 227 54 64
Email: atencdb@clinic.cat

Clinical information (Mandatory)

Patient clinical data:

The diagnostic request must always be accompanied by:

- Referring physician information.
- Patient clinical data.
- Authorization.

Referring physician information:

Referring Physician*:

Department and Hospital*:

Physician Email*:

Patient clinical information:

Patient full name or identification*:

Date of Birth*: / /

Sex*: ○ Male ○ Female

Sample Type*: ○ Serum ○ CSF

Clinical course summary*:

*Essential to determine the most appropriate or additional tests in cases of inconclusive results or when specific confirmatory tests are required.

Clinical course (Optional– check as applicable)

Course type:

- ☐ Acute
- ☐ Subacute
- ☐ Progressive

Specific clinical features:

- ☐ Behavioral changes
- ☐ Psychiatric symptoms
- ☐ Memory impairment
- ☐ Language disturbances
- ☐ Seizures
- ☐ Status epilepticus
- ☐ Sleep disorders
- ☐ Abnormal movements
- ☐ Gait instability
- ☐ Rigidity
- ☐ Neuromyotonia
- ☐ Decreased level of consciousness consciousness
- ☐ Dysautonomia
- ☐ Central hypoventilation
- ☐ Sensory deficit
- ☐ Motor deficit
- ☐ Visual impairment
- ☐ Brainstem/cerebellar involvement
- ☐ Mild cognitive impairment
- ☐ Rapidly progressive cognitive impairment
- ☐ Other (please specify):

Tumor presence:

- ☐ Lung
- ☐ Ovary
- ☐ Breast
- ☐ Testicular
- ☐ Hodgkin
- ☐ Thymoma
- ☐ Other (please specify)

Complementary studies:

- ☐ Brain MRI:
- ☐ EEG:
- ☐ Spinal MRI:
- ☐ Pleocytosis
- ☐ Elevated CSF protein
- ☐ Oligoclonal bands

Laboratory test request:

Check	Catalogue ID	Description	Method	Disease
☐	54232 (CSF) 54233 (serum)	**Onconeural and/or intracellular** antibodies (Onco+GAD), serum/CSF. Hu, Ri, Yo, CV2 (CRMP5), Ma2/Ma1, Amphiphysin, Tr (DNER), ZIC4, SOX1, GAD, GFAP, AK5, and other less frequent antibodies[¥].	Immunohistochemistry screening on tissue (cerebellum / brain)[*].	• Paraneoplastic syndrome. • Autoimmune cerebellar ataxia. • Autoimmune encephalitis. • Stiff Person syndrome.
☐	54529 (CSF) 54528 (serum)	**Neuronal surface** antibodies, serum/CSF. NMDAR, AMPAR, GABA_B receptor, LGI1, CASPR2, GABA_A receptor, mGluR1, mGluR2, mGluR5, DPPX, IgLON5, Neurexin-3a, SEZ6L2, GluK2, and other less frequent antibodies.	Immunohistochemistry screening on tissue (cerebellum / brain)[*].	• Autoimmune encephalitis. • Cerebellar syndrome.
☐	54226 (CSF) 54227 (serum)	Anti-**Recoverin** antibodies, serum/CSF.	Inmunoblot.	• Cancer-associated retinopathy.
☐	54228 (CSF) 54229 (serum)	Anti-Glycine receptor (**GlyR**) antibodies, serum/CSF.	Cell based assay (live or fixed).	• Autoimmune encephalitis. • Stiff Person syndrome / PERM.
☐	54235 (CSF) 54236 (serum)	Anti-**AQP4** (NMO) and anti-**MOG** antibody profile, serum/CSF.	Cell based assay (live or fixed).	• Neuromyelitis Optica Spectrum Disorders (NMOSD). • MOG Antibody–Associated Disease (MOGAD).
☐	54237 (CSF) 54238 (serum)	Anti-**D2R** (dopamine receptor) antibodies, serum/CSF.	Cell based assay (live or fixed).	• Basal ganglia encephalitis.
☐	54537 (serum)	Anti-**MAG** antibodies (IgM), serum.	ELISA.	• Anti MAG–associated demyelinating neuropathy.
☐	54856 (serum)	Anti-**ganglioside** antibodies (IgG and IgM), serum. GM1, GM2, GM3, GM4, GD1a, GD1b, GD2, GD3, GT1a, GT1b, GQ1b, sulfatides.	Inmunoblot.	• Autoimmune neuropathies (GBS, CIDP, MMN, etc.).

Laboratory test request:

Check	Catalogue ID	Description	Method	Disease
☐	54065 (CSF)	**IgG oligoclonal bands**, CSF (serum required).	Isoelectric focusing.	• Multiple sclerosis • Other inflammatory disorders of the central nervous system (CNS).
☐	54234 (CSF)	**IgM oligoclonal bands**, CSF (serum required).		
☐	54290 (CSF)	**Prion protein** detection for Creutzfeldt Jakob disease (**PrP RT QuIC**), CSF.	RT-QuIC (*Real-time quaking-induced conversion*).	• Prion diseases.
☐	54222 (CSF)	**Protein 14 3 3**, CSF.	ELISA.	
☐	54999 (whole blood)	**PRNP gene** study, whole blood (EDTA).	Sanger.	
☐	54894 (CSF)	**Alpha synuclein** detection by **RT QuIC**, CSF.	RT-QuIC (*Real-time quaking-induced conversion*).	• Alpha-synucleinopathies (Parkinson's disease, dementia with Lewy bodies, multiple system atrophy).
☐	54874 (serum)	Neurofilament light chain (**NfL**) quantification, serum/CSF.	Simoa.	• Biomarker of neuronal damage.
☐	54890 (CSF)			

* Positive results will be confirmed by immunoblot or cell based assays, as appropriate.

¥ After consultation with the laboratory, other less frequent antibodies may be tested (e.g. Septin 5, KLHL 11 and others associated with cerebellar ataxias).

Research or special request studies:

Check	Catalogue ID	Description	Method	Disease
☐	54892 (serum)	pTau 181 quantification, serum/CSF.	Simoa.	• Alzheimer.
☐	54892 (CSF)			
☐	54224 (serum)	Neuro 2 Plex (NfL, GFAP), serum/CSF.	Simoa.	• Biomarker of neuronal damage.
☐	54223 (CSF)			
☐	54893 (serum)	Neuro 4 Plex (NfL, UCH1, GFAP, TAU), serum/CSF.	Simoa.	
☐	54893 (CSF)			

Samples submission

Sample Type

Most anti neuronal antibodies can be determined in serum or CSF; however, **CSF submission is recommended** in the following clinical scenarios:

- Autoimmune limbic encephalitis.
- Neurological disorders associated with anti GAD65 antibodies.
- GFAP astrocytopathy.
- Stiff Person syndrome / PERM with anti GlyR antibodies.

Prion protein detection for the diagnosis of Creutzfeldt–Jakob disease (RT-QuIC), as well as 14-3-3 protein quantification, are performed in cerebrospinal fluid (CSF) samples, as is the detection of alpha-synuclein by RT-QuIC.

Anti-MAG (IgM) and anti-ganglioside antibodies (IgG and IgM) are exclusively analyzed in serum samples.

For the evaluation of IgG and IgM oligoclonal bands, the availability of both serum and CSF samples is required in order to determine the presence of intrathecal synthesis.

Shipping Conditions

- Samples may be sent at room temperature and **must be shipped by courier**, as they **must arrive at the laboratory within 24 hours of sample collection**.
- If samples are previously frozen or if a delivery delay is expected, shipment of frozen samples is recommended.

Shipments from outside the European Union

In the case of shipments from outside the European Union, please contact the CDB External Agreements Department via email: LD_convenisexterns@clinic.cat

Turnaround times : (Catalogue)

- Onconeural/intracellular antibodies (**Onco + GAD**).
- Study of **neuronal surface** antibodies.
- Anti **Recoverin** antibodies.
- Anti **GlyR** antibodies.
- **AQP4** (NMO) and **MOG** antibodies.
- Anti **D2R** antibodies (dopamine receptor).
- Anti **MAG** antibodies (IgM).
- Prion protein detection for the diagnosis of Creutzfeldt–Jakob disease.
- **Protein 14 3 3**.

14 days

- Anti ganglioside antibodies (IgG and IgM).

15 days

- IgG oligoclonal bands.

21 days

- **IgM oligoclonal bands.**
- **Alpha synuclein** detection by RT QuIC.
- Neurofilament light chain (**NfL**) quantification.

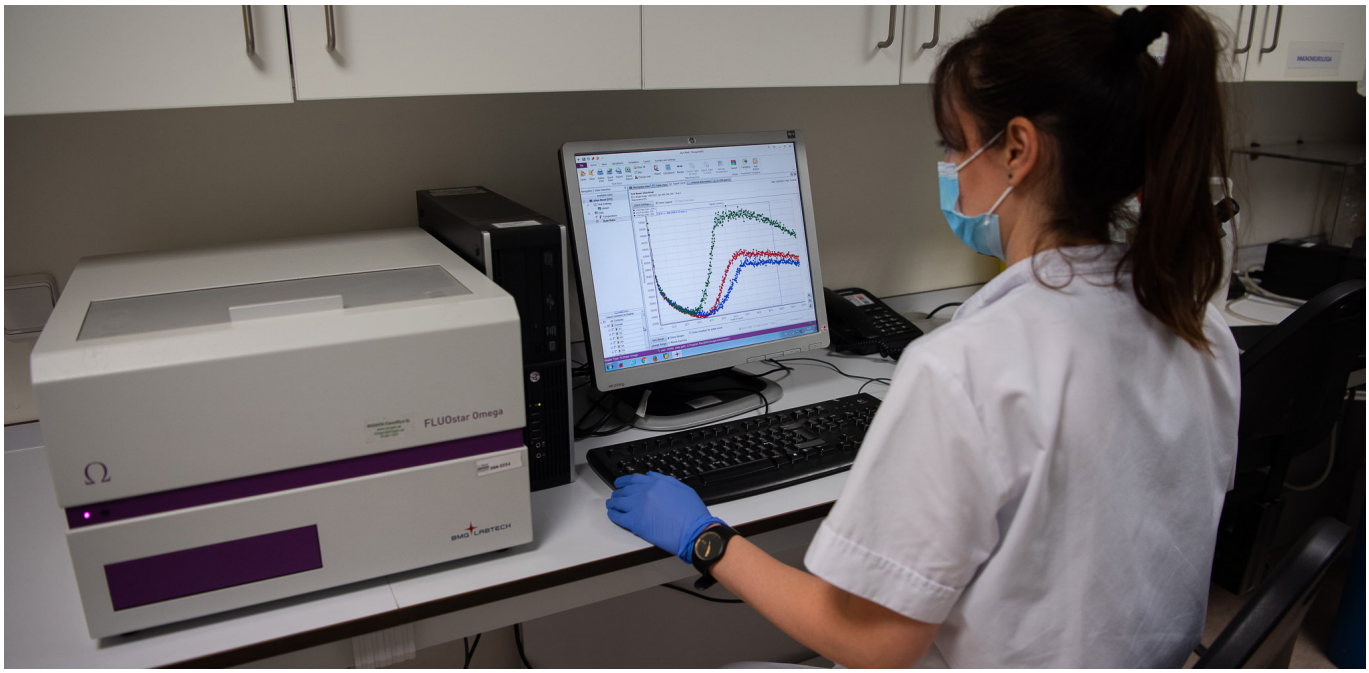
30 days

- Genetic study of **Creutzfeldt–Jakob** disease.

60 days

Immunoneurology laboratory: Contact information

Dra. Raquel Ruiz García (rruizg@clinic.cat)
Dra. Laura Naranjo Rondán (lanaranjo@clinic.cat)
Phone number: +34 617 304 306



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