

Analys av anti-neuronala antikroppar

När, var, hur ?

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Neuromuskulära synapsen

«Neuroimmunologins vagga»

Myastenia Gravis

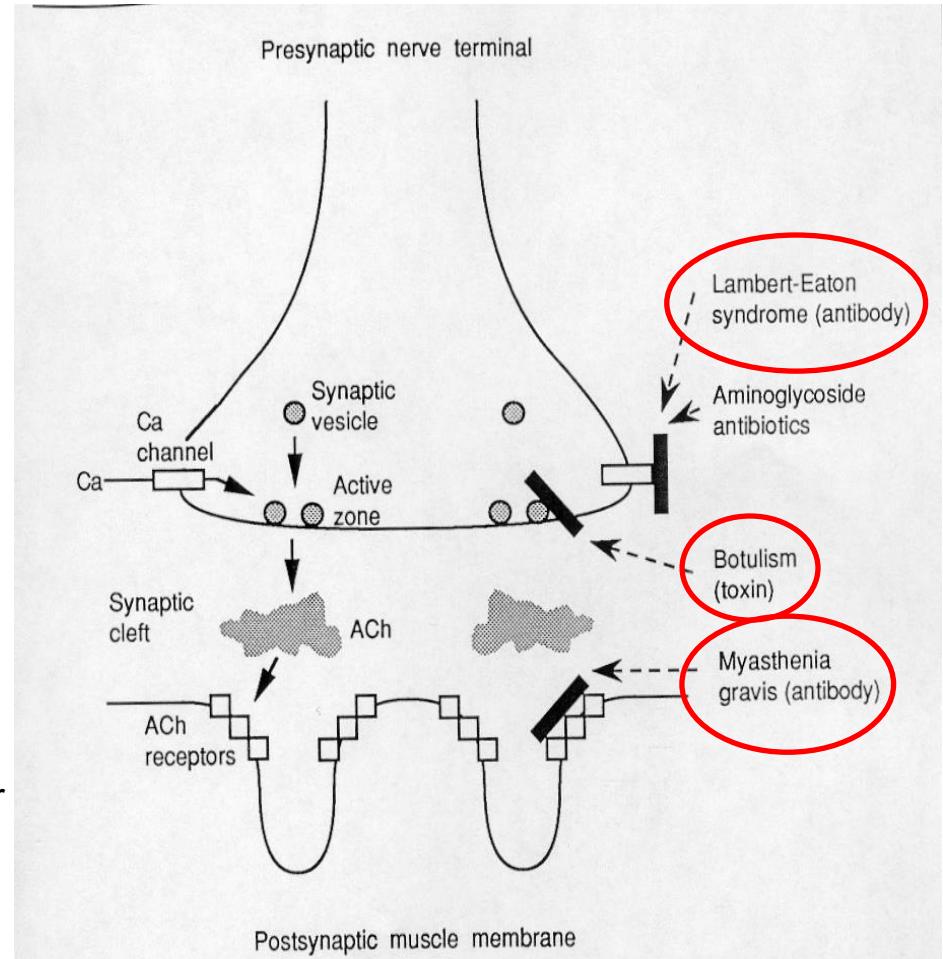
- Antikroppar mot Acetylkolin-receptor
- Ger slappa pareser
- Typisk uttröttbarhet
- Behandlas genom att hämma nedbrytning av acetylkolin

LEMS – Lambert-Eatons myastena syndrom

- Antikroppar mot spänningsskänsliga calciumkanaler, VGCC
- Slappa pareser, uttröttbarhet, facilitering
- Blockad av Ach – frisättning
- Majoriteten paramaligna, SCLC.

Neuromyotoni / Morvan's syndrom

- Anti-VGKC – LGI/CASPR3
- Svaghet, svettning, myokymier
- CNS-symptom, konfusion, paranoia, kramper
- Autoimmun eller paramalign,
- SCLC, Thymom



Paraneoplastiska neurologiska syndrom (PNS)

- Neurologisk fjärr - effekt av cancer
- Omkring 1-2% av all cancer
- Debuterar före kliniska symptom av cancer i 60-70% av fallen
- Onconeurala antikroppar biomarkörer
- Kan medföra tidig diagnos och behandling

Paraneoplastiska neurologiska syndrom, PNS

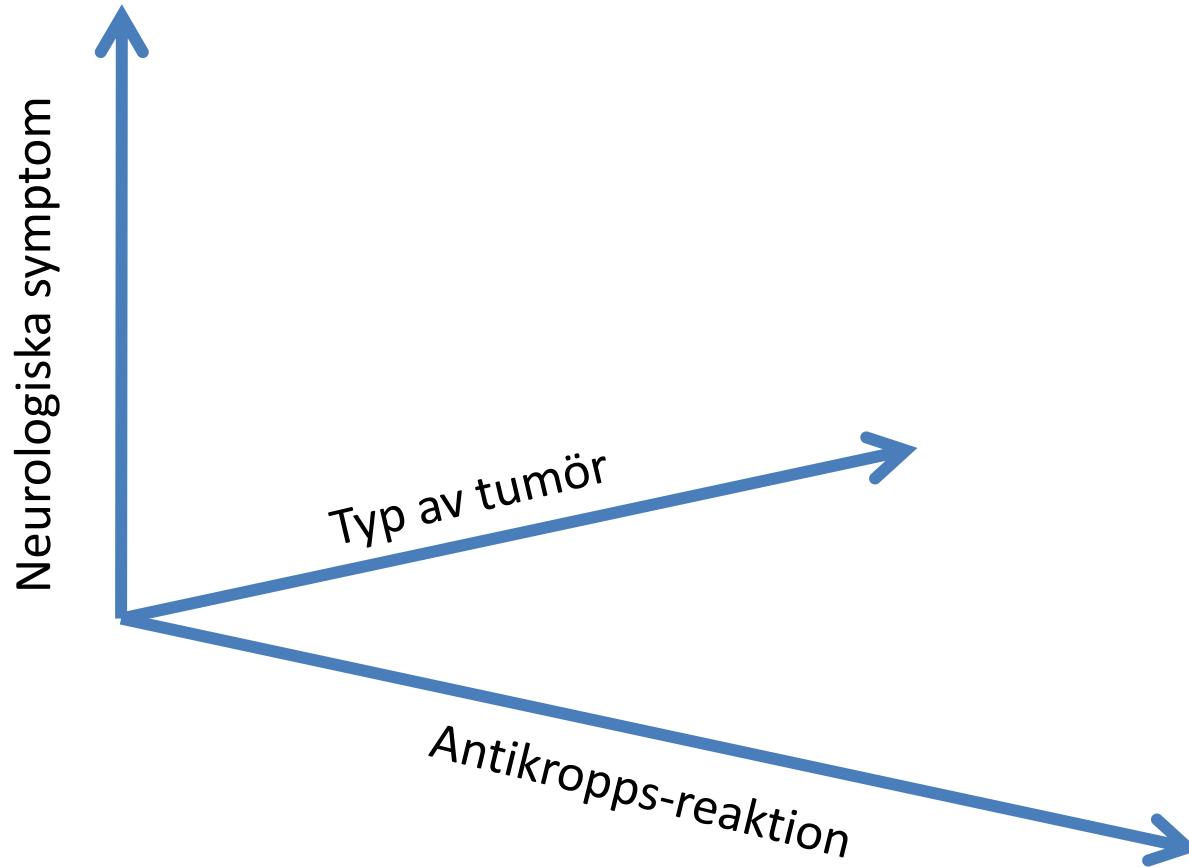
- PEM - Paraneoplastisk encefalomyelit
- PSN - Paraneoplastisk sensorisk neuronopati
- PCD - Paraneoplastisk cerebellär degeneration
- LEMS – Lambert Eatons myastena syndrom
- MG – Myastenia gravis
- LE – Limbisk Encefalit
 - Inkl NMDA-rec encefalit

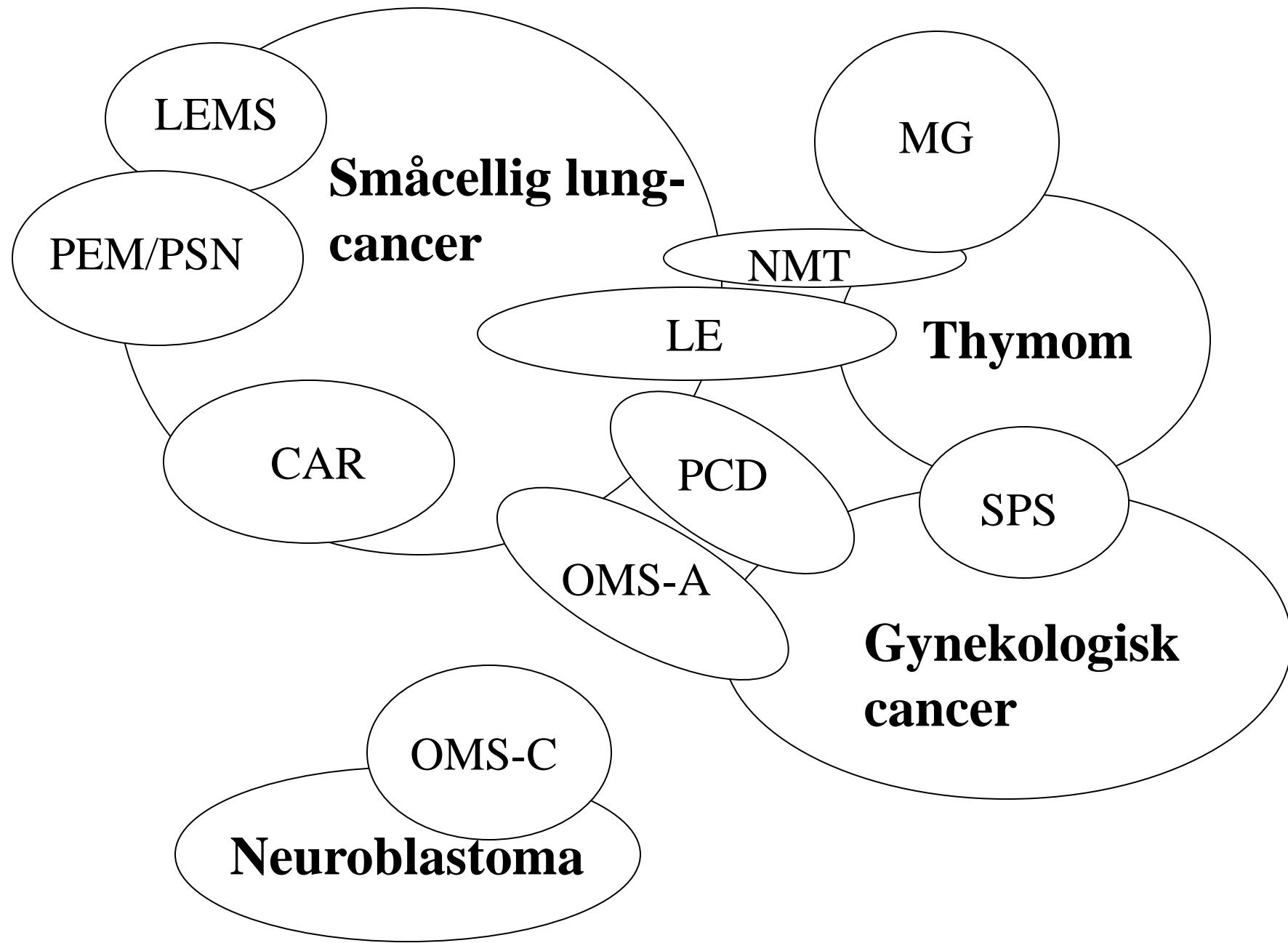
Ytterligare paraneoplastiska CNS syndrom

- Stiff-person syndrome (SPS)
 - Muskelrigiditet och spasmer
- Anti-GAD
- Anti-amphiphysin (bröstcancer)
- Cancer-associerad retinopati (CAR)
 - Synnedsättning
 - Förlust av foto-receptorer, (stavar/tappar)
 - Anti-recoverin (SCLC)

Paraneoplastiska CNS syndrom

Utredning i tre dimensioner





	Syndrom	Associerade cancer-former
Well characterised paraneoplastic ab		
Anti-Hu	PEM-cortical, limbic, brainstem, PCD PSN, autonomic dysfunciton.	SCLC - other
Anti-Yo (PCA-1)	PCD	Gyn, Breast
Anti-Ri	PCD, Brainstem encephalit, ONS	Breast, Gyn, SCLC
Anti-CV2 / CRMP5	PEM	SCLC, Thymom, other
Anti-Ma-prot (Ma1/2)	Limbic, hypothalamic, brainstem encephalitis	Testis, non-SCLC, solid tumors
Anti-Amphiphysin	PEM, LE, Myelopati, Stiff person syndrome	SCLC, Breast-Ca
Partly characterised paraneoplastic ab		
Anti-Tr	PCD	Hodgkin
Anti-Zic4	PCD	SCLC
mGluR1	PCD	Hodgkin
ANNA-3	Various PND in CNS	SCLC
PCA-2	Various PND in CNS	SCLC
Ab that occurs with or without cancer association		
Anti-NMDA-rec	Characteristic encephalitis	Teratom, ovary
Anti-VGKC / LG1/CASPR2	Limbic encephalitis, Neuromyotoni, Morvans	Thymom, SCLC, other
Anti-VGCC	LEMS	SCLC
Anti-AchR	MG	Thymom
Anti-nAchR	Pandysautonomi	SCLC
Anti-GAD	Stiff person syndrome, LE <small>Clas Malmeström</small>	Thymom, other

Varför så rörig nomenklatur ?

- Namn efter index-patient...
 - Hu - Hull
 - Yo – Young
 - Ma – Margret
- Efter metod...
 - Anna – anti-nucleär neuronal ak
- Känt specifikt Ag eller inte...
 - NOVA – (= Ri, Anna-2)

Association PNS-ab / Tumors

Table 1 Patient characteristics

	Anti-Hu	Anti-Yo	Anti-CV2	Anti-Ma/Ta	Anti-Ri	Anti-Tr	
No of patients	170	59	23	19	15	9	= 295
Sex (F/M)	67/103	57/2	7/16	4/15	12/3	2/7	
Age (year) (mean (Q1–Q3))	66 (58–72)	65 (59–72)	68 (61–78)	55 (42–69)	66 (52–75)	58 (50–71)	
Neurological syndrome							
Peripheral nerve disorders	74	1	9	0	0	0	
Limbic encephalitis	14	0	1	11	3	1	
Brainstem encephalitis	16	1	0	4	9	0	
Cerebellar degeneration	12	54	3	3	3	8	
PEM	29	1	2	0	0	0	
Other	25	2	8	1	0	0	
Cancer							
SCLC	109	0	12	0	0	0	
NSCLC	11	1	2	1	1	0	
Testicular	0	0	0	6	1	0	
Breast	4	11	1	2	8	0	
Gynaecological	0	32	0	0	0	0	
Hodgkin	0	0	0	0	0	6	
No tumour	23	5	4	6	2	1	
Other	23	10	4	4	3	2	

NSCLC, non-small cell lung cancer; PEM, paraneoplastic encephalomyelitis; SCLC, small cell lung cancer; Q1, first quartile; Q3, third quartile.

J Neurol Neurosurg Psychiatry 2010;81:42–45.

Table 1 Classical and non-classical paraneoplastic neurological syndromes

Syndromes of the central nervous system

(Encephalomyelitis)
Limbic encephalitis
Brainstem encephalitis
Subacute cerebellar degeneration
Opsoclonus-myoclonus*
Optic neuritis†
Cancer associated retinopathy†
Melanoma associated retinopathy†
Stiff person syndrome
Necrotising myelopathy‡
Motor neuron diseases‡

Syndromes of the peripheral nervous system

Subacute sensory neuropathy
Acute sensorimotor neuropathy
Guillain-Barré syndrome‡
Brachial neuritis‡
Subacute/chronic sensorimotor neuropathies*
Neuropathy and paraproteinæmia†
Neuropathy with vasculitis‡
Autonomic neuropathies
Chronic gastrointestinal pseudo-obstruction
Acute pandysautonomia‡

Syndromes of the neuromuscular junction and muscle

Myasthenia gravis†
Lambert-Eaton myasthenic syndrome‡
Acquired neuromyotonia‡
Dermatomyositis‡
Acute necrotising myopathy‡

Classical syndromes are underlined.

*Associated with onconeural antibodies only with particular tumour types.

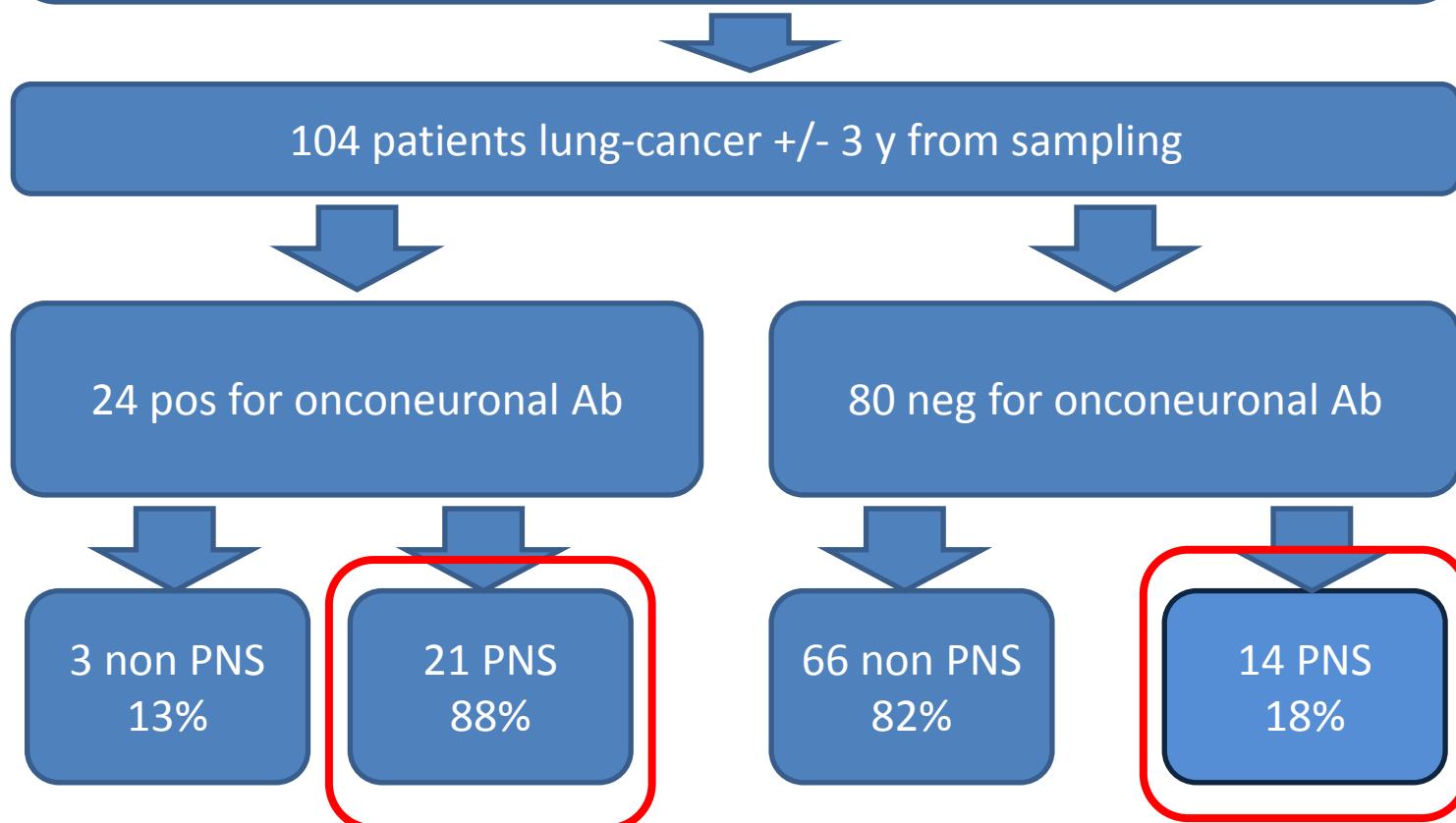
†Syndromes not included in the present recommendations.

‡Neurological syndromes not associated with known onconeural antibodies.

antikroppar / antigen

Antibody	Synonym	Antigen	Fluorescence-pattern	Paraneoplastic syndrome	Associated tumor
Anti-Hu	ANNA-1	HuD-prot (38 kDa)	All nuclei both CNS / PNS; granular floourescence	PCD, PEM, SN	SCLC
Anti-Ri	ANNA-2	NOVA	All nuclei in CNS; granular floourescence	OM, PCD, LE	Breast, SCLC, Gyn
Anti-Yo	PCA-1	CDR2, CDR62	Purkinjecell cytoplasma / axon extensive staining	PCD	Breast, Ovary
PCA-2		Purkinjecell prot	Purkinjecell cytoplasma / other neurons	PEM, PCD, LEMS	SCLC
ANNA-3			Purkinjecell nuclei & nucleus and glomerula podocytes	PCD, PEM, SN	SCLC
Tr			Purkinjecell cytoplasma w. dots in molecular layer	PCD	Hodgkins
AGNA	SOX1	SOX-1	Nuclei of Bergman glia and glia in white matter.	PND	SCLC
Ma	Ma1 / PNMA1	Ma-prot (37 kDa)	Neuronala nuclei	PCD, BE	Various Cancer
Ma2	Ta/ PNMA2	Ma-prot (40 kDa)	Neuronala nuclei / pericaryon	PCD, LE	Testis
Anti-CV2	CRMP5	66 kDa prot	Oligodendrocyt cytoplasma	PEM, SN	SCLC, Thymom
Anti-Amphiphysin		Amphiphysin (128 kDa)	Central presynaptic terminals	SPS, SN	Breast, SCLC
Anti-GAD		Glut acid decarbox (65 kDa)	Islet cells & gray matter / granulosum and moleculare	SPS	Breast, Colon, SCLC
Anti-Recoverin 2018-05-21			Retinal photoreceptor Gösta Malmeström	CAR	SCLC

3679 patients referred for analyzing onconeural Ab
1995 - 2005



Cristian Vedeler et al, Haukeland, Bergen, ISNI – Boston, 2012

Pat med PNS och CSF+ har bättre överlevnad

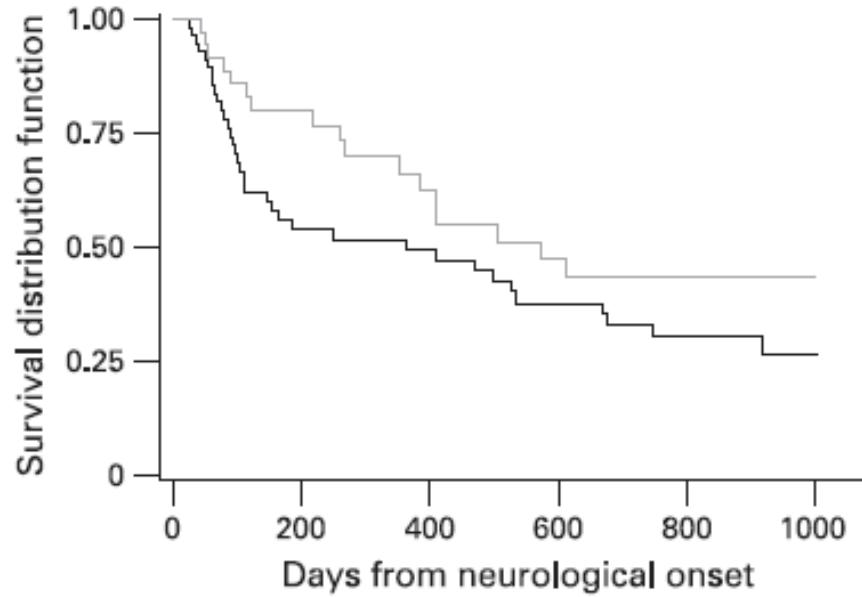


Figure 2 Survival of patients with anti-Hu antibodies who had a CSF study within 90 days after neurological onset. Patients were divided into two groups; those with a normal cell count in the CSF (black curve; $n = 56$) and those with more than 5 white cells/mm³ (grey curve; $n = 35$). The group with CSF inflammation showed a better median survival than the group without (572 days vs 365 days; $p = 0.05$).

Limbic Encefalit – sedan 1968

- Subakut onset och progressiv affektion av korttids- minne, konfusion, psykiatriska symptom och kramper.
- EEG visar fokal eller generaliserad låg frekvent eller epileptiform aktivitet.
- Association med tumör eller autoimmun...
 - Ett flertal olika tumörer finns beskrivna.
 - SCLC
 - Teratom
 - Testis-Ca
 - Bröst-Ca
 - Hodgkins
 - mfl
 - Om paraneoplastiskt – sämre prognos.
 - Liksom vid övriga paraneoplastiska tillstånd kan tumören vara svår att hitta.

Kliniska symptom vid limbisk encefalit

Nedsatt korttidsminne	84 % - 92 %
Akut konfusion	46 %
Krampanfall	50% - 58 %
Psykiatriska symptom	42 % - 50 %
"Extralimbisk" neurologisk påverkan	60 % - 42 %
Hypothalamiska symptom	22%
(Gultkien Brain 2000 / Lawn, Mayo clin proc. 2003)	

Differentialdiagnoser – Limbisk encefalit

Infection

Herpes simplex type 1 and 2, Varicella zoster virus, Enterovirus, Neuroborreliosis,
Adenovirus, HIV, TB, Listeria
Cytomegalovirus, Human herpesvirus-6/7, JC virus, Epstein-Barr virus, fungal/
parasitic (in immunocompromised patients)
Arboviruses, Poliomyelitis, Rabies, West Nile virus (if patient travelled abroad)
Systemic
Neurosypilis

Acute demyelinating encephalomyelitis (ADEM)

Degenerative diseases

Creutzfeldt-Jakob disease
Rapidly progressive Alzheimer's disease or dementia with Lewy bodies

Nutritional/toxic/drug

Wernicke encephalopathy (Thiamine deficiency)
Alcohol, including alcohol withdrawal syndrome
Other recreational drugs
Chemotherapy (such as Methotrexate)
Lithium

Metabolic

Uremic encephalopathy
Hepatic encephalopathy
Electrolyte disturbances

Connective tissue disorders and vasculitis

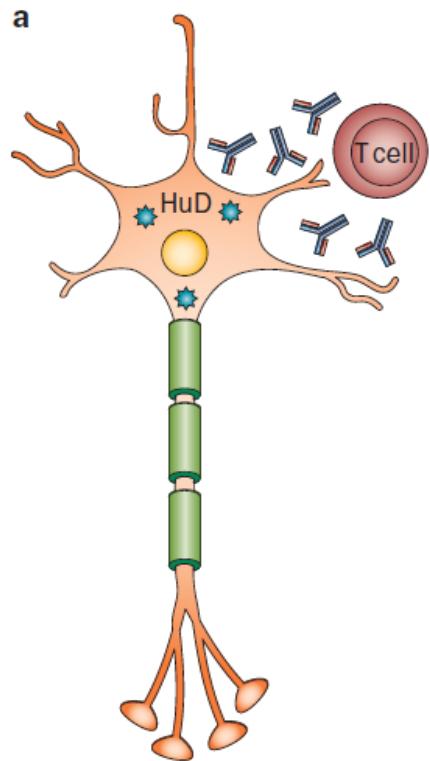
Systemic lupus erythematosus (SLE)
Behçet's disease
Sjogren's syndrome
Primary CNS vasculitis/angiitis

Primary or secondary CNS malignancy

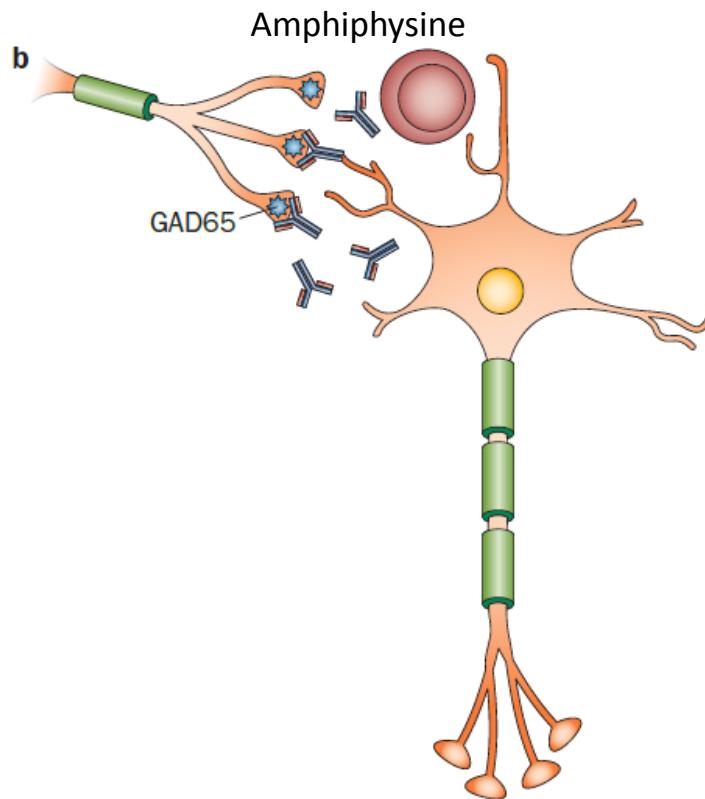
Gliomas
Cerebral metastasis
Primary CNS lymphoma
Intravascular lymphoma

LE first associated with ab against intracellular proteins

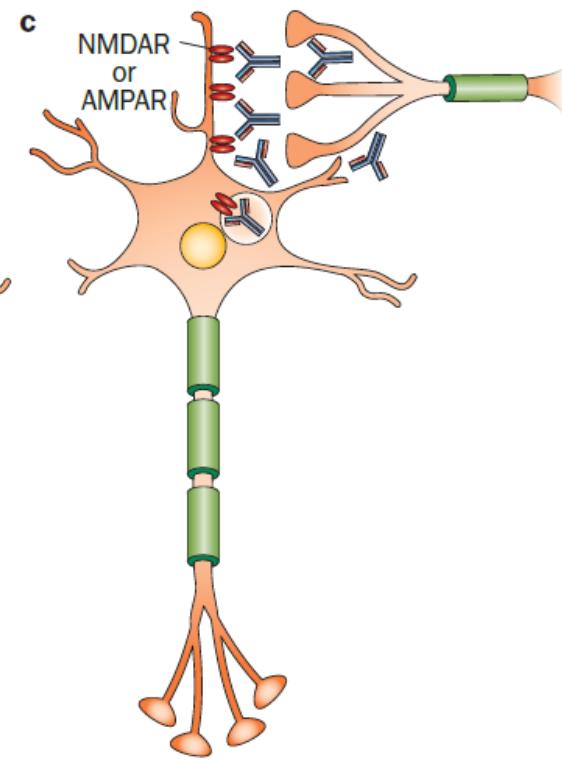
- Hu - ANNA1 (Anti Neuronal Nuclear Antigen 1)
 - In all nuclei in CNS & PNS
- Ri – ANNA2 (Anti Neuronal Nuclear Antigen 2)
 - In all nuclei in CNS
- Yo – PCA1 (Purkinjecell antigen 1)
- Amphiphysin
 - Presynaptic terminals
- CV2 / CRMP5
 - Oligodendrocyte cytoplasma



Intracellulära Ag
Generellt dålig effekt
av immunomodulation

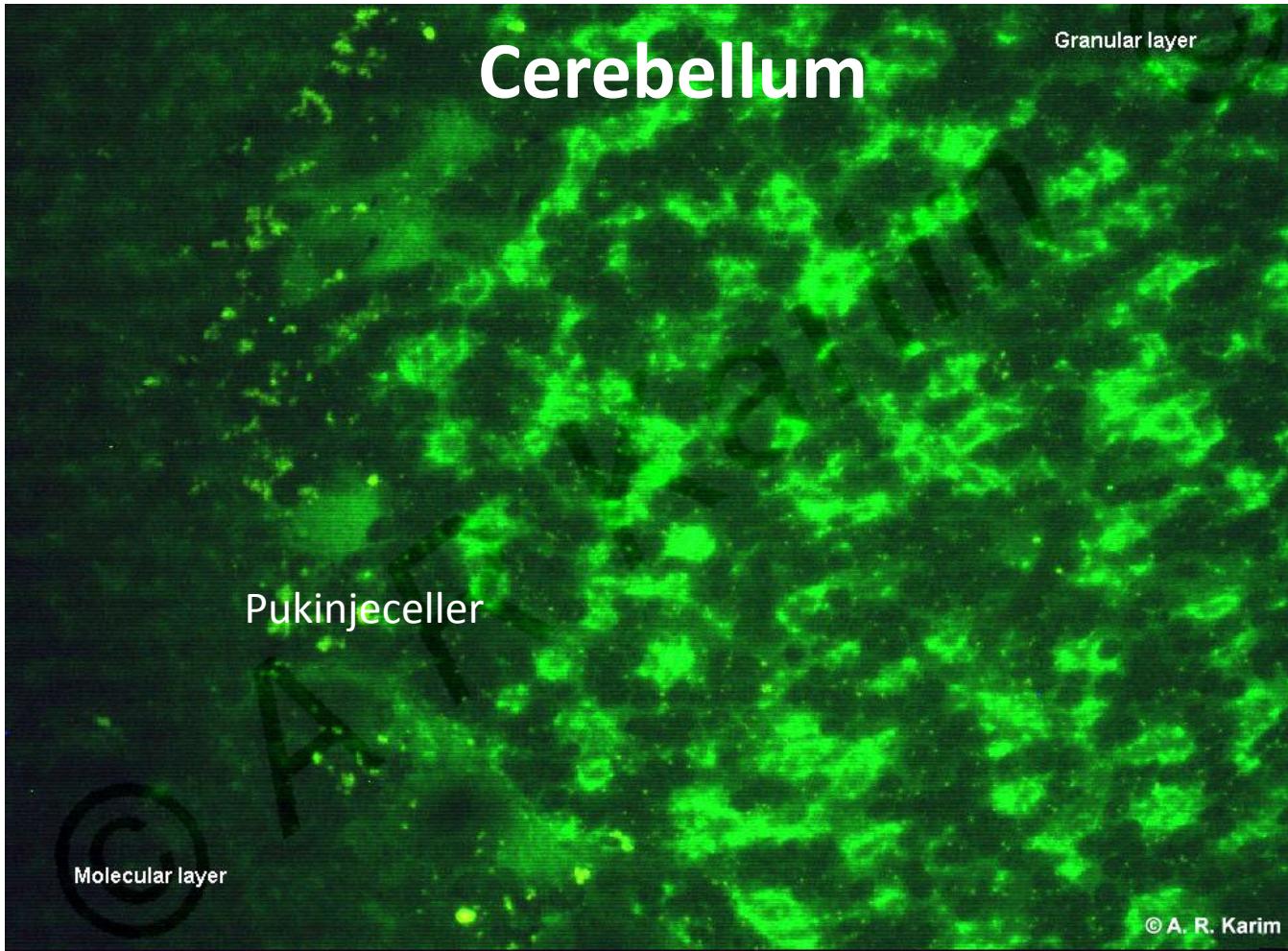


Synaptiska Ag
Generellt måttlig effekt
av immunomodulation



Membranbundna Ag
Ofta receptorfunktion.
Generellt god effekt av
immunomodulation

Anti-GAD associerad epilepsi



Anti-GAD associerad epilepsi

- GAD-antibodies directed against glutamic acid decarboxylase, responsible for synthesis of the inhibitory neurotransmitter GABA
- GAD antibodies are found in 60–80% of patients with type 1 diabetes at low levels.
- Higher levels have been demonstrated in various neurological conditions including cerebellar ataxia and stiff-person syndrome (SPS).

- Epilepsy co-exists in up to 30% of the patients with SPS.
- More associated with a chronic course of Ep.
- GAD is a intracellular antigen – hence anti-GAD EP is not expected to respond swiftly to immunotherapy.
- Conflicting reports on treatment-response of IVIG, Ritux, etc.

Antibodies against surface ag.

Table 2 Neuronal surface antibody associated syndromes

Syndrome	Antibodies	Particular clinical features	Possible tumours	Immunotherapy response	In vitro evidence of Ab pathogenicity	Frequency or No of cases reported
NMDAR-Ab encephalitis	NMDAR	Dyskinetic movements, decreased consciousness, psychiatric presentation in young women. Epilepsy and abnormal movements more frequent at onset in children	Ovarian teratoma. Rare in children. Up to 50% after age 18 years	Yes	In vitro and in vivo reduction of NMDA receptors	Common syndrome. More than 500 cases reported, mainly in USA
LE	LGI1	Male predominance, hyponatraemia, faciobrachial dystonic seizures, myoclonus	Rare with LGI1-Ab. Thymoma in some with CASPR2-Ab	Yes	In vitro production of epileptogenic activity in brain slices	Common syndrome
	CASPR2 (<10%)	Possible isolated psychiatric symptoms	70% (lung, breast, thymus)	Yes, frequent relapses	Downregulation of AMPA receptors	More than 600 cases reported, mainly in UK
	AMPAR	Prominent seizures	60% (SCLC)	Yes	None	14
	GABA _B R	Ophelia syndrome	Hodgkin lymphoma	Unknown	None	25
Morvan's syndrome	CASPR2	Encephalopathy, peripheral nerve hyperexcitability, dysautonomia	Thymoma	Yes	Not tested	9
PERM	GlyR	Encephalomyelitis with myoclonus, rigidity and brainstem signs	Thymoma	Yes	Not tested	6
Cerebellar ataxia	VGCC	Possible coexistence of LEMS	SCLC	Poor	Not tested	16
	mGluR1	Remote history of Hodgkin lymphoma	Hodgkin lymphoma	Yes	In vivo	3

- Ab against NMDA-receptor.
 - NMDA-receptor expressed mainly in hippocampus.
 - Approx 90% of all cases of Limbic Encephalitis
 - 45 % Associated with tumor
 - mainly teratoma; >3/4; young women.
 - 45% normal brain MRI
 - 90 % pathological CSF-exams
 - Elevated lymphocyte-count, elevated protein, with/without OB's

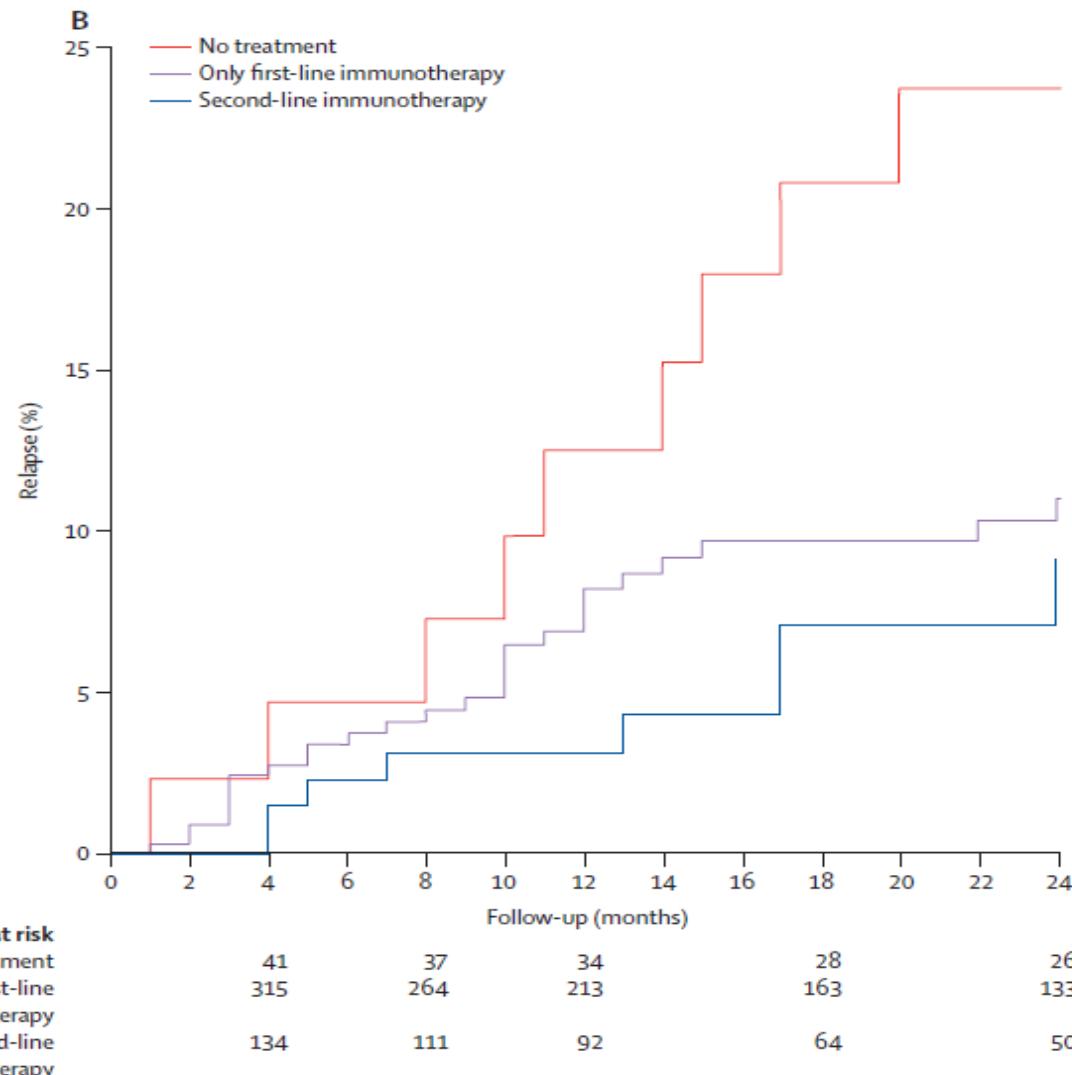
Ab's directed against membrane-antigens/ ionchannels, so
function is affected
pathogenic

Sammanfattning indelning LE

Tre övergripande grupper

1. LE associerad med "klassiska onconeuronala antikroppar" mot intracellulära neuronala antigen.
Majoriteten av dessa fall är associerade med tumör, dvs paraneoplastisk LE
2. LE associerad med antikroppar mot neuronala yt - eller synaps – antigen
En del av dessa fall är också associerade med tumör (paraneoplastisk LE)
Ingen tumör hittas i många fall.
3. LE utan detekterbar känd autoantikropp – seronegativ LE. Många av dessa fall är associerade med tumör

Risk för återfall



Association between Herpes enc. and NMDA-enc.

Viral triggering of anti-NMDA receptor encephalitis in a child - an important cause for disease relapse.

Wickström R¹, Fowler A², Cooray G³, Karlsson-Parra A⁴, Grillner P².

Abstract

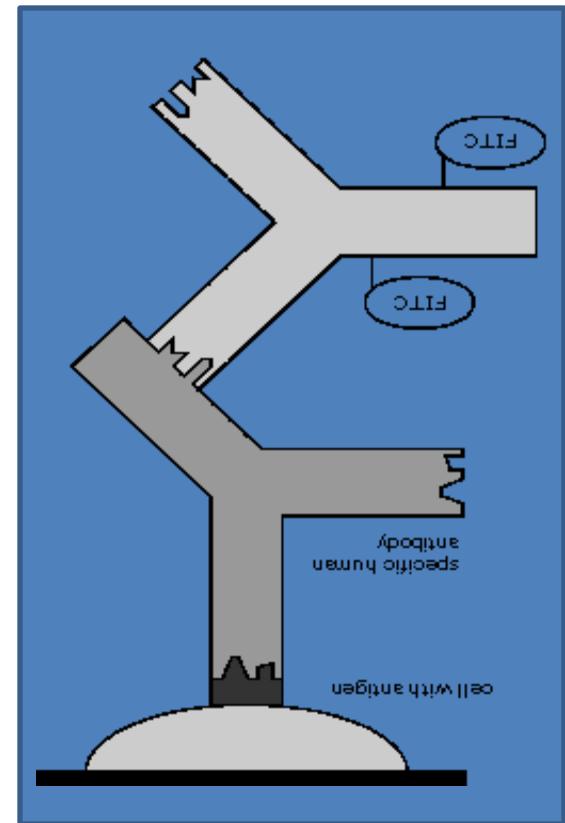
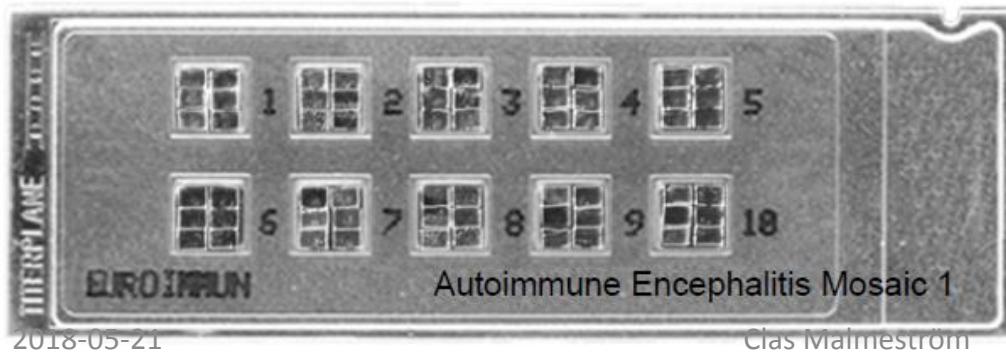
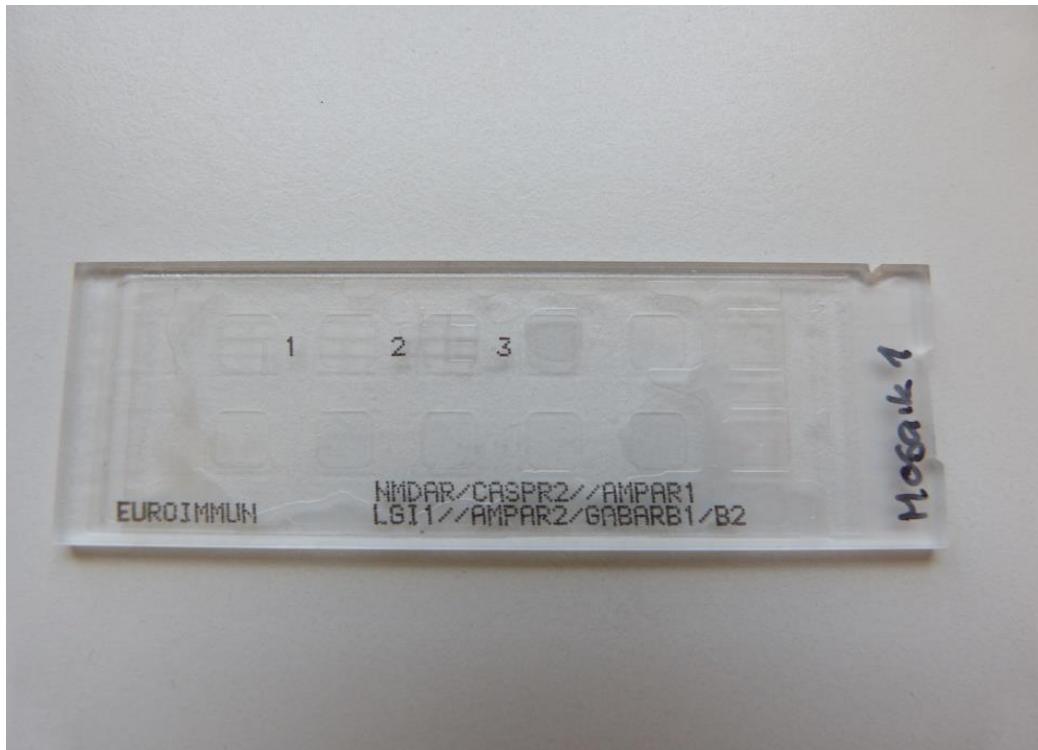
.....We conclude that relapse or persisting symptoms in HSE in children may represent an immune-mediated mechanism rather than a viral reactivation and that NMDAR antibodies should be analyzed as this may be of importance for the choice of therapy.

Eur J Paediatr Neurol. 2014 Jul;18(4):543-6

Metodval

- Indirekt immunfluorescens
 - Vävnad
 - CBA – Cell baserade assays.
- Western blot / Line-blot
- Elisa ofta för okänsliga
 - Antigenen konformationkänsliga, förlorar sin antigenicitet då de fixeras på exempelvis plast
 - Exempelvis vid NMDA-rec Ak, NMO-ak mfl.

Indirect immunofluorescence



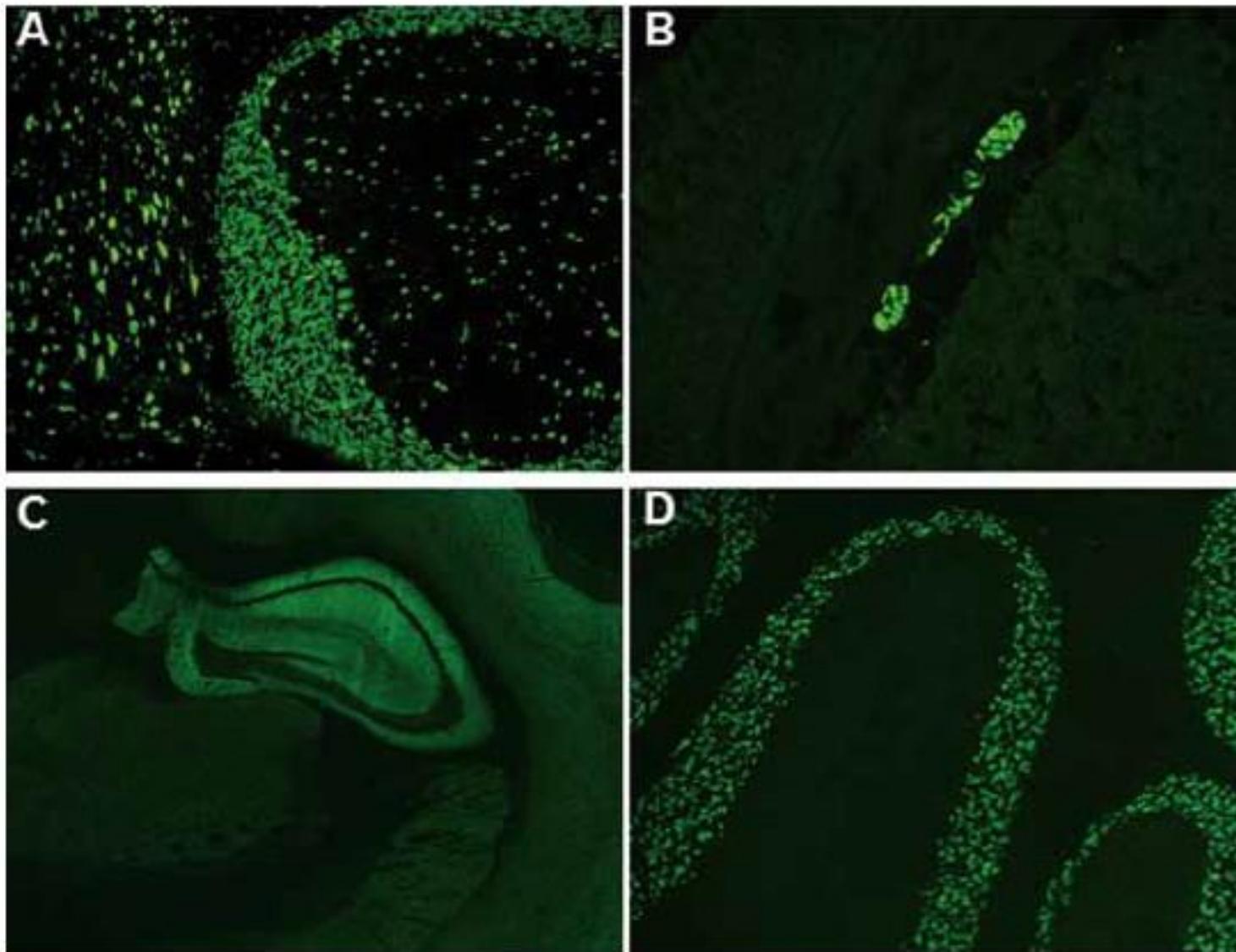
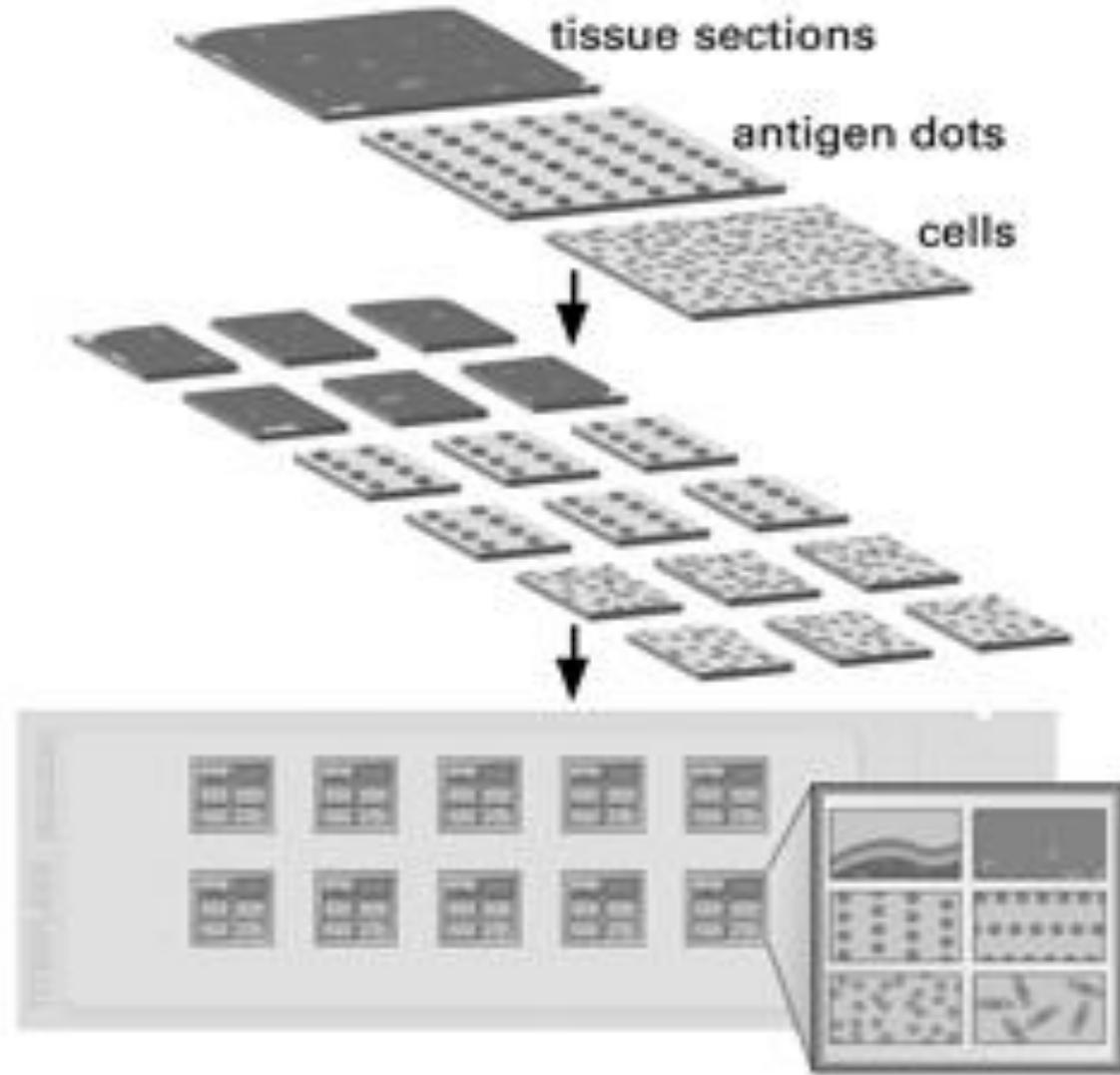
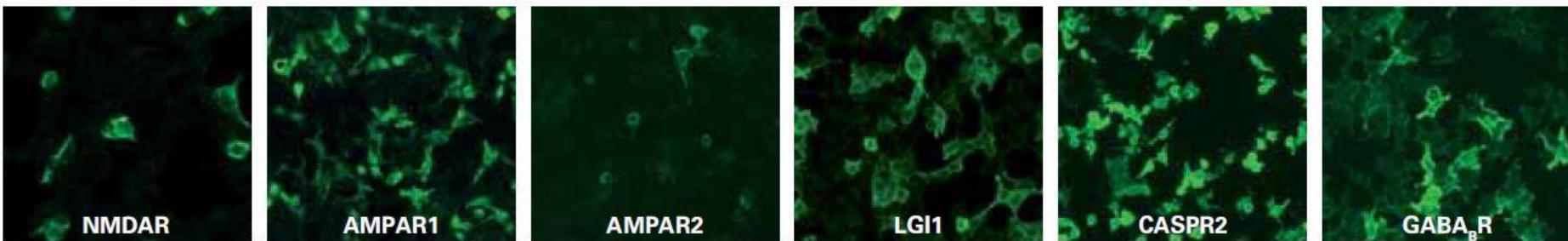


Figure 1. Immunofluorescence patterns of ANNA1 and NMDA receptor antibody reactivities on substrate of mouse tissues. ANNA1 binds to nuclei (and less intensely to perikarya) of all neurons, including cerebellar Purkinje, granular layer and molecular layer (A, right), midbrain (A, left) and myenteric plexus (B). NMDA receptor antibody binds to neural synapses, most prominently in hippocampus (C) and cerebellar granular layer (D).





IIFT Autoimmune Encephalitis Mosaic 1

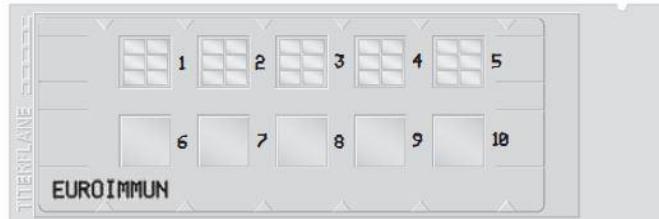


- BIOCHIP Mosaic for the detection of antibodies relevant for differential diagnosis in autoimmune encephalitides
- Highly sensitive and monospecific determination of antibodies using recombinant cell lines

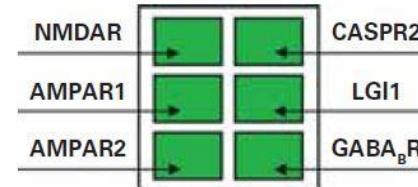


BIOCHIP arrangement

The Autoimmune Encephalitis Mosaic 1 is available in two formats: slides with three or five fields each. One field consists of six BIOCHIPS.

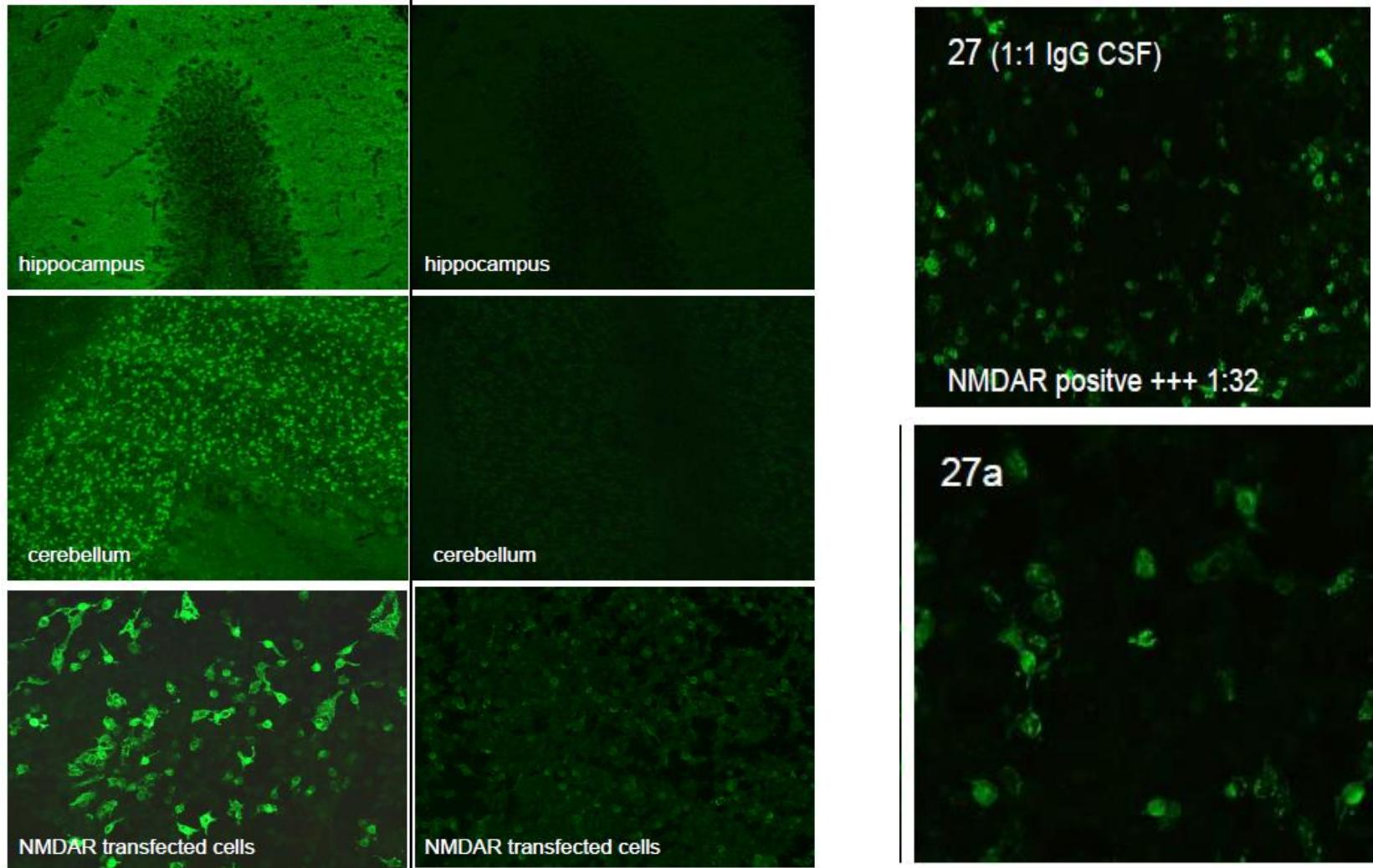


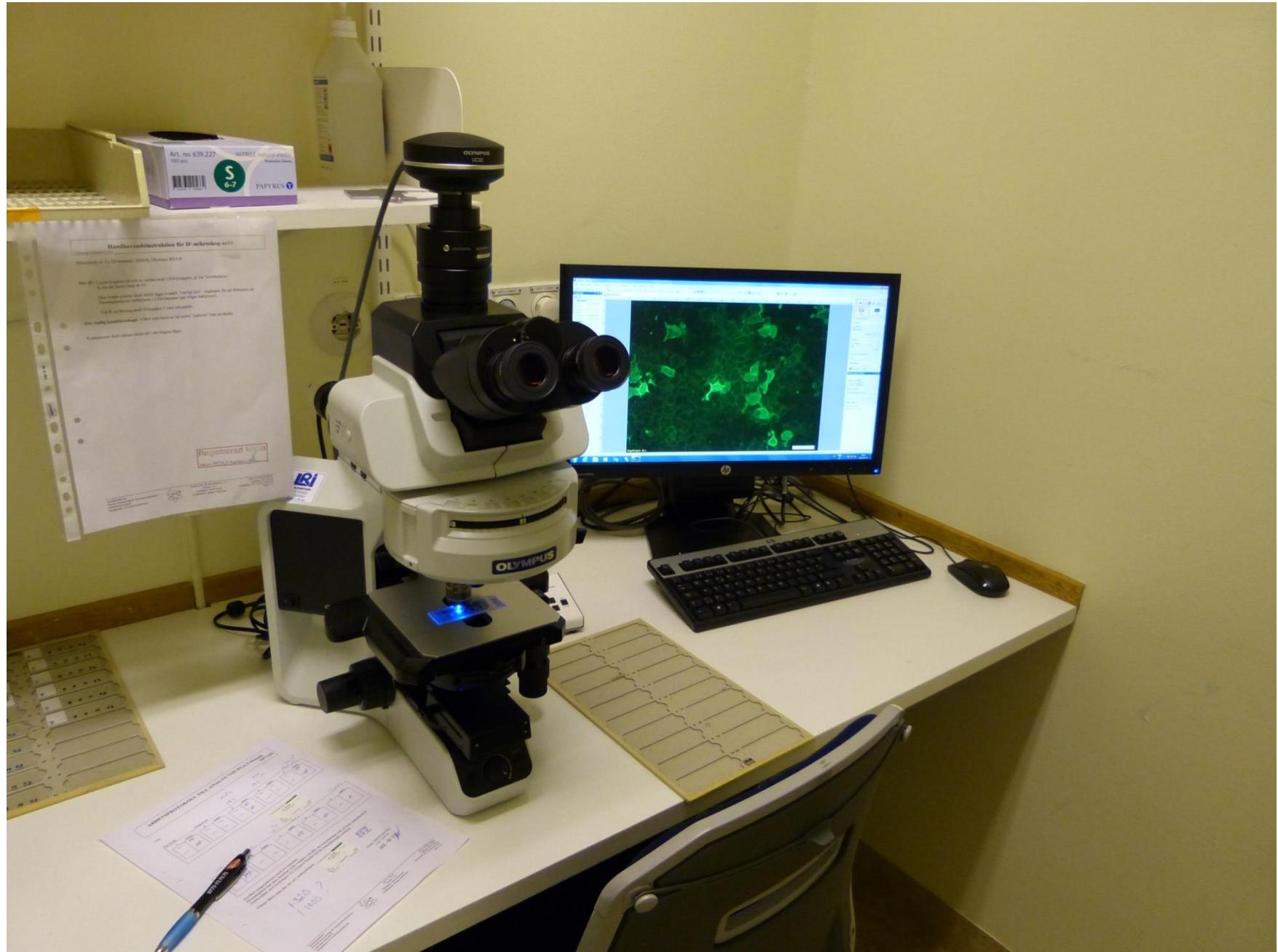
2018-05-21



Clas Malmeström

Anti-NMDA Ab in IIF and CBA





2018-05-21

Clas Malmeström

Anti – Hu (ANNA-1) Cerebellum

Anti – Hu (ANNA-1) Gut

Anti – Ri (ANNA-2) Cerebellum

Anti – GAD Cerebellum

Anti – NMDA, transfekterade EU-90

Anti – CASPR2, transfekterade EU-90

Immunoblot automatiserad robot



Immunoblot

EUROLinescan - Protocol

Date: 2012-11-27
Printed: 2012-11-28

Strip

NEURO4/ 47- 05

La	Co	Titin	SOX1	Rec	Hu	Yo	Ri	Ma2/Ta	CV2	Amp
NEURO4/ 47- 05										
-1	142	4	2	1	98	4	3	8	2	2
0	+++	0	0	0	+++	0	0	(+)	0	0

NEURO4/ 47- 08

Ta, CV2, Amphiphysin

Immunoblot

EUROLinescan - Protocol

Date:
Printed:

2012-11-27
2012-11-28

Strip

NEURO4/ 47- 05

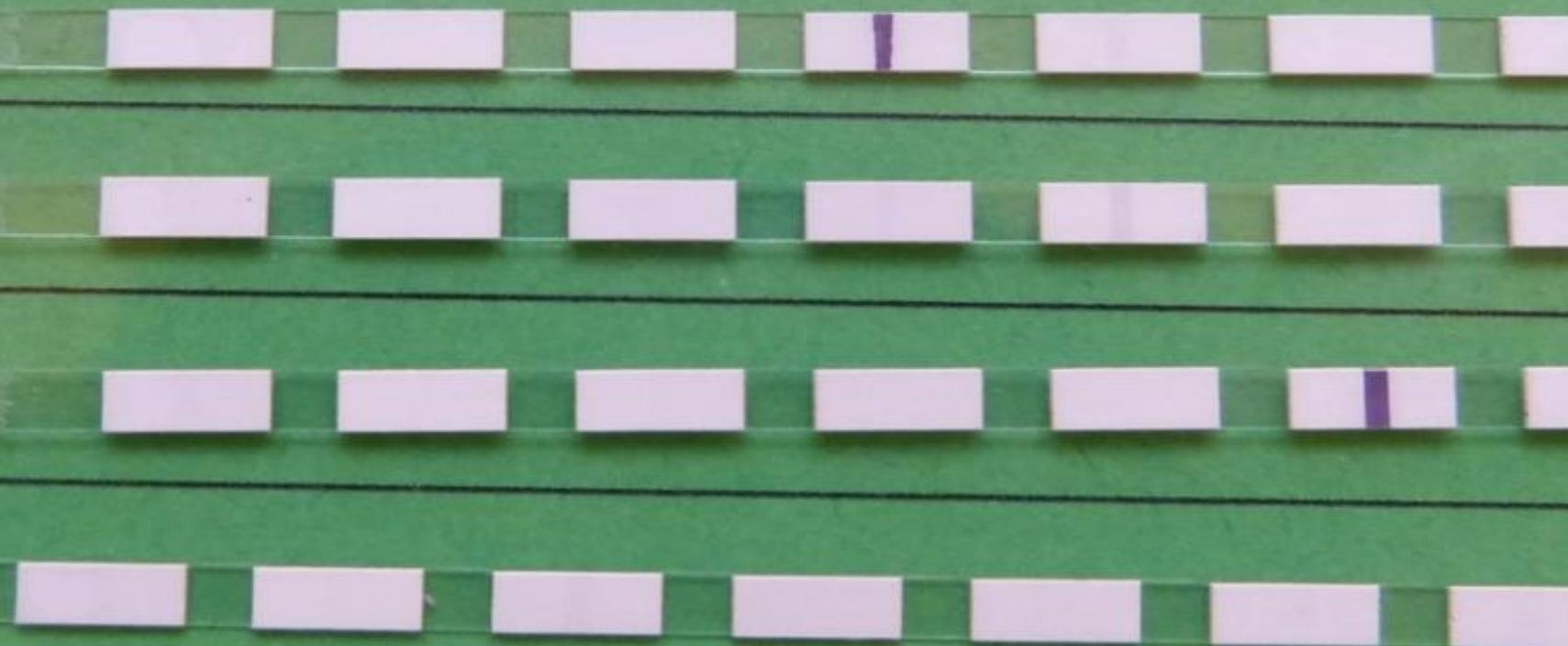
NEURO4/ 47- 06

NEURO4/ 47- 07

	La	Co	Titin	SOX1	Rec	Hu	Yo	Ri	Ma2/Ta	CV2	Amp
N	0	+++	○	○	○	○	○	+++	(+)	○	○
NEURO4/ 47- 07	-1	128	5	2	2	3	3	105	6	2	3
	0	+++	0	0	0	0	0	+++	(+)	0	0

Ta, CV2, Amphiphysin

Immunoblot



Association PNS-ab / Tumors

Table 1 Patient characteristics

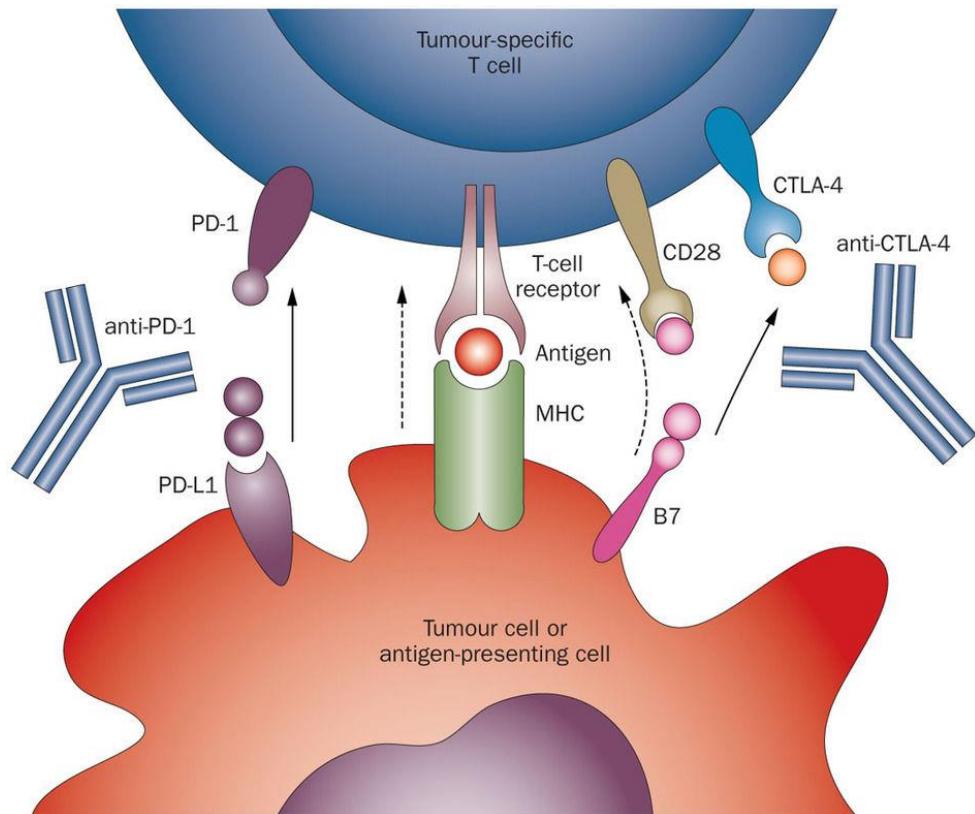
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J Neurol Neurosurg Psychiatry 2010;81:42–45.

Biverkningar av PD1-hämmare ny marknad för neuroimmunologi ?

- Framgångsrika mot tumör-sjukdomar
- Trycker på gasen och släpper på bromsen....
- Vad händer då?



Drake, C. G. et al. (2013) Breathing new life into immunotherapy: review of melanoma, lung and kidney cancer
Nat. Rev. Clin. Oncol. doi:10.1038/nrclinonc.2013.208

- Nivolumab – Opdivo
 - *Melanom*
 - *Icke-småcellig lungcancer (NSCLC)*
 - *Njurcellscancer (RCC)*
 - *Klassiskt Hodgkins lymfom*
 - *Skivepitelial huvud- och halscancer (SCCHN)*
 - *Urotelialcellscancer*
- Pembrolizumab – Keytruda
 - Malignt melanom (inoperabelt eller metastaserat)
 - NSCLC
 - Hodgkins lymfom, klassiskt recidiverande eller refraktär
 - Urotelial cancer metastaserad

FASS

PD1 resp CTLA-4.

- Ger immunsystemet ökade möjligheter att angripa tumören (non-self), tyvärr ökar även reaktivitet mot egen vävnad
- Lista på biverkningar från ett pressmeddelande från BMS :
 - Immune-mediated -
 - -Pneumonitis
 - -Colitis
 - -Hepatitis
 - -Neuropathies
 - -Endocrinopathies
 - -Nephritis
 - -Skin Adverse Reactions and Dermatitis
 - -Encephalitis
 - other Immune-mediated Adverse Reactions

Sammanfattnings

- De flesta paraneoplastiska Abs framkommer i ett bredare spektrum av neurologiska manifestationer än den ursprungliga syndrom-presentationen
- Antalet antikroppar fortsätter att växa
- Diagnostiskt viktiga antikroppar kan missas om man begränsar sig till 2-3 individuella tester.
- Kommande behandlingar av tumörer kan ge autoimmuna tillstånd som biverkningar

REMISS IMMUNOLOGI 1 AUTOIMMUNITET

Avsändare

www.immunologi.se

Patient: personnummer, efternamn, förnamn

Provet utgörs av:

- Likvor
- serum/blod utan tillsats
- Faeces
- EDTA-blod*
- Annat.....

Kliniska data

Akuta analyser under vardagar ring 031-3424708

På helger mellan 09:00-12:00 ring Sahlgrenska Universitetssjukhusets växel för att nå personal i beredskap

- Vaskulit Screen: Pr-3, MPO, och z-GMB (semikvantitativ)

Antikroppar vid reumatiska sjd

- ANA-Screen
(ANA + ds DNA, SS-A-52, SS-A-60 SS-B, Sm, RNP, Scl-70, Jo-1, Cent B, Ribon P)
- ANA (cellkärnor)IF
Ds DNA
- SS-A, SS-B
- Sm, RNP
- Scl-70
- Jo-1
- Cent B
- Histon
- C1q
- Sklerodermi Ak
(Scl-70, Cent-A, Cent-B, RP-155
RP-11, Fibrillarin, NOR-90, Th/To PM/
Scl-75, PM/Scl-100, Ku, PDGFR)
- Myosit Ak
(OJ, EJ, PL-12, SRP, Jo-1,
PM/Scl-75, PM/Scl-100, Ku, SAE1
NXP2, MDAS, TIF1-γ, MI-2b, MI-2a)
- c-ANCA (Mup44) Ak
(inklusionskroppsmyosit)
- HMGCR Ak
(nekrotiseringande autoimmun myopati)
- RF IgM
- RF IgG
- RF IgA
- Citrulin (CCP)
- ANCA-screen (ANCA+PR3+MPO)
- ANCA IF
- PR3
- MPO
- GBM (Glomerulär Basalmembran)
- Kardiolipin
- Kardiolipin och Beta2-glykoprotein-1

Ak mot diabetes Ag

- GAD
- ICA
- IA-2
- ZnT8
- Insulin

Ak mot hud Ag (biopsi)

- Hudbiopsi, immunfluorescens,
basalmembran,
intercellulärsubstans

Ak mot hud Ag (serum)

- Basalmembran och
intercellulärsubstans
- Desmoglein1 (pemfigus)
- Desmoglein3 (pemfigus)
- BP180 (pemfigoid)
- BP230 (pemfigoid)
- Envoplakin (paraneoplastisk
pemfigus)
- Salt split

Tester vid mag-tarm sjd

- ANCA-screen (ANCA, PR3, MPO)
- Saccharomyces cerevisiae, IgA,
IgG (ASCA)
- Parietalceller Ak
- Intrinsic faktor Ak
- Transglutaminas IgA Ak och
Deaminater gladin IgG AK
- Transglutaminas IgA Ak och
Elastas i faeces

Ak vid leversjd

- Mitokondri/Glatt musk. IF
(AMA/SMA) IF
- Liver-Kidney Microsomalantigen
(LKM)
- Lever ak panel (AMA-M2,
Sp 100, PML, gp 210, LKM-1, LC-1,
SLA/LP, M2-3E (BPO))
- IgD
- Komplementdefektscreening
- Survivin
- Calprotectin i serum
- C3,C4,C3d komplementfaktorer

Ak vid misst. paraneoplastisk neuronalt syndrom (PNS)

- Hu, Ri, Yo
- PCA-2
- Tr
- Amphiphysin
- CV2
- Ma/Ta
- Recoverin
- Sox1
- Zic4

Ak vid autoimmun encefalit

- NMDA-receptor
- AMPA1/2-receptor
- DPPX
- LGI-1 (VGKC)
- CASPR2 (VGKC)
- GABA-B
- GAD65

Ak mot övriga neuronala Ag

- VGCC N-typ
- VGCC PQ-typ
- Aquaporin-4 (NMO)
- MOG

Ak mot neuromuskulära Ag

- Acetylkolinreceptor
- MuSK
- Titin
- MAG
- Tvärstrimlig muskel
- Glykolipid/Gangliosider (GM1, GM2,
GD1a, GD1b, GO1b, MAG)

Ak mot övriga Ag

- Binjurebark
- PLA-2 (Fosfolipas)
- THSD7A
- TPO IgG(thyreoidaeperoxidaser)
- Tyreoglobulin IgG
- GM-CSF

Övriga tester

- SAA (serumamyloid A)
- IgD
- Komplementdefektscreening
- Survivin
- Calprotectin i serum
- C3,C4,C3d komplementfaktorer

REMISS IMMUNOLOGI 2 CELLÄR IMMUNITET

Avsändare

www.immunologi.se

Patient: personnummer, efternamn, förnamn

Provet utgörs av:

- heparinblod**
- serum/blod utan tillsats
- EDTA-blod*
- urin
- benmarg
- annat
- likvör

Provtagn. datum

Remitterande läkare

Provtagningsansvariges namn och telefonnr

Debiteringsadress om annan än avsändaren

Kliniska data

Om akutbehandling av provet önskas v.g. ring 031-342 49 17

Lymfocytsubpopulationer(FACS)

- CD3*
- T- och B-lymfocyter*
- CD4/CD8-kvot i blod*
- CD4/CD8-kvot i likvör (ska förbeställas tel 031-3424708)
- CD19/CD20*
- NK-cell*
- Immunbristpanel, barn*
- Immunbristpanel, vuxen*
- Kontroll stamcelltransplantation*
- CVID
- Andra ytantigener*

Funktionell celltester (ska förbeställas på tel 031-3424703)

- FASCIA Utökad lymfocytstimulering**
- Lymfocytstimulering*
- Lymfocytstimulering med PPD och /eller Candida**
- Immunoglobulinproducerande celler (ELISPOT)**
- Immunoglobulinproducerande celler efter stimulering (ELISPOT)**
- ML (Mixed Lymphocyte Culture)**
- FANKA (NK-celleaktivitet, lytisk aktivitet)**
- BAT (Basofilaktiveringstest)**
- BAT (Basofilaktiveringstest läkemedel)**, ange läkemedel
efter samtal med lab.
- T-cells stimulering, ange läkemedel efter samtal med lab.

Fagocytfunktionstest (Ska förbeställas på tel 031-3424703)

- Fagocyt**
- Fagoburst**
- Uttryck av adhesionsmolekyler (CD11b, CD18)**

Cytokinanalyse

- Cytokiner i serum eller likvör
- Cytokinproduktionefter stimulering av celler från
heparinblod**. Ska förbeställas på tel 031-3424703

Markera vilka cytokiner som önskas

Serum	Likvör	Cytokinproduktion
<input type="checkbox"/> IL-1β	<input type="checkbox"/> IL-1β	<input type="checkbox"/> IL-1β
<input type="checkbox"/> IL-2	<input type="checkbox"/> IL-2	<input type="checkbox"/> IL-2
<input type="checkbox"/> IL-4	<input type="checkbox"/> IL-4	<input type="checkbox"/> IL-4
<input type="checkbox"/> IL-5	<input type="checkbox"/> IL-5	<input type="checkbox"/> IL-5
<input type="checkbox"/> IL-6	<input type="checkbox"/> IL-6	<input type="checkbox"/> IL-6
<input type="checkbox"/> IL-8	<input type="checkbox"/> IL-8	<input type="checkbox"/> IL-8
<input type="checkbox"/> IL-10	<input type="checkbox"/> IL-10	<input type="checkbox"/> IL-10
<input type="checkbox"/> IL-12	<input type="checkbox"/> IL-12	<input type="checkbox"/> IL-12
<input type="checkbox"/> IL-18	<input type="checkbox"/> IL-18	<input type="checkbox"/> IL-18
<input type="checkbox"/> IFN-γ	<input type="checkbox"/> IFN-γ	<input type="checkbox"/> IFN-γ
<input type="checkbox"/> TNF-α	<input type="checkbox"/> TNF-α	<input type="checkbox"/> TNF-α
<input type="checkbox"/> GM-CSF	<input type="checkbox"/> GM-CSF	<input type="checkbox"/> GM-CSF

Sahlgrenska universitetssjukhuset/Sahlgrenska

Immunoanalytika laboratorium Box 7193, 402 34 Göteborg,

Besöksadress: Guldhedsgatan 10A

tel 342 49 17 (exp och provvari), 342 47 08, 342 49 26 (serologi),

342 47 03 (celltest), 342 18 87 (allergitester). Fax 031-82 67 91

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Type I error
(false positive)



Type II error
(false negative)



Figure 3.1 Type I and Type II errors