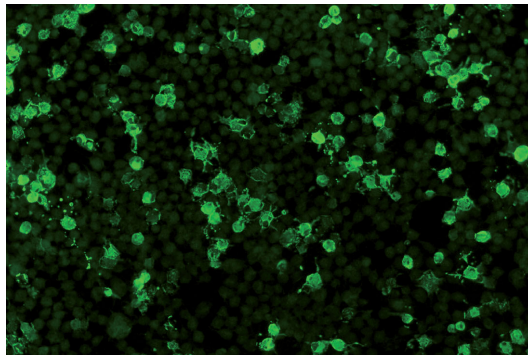
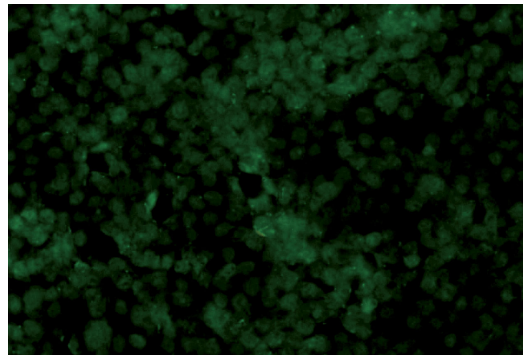


# Anti-Glutamate Receptor (Type NMDA) IIFT



NMDA-receptor (transfected cells)



Non-transfected cells

Anti-NMDA-receptor

**Indication:** Test system for the in vitro determination of antibodies against glutamate receptors (type NMDA) in human serum, plasma or cerebrospinal liquid (CSF) for the diagnosis of the following disease: autoimmune encephalitis (anti-NMDA receptor encephalitis).

**Clinical significance:** Antibodies against glutamate receptors (type NMDA) are specific markers for anti-NMDA receptor encephalitis, an inflammatory encephalopathic autoimmune disease which was first described in 2007 in patients with ovarian tumours and is currently a still widely underdiagnosed disease.

The disease often starts with a flu-like preliminary stage, followed by psychiatric symptoms such as anxiety, excitement, strange behaviour, delusions and hallucinations. A large proportion of patients end up in psychiatric therapy. Within a few weeks epileptic attacks and catatonia-like consciousness disorders follow. Many patients have ovarian tumours (teratoma), which amongst other things contain nerve cells. In these patients, anti-NMDA receptor encephalitis is a paraneoplastic syndrome.

In the serum and CSF of patients with anti-NMDA receptor encephalitis are autoantibodies directed against the extracellular domain of the receptor NR1 subunit. These are not identical with autoantibodies against the NR2 subunit of the NMDA receptor, which have occasionally been discussed (controversial findings) as indicators of a neurological involvement in SLE (neuropsychiatric lupus).

Anti-NMDA receptor encephalitis is increasingly diagnosed not just in young women, but also in older female patients, in women without teratoma, in men (some with teratoma of the testis) and in children. Prognosis for patients is improved with appropriate immunomodulatory therapy, and, in PNS, tumour detection and resection as early as possible. In around 75% of cases a substantial regression of symptoms can be achieved. However, 25% of patients die or suffer from severe neurological deficits. Survivors have memory loss (amnesia) for the duration of the illness, and there is a risk of relapses of the encephalitis syndrome, the latter in particular when the tumour is removed too late or not at all or if no tumour could be found.

**Application of the Anti-Glutamate Receptor (Type NMDA) IIFT:** Diagnosis of anti-NMDA receptor encephalitis is based on a combination of the characteristic clinical picture, with supporting results from brain MRT, EEG and CSF analysis if necessary, and the detection of anti-glutamate receptor (type NMDA) antibodies in serum/CSF, which are directed against the NR1 subunit of the receptor. Infectious encephalitides (especially HSV) and other autoimmune aetiologies (limbic encephalitis with autoantibodies against Hu, Ma2, CV2 and amphiphysin) must be excluded by differential diagnostics. In general, antibodies against glutamate receptors (type NMDA) should be determined in all patients with encephalitis where no pathogen has been detected and in suspected cases of limbic encephalitis. When a positive serological result is obtained a comprehensive teratoma investigation should be undertaken.

Indirect immunofluorescence (IIFT) is a simple and modern method that enables highly sensitive, monospecific detection of anti-glutamate receptor (type NMDA) antibodies by means of a recombinant cell line transfected with expression constructs for the receptor subunit NR1.

## EUROIMMUN IIFT Autoimmune Diagnostics

**tissue/cell substrates:**  
adrenal gland, monkey  
bladder, rat  
cartilage (trachea), monkey\*  
cerebellum, monkey  
cerebrum, monkey  
Crithidia luciliae  
DNS-bound lactoferrin  
erythrocytes, human\*  
eye, monkey\*  
granulocytes, human (ethanol-fixed)  
granulocytes, human (formaldehyde-fixed)  
granulocytes, human (methanol-fixed)  
heart, monkey  
HEp-2 cells  
HEp-20-10 cells  
HUVEC  
hypothalamus, monkey\*  
intestine, monkey  
kidney, monkey  
kidney, mouse  
kidney, rat  
lacrimal gland, monkey  
lip, monkey\*  
liver, monkey  
liver, mouse  
liver, rat  
lobus temporalis, monkey\*  
lung, monkey  
lymph nodes, monkey\*  
lymphocytes, human\*  
mammary gland, monkey\*  
mouth mucosa, monkey\*  
nerve, monkey  
oesophagus, monkey  
oesophagus, rat  
ovary, monkey  
pancreas, monkey  
parathyroid gland, monkey  
parotid gland, monkey  
pituitary gland, monkey  
placenta, monkey\*  
prostate, monkey  
Saccharomyces cerevisiae  
skeletal muscle, monkey  
spermatozoa, human  
spleen, monkey\*  
spinal cord, monkey  
stomach, monkey  
stomach, mouse  
stomach, rat  
synovium, monkey  
testis, monkey  
thrombocytes, human  
thymus, monkey  
thyroid gland, monkey  
tongue, monkey  
VSM47 cells  
umbilical cord, human

**EUROPLUS™ substrates:**  
AIH (LC-1 + SLA/LP)  
BP180  
GBM  
gliadin  
intrinsic factor  
myeloperoxidase (MPO)  
PBC (AMA M2 + Sp100)  
proteinase 3 (PR3)  
ribosomal P:proteins + Jo-1  
SS-A + SS-B  
SS-B + ribosomal P:proteins + Jo-1  
SS-B + Sol-70 + Jo-1  
thyroglobulin (TG)

**transfected cells:**  
aquaporin-4  
BP230  
desmoglein 1 + 3  
NMDA receptor  
rPAG 1 + 2 (pancreas antigen 1 + 2)

**BIOCHIP Mosaics™:**  
ANA global test: HEp-20-10/monkey liver  
Autoantibody Profile: combination of 30 different tissues per slide  
CIBD Profile: monkey pancreas/intest. goblet cells (culture)/granulocytes (EOH)/Saccharomyces cerevisiae  
Basic Profile: HEp-20-10/monkey liver/rat kidney/rat stomach  
EUROPLUS endomysium + gliadin: monkey intestine/monkey liver/gliadin  
Granulocyte Mosaic: granulocytes (EOH)/granulocytes (HCHO)/HEp-2/monkey liver  
Liver Mosaic: HEp-2/monkey liver/rat liver/rat kidney/rat stomach/monkey heart  
Neuronal Antibody Screen: monkey cerebellum/monkey nerve/monkey intestine  
Polyendocrinopathy Mosaic: monkey thyroid/monkey pancreas/monkey adrenal/monkey ovary/monkey testis/monkey stomach

Other mosaics also available  
Special substrate combinations on request

\* Currently not available as IVD in the EU.

Made in Germany

# Test Characteristics

## Anti-Glutamate Receptor (Type NMDA) IIFT

**Viruses:**  
Adenoviruses  
Chikungunya virus  
Coxsackieviruses  
Crimean Congo fever virus (CCHFV)\*  
Cytomegalovirus (CMV)  
Dengue viruses types 1-4 (DENV)  
ECHO virus  
Epstein-Barr virus capsid antigen (EBV-CA)  
Epstein-Barr virus early antigen (EBV-EA)  
Epstein-Barr virus nuclear antigen (EBNA)  
Hantaviruses (types Hantaan, Puumala, Seoul, Saaremaa, Dobrava, Sin Nombre, Andes\*)  
Herpes simplex virus types 1 and 2 (HSV-1/2)  
Human herpes virus type 6 (HHV-6)  
HIV-1 and -2\*  
Influenza virus A (Shangdong, Singapore, Beijing)  
Influenza virus B (Panama)  
Japanese encephalitis virus (JEV)\*  
Measles virus  
Mumps virus  
Parainfluenza viruses types 1-4  
Respiratory syncytial virus (RSV)  
Rubella virus\*  
Sandfly fever virus\*  
(types Sicilian, Naples, Toscana, Cyprus)  
SARS Coronavirus (SARS-CoV)  
Tick-borne encephalitis (TBE) virus  
Varicella zoster virus (VZV)  
West Nile virus (WNV)  
Yellow fever virus (YFV)

**Bacteria:**  
Afipia felis\*  
Bartonella henselae  
Bartonella quintana  
Bordetella parapertussis  
Bordetella pertussis  
Borrelia afzelii  
Borrelia burgdorferi  
Borrelia garinii  
Campylobacter coli\*  
Campylobacter jejuni\*  
Chlamydia pneumoniae  
Chlamydia psittaci  
Chlamydia trachomatis  
Haemophilus influenzae\*  
Helicobacter pylori  
Klebsiella pneumoniae\*  
Legionella bozemanii\*  
Legionella dumoffii\*  
Legionella gormanii\*  
Legionella jordanis\*  
Legionella longbeachae\*  
Legionella micdadei\*  
Legionella pneumophila serotypes 1-14  
Listeria monocytogenes 1/2 a, 4b\*  
Mycoplasma hominis  
Mycoplasma pneumoniae  
Treponema pallidum  
Treponema phagedenis  
Ureaplasma urealyticum  
Yersinia enterocolitica\*

**EUROPLUS™ substrates:**  
Borrelia VisE (recombinant)  
Borrelia OspC  
EBV p19 + gp125

**Yeasts:**  
Candida albicans  
Candida glabrata\*  
Candida krusei\*  
Candida parapsilosis\*  
Candida tropicalis\*

**Parasites:**  
Echinococcus granulosus  
Leishmania donovani  
Plasmodium falciparum HRP-2/MSP-2 (rec.)\*  
Plasmodium vivax MSP/CSP (recombinant)\*  
Toxoplasma gondii

**Profiles:**  
Accompanying hepatitis profile  
Central nervous system profile  
Exanthema profile  
Fever profile South East Asia  
Flavivirus profile  
Gastrointestinal tract profile  
Infectarthritis profile  
Infectarthritis profile (The Tropics)  
Lymphadenitis profile  
Myocarditis profile  
Ophthalmology profile  
Otitis profile  
Pregnancy profile  
Respiratory tract profile  
Sexually transmitted diseases (STD) profile  
TORCH profile

\* Currently not available as IVD in the EU.

Special substrate combinations  
on request

**Made in Germany**

Version: 01/10  
FA\_112d\_D\_UK\_A01

**Test principle:** The test system exclusively serves for the in vitro determination of human antibodies in human serum, plasma or CSF. The determination can be performed qualitatively or quantitatively. BIOCHIPS are incubated with diluted patient samples. In the case of positive reactions, specific antibodies of the classes IgA, IgG and IgM will bind to the antigens. In a second step, the attached antibodies are stained with fluorescein-labelled anti-human antibodies and made visible with the fluorescence microscope.

**Test procedure:** EUROIMMUN BIOCHIP slides are incubated using the proprietary TITERPLANE Technique. This technique enables multiple samples to be incubated next to each other and simultaneously under identical conditions. Results are evaluated by fluorescence microscopy.

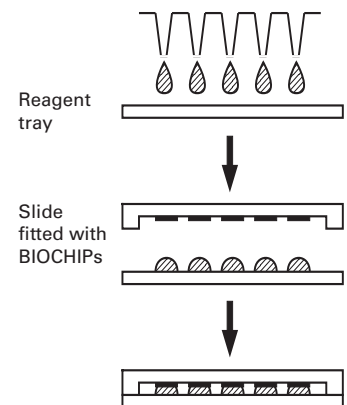
**Intra-assay reproducibility:** Ten determinations for each of two characterised samples were incubated in parallel. The deviation in the fluorescence intensity of the IIFT amounted to no more than  $\pm 1$  intensity levels for all samples.

**Inter-assay reproducibility:** Two characterised samples were incubated in duplicate on at least 2 different days in 5 test runs. In quantitative evaluation of results, no deviation in the fluorescence intensity was found.

**Inter-lot reproducibility:** Three slide lots were tested with different characterised sera to estimate any deviations between individual lots. The deviation in the fluorescence intensity of the IIFT amounted to no more than  $\pm 1$  intensity levels for all samples.

**Sensitivity and specificity:** The clinical sensitivity and specificity of the test system are 100%. Samples from patients with Anti-NMDAR encephalitis (n=39), patients with other encephalitides (n=31) and healthy blood donors (n=100) were investigated. Reference: Wandinger, Dalmau et al., From Pathogenesis to Therapy of Autoimmune Diseases. Autoantigens, Autoantibodies, Autoimmunity 6:434-435, Pabst Science Publishers (2009)

### Incubation with the TITERPLANE™ Technique



Sample characterisation	n	Anti-glutamate-receptor (type NMDA) Ab pos.
Patients with anti-NMDAR encephalitis	39	100 %
Patients with other encephalitides	31	0 %
Blood donors	100	0 %

### Technical data:

Antigen substrate	Transfected cells and non-transfected cells (EU 90)
Sample dilution	Serum or plasma. Qualitative: 1:10, CSF: undiluted quantitative: 1:10/100/1000 etc.
Conjugate	IgG
Test procedure	30 min (sample) / 30 min (conjugate). Room temperature.
Microscopy	Objective 40x, excitation filter: 488 nm, colour separator: 510 nm, blocking filter: 520 nm, light source: EUROIMMUN LED or mercury vapour lamp, 100 W
Reagents	Ready for use, with the exception of the PBS Tween buffer.
Stability	Stable at +2°C to +8°C for 18 months after the date of manufacture.
Test kit format	10 or 20 slides, each containing 3, 5 or 10 test fields. Kits include all necessary reagents.
Order no.	FA 112d-####-51
Related products	FA 111m-3: hippocampus, rat/cerebellum, rat/NMDA-R/EU 90