

Autoantikroppar vid neuromuskulär transmissionsrubbning

Clas Malmeström

Med Dr, Överläkare

MS-Centrum, Neurosjukvården

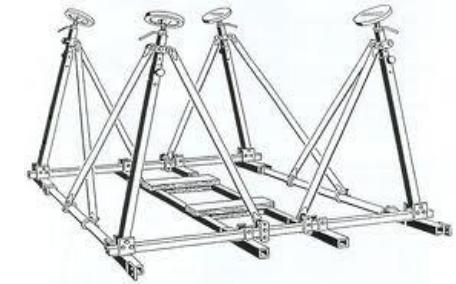
Klinisk Immunologi och transfusionsmedicin
Sahlgrenska Universitetssjukhuset

Disclosures

- Clas Malmeström
- Har erhållit ekonomisk ersättning för undervisningsuppdrag, deltagande i Ad-board samt erhållit resebidrag och icke villkorade forskningsbidrag inom MS-fältet från bland andra Biogen, Genzyme, Merck, Novartis, Roche, Sanofi.
- Är styrelseledamot i Alzinova AB, som utvecklar vaccin mot Alzheimers sjukdom.
- Äter 15 ml Möllers tran dagligen alla månader med bokstaven R

Neuromuskulära synapsen

«Neuroimmunologins vagga»



Myastenia Gravis

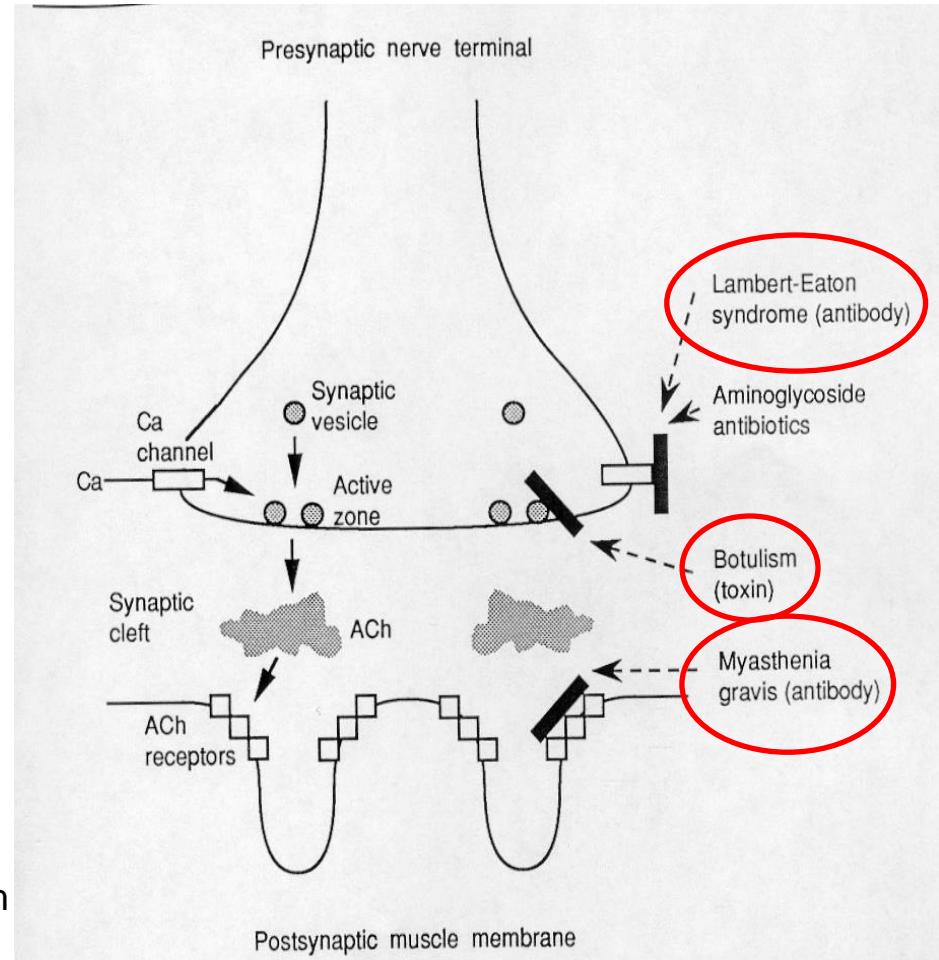
- Antikroppar mot Acetylkolin-receptor
- Ger slappa pareser
- Typisk uttröttbarhet
- Behandlas genom att hämma nedbrytning av acetylkolin

LEMS – Lambert-Eatons myastena syndrom

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

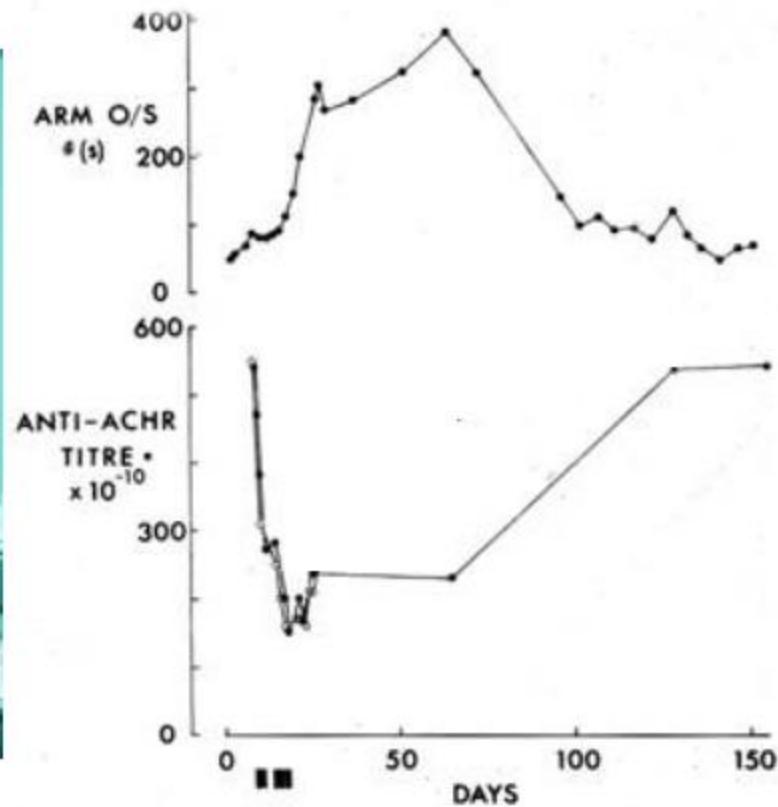
Neuromyotoni / Morvan's syndrom

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



Plasmaferes som behandling av Myastenia Gravis

University of Oxford



John Newsom-Davis d 2007

Pinching, Peters and Newsom-Davis 1977;
Newsom-Davis et al 1978

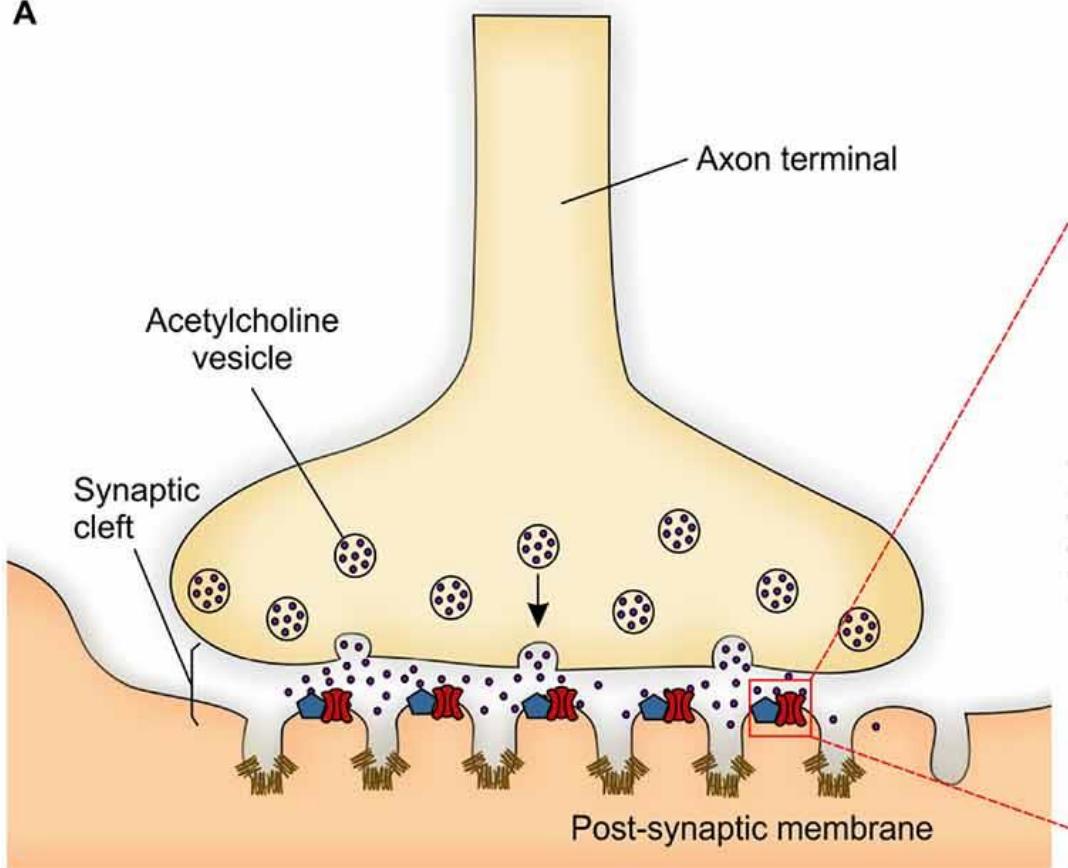
2018-05-23

Clas Malmeström

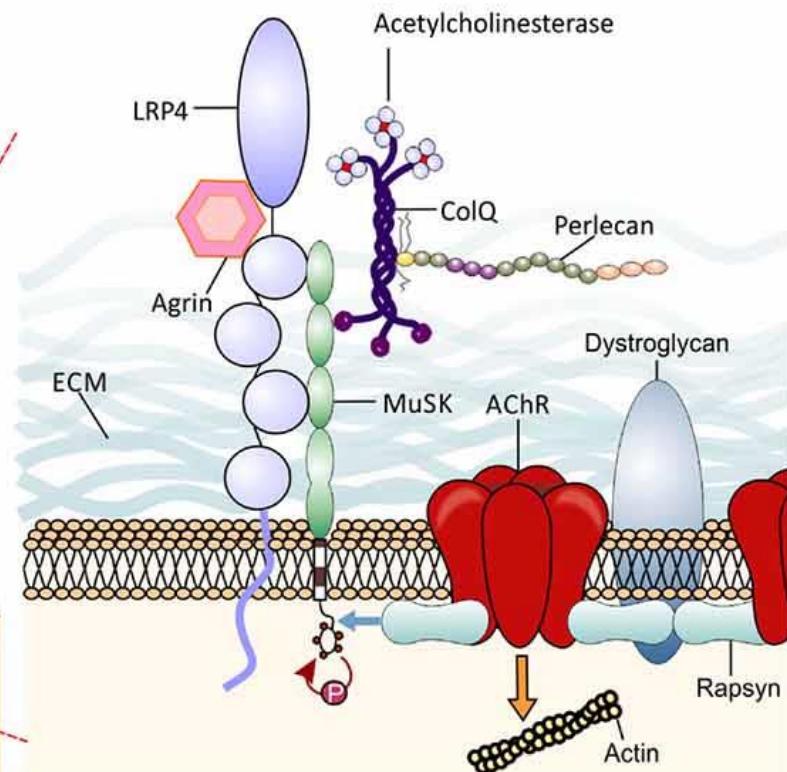
Adapted from Prof. Angela Vincent

Antigenens relation till varandra

A



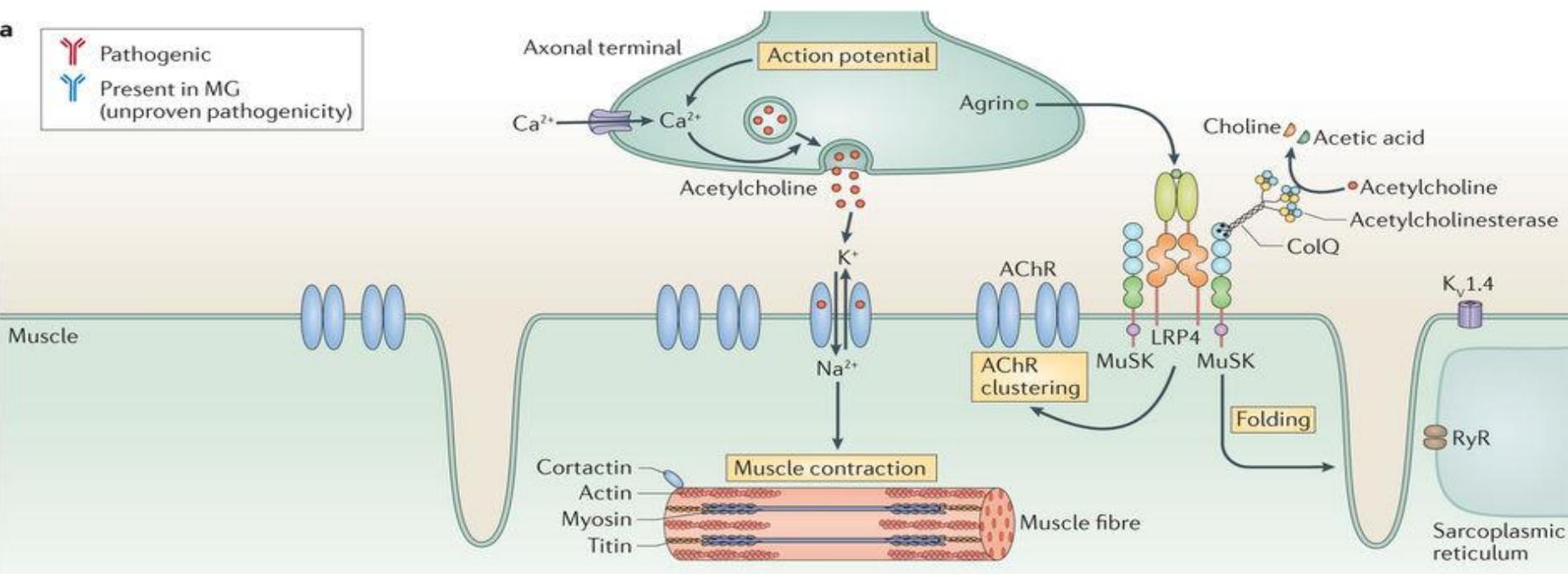
B

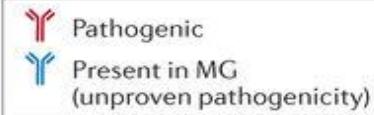
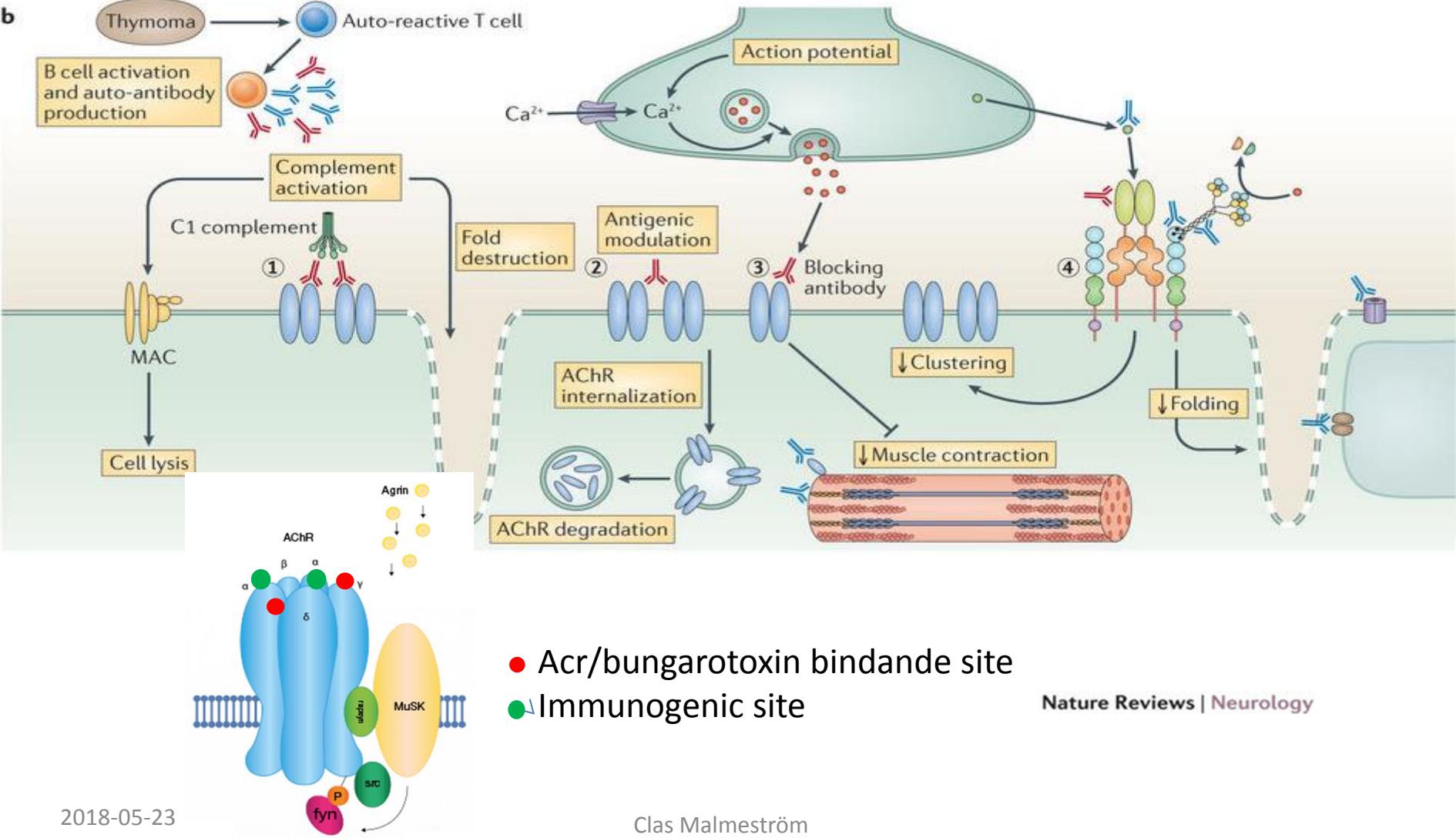


Front. Mol. Neurosci., 27 December 2016

a

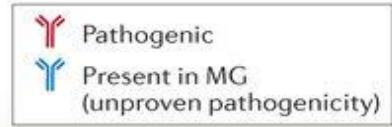
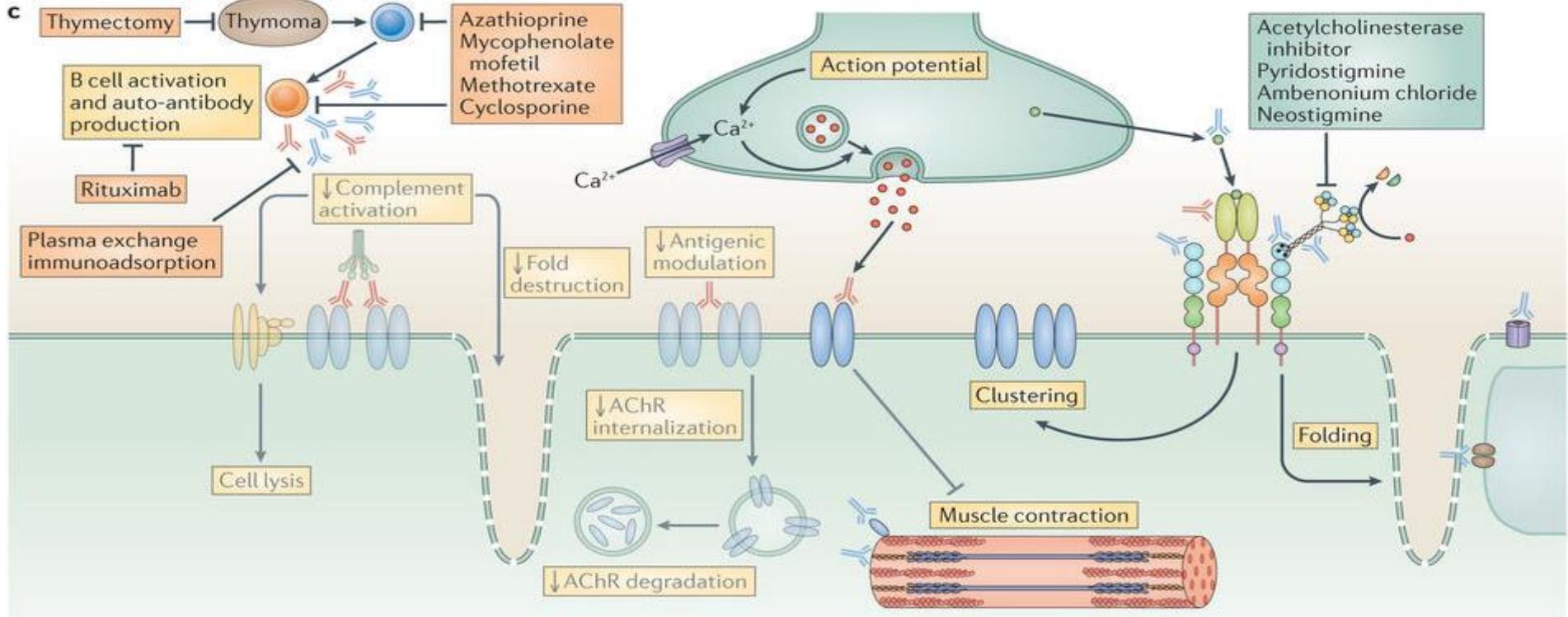
- Pathogenic
- Present in MG (unproven pathogenicity)



a**b**

Antigen	Age/onset	M:F	Weakness pattern	% ocular MG	Thymus changes
	<50	1:4.5	Any	10-15	Follicular hyperplasia
AChR	40-60	1:1	Any	2-3	AB, B Thymoma
	>50	1.8:1	Any	20	Atrophy, rare germinal centers
MuSK	Any	1:4	Bulbar	Rare	-
LRP4	Any	1:2	Mild general	20	?

Curr opin Neurol 2017, 30:464

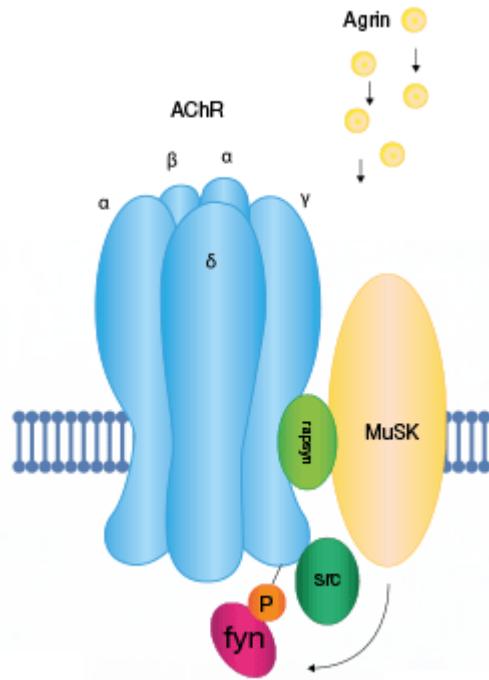
a**c**

Nature Reviews | Neurology

MuSK – antikroppar anti - muskelspecifikt kinas

- Mestadels unga vuxna kvinnor.
 - M:F ratio: 1:4
- Ofta bulbär påverkan
- Okulär myasteni ovanlig
- Svarar sämre på acetylcholin-esterashämmare
- Thymectomi vanligtvis inte indicerad
- Anti-CD20 tycks effektiv

IBL International MuSK-Ab ELISA



Muskel specific thyrosin kinase, MuSK is part of an agrin receptor complex and mediates the agrin-induced clustering of acetylcholine receptors

- The world's first commercially available ELISA for measuring MuSK autoantibodies
- Excellent clinical sensitivity of 95.8 % and specificity of 100 %
- Qualitative (cut-off) and quantitative (standard curve) evaluation of results
- High-performance assay: low cross-reactivity, good linearity and high precision

Metoder

- RIA –
 - Radio immunprecipitation assay
- Elisa –
 - Enzyme linked innumosorbent assay
- CBA –
 - Cell based assays



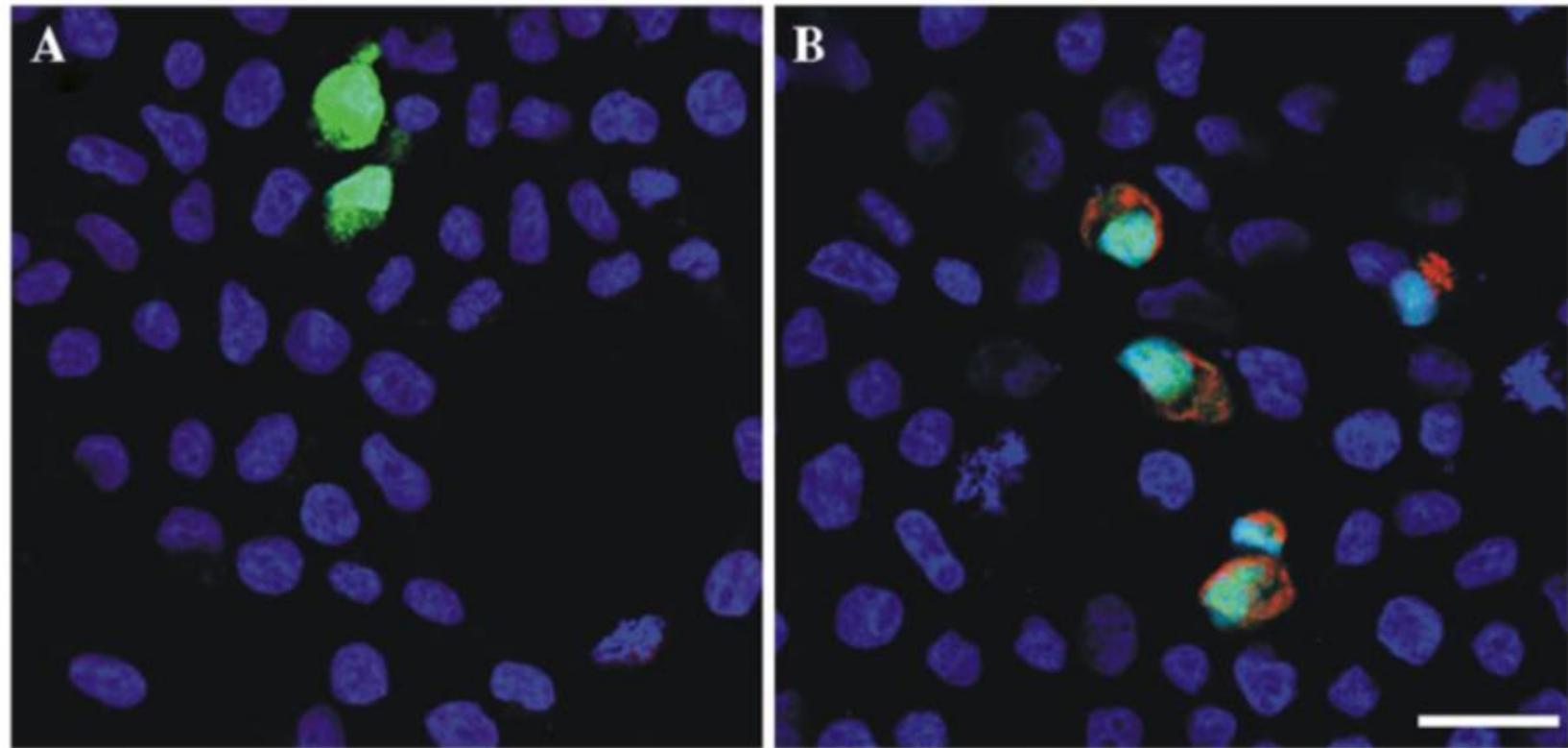
Bungarus multicinctus^[1]

$^{125}\text{I}-\alpha$ -bungarotoxin

RIA är på väg att fasas ut i
många lab pga arbetsmiljö-skäl



LRP4- CBA



binding of HEK293 cells transfected with huLRP4 by double-
ve antisera. Confocal images are shown of HEK293 cells

(serum 4, **a**), others strongly reacted with LRP4-exp
(serum 6, **b**), indicated by *red fluorescence*. Both sera

LRP4 – antikroppar

Table 1. LRP4 antibody-positive MG

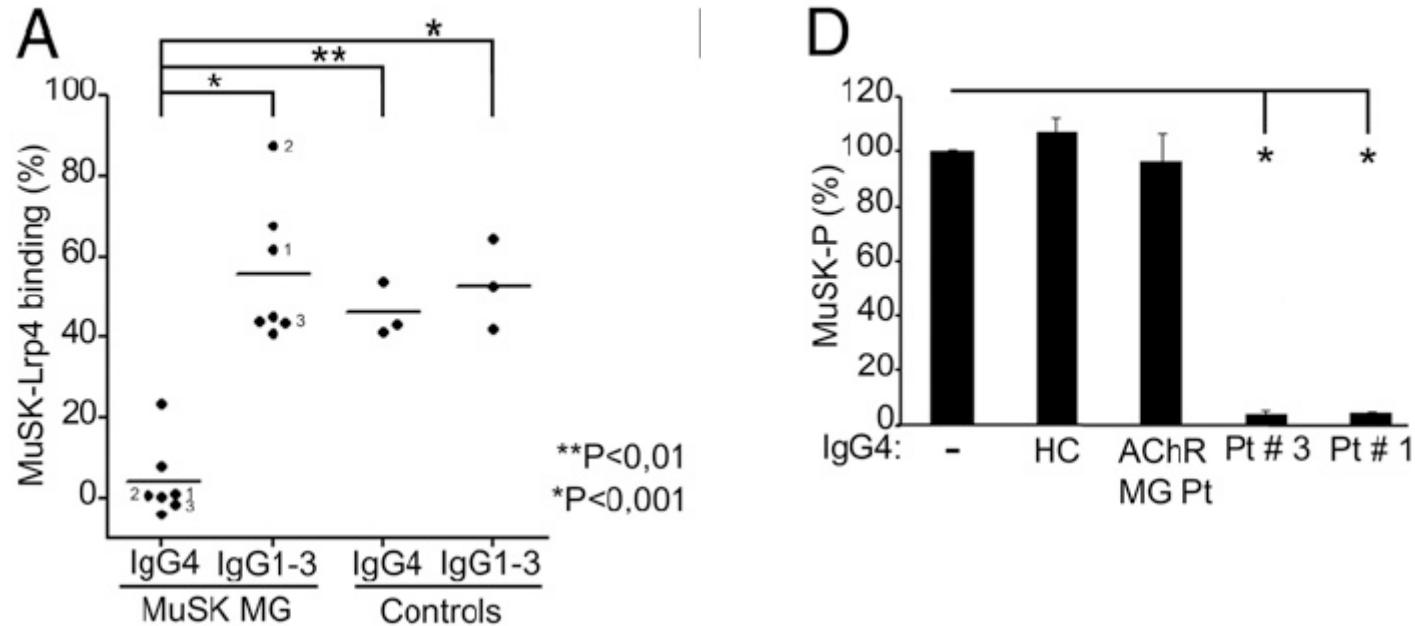
Reference	Assay	Cutoff	AChR ab ⁺	AChR ab ⁻ , MuSK ab ⁺	DNMG	Generalized MG	Thymoma	Cohort
52	LUCIP	Mean + 4 SD	0% (0/100)	11% (3/28)	2.2% (6/272)	Yes	No	Japan
51	CBA				53.8% (6/13)	Yes	No	Germany
50	ELISA	Mean + 4 SD	0% (0/61)	2.8% (1/36)	9.2% (11/120)	Yes	No	United States and Greece
54	CBA				8.2% (6/73)	Yes	No	Norway, Italy, the Netherlands, United States, and Japan
64	CBA		7.5% (8/107)	14.9% (10/67)	18.7% (119/635)	Yes	No	Europe and Israel
62	FACS	Mean + 2.5 SD	13% (3/23)	13% (3/23)	14.5% (8/55)	Yes	1	Italy
66	CBA				1.4% (2/145)	Yes	No	United Kingdom
65	CBA				4% (2/50)	Yes	/	China
63	CBA				10.3% (6/58)	Yes	No	China

Abbreviations: LECIP, luciferase-reporter immunoprecipitation; ELISA, enzyme-linked immunosorbent assay; CBA, cell-based assay; FACS, fluorescence-activated cell sorting; ab, antibody.

Ann. N.Y. Acad. Sci. 1413 (2018) 126–135 © 2018 New York Academy of Sciences.

MuSK IgG4 autoantibodies cause myasthenia gravis by inhibiting binding between MuSK and Lrp4

Maartje G. Huijbers^{a,b,1,2}, Wei Zhang^{c,2}, Rinse Klooster^b, Erik H. Niks^a, Matthew B. Friese^c, Kirsten R. Straasheijm^b, Peter E. Thijssen^b, Hans Vrolijk^d, Jaap J. Plomp^{a,d}, Pauline Vogels^b, Mario Losen^e, Silvère M. Van der Maarel^{b,3}, Steven J. Burden^{c,3}, and Jan J. Verschueren^{a,3}



A: IgG4 men inte IgG1-3 från samma patient inhiberar agrin-beroende bindning mellan MusK och Lsp4
D: IgG4 reducerar fosforylering av MuSK



Spectrums of IgG Classes

Name	Percent	Complement activator	Binds to <u>Fc receptor</u> on phagocytic cells
IgG1	66%	second-highest	high affinity
IgG2	23%	third-highest	extremely low affinity
IgG3	7%	highest	high affinity
IgG4	4%	no	intermediate affinity

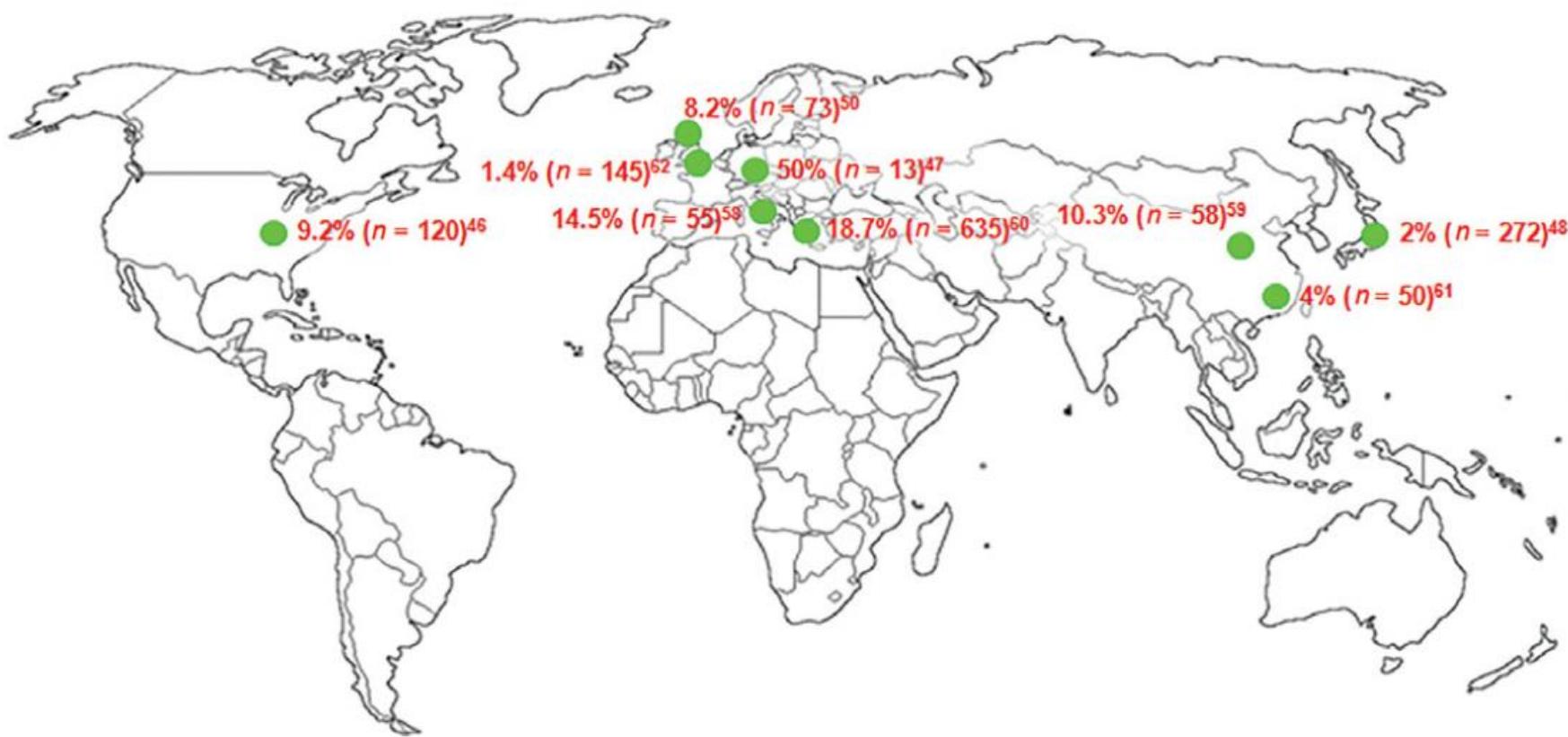
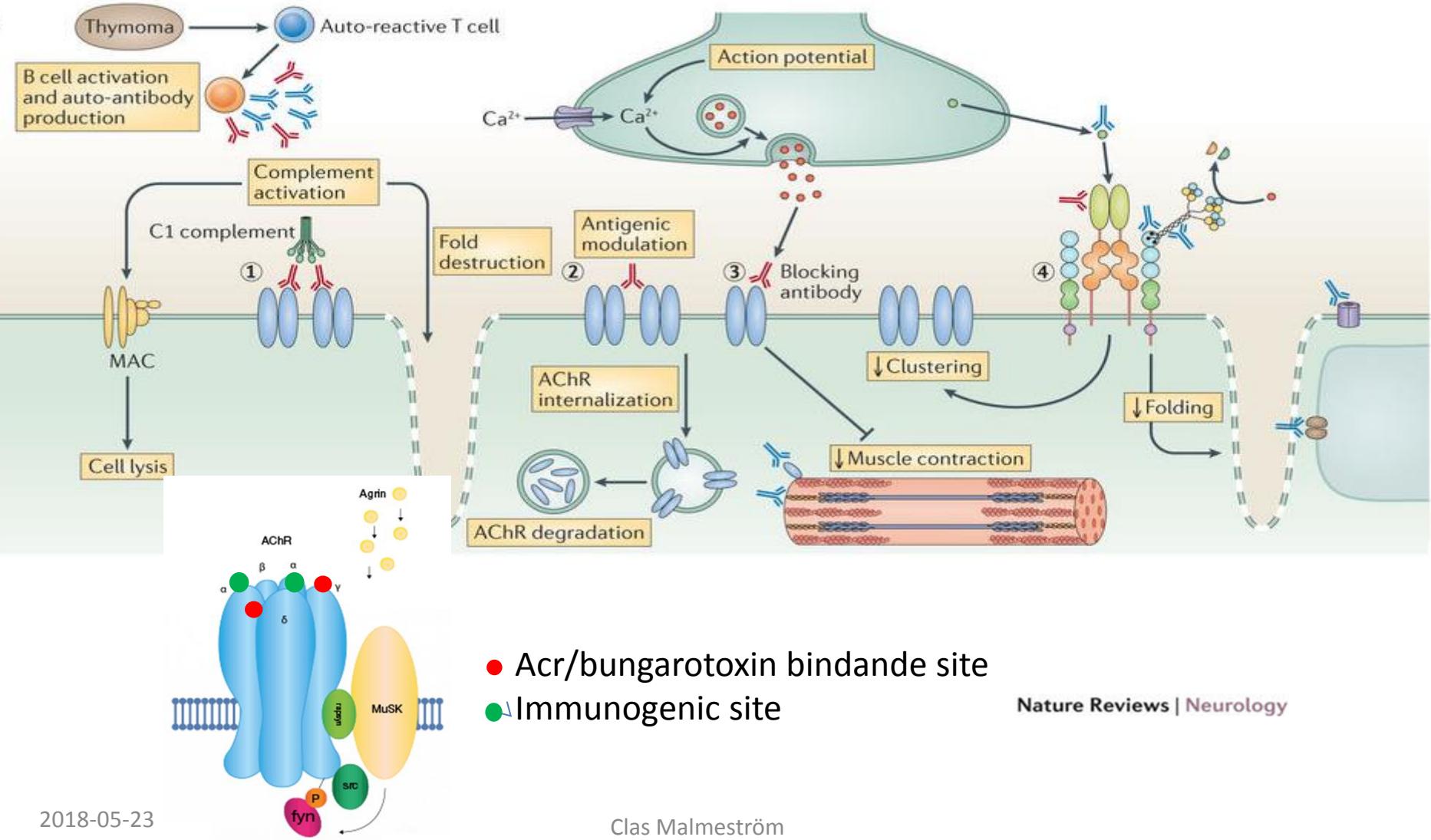


Figure 3. Prevalence of anti-LRP4 antibodies in double-seronegative MG.

1 – 2 – 4 – 8 – 9 – 10 - 14 – 19 – 50 % av dubbel seronegativa MG

Ann. N.Y. Acad. Sci. 1413 (2018) 126–135 © 2018 New York Academy of Sciences.

b



OUH Home ▶ Immunology ▶ Diagnostic tests ▶ Clustered AchR and MuSK

CLUSTERED ACHR AND MUSK

For the detection of low affinity antibodies

Specimen requirements

Serum 1ml; plasma is acceptable but CSF not required

Cost

100 UKP - UK NHS, International and Private; price includes AChR, MuSK and LRP4

Laboratory turnaround time

21 days

Laboratory method

Cell based assay

Deficiency range / units

DIAGNOSTIC TESTS

The diagnostic laboratory

How to order tests

Allergy serology

Autoimmunity

Immunochemistry

Immunodeficiency

Infectious immunology

Neuroimmunology

Announcements and amendments to testing

◀ Immunology

Neuromuskulära synapsen

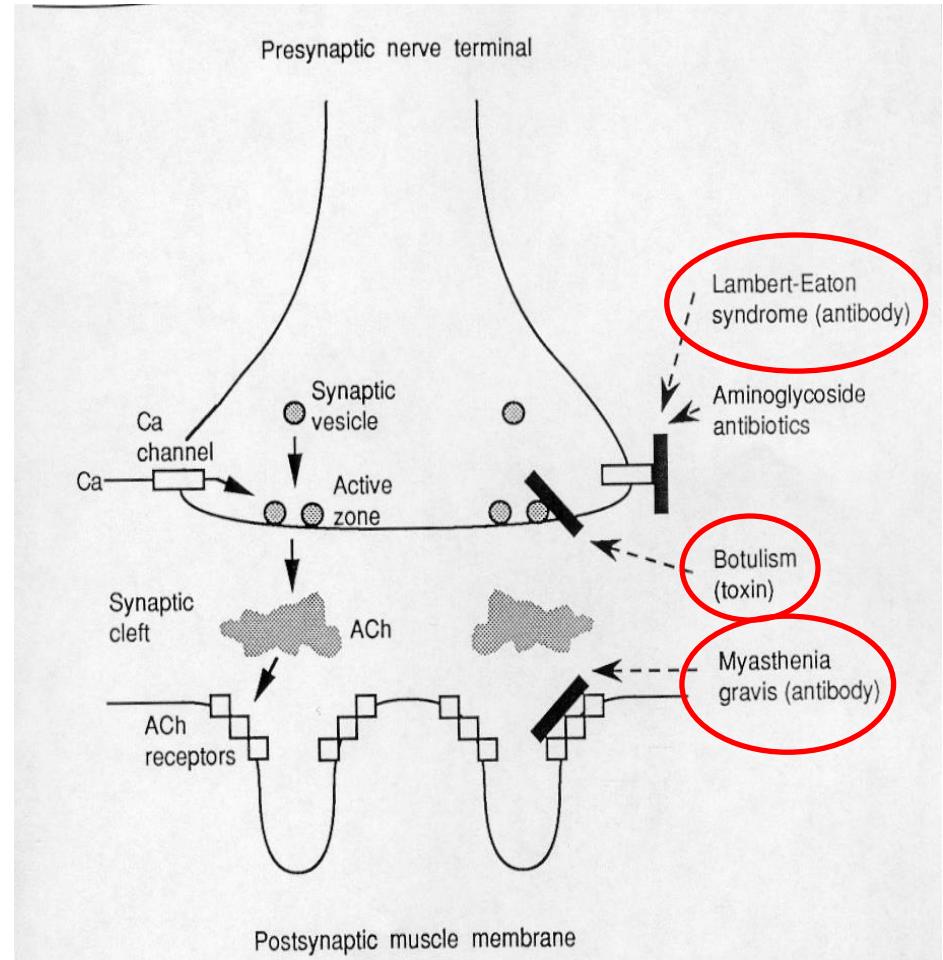
«Neuroimmunologins vagga»



LEMS – Lambert-Eatons

LEMS – Lambert-Eaton myastena syndrom

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



Lambert-Eatons / LEMS

Type	Voltage	α_1 subunit (gene name)	Associated subunits	Most often found in
L-type calcium channel ("Long-Lasting" AKA "DHP Receptor")	HVA (high voltage activated)	$\text{Ca}_v1.1$ (CACNA1S) $\text{Ca}_v1.2$ (CACNA1C) $\text{Ca}_v1.3$ (CACNA1D) $\text{Ca}_v1.4$ (CACNA1F)	$\alpha_2\delta$, β , γ	Skeletal muscle, smooth muscle, bone (osteoblasts), ventricular myocytes** (responsible for prolonged action potential in cardiac cell; also termed DHP receptors), dendrites and dendritic spines of cortical neurones
P-type calcium channel ("Purkinje") / Q-type calcium channel	HVA (high voltage activated)	$\text{Ca}_v2.1$ (CACNA1A)	$\alpha_2\delta$, β , possibly γ	Purkinje neurons in the cerebellum / Cerebellar granule cells
N-type calcium channel ("Neural"/"Non-L")	HVA (high voltage activated)	$\text{Ca}_v2.2$ (CACNA1B)	$\alpha_2\delta/\beta_1$, β_3 , β_4 , possibly γ	Throughout the brain and peripheral nervous system.
R-type calcium channel ("Residual")	intermediate voltage activated	$\text{Ca}_v2.3$ (CACNA1E)	$\alpha_2\delta$, β , possibly γ	Cerebellar granule cells, other neurons
T-type calcium channel ("Transient")	low voltage activated	$\text{Ca}_v3.1$ (CACNA1G) $\text{Ca}_v3.2$ (CACNA1H) $\text{Ca}_v3.3$ (CACNA1I)		neurons, cells that have pacemaker activity, bone (osteocytes)

- Spänningsskänsliga kalciumkanaler (VGCC) ; Spänningsskänsliga jonkanaler i membranet i exciterbara celler, såsom muskler, neuron och glialceller
- Permeabilitet för kalciumjonen, Ca^{2+} .
- Vid fysiologisk eller vilande membranpotential stängs VGCCs normalt.
- De aktiveras vid depolariserade membranpotentialer

VGCC P/Q-typ vs VGCC N-typ

- Anti- VGCC P/Q –typ har en patogen roll vid LEMS
- Kliniska relevansen av VGCC N-typ är mer oklar – jonkanalen uttrycks i nervvävnad och är associerad med störningar i autonoma nervsystemet samt lillhjärnspåverkan.
- Inga riktigt validerande studier finns för VGCC N-typ
- ”LEMS - 84% seropositiva för VGCC, (P/Q-typ 74%; N-typ 58%), associerade med tumör, ffa SCLC”

Martin-Moutot, Rev Neurol, 2004

Table 7
Retrospective studies on Lambert-Eaton myasthenic syndrome (LEMS).

Référence	N pts ^a	Histology	LEMS diagnostic criteria	Antibodies tested	Anticancer treatment	Evolution
Chalk et al. [181]	16	SCLC	Clinic + EMG	ND	CT ± RT ± surgery (n = 11)	Improvement 10 No Improvement 1
Bady et al. [182]	18	SCLC 15 Squamous 3	Clinic + EMG	Anti-AChR Anti-VGCC Antinuclear	CT ± RT (n = 3)	EMG improvement
Bady et al. [183]	17	SCLC 14 Squamous 3	Clinic + EMG	Anti-AChR Anti-VGCC	CT ± RT (n = 2)	Neurological and EMG improvement
Gutmann et al. [184]	14	SCLC 12 Atypical carinoïd 2	Clinic + EMG	ND	ND	ND
Sakuragi et al. [185]	1	SCLC	Unspecified	ND	CT	Improvement
Oh et al. [186]	6	SCLC	Clinic + EMG	ND	CT ± RT ± Surgery (n = 6)	Improvement
Tim et al. [187]	24	SCLC	Clinic + EMG	Anti-AchR Anti-VGCC	CT (n = 19)	Improvement in strength (16%) No improvement (58%)
O'Suilleabhain et al. [188]	8	SCLC	Clinic + EMG	Anti-N-type Anti-P/Q-type Anti-Hu Anti-Ri Anti-Amphiphysine Anti-GAD65 Anti-AChR	ND	ND
Maddison et al. [189]	15	SCLC	Clinic + EMG + Raised titers of Anti-P/Q-type	Anti-P/Q-type	ND	ND
Moon et al. [190]	7	SCLC	Clinic + EMG	ANA Anti-VGCC Search only in no SCLC patients	CT ± RT ± Surgery (n = 7)	2 complete remissions
Tim et al. [191]	31	SCLC 29 Squamous 1 LC 1	Clinic + EMG	Anti-VGCC	ND	Improvement (35%)
Nakao et al. [192]	67	SCLC	Clinic + EMG	Anti-P/Q-type	ND	ND
Wirtz et al. [193]	14	SCLC	Clinic + EMG	Anti-AChR	ND	ND
Wirtz et al. [194]	7	SCLC	Clinic + EMG or high titer of Anti-VGCC	ND	ND	ND
Zambelis et al. [195]	3	SCLC	Clinic + EMG ± Anti-VGCC	Anti-AchR Anti-VGCC	ND	ND
Wirtz et al. [196]	9	SCLC	Clinic + EMG, Anti-VGCC (P/Q)	Anti-P/Q-type Anti-Hu	ND	ND
Wirtz et al. [197]	26	SCLC	Clinic + Anti-VGCC ± EMG	Anti-P/Q-type	ND	ND
Oh et al. [198]	17	SCLC	Clinic + Anti-VGCC, dysautonomia, or postexercise improvement	Anti-VGCC	ND	ND
Wirtz et al. [199]	13	SCLC	Clinic + Anti-VGCC or EMG	ND	ND	ND
Titulaer et al. [200]	54	SCLC	Clinical features + Anti-VGCC ± EMG	Anti-VGCC	ND	ND
Titulaer et al. [201]	53	SCLC	ND	ND	ND	ND
Titulaer et al. [202]	52	SCLC	Clinic + Anti-VGCC or EMG	ND	ND	ND
Titulaer et al. [203]	58	SCLC	Clinic + EMG or Anti-VGCC	Anti-SOX1 Anti-VGCC	ND	ND
Crone et al. [204]	4	SCLC	Clinic + EMG	Anti-VGCC Anti-Hu	CT	Improvement

SCLC = small cell lung cancer; LEMS = Lambert Eaton Myasthenic Syndrome; pts = patients; LC = lung cancer; EMG = electromyography; ND = no data; CT = chemotherapy; RT = radiotherapy.

^a Only patients with LEMS and lung cancer are reported in the table.

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, TIF-1γ, MI-2b, MI-2a)
- c-NA (Mup44) Ak
(inklusionskroppsmysot)
- 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

Provagn. datum

Remitterande läkare

Provtagningsansvariges namn och telefonnr

Debiteringsadress om annan än avsändaren

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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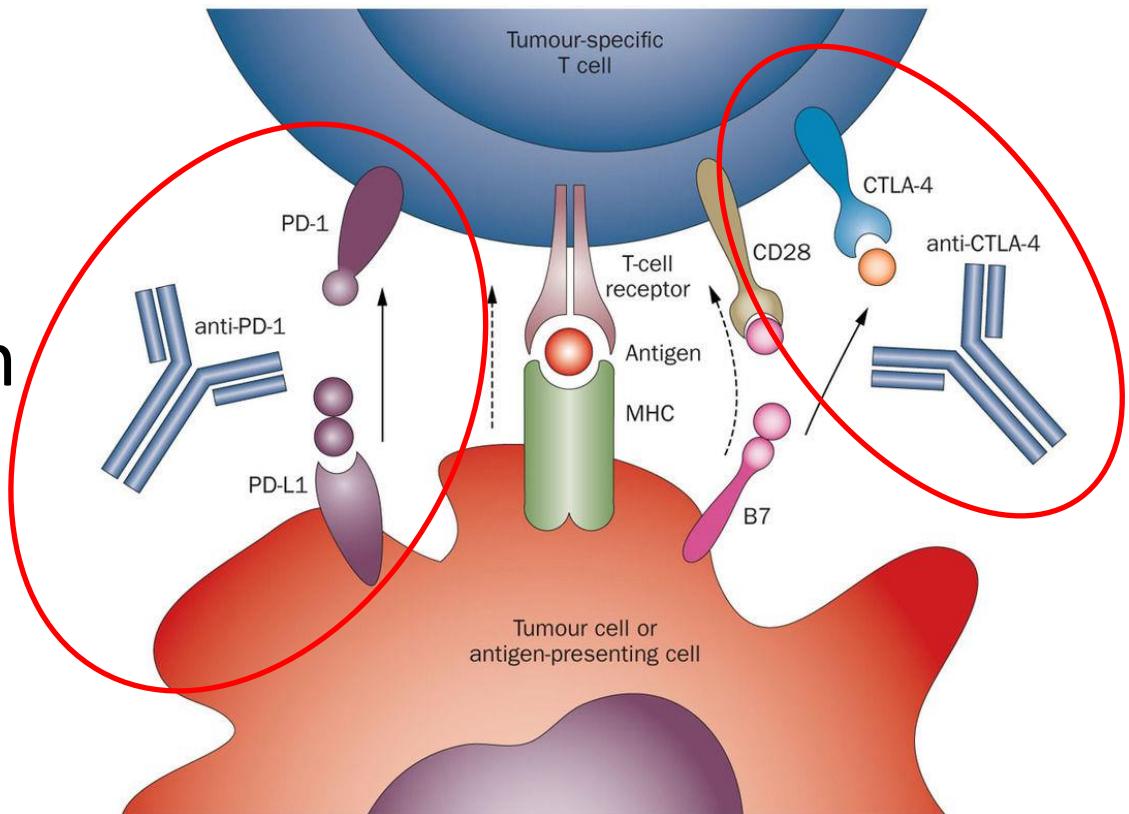
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Biverkningar av PD1-hämmare ny marknad för neuroimmunologi ?

- 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 2018

FDA Approves Keytruda (pembrolizumab) as First Cancer Treatment for any Solid Tumor with a Specific Genetic Feature



May 23, 2017 -- The U.S. Food and Drug Administration today granted accelerated approval to a treatment for patients whose cancers have a specific genetic feature (biomarker). This is the first time the agency has approved a cancer treatment based on a common biomarker rather than the location in the body where the tumor originated.

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



Review

Autoimmune paraneoplastic syndromes associated to lung cancer: A systematic review of the literature: Part 5: Neurological auto-antibodies, discussion, flow chart, conclusions



Claudine Sculier^a, Georgiana Bentea^a, Lucien Ruelle^a, Bogdan Grigoriu^a, Michelle Coureau^a, Julie Gorham^a, Spyridon Sideris^a, Stéphane Holbrechts^b, Jean-Jacques Lafitte^c, Anne-Pascale Meert^a, Valérie Durieux^{d,e}, Thierry Berghmans^{a,e}, Jean-Paul Sculier^{a,e,*}

A B S T R A C T

The development of new immune treatment in oncology and particularly for lung cancer may induce new complications, particularly activation or reactivation of auto-immune diseases. In this context, a systematic review on the auto-immune paraneoplastic syndromes that can complicate lung cancer appears useful. This article is the last of a series of five and deals mainly with onconeural antibodies involved in neurological paraneoplastic syndromes and provides the final discussion.

DE FARLIGASTE MATVAROR ENLIGT NÄRINGSSPECIALISTERNA

