5th Congress of the European Academy of Neurology

Oslo, Norway, June 29 - July 2, 2019

Teaching Course 9

Antibodies: From autoimmune encephalitis to paraneoplastic myelopathies (Level 2)

Antibody-mediated neuropathies

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ANTIBODY-MEDIATED NEUROPATHIES

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Hospital de la Santa Creu i Sant Pau – Barcelona (SPAIN)
EAN 2019 // OSLO - NORWAY

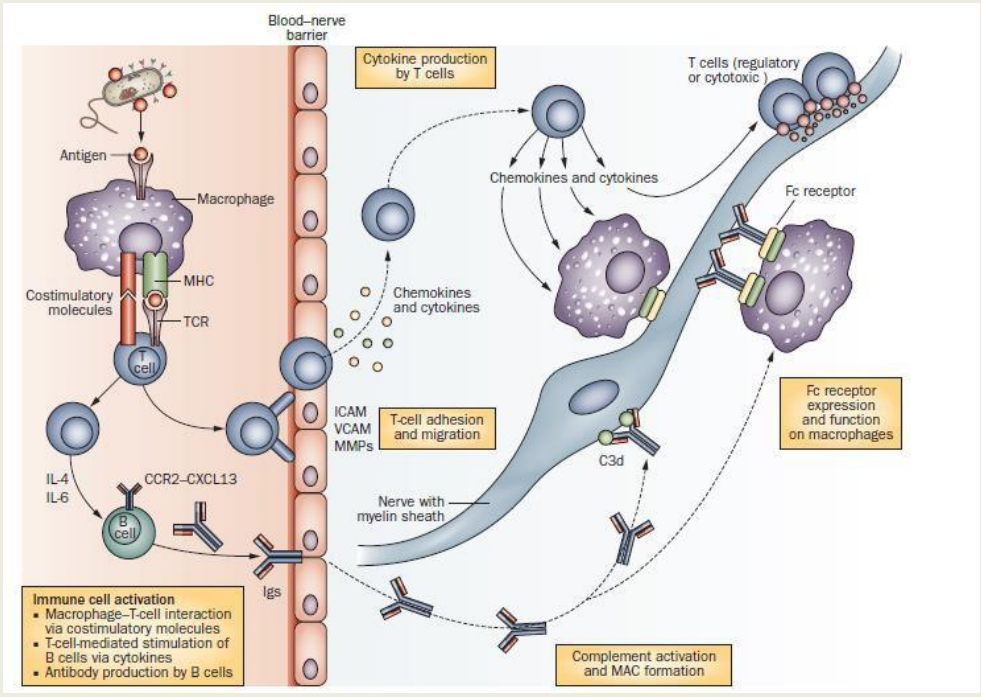
NEUROMUSCULAR BCN
HOSPITAL DE LA SANTA CREU I SANT PAU-UAB. BARCELONA

ciberer
Centro de Investigación Biomédica en Red
Enfermedades Raras

HOSPITAL DE LA SANTA CREU I SANT PAU
UNIVERSITAT AUTÒNOMA DE BARCELONA

DISCLOSURES

- LQ received research grants from Instituto de Salud Carlos III – Ministry of Economy and Innovation (Spain), GBS-CIDP Foundation International, Novartis Pharma Spain, Sanofi Genzyme and Grifols (SPIN Award)
- LQ provided expert testimony to Grifols, CSL Behring, Novartis, Sanofi-Genzyme and Roche
- LQ received travel grants from Merck-Serono, Biogen and CSL Behring.

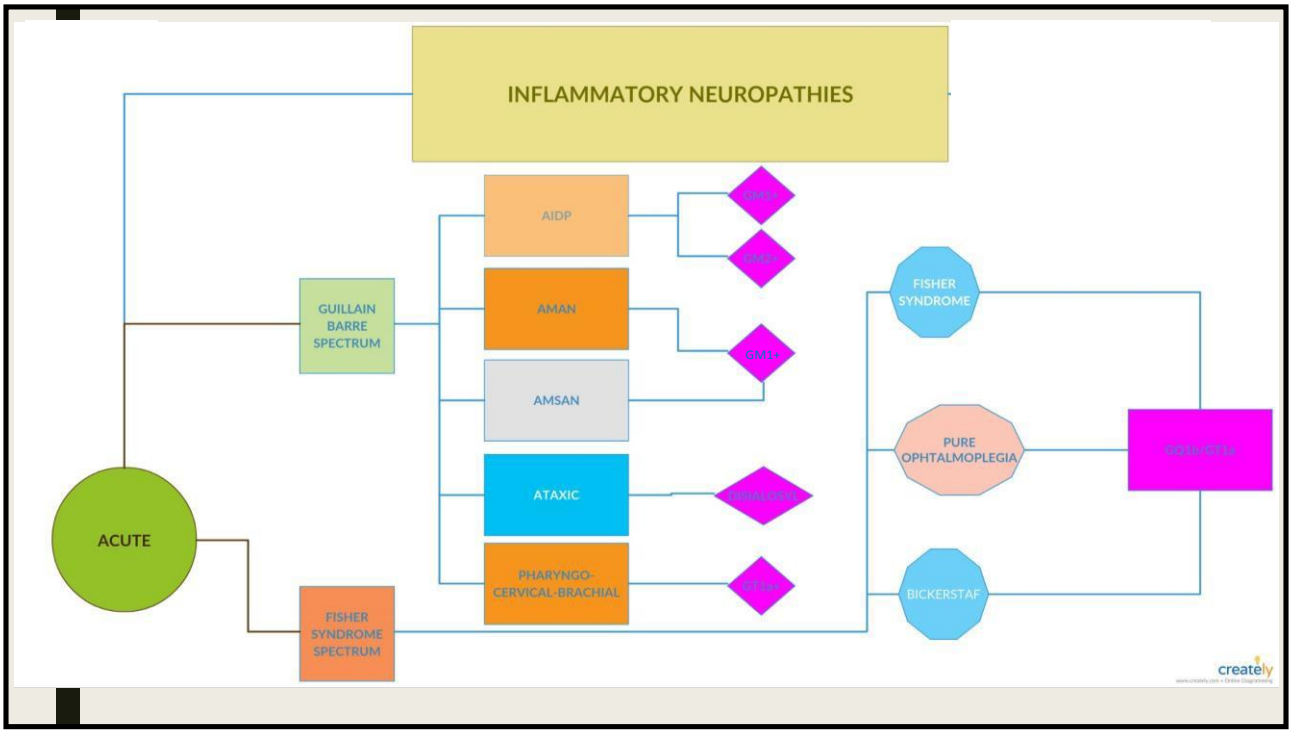

Blood–nerve barrier
Cytokine production by T cells
T cells (regulatory or cytotoxic)
Antigen
Macrophage
Chemokines and cytokines
Fc receptor
MHC
Costimulatory molecules
TCR
T cell
Chemokines and cytokines
ICAM
VCAM
MMPs
T-cell adhesion and migration
Fc receptor expression and function on macrophages
C3d
IL-4
IL-6
CCR2–CXCL13
B cell
Nerve with myelin sheath
Igs
Immune cell activation
▪ Macrophage–T-cell interaction via costimulatory molecules
▪ T-cell-mediated stimulation of B cells via cytokines
▪ Antibody production by B cells
Complement activation and MAC formation

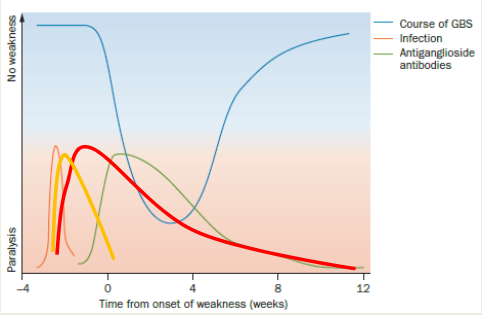
WHY AUTOANTIBODIES?

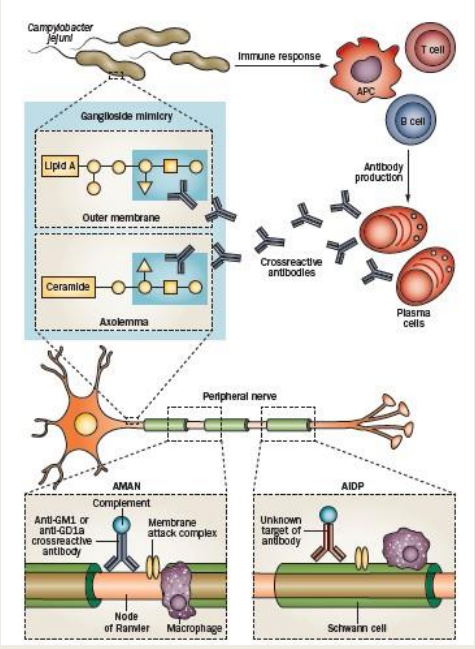
RESPONSE TO THERAPY	• IVIG • Plasma Exchange
GENETICS	• FcgRIIb polymorphisms • HLA class II
PATHOLOGY	• IgG/IgM deposition • Complement
MODELS	• Passive transfer of disease
AUTOANTIBODIES	• MAG • Gangliosides • Nodo/Paranodal

GUILLAIN BARRE SYNDROME

AND VARIANTS







Van den Berg et al 2014

PRECEDING INFECTIONS

CLASSICAL

- Campylobacter
- CMV
- Mycoplasma
- Haemophilus
- Surgery

RECENT

- Hepatitis E
- Zika
- Immune-checkpoint inhibitors

Guillain-Barré Syndrome outbreak associated with Zika virus infection in French Polynesia: a case-control study

Van-Mai Cao-Lormeau*, Alexandre Blake*, Sandrine Mons, Stéphane Lastère, Claudine Roche, Jessica Vanhomwegen, Timothée Dub, Laure Baudouin, Anita Teissier, Philippe Larre, Anne-Laure Vial, Christophe Decam, Valérie Choumet, Susan K Halstead, Hugh J Willison, Lucile Musset, Jean-Claude Manuguerra, Philippe Despres, Emmanuel Fournier, Henri-Pierre Mallet, Didier Musso, Arnaud Fontanet*, Jean Neil*, Frédéric Ghawché*

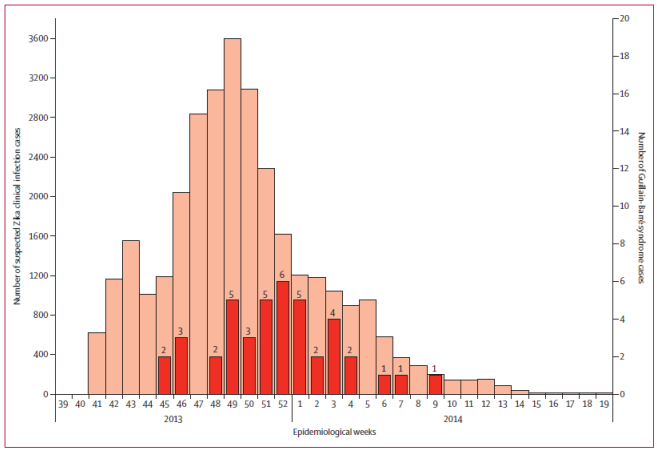
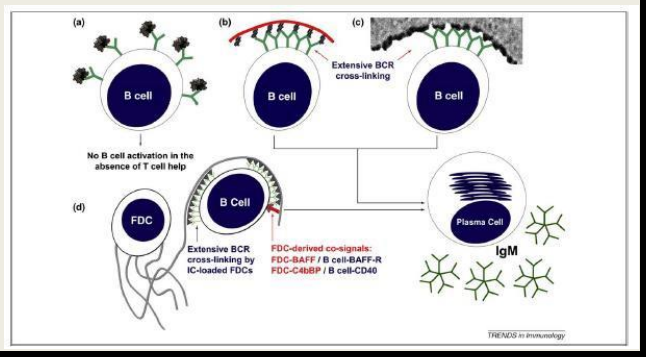
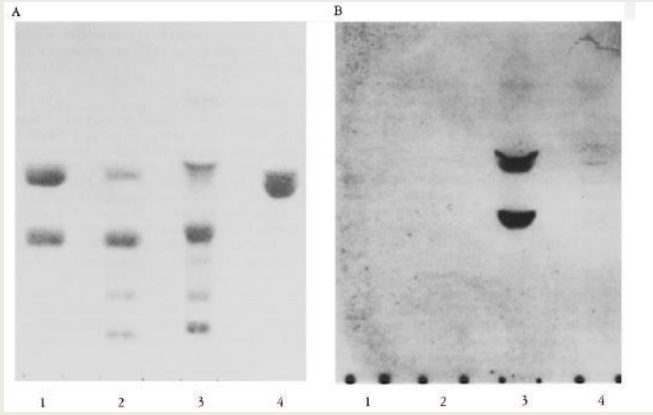


Figure: Weekly cases of suspected Zika virus infections and Guillain-Barré syndrome in French Polynesia between October, 2013, and April, 2014



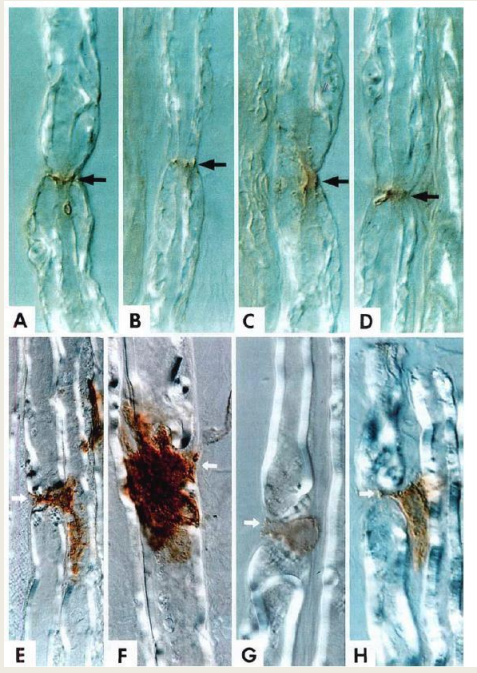
Serum Antibodies to Gangliosides in Guillain-Barré Syndrome

A. A. Ilyas, PhD,* H. J. Willison, MBBS,* R. H. Quarles, PhD,* F. B. Jungalwala, PhD,† D. R. Cornblath, MD,‡ B. D. Trapp, PhD,‡ D. E. Griffin, MD,‡ J. W. Griffin, MD,‡ and G. M. McKhann, MD‡



Acute Motor Axonal Neuropathy: An Antibody-mediated Attack on Axolemma

Charlene Hafer-Macko,* Sung-Tsang Hsieh,* Chun Yan Li,† Tony W. Ho,* Kazim Sheikh,* David R. Cornblath,* Guy M. McKhann,*‡ Arthur K. Asbury,§ and John W. Griffin*‖



Brain (1995), **118**, 597–605

Guillain–Barré syndrome in northern China
Relationship to *Campylobacter jejuni* infection and anti-glycolipid antibodies

T. W. Ho,[1] B. Mishu,[4] C. Y. Li,[7] C. Y. Gao,[7] D. R. Cornblath,[1] J. W. Griffin,[1,2] A. K. Asbury,[6] M. J. Blaser[4,5] and G. M. McKhann[1,3]

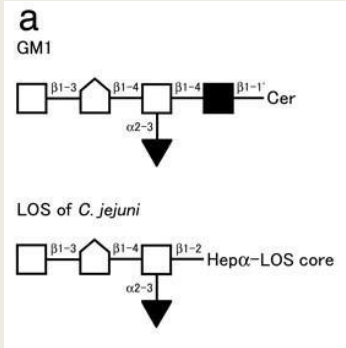
Table 4 *Percent of patients with anti-glycolipid IgG antibodies*

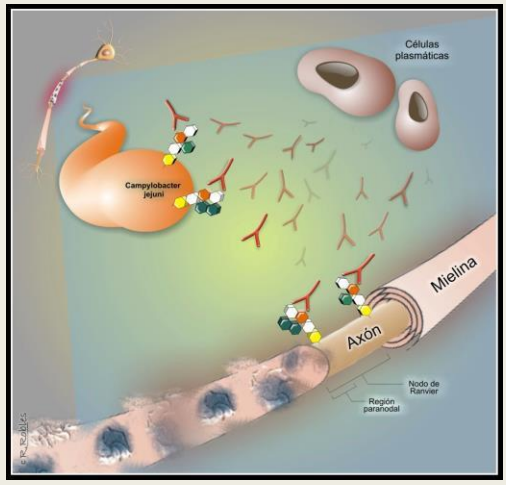
	No. of patients	Percentage of patients						
		GM1	GA1	LK1	3'LM1	GM2	GD1a	GD1b
All patients	38	42*	26	17	17	17	26	18
C. jejuni-positive	25	44*	28	12	8	16	24	24
C. jejuni-negative	13	38**	23	23	31	15	31	8
AMAN	21	48	19	14	19	10	33	25
AIDP	12	33	33	25	8	25	8	25
Village controls	17	6	12	24	29	18	6	6

*$P < 0.01$ when compared with village controls; **$P < 0.02$ when compared with village controls.

A Bacterium Lipopolysaccharide That Elicits Guillain-Barré Syndrome Has a GM1 Ganglioside-like Structure

By Nobuhiro Yuki,* Takao Taki,‡ Fuyuhiko Inagaki,‖ Takeshi Kasama,§ Masaki Takahashi,¶ Kahiko Saito,¶ Shizuo Handa,‡ and Tadashi Miyatake*



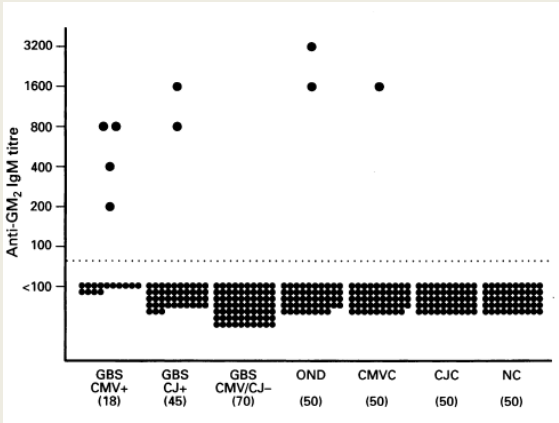


Journal of Neurology, Neurosurgery, and Psychiatry 1997;62:641–643

SHORT REPORT

Cytomegalovirus infections and anti-GM2 antibodies in Guillain-Barré syndrome

B C Jacobs, P A van Doorn, J H M Groeneveld, A P Tio-Gillen, F G A van der Meché



Original Article

Acute axonal Guillain-Barré syndrome with IgG antibodies against motor axons following parenteral gangliosides

Isabel Illa MD[1], Nicolau Ortiz MD[1], Eduard Gallard PhD[1], Candido Juarez PhD[2], Josep M. Grau MD[1], Dr Marinos C. Dalakas MD Chief[3,*]

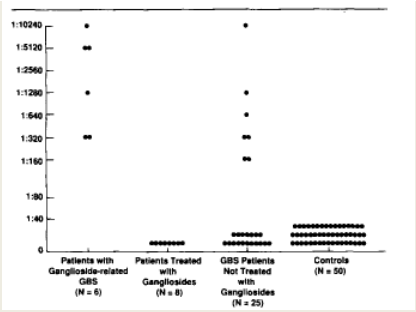
Article first published online: 8 OCT 2004

DOI: 10.1002/ana.410380214

Issue

Annals of Neurology

Volume 38, Issue 2, pages 218–224, August 1995



THE ATAXIC VARIANTS

Fisher Syndrome

Acute Ataxic Neuropathy

The New England
Journal of Medicine

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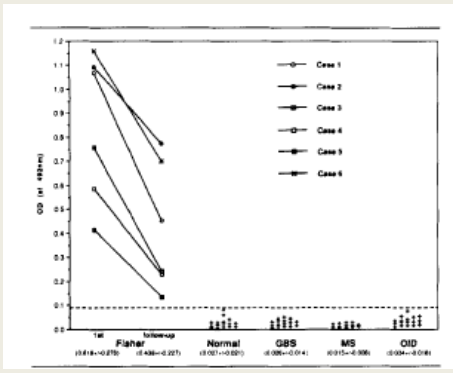
Volume 255 JULY 12, 1956 Number 2

AN UNUSUAL VARIANT OF ACUTE IDIOPATHIC POLYNEURITIS (SYNDROME OF OPHTHALMOPLEGIA, ATAXIA AND AREFLEXIA)*

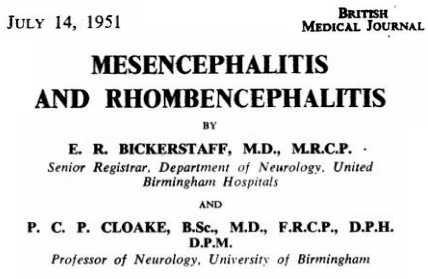
MILLER FISHER, M.D.†

Serum IgG Antibody to Ganglioside GQ1b Is a Possible Marker of Miller Fisher Syndrome

Atsuro Chiba, MD, Susumu Kusunoki, MD,
Teruo Shimizu, MD, and Ichiro Kanazawa, MD



BICKERSTAFF ENCEPHALITIS



JULY 14, 1951 BRITISH MEDICAL JOURNAL

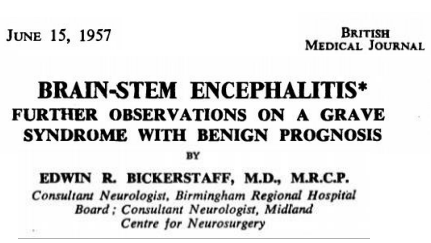
MESENCEPHALITIS AND RHOMBENCEPHALITIS

BY

E. R. BICKERSTAFF, M.D., M.R.C.P.
Senior Registrar, Department of Neurology, United Birmingham Hospitals

AND

P. C. P. CLOAKE, B.Sc., M.D., F.R.C.P., D.P.H. D.P.M.
Professor of Neurology, University of Birmingham



JUNE 15, 1957 BRITISH MEDICAL JOURNAL

BRAIN-STEM ENCEPHALITIS*
FURTHER OBSERVATIONS ON A GRAVE SYNDROME WITH BENIGN PROGNOSIS

BY

EDWIN R. BICKERSTAFF, M.D., M.R.C.P.
Consultant Neurologist, Birmingham Regional Hospital Board; Consultant Neurologist, Midland Centre for Neurosurgery

1951: 3 patients

Ataxia
Ophtalmoplejia
Consciousness

1957: 8 patients

Ataxia
Ophtalmoplejia
Consciousness

Good prognosis
No sequelae

ENCEFALITIS DE BICKERSTAFF

Historia

Serum IgG Antibody to Ganglioside GQ1b Is a Possible Marker of Miller Fisher Syndrome

Atsuro Chiba, MD, Susumu Kusunoki, MD, Teruo Shimizu, MD, and Ichiro Kanazawa, MD

Ann Neurol 1992;31:677–679

1992: antiGQ1b in Miller-Fisher

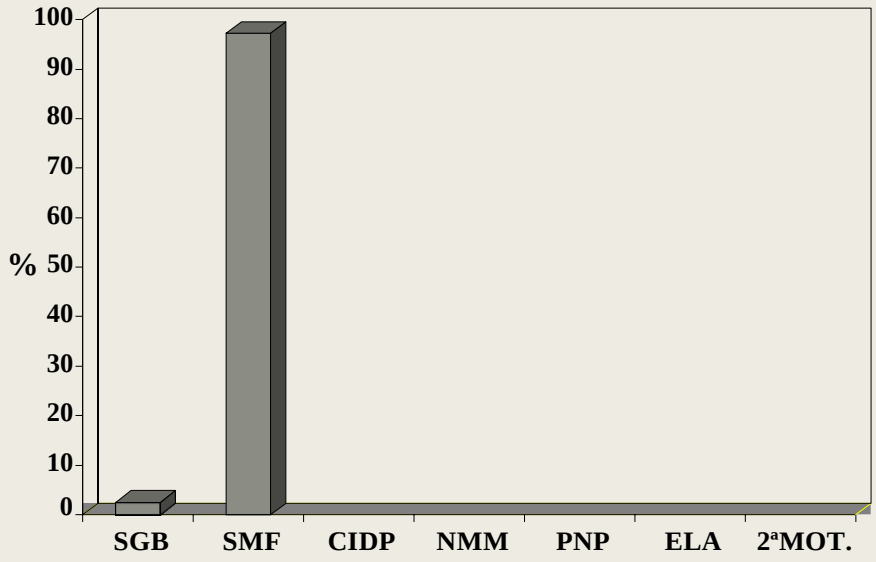
Journal of the Neurological Sciences, 118 (1993) 83–87

An immunologic abnormality common to Bickerstaff's brain stem encephalitis and Fisher's syndrome

N. Yuki [a], S. Sato [a], S. Tsuji [a], I. Hozumi [a] and T. Miyatake [b]

1993: antiGQ1b in Bickerstaff

Fisher-Bickerstaff syndrome



Acute sensory ataxic neuropathy associated with monospecific anti-GD1b IgG antibody

C.-L. Pan, N. Yuki, M. Koga, M.-C. Chiang and S.-T. Hsieh
Neurology 2001;57;1316-1318

GD1b-specific antibody induces ataxia in Guillain-Barré syndrome

K. Kaida, K. Kamakura, G. Ogawa, M. Ueda, K. Motoyoshi, M. Arita and S. Kusunoki
Neurology 2008;71;196-201
DOI: 10.1212/01.wnl.0000317093.57106.33

MFS

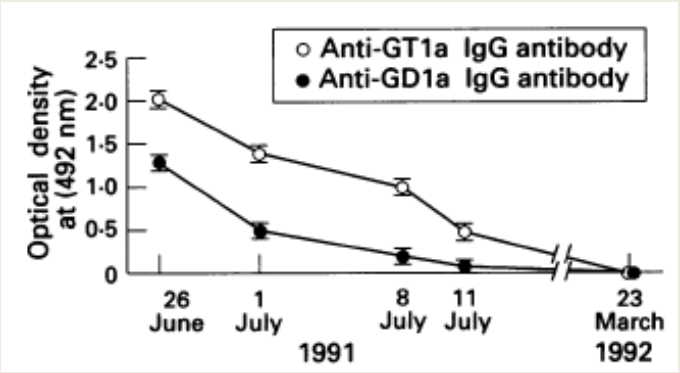
ACUTE ATAXIC NEUROPATHY

Journal of Neurology, Neurosurgery, and Psychiatry 1994;57:1121–1123

SHORT REPORT

Two species of antiganglioside antibodies in a patient with a pharyngeal-cervical-brachial variant of Guillain-Barré syndrome

Kouichi Mizoguchi, Asako Hase, Tomokazu Obi, Hiroaki Matsuoka, Masami Takatsu, Yoshirou Nishimura, Fumitoshi Irie, Yousuke Seyama, Yoshio Hirabayashi



Journal of Neurology, Neurosurgery, and Psychiatry 1996;61:649–651

SHORT REPORT

Acute oropharyngeal palsy is associated with antibodies to GQ1b and GT1a gangliosides

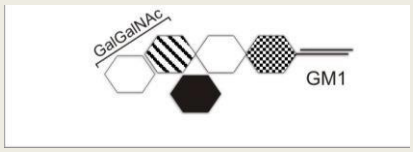
C P O'Leary, J Veitch, W F Durward, A M Thomas, J H Rees, H J Willison

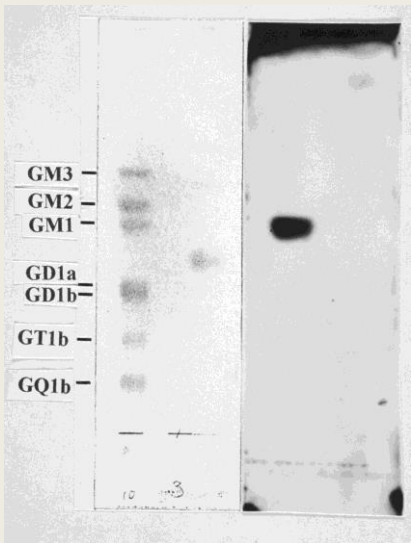
Table 1 Clinical features of the three oropharyngeal patients and the 10 Miller Fisher (MFS) patients

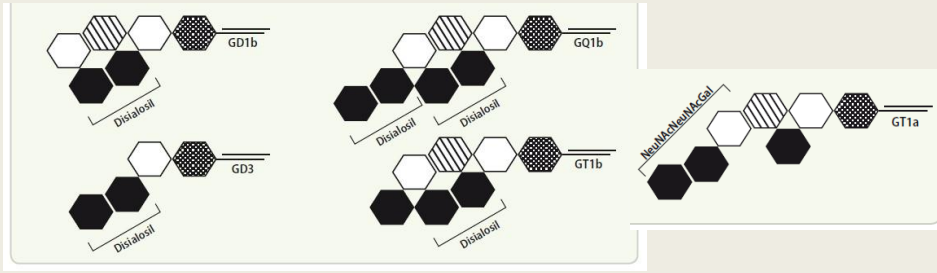
	Patient 1	*Patient 2*	*Patient 3*	*10 MFS patients*
Clinical features:				
Age/sex	39 F	49 M	52 M	17–57 (mean 34) M:F = 7:3
Preceding infection	URTI	C Jejuni enteritis	URTI	10/10
Symptoms at onset	Bulbar	Bulbar and sensory	Bulbar and sensory	6/10 ocular 5/10 ataxia 5/10 sensory
Dysarthria	+ +	+ +	+ +	9/10
Dysphagia	+ +	+ +	+ + +	9/10
Perioral paraesthaesia	−	−	+	5/10
Facial weakness	−	−	+ +	9/10
Ptosis	−	−	−	7/10
Ophthalmoplegia	−	−	−	10/10
Ataxia	−	+	−	10/10
Areflexia	Partial	Complete	Complete	10/10
Limp paraesthesiae	Distal	Distal	−	5/10
Limb weakness (MRC grade)	No	No	Yes (4)	6/10 No 4/10 grade 4
Ventilated	No	No	No	1/10 (4 days)
Tube fed	No	No	Yes	3/10
Specific treatment	None	None	HIg	9/10 (6 × HIg, 3 × PE)

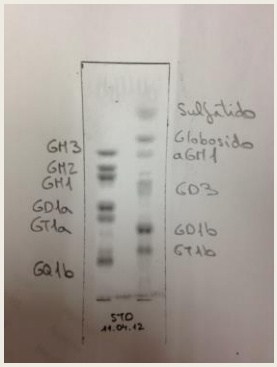
URTI = Upper respiratory tract infection; HIg = human immune globulin; PE = plasma exchange; + = mild; + + = moderate; + + + = severe; − = absent.

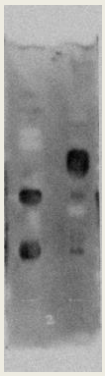
TECHNICAL COMMENTS











FS

ACUTE
ATAXIC

1985

1992

FUTURE

IGOS International GBS Outcome Study

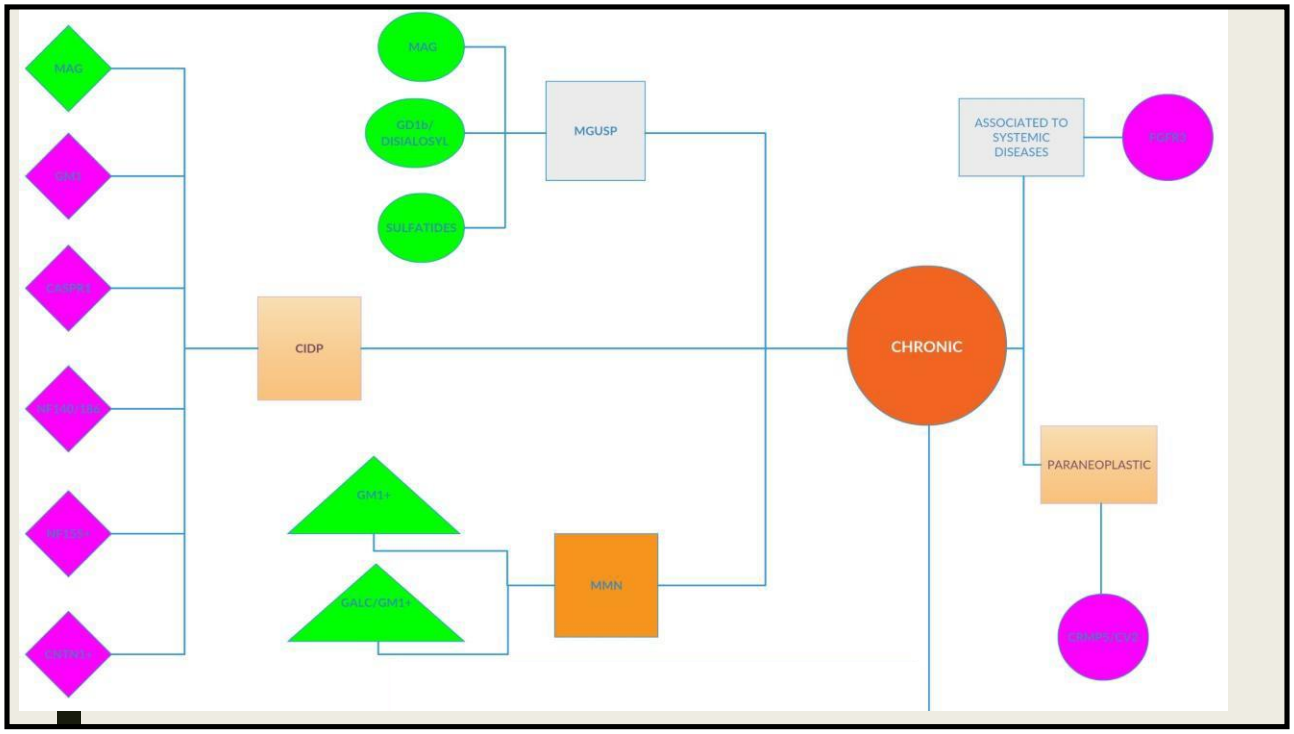
doi:10.1093/brain/awy232 BRAIN 2018: Page 1 of 12 | 1

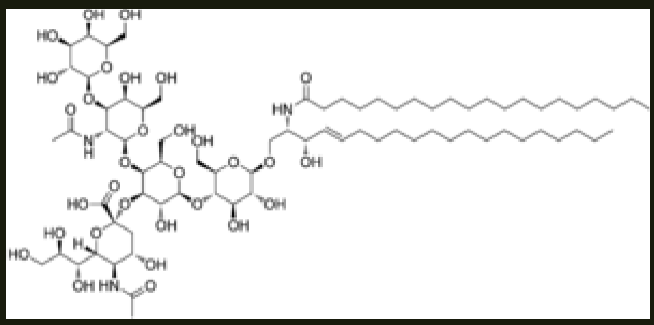
BRAIN
A JOURNAL OF NEUROLOGY

Regional variation of Guillain-Barré syndrome

Alex Y. Doets,[1,*] Christine Verboon,[1,*] Bianca van den Berg,[1,*] Thomas Harbo,[2] David R. Cornblath,[3] Hugh J. Willison,[4] Zhahirul Islam,[5] Shahram Attarian,[6] Fabio A. Barroso,[7] Kathleen Bateman,[8] Luana Benedetti,[9] Peter van den Bergh,[10] Carlos Casasnovas,[11] Guido Cavaletti,[12] Govindsinh Chavada,[4] Kristl G. Claeys,[13,14] Efthimios Dardiotis,[15] Amy Davidson,[4] Pieter A. van Doorn,[1] Tom E. Feasby,[16] Giuliana Galassi,[17] Kenneth C. Gorson,[18] Hans-Peter Hartung,[19] Sung-Tsang Hsieh,[20] Richard A.C. Hughes,[21] Isabel Illa,[22] Badrul Islam,[5] Susumu Kusunoki,[23] Satoshi Kuwabara,[24] Helmar C. Lehmann,[25] James A.L. Miller,[26] Quazi Deen Mohammad,[27] Soledad Monges,[28] Eduardo Nobile Orazio,[29] Julio Pardo,[30] Yann Pereon,[31] Simon Rinaldi,[32] Luis Querol,[22] Stephen W. Reddel,[33] Ricardo C. Reisin,[34] Nortina Shahrizaila,[35] Soren H. Sindrup,[36] Waheed Waqar,[37] Bart C. Jacobs[1,38] and the IGOS Consortium[#]

CHRONIC NEUROPATHIES





MULTIFOCAL MOTOR NEUROPATHY

ANTI-GM1 IgM

A Treatable Multifocal Motor Neuropathy with Antibodies to GM1 Ganglioside

A. Pestronk, MD,* D. R. Cornblath, MD,* A. A. Ilyas, PhD,† H. Baba, MD,† R. H. Quarles, PhD,† J. W. Griffin, MD,* K. Alderson, MD,* and R. N. Adams, MSc*

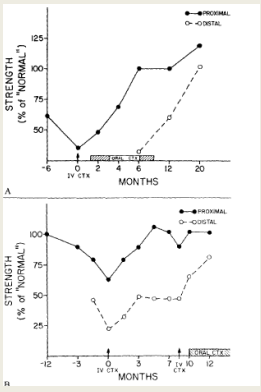
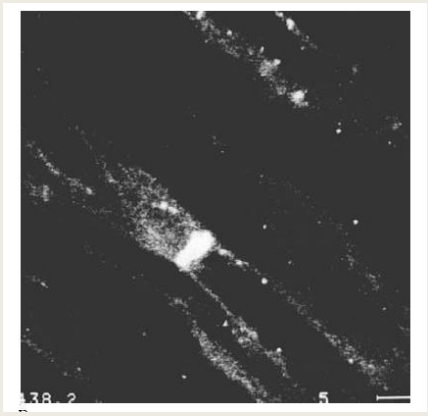
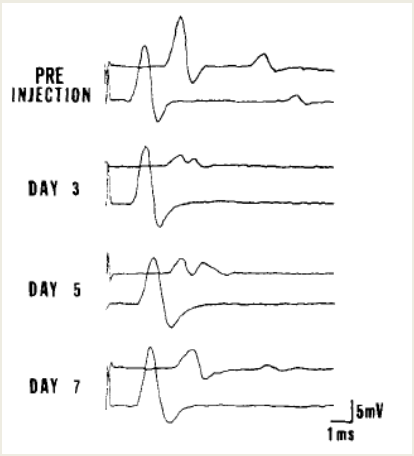


Table 2. Longitudinal Study of Antibody Titers[a]

		GM1[b]	GD1b[b]
Patient 1	Pretreatment	3880 ± 328 (6)	3967 ± 301 (6)
	After IV CTX		
	10 mo (end of oral CTX)	909 ± 51 (3)	435 (2)
	16 mo	1100 ± 114 (6)	696 ± 187 (4)
	21 mo	2820 ± 152 (3)	ND
Patient 2	Pretreatment	1553 ± 174 (12)	—
	After IV CTX #1		
	1 mo	995 ± 98 (6)	—
	3 mo	1037 ± 61 (6)	—
	8½ mo (IV CTX #2)		
	10 mo (start oral CTX)	667 (2)	ND
	12 mo	395 (2)	ND




PRE
INJECTION
DAY 3
DAY 5
DAY 7
5mV
1 ms

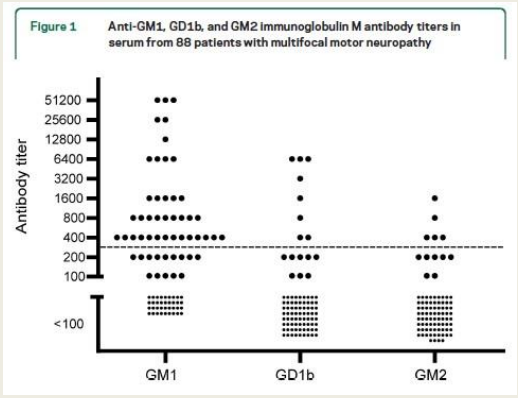
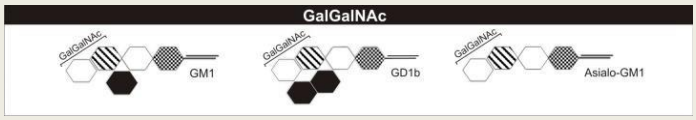


Figure 1
Anti-GM1, GD1b, and GM2 immunoglobulin M antibody titers in serum from 88 patients with multifocal motor neuropathy
Antibody titer
51200
25600
12800
6400
3200
1600
800
400
200
100
<100
GM1
GD1b
GM2


GalGalNAc
GM1
GD1b
Asialo-GM1

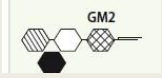

GM2

Table 2 Comparison of patients with and without anti-GM1 IgM antibodies

	Anti-GM1 IgM negative (n = 50)[a]	Anti-GM1 IgM positive (n = 38)[a]	p (2-tailed)
Male	37 (74)	27 (71)	0.76
Age at onset, y	40 (22-63)	38 (23-66)	0.39
Time to treatment, y	5 (0-16)	5 (1-22)	0.33
Duration of MMN, y	11 (2-43)	12 (2-38)	0.90
Age at inclusion, y	52 (30-73)	55 (27-78)	0.37
MRC sumscore	169 (126-179)	158 (108-179)	<0.01
Abnormal vibration sense	7 (14)	12 (32)	0.06
Maintenance IVIg	38 (76)	29 (76)	0.97
IVIg grams per week	13 (8-35)	15 (5-100)	0.09
ODSS arms and legs	3 (0-6)	4 (1-9)	<0.01
Definite motor CB	1 (0-8)	1 (0-6)	0.59
Probable motor CB	2 (0-7)	2 (0-9)	0.41
Demyelination[b]	1 (0-6)	2 (0-9)	0.48
Axon loss[c]	2 (0-7)	2 (0-10)	0.05

HIGHLIGHT CME

Multifocal motor neuropathy with and without conduction block

A single entity?

E. Delmont, MD; J.P. Azulay, PhD, MD; R. Giorgi, PhD, MD; S. Attarian, MD; A. Verschueren, MD; D. Uzenot, MD; and J. Pouget, MD

Table 1 *Clinical features of 13 cases of MMN without CB at diagnosis, after 4 years of follow-up and at last examination*

Age/sex	Diagnostic delay/ follow-up	Involved nerve			Deep tendon reflex	F/C	Muscle atrophy
		At diagnosis	At 4 y	At last examination			
Case 1 52/M	1 y/12 y	R and L ulnar and median	Same	Same	+	F/C	+
Case 2 45/m	4 y/16 y	L and R radial, L peroneal, R tibial	Same	+L median +R peroneal	+	F	+
Case 3 57/M	2 y/4 y	L radial, L ulnar	−L ulnar		+		No
Case 4 27/F	3 y/14 y	R median, R ulnar	Same	Same	+	F/C	+
Case 5 54/M	1 yr/5 y	L and R ulnar	Same		+	F/C	+
Case 6 47/F	10 y/22 y	L median, L ulnar	Same	+R peroneal +R tibial	+	C	+
Case 7 30/F	0,5 y/22 y	L and R ulnar, L and R tibial	+L and R radial	Same	+		+
Case 8 43/M	0,5 y/5 y	L peroneal, R femoral	Same	Same	−		No
Case 9 46/M	8 y/10 y	R radial, R ulnar	Same	Same	−	F/C	+
Case 10 54/M	2 y/7 y	L and R radial, R ulnar	−R ulnar	Same	+	F/C	+
Case 11 50/M	6 y/7 y	L and R axillary, radial, ulnar	Same	Same	+	F/C	+
Case 12 59/M	3 y/4 y	R radial	+R ulnar		+	F	+
Case 13 40/F	4 y/5 y	R median, radial, ulnar	Same		+	F	+

RESEARCH PAPER

Sensitivity and predictive value of anti-GM1/galactocerebroside IgM antibodies in multifocal motor neuropathy

Eduardo Nobile-Orazio,[1] Claudia Giannotta,[1] Lucile Musset,[2] Paolo Messina,[3] Jean-Marc Léger[4]

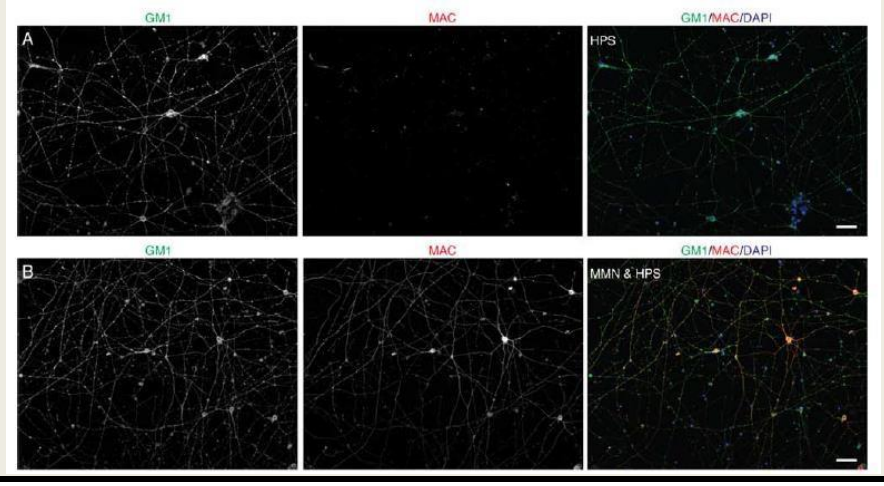
Table 1 Antibody testing in MMN

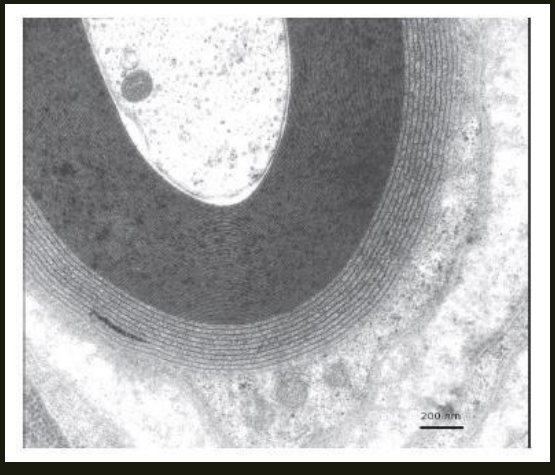
IgM antibody	Frequency versus controls* (p value)	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
GM1	<0.00001	48	93	66	86
GM1(>1:2560)	<0.00001	28	99	85	83
GM2	0.12	8	98	50	79
NS6S	0.053	23	90	39	81
Galactocerebroside	0.002	55	73	36	85
GM1/GalC	<0.00001	75	85	59	92
GM1/GalC (≥1:2560)	<0.00001	60	92	67	89
GM1/GalC (>1:5120)	<0.00001	40	99	89	85

Italics indicate that data refer to serum dilutions different from the other data.
*Fisher exact test, two-tailed.
MMN, multifocal motor neuropathy.

Autoantibody Pathogenicity in a Multifocal Motor Neuropathy Induced Pluripotent Stem Cell–Derived Model

Oliver Harschnitz, MD,[1,2] Leonard H. van den Berg, MD, PhD,[1] Lill Eva Johansen, MSc,[2] Marc D. Jansen, DI,[1] Sandra Kling, PhD,[1] Renata Vieira de Sá, MSc,[2] Lotte Vlam, MD,[2] Wouter van Rheenen, MD,[1,2] Henk Karst, PhD,[2] Corette J. Wierenga, PhD,[3] R. Jeroen Pasterkamp, PhD,[2] and W. Ludo van der Pol, MD, PhD[1]





MGUSP

ANTI-MAG / CANOMAD / SULFATIDES

Monoclonal IgM Neuropathies

- MAG+
- MAG-
  - Demyelinating
    - CIDP
  - Axonal
    - GD1b
    - SULFATIDES

European Journal of Neurology 2010, 17: 356–363 doi:10.1111/j.1468-1331.2009.02930.x

EFNS TASK FORCE/CME ARTICLE

European Federation of Neurological Societies/Peripheral Nerve Society Guideline on management of chronic inflammatory demyelinating polyradiculoneuropathy: Report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Society — First Revision

Members of the Task Force: P. Y. K. Van den Bergh[a], R. D. M. Hadden[b], P. Bouche[c], D. R. Cornblath[d], A. Hahn[e], I. Illa[f], C. L. Koski[g], J.-M. Léger[h], E. Nobile-Orazio[i], J. Pollard[j], C. Sommer[k], P. A. van Doorn[l] and I. N. van Schaik[m]

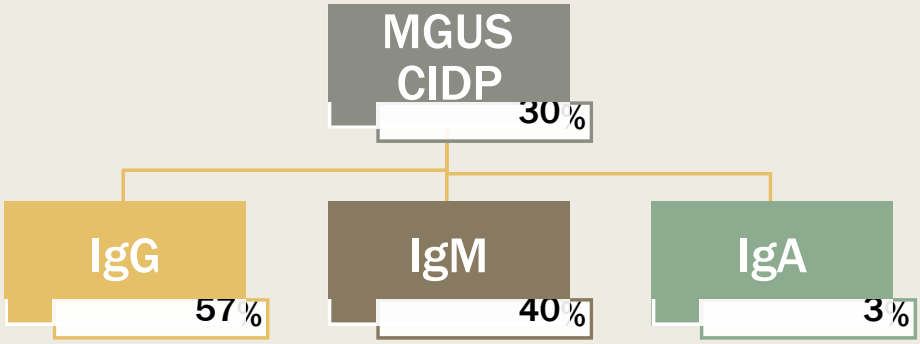
Table 4 Clinical diagnostic criteria

(1) Inclusion criteria
- (a) Typical CIDP
  - Chronically progressive, stepwise, or recurrent symmetric proximal and distal weakness and sensory dysfunction of all extremities, developing over at least 2 months; cranial nerves may be affected; and
  - Absent or reduced tendon reflexes in all extremities
- (b) Atypical CIDP (still considered CIDP but with different features)
  - One of the following, but otherwise as in (a) (tendon reflexes may be normal in unaffected limbs):
  - Predominantly distal (distal acquired demyelinating symmetric, DADS) or
  - Asymmetric [multifocal acquired demyelinating sensory and motor neuropathy (MADSAM), Lewis–Sumner syndrome] or
  - Focal (e.g., involvement of the brachial or lumbosacral plexus or of one or more peripheral nerves in one upper or lower limb)
  - Pure motor or
  - Pure sensory (including chronic immune sensory polyradiculopathy affecting the central process of the primary sensory neuron)

(2) Exclusion criteria
- Borrelia burgdorferi infection (Lyme disease), diphtheria, drug or toxin exposure probably to have caused the neuropathy
- Hereditary demyelinating neuropathy
- Prominent sphincter disturbance
- Diagnosis of multifocal motor neuropathy
- IgM monoclonal gammopathy with high titre antibodies to myelin-associated glycoprotein
- Other causes for a demyelinating neuropathy including POEMS syndrome, osteosclerotic myeloma, diabetic and non-diabetic lumbosacral radiculoplexus neuropathy. PNS lymphoma and amyloidosis may occasionally have demyelinating features

Chronic inflammatory demyelinating polyradiculoneuropathy:
Comparison of patients with and without an associated monoclonal gammopathy

Mark B. Bromberg, MD, PhD; Eva L. Feldman, MD, PhD; and James W. Albers, MD, PhD



ANTI-MAG + MGUS-P

Complement-fixing antiperipheral nerve myelin antibodies in patients with inflammatory polyneuritis and with polyneuropathy and paraproteinemia

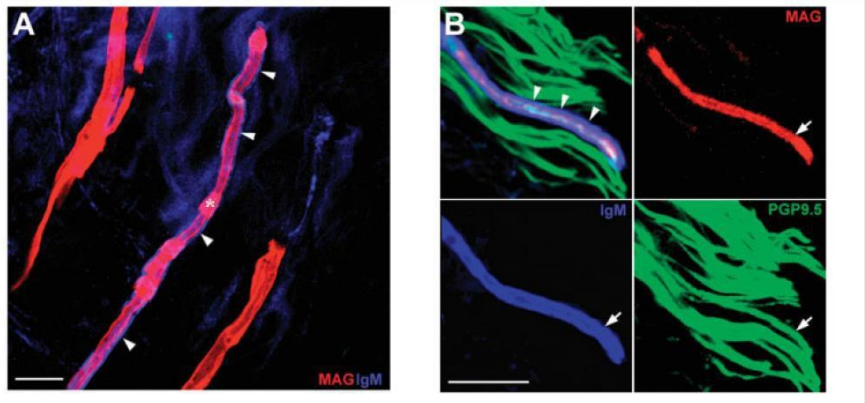
Norman Latov, Robin B. Gross, James Kastelman, Tracy Flanagan, Stella Lamme, Daniel A. Alkaitis, Marcelo R. Olarte, William H. Sherman, Leonard Chess, and Audrey S. Penn

Addendum. Since this manuscript was accepted, we found that the IgM paraproteins from the four patients with antimyelin antibodies all react with the same myelin protein of approximately 90,000 daltons.[36]

ANTI-MAG

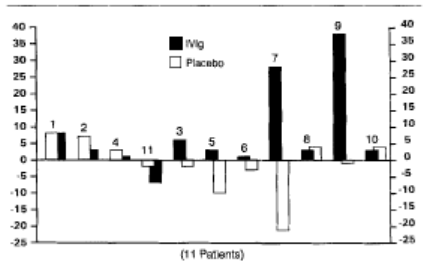
IgM Deposits on Skin Nerves in Anti–Myelin-Associated Glycoprotein Neuropathy

Raffaella Lombardi, PhD,[1,2] Beat Erne, MSc,[1] Giuseppe Lauria, MD,[2] Davide Pareyson, MD,[3] Monica Borgna, PhD,[2] Michela Morbin, MD, PhD,[4] Andreas Arnold, MD,[5] Adam Czaplinski, MD,[1] Peter Fuhr, MD,[1] Nicole Schaeren-Wiemers, PhD,[1] and Andreas J. Steck, MD[1]



A Controlled Study of Intravenous Immunoglobulin in Demyelinating Neuropathy with IgM Gammopathy

Marinos C. Dalakas, MD, Richard H. Quarles, PhD, Robert G. Farrer, PhD, James Dambrosia, PhD, Shawke Soueidan, MD, Daniel P. Stein, MD, Edward Cupler, MD, Elizabeth A. Sekul, MD, and Carlos Otero, MD



A randomised controlled trial of intravenous immunoglobulin in IgM paraprotein associated demyelinating neuropathy

Giancarlo Comi
Luisa Roveri
Antony Swan
Hugh Willison
Martin Bojar
Isabel Illa
Clementine Karageorgiou
Eduardo Nobile-Orazio
Peter van den Bergh
Tony Swan
Richard Hughes and the Inflammatory Neuropathy Cause And Treatment (INCAT) Group*

Table 4 Secondary endpoints at week 4

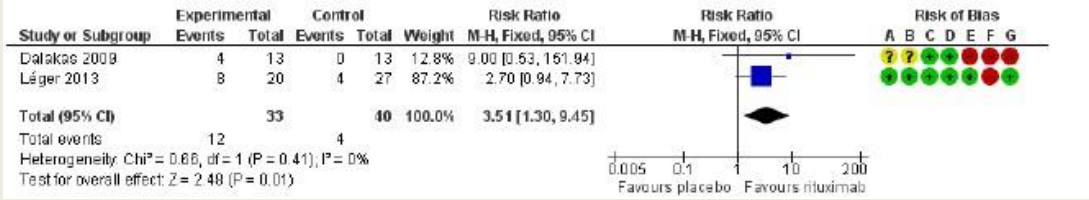
Assessment[a]	IVIg (mean+SD)			Placebo (mean+SD)			
	Baseline	Week 4	p[b]	Baseline	Week 4	p[b]	p[c]
Rankin scale	2.5 (0.9)	2.1 (1.0)	**0.049**	2.2 (0.9)	2.4 (0.9)	NS	NS
Rotterdam scale	28.7 (5.4)	29.8 (5.5)	0.07	30.0 (5.2)	29.4 (5.3)	NS	NS
10 m. walking time (sec)	10.5 (4.2)	9.7 (4.3)	NS	10.8 (4.8)	9.7 (4.0)	0.03	NS
9 hole peg board (sec)	37.9 (15.2)	36.9 (16.6)	NS	38.7 (14.7)	38.1 (15.4)	NS	NS
SF36	43.3 (26.5)	48.6 (25.0)	NS	46.4 (26.3)	42.8 (25.0)	NS	NS
Hand Grip	68.6 (26.5)	77.2 (28.6)	**0.014**	71.8 (25.1)	71.0 (24.8)	NS	**0.049**
MRC	55.9 (4.5)	56.7 (3.9)	NS	56.1 (3.4)	56.4 (3.9)	NS	NS
Distal CMAP Amplitude	9.3 (5.9)	10.0 (6.3)	NS	10.6 (7.0)	10.2 (6.3)	NS	NS
Proximal CMAP Amplitude	7.3 (6.1)	7.7 (5.8)	NS	7.8 (5.9)	7.5 (6.1)	NS	NS
Motor conduction velocity	30.6 (9.9)	29.9 (10.7)	NS	30.6 (10.9)	30.5 (10.3)	NS	NS
Sensory Symptoms Score	6.9 (3.6)	6.1 (3.4)	NS	6.2 (3.1)	6.0 (3.5)	NS	NS
Sensory Sum Score	10.1 (6.3)	7.2 (5.6)	**0.002**	10.2 (6.3)	8.7 (5.5)	NS	NS

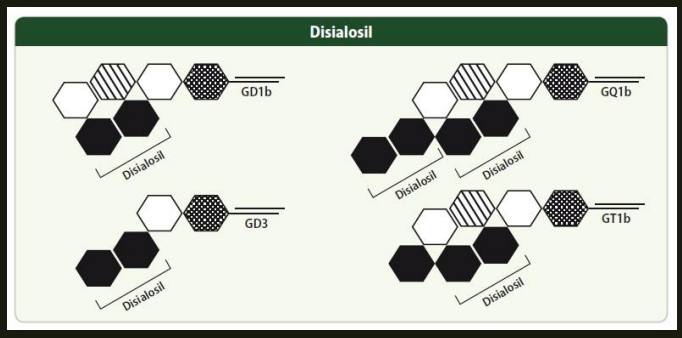
Cochrane Library

Cochrane Database of Systematic Reviews

Immunotherapy for IgM anti-myelin-associated glycoprotein paraprotein-associated peripheral neuropathies (Review)

Lunn MPT, Nobile-Orazio E





CANOMAD
CHRONIC ATAXIC NEUROPATHY

Disialosyl Antibodies

Sensory Neuropathy Associated with Monoclonal Immunoglobulin M to GD1b Ganglioside

Geneviève C. Daune, PhD,* Robert G. Farrer, PhD,*
Marinos C. Dalakas, MD,† and Richard H. Quarles, PhD*

A 67-year-old woman with a sensory polyneuropathy was shown to have a serum monoclonal immunoglobulin M λ antibody with a titer of 1:10,000 toward GD1b ganglioside. The immunoglobulin M also reacted with some other gangliosides containing disialosyl groups such as GD2, GD3, and GQ1b, but it did not react with GM1, LM1, or GD1a. The principal reactive ganglioside in human cauda equina was GD1b.

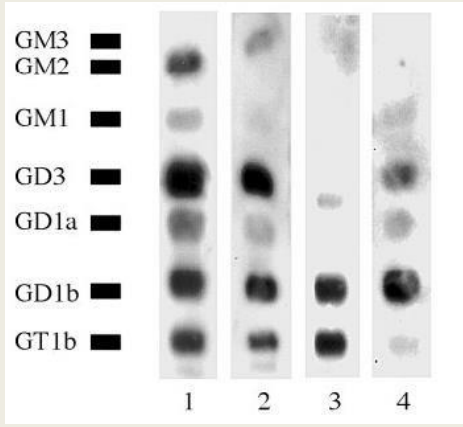


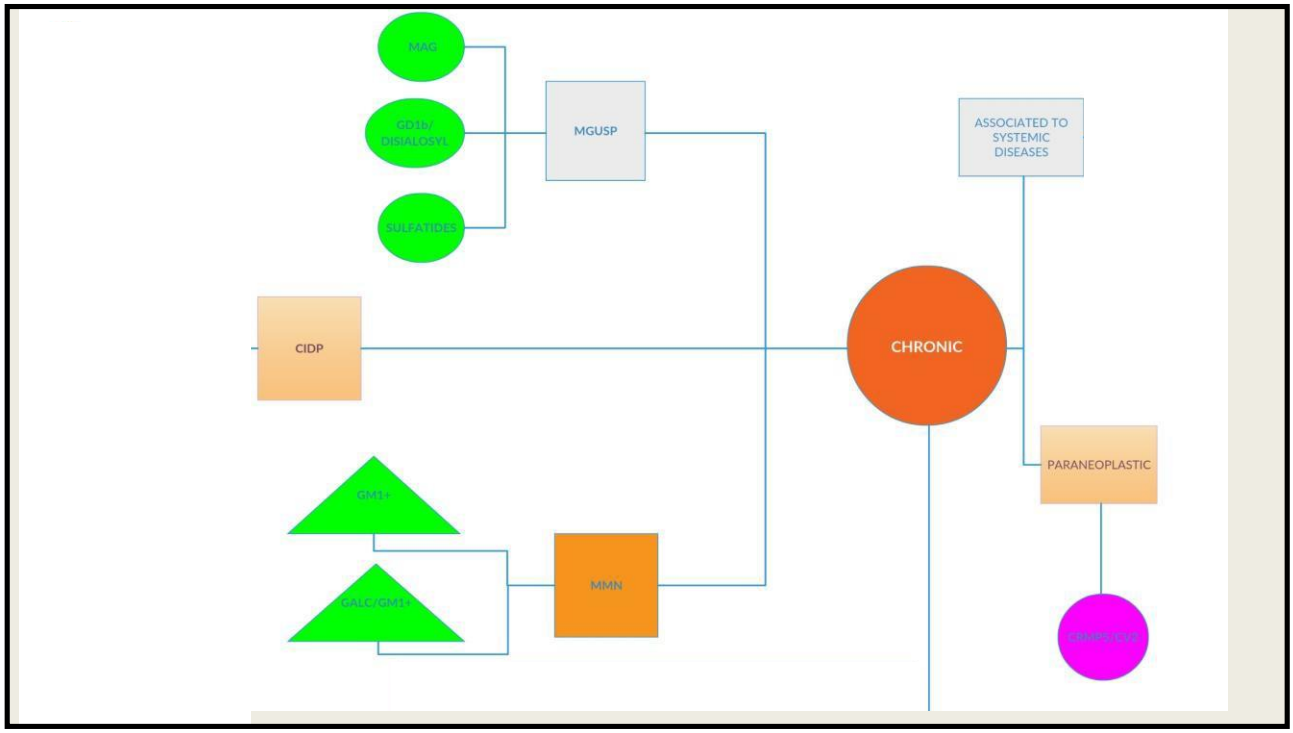
Table 1 *Clinical data*

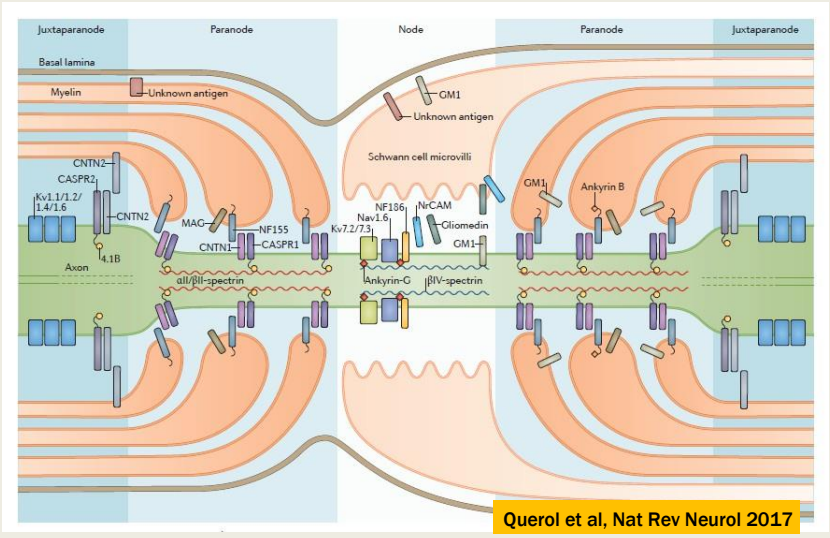
Case	Referral source*	Sex	Age at onset (years)	Duration (years)	Mode of onset	Relapses	Cranial nerve involvement			Limb involvement					
							III, IV, VI	V	VII	Bulbar	Paresis	Paraesth.	UL ataxia	LL ataxia	Gait ataxia
1	2	F	57	8	A	+ (smb)	+	+		+	+	+			
2	9	M	72	15	C						+	+	++	++	++
3	3	M	67	4	S	+ (so)	++	+		+		+	+	+	+
4	3	M	41	9	S	+ (sbo)	+	+	+	+	+	+	++	++	++
5	3	M	72	7	C		+					+	+	+	+
6	6	M	28	27	C	+ (o)	+				++	+	++	+	
7	6	F	40	7	C	+ (bo)	+	+		+	++	+	++	++	+
8	7	M	46	13	C		+	+		+	++	+	+	+	+
9	12	M	42	20	A	+ (smbor)	+			+	+	+	+	+	+
10	4	M	58	12	C		++				++		++	++	++
11	8	M	64	6	C	+ (so)	+	+			+	++	+	+	+
12	10	F	41	25	A	+ (mbor)	++	+	++	++	+	++	++	++	+
13	8	M	58	7	C	+ (s)	+					+	+	++	+
14	11	M	64	19	C	+ (smb)	+		+	+	+		+	+	++
15	6	M	42	6	C					+		+			
16	1	F	56	13	C	+ (so)	+	+		+	+		+	++	++
17	1	M	59	6	C	+ (sbo)	++		+	+	+		+	+	+
18	5	M	51	29	A	+ (smbo)	+	+		+	+	+	++	++	+

*Referral source numbered as per the list of authors. A = acute; S = subacute; C = chronic; b = bulbar; m = motor; o = ophthalmoplegia; r = respiratory; s = sensory; + = present; ++ = substantive feature.

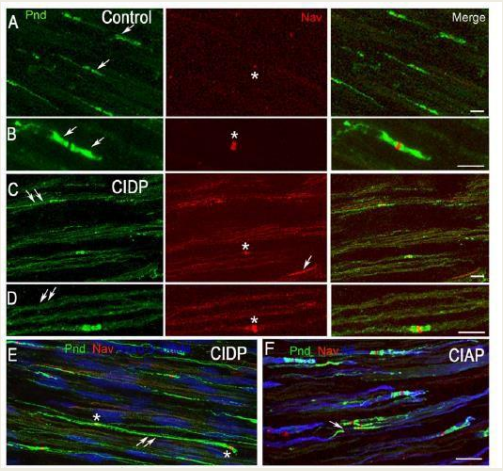
CIDP

A SYNDROME WITH MANY FACES…





Querol et al, Nat Rev Neurol 2017



Journal of the Peripheral Nervous System 18:168–176 (2013)

RESEARCH REPORT

Disruption of nodal architecture in skin biopsies of patients with demyelinating neuropathies

Kathrin Doppler, Christian Werner, and Claudia Sommer

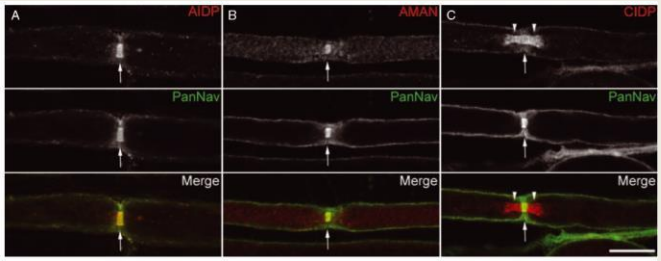
Department of Neurology, University of Würzburg, Würzburg, Germany

Control **CIDP**

RESEARCH REPORT

Nodal proteins are target antigens in Guillain-Barré syndrome

Jérôme J. Devaux[1], Masaaki Odaka[2], and Nobuhiro Yuki[3]



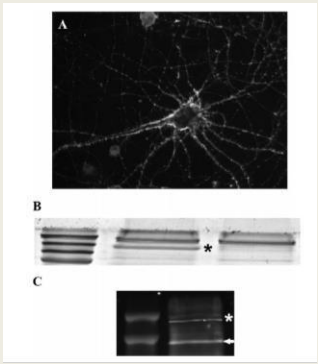
	Reactivity against						
	NF186	Gliomedin	NrCAM	Contactin	Any antigens	Only one antigen	Multiple antigens
GBS	15 (3)	12 (1)	4	12 (2)	26†	16	10
AIDP	12 (1)	14 (1)†	6	16 (2)	28*	16	12
AMAN	18 (2)†	10	2	8	24†	16	8
CIDP	12 (2)	6	2	16 (2)	24†	16	8
OND	0	1.3	0	3.8	3.8	2.5	1.3
NC	2	0	2	2	4	2	2

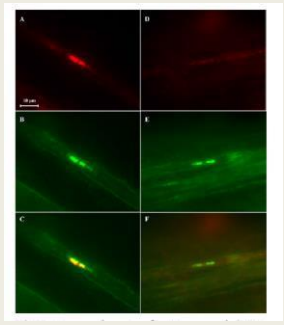
CONTACTIN-1

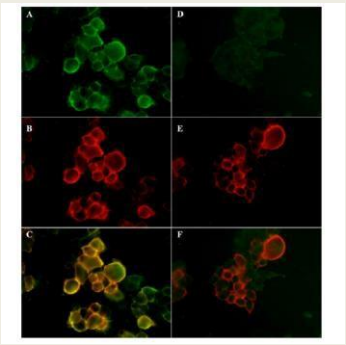
Antibodies to Contactin-1 in Chronic Inflammatory Demyelinating Polyneuropathy

Luis Querol, MD,[1,2] Gisela Nogales-Gadea, PhD,[1,2] Ricard Rojas-Garcia, MD, PhD,[1,2] Eugenia Martinez-Hernandez, MD,[1,2] Jordi Diaz-Manera, MD,[1,2] Xavier Suárez-Calvet, MSc,[1,2] Miquel Navas,[1,2] Josefa Araque, RPN,[1,2] Eduard Gallardo, PhD,[1,2] and Isabel Illa, MD, PhD[1,2]

3 patients!







CONTACTIN-1 PATIENTS

- ~~*Older*~~
  - 2 year old kid recently detected (Carrera-Garcia et al, Neurol NeuroImmunol Neuroinflammat *in press*)
- *Aggressive neuropathy - GBS misdiagnosis*
- ~~*Predominantly motor*~~
  - Very ataxic forms
- *Demyelinating features, early axonal damage*
- *Poor response to IVIg*
- *Response to plasma exchange*
- *Partial response to steroids*
- *IgG4 isotype antibodies*

doi:10.1093/brain/awv054 BRAIN 2015: Page 1 of 8 | 1

BRAIN
A JOURNAL OF NEUROLOGY

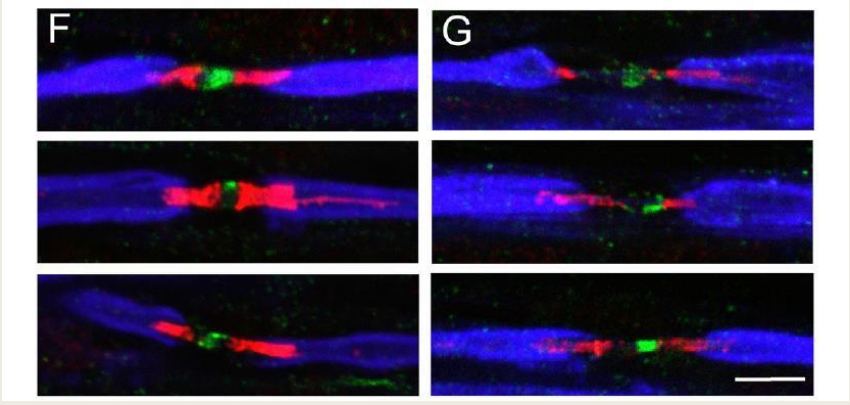
REPORT

Contactin 1 IgG4 associates to chronic inflammatory demyelinating polyneuropathy with sensory ataxia

Yumako Miura,[1,*] Jérôme J. Devaux,[2,*] Yuki Fukami,[1] Constance Manso,[2] Maya Belghazi,[2] Anna Hiu Yi Wong,[1] Nobuhiro Yuki[1,3] and for the CNTN1-CIDP Study Group[†]

CONTACTIN-1

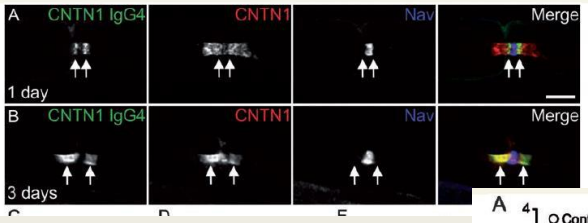
CIDP autoantibodies against contactin-1 induce paranodal alterations in myelinated DRG neurons in culture.
(DRG neuron/Schwann cell)

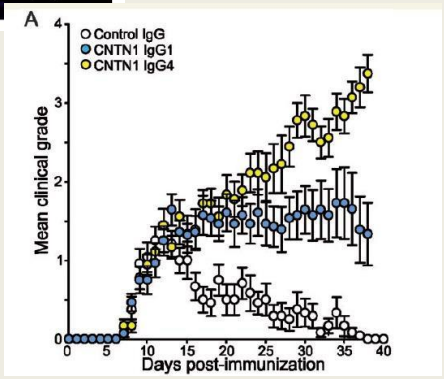


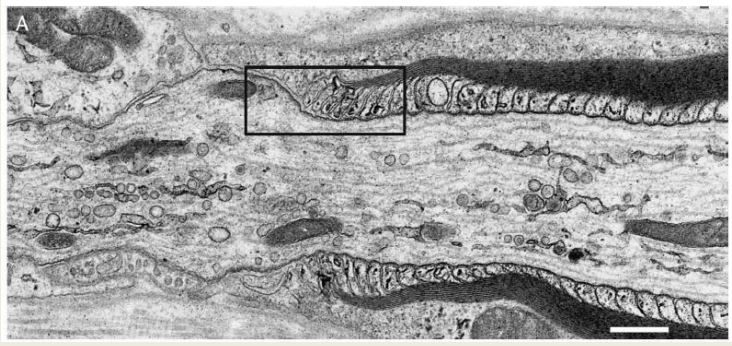
J Biol Chem 2014

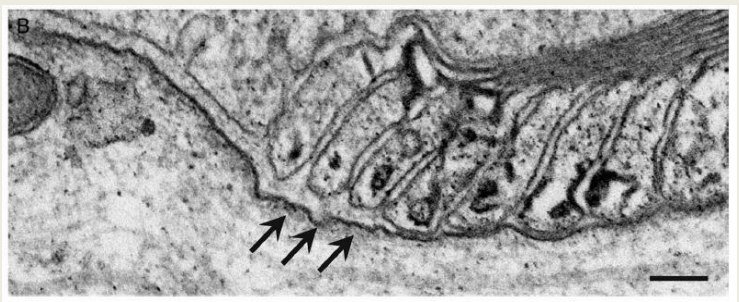
Contactin-1 IgG4 antibodies cause paranode dismantling and conduction defects

Constance Manso,[1] Luis Querol,[2] Mourad Mekaouche,[1] Isabel Illa[2] and Jérôme J. Devaux[1]









Koike et al, JNNP 2017

Neurobiology:
Specific Contactin *N*-Glycans Are Implicated in Neurofascin Binding and Autoimmune Targeting in Peripheral Neuropathies

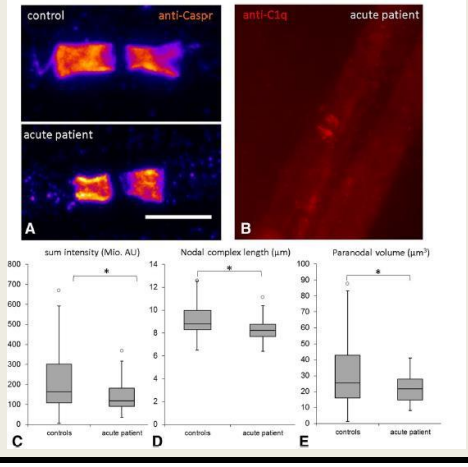
Marilyne Labasque, Bruno Hivert, Gisela Nogales-Gadea, Luis Querol, Isabel Illa and Catherine Faivre-Sarrailh
J. Biol. Chem. 2014, 289:7907-7918.

Functional disruption

RESEARCH Open Access

Anti-CNTN1 IgG3 induces acute conduction block and motor deficits in a passive transfer rat model

Kathrin Doppler[1*], Yasmin Schuster[1], Luise Appeltshauser[1], Lydia Biko[1], Carmen Villmann[2], Andreas Weishaupt[1], Christian Werner[3] and Claudia Sommer[1]



HLA ASSOCIATION

DRB1*11 (DR11):

- 53,3 % CNTN1+ patients
- 35,3 % seronegative CIDP patients
- 28,8 % general population

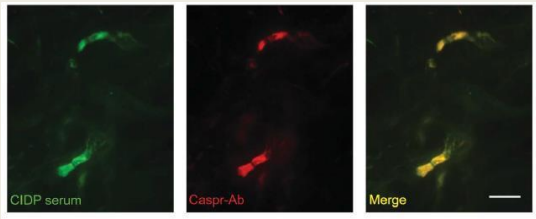
NEUROFASCIN 155

Neurology®

Neurofascin as a target for autoantibodies in peripheral neuropathies

Judy King Man Ng, Joachim Malotka, Naoto Kawakami, et al.

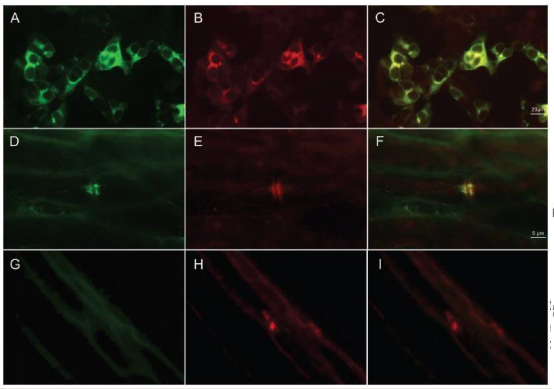
Neurology; Published online before print October 24, 2012;
DOI 10.1212/WNL.0b013e31827689ad

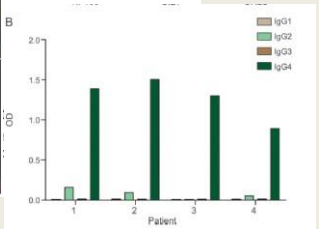


Neurofascin IgG4 antibodies in CIDP associate with disabling tremor and poor response to IVIg

Luis Querol, MD, PhD
Gisela Nogales-Gadea, PhD
Ricardo Rojas-Garcia, MD, PhD
Jordi Diaz-Manera, MD, PhD
Julio Pardo, MD, PhD
Angel Ortega-Moreno, MD
Maria Jose Sedano, MD
Eduard Gallardo, PhD
Jose Berciano, MD, PhD
Rafael Blesa, MD, PhD
Josep Dalmau, MD, PhD
Isabel Illa, MD, PhD

Correspondence to Prof. Illa: iilla@santpau.cat





ANTI-NF155 CLINICAL FEATURES

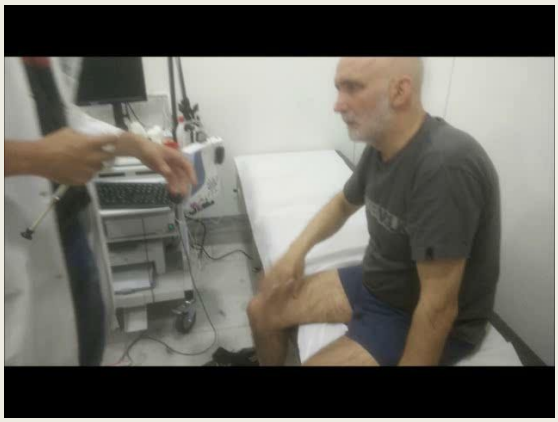
- DADS phenotype
- Ataxia
- Slow, prominent tremor (3-6Hz)
- Demyelinating EMG
- Poor response to IVIg (some may respond well to steroids)
- Response to Plasma Exchange.
- IgG4 antibodies

ANNALS of Clinical and Translational Neurology
Open Access
BRIEF COMMUNICATION

Head and voice tremor improving with immunotherapy in an anti-NF155 positive CIDP patient

Cèlia Painous[1], Mª Ángeles López-Pérez[2], Isabel Illa[1,3] & Luis Querol[1,3]

[1]Neuromuscular Diseases Unit, Department of Neurology, Hospital de la Santa Creu i Sant Pau, Universitat Autònoma de Barcelona, Barcelona, Spain
[2]Department of Neurology, Hospital San Pedro, Logroño, Spain
[3]Centro para la Investigación Biomédica en Red en Enfermedades Raras, CIBERER (Centre for Biomedical Network Research on Rare Diseases), Madrid, Spain



Published Ahead of Print on February 3, 2016 as 10.1212/WNL.0000000000002418

ARTICLES

Neurofascin-155 IgG4 in chronic inflammatory demyelinating polyneuropathy

Jérôme J. Devaux, PhD*
Yumako Miura, PhD*
Yuki Fukami, MD
Takayuki Inoue, PhD
Constance Manso, BSc
Maya Belghazi, PhD
Kenji Sekiguchi, MD, PhD
Norito Kokubun, MD, PhD
Hiroo Ichikawa, MD, PhD
Anna Hiu Yi Wong, MRCP
Nobuhiro Yuki, MD, PhD

Correspondence to Prof. Yuki:

ABSTRACT

Objective: We report the clinical and serologic features of Japanese patients with chronic inflammatory demyelinating polyneuropathy (CIDP) displaying anti-neurofascin-155 (NF155) immunoglobulin G4 (IgG4) antibodies.

Methods: In sera from 533 patients with CIDP, anti-NF155 IgG4 antibodies were detected by ELISA. Binding of IgG antibodies to central and peripheral nerves was tested.

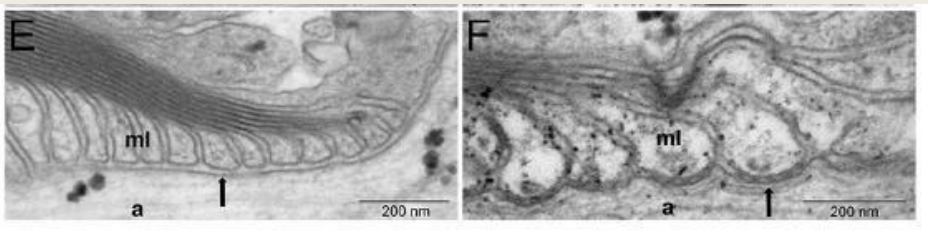
Results: Anti-NF155 IgG4 antibodies were identified in 38 patients (7%) with CIDP, but not in disease controls or normal participants. These patients were younger at onset as compared to 100 anti-NF155–negative patients with CIDP. Twenty-eight patients (74%) presented with sensory ataxia, 16 (42%) showed tremor, 5 (13%) presented with cerebellar ataxia associated with nystagmus, 3 (8%) had demyelinating lesions in the CNS, and 20 of 25 (80%) had poor response to IV immunoglobulin. The clinical features of the antibody-positive patients were statistically more frequent as compared to negative patients with CIDP (n = 100). Anti-NF155 IgG antibodies targeted similarly central and peripheral paranodes.

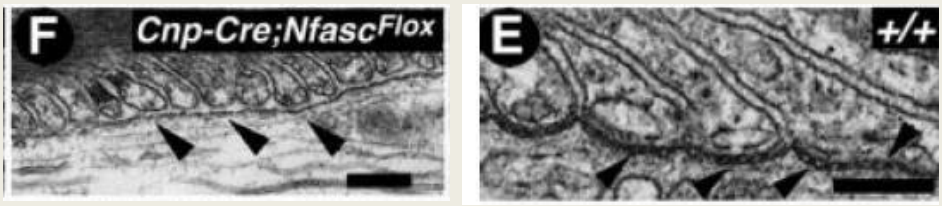
Conclusion: Anti-NF155 IgG4 antibodies were associated with a subgroup of patients with CIDP showing a younger age at onset, ataxia, tremor, CNS demyelination, and a poor response to IV immunoglobulin. The autoantibodies may serve as a biomarker to improve patients' diagnosis and guide treatments. *Neurology*® 2016;86:1-8

Short communication

Paranodal lesions in chronic inflammatory demyelinating polyneuropathy associated with anti-Neurofascin 155 antibodies

Jean-Michel Vallat [a,*], Nobuhiro Yuki [b], Kenji Sekiguchi [c], Norito Kokubun [d], Nobuyuki Oka [e], Stéphane Mathis [f], Laurent Magy [a], Diane L. Sherman [g], Peter J. Brophy [g], Jérôme J. Devaux [h]





Martinez-Martinez *et al. Journal of Neuroinflammation* (2017) 14:224
DOI 10.1186/s12974-017-0996-1

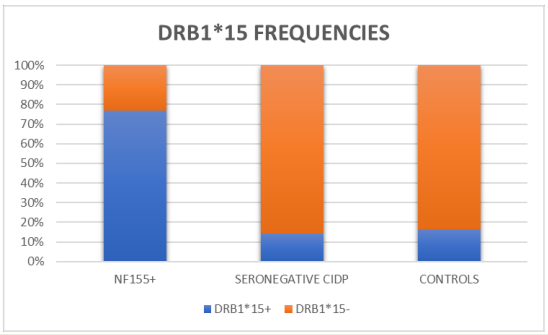
Journal of Neuroinflammation

RESEARCH Open Access

Anti-NF155 chronic inflammatory demyelinating polyradiculoneuropathy strongly associates to HLA-DRB15

Laura Martinez-Martinez[1], Ma. Cinta Lleixà[2,3], Gemma Boera-Carnicero[1], Andrea Cortese[4,5], Jérôme Devaux[6], Ana Siles[2,3], Yusuf Rajabally[7], Alicia Martinez-Piñeiro[8], Alejandra Carvajal[9], Julio Pardo[10], Emilien Delmont[6,11], Shahram Attarian[11], Jordi Diaz-Manera[2,3], Ilaria Callegari[4,12], Enrico Marchioni[4], Diego Franciotta[4], Luana Benedetti[13], Guiseppe Lauria[14,15], Oscar de la Calle Martin[1], Cándido Juárez[1], Isabel Illa[2,3] and Luis Querol[2,3]*

A



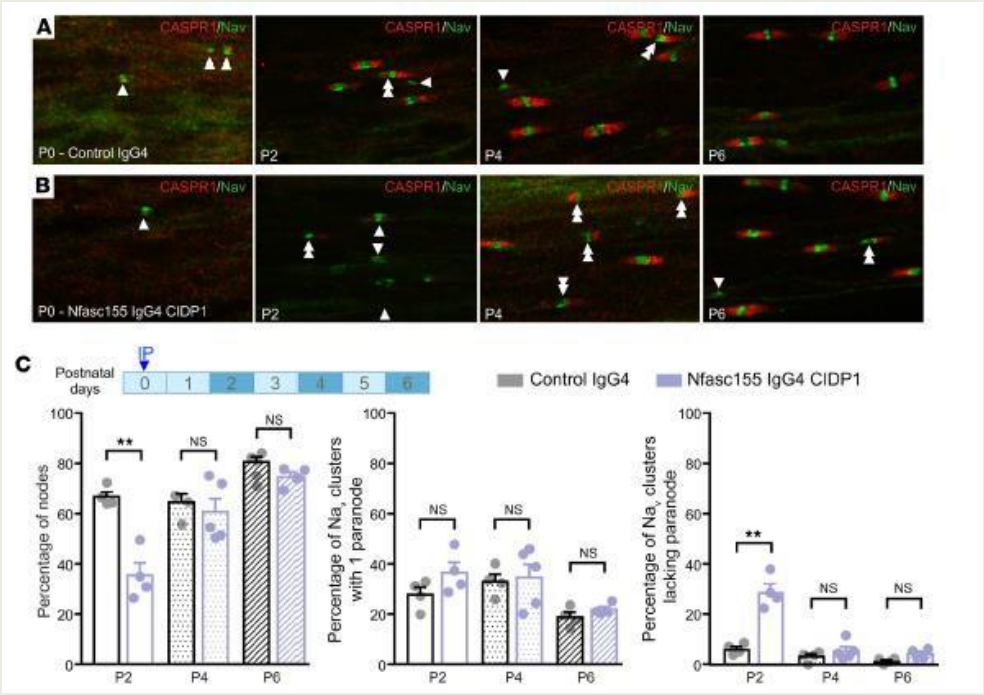
The Journal of Clinical Investigation

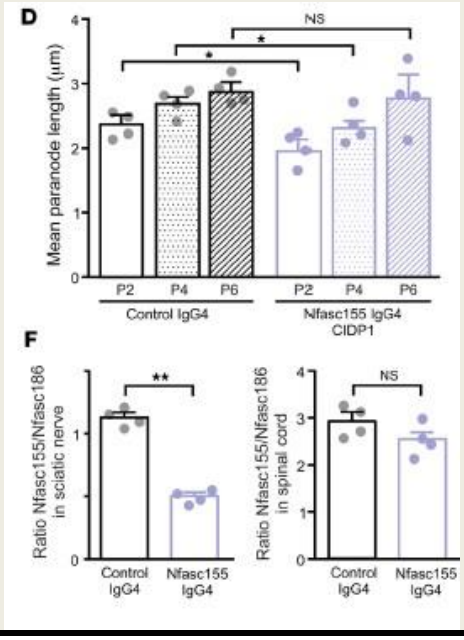
RESEARCH ARTICLE

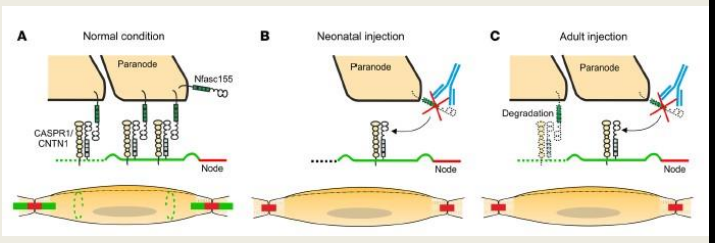
Anti–neurofascin-155 IgG4 antibodies prevent paranodal complex formation in vivo

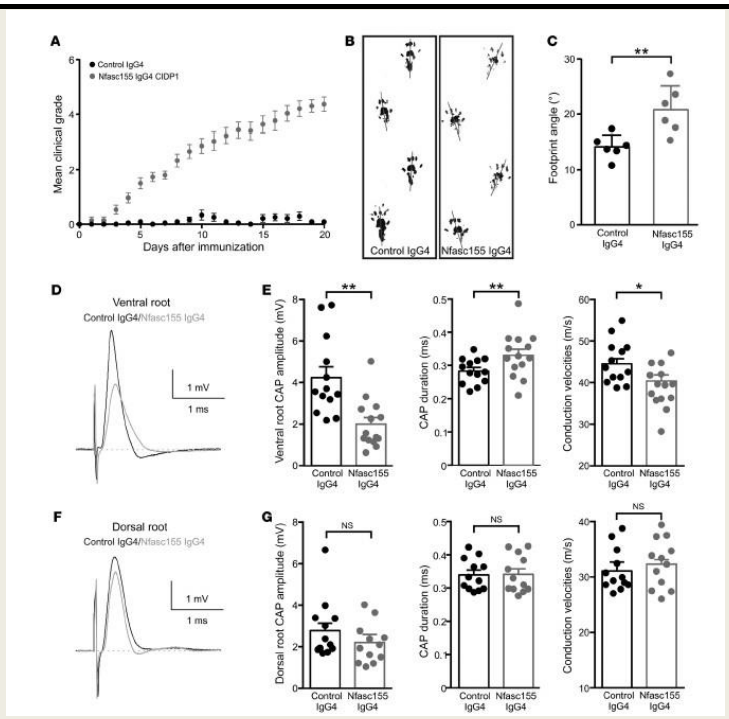
Constance Manso,[1,2] Luis Querol,[3,4] Cinta Lleixà,[3,4] Mallory Poncelet,[5] Mourad Mekaouche,[1,6] Jean-Michel Vallat,[7] Isabel Illa,[3,4] and Jérôme J. Devaux[1,5]

[1]Aix Marseille Université, CNRS, CRN2M-UMR7286, Marseille, France. [2]Université de Bordeaux, Interdisciplinary Institute for Neuroscience, UMR5297, Bordeaux, France. [3]Neuromuscular Diseases Unit, Hospital de la Santa Creu i Sant Pau, Universitat Autònoma de Barcelona, Barcelona, Spain. [4]Centro para la Investigación en Red en Enfermedades Raras (CIBERER), Madrid, Spain. [5]Institute for Neurosciences of Montpellier, INSERM U1051, Montpellier University, Hopital Gui de Chauliac, Montpellier, France. [6]Aix Marseille Université, CNRS, INP UMR7051, Marseille, France. [7]National Reference Center for "rare peripheral neuropathies" and Department of Neurology, University Hospital, Limoges, France.


A
CASPR1/Nav
P0 - Control IgG4
P2
P4
P6
B
P0 - Nfasc155 IgG4 CIDP1
C
IP
Postnatal days
0 1 2 3 4 5 6
Control IgG4
Nfasc155 IgG4 CIDP1
Percentage of nodes
Percentage of Na+ clusters with 1 paranode
Percentage of Na+ clusters lacking paranode
**
NS


D
Mean paranode length (µm)
NS
*
Control IgG4
Nfasc155 IgG4 CIDP1
F
Ratio Nfasc155/Nfasc186 in sciatic nerve
Ratio Nfasc155/Nfasc186 in spinal cord
Control IgG4
Nfasc155 IgG4


A
Normal condition
B
Neonatal injection
C
Adult injection
Paranode
Nfasc155
CASPR1/ CNTN1
Degradation
Node



Unpublished

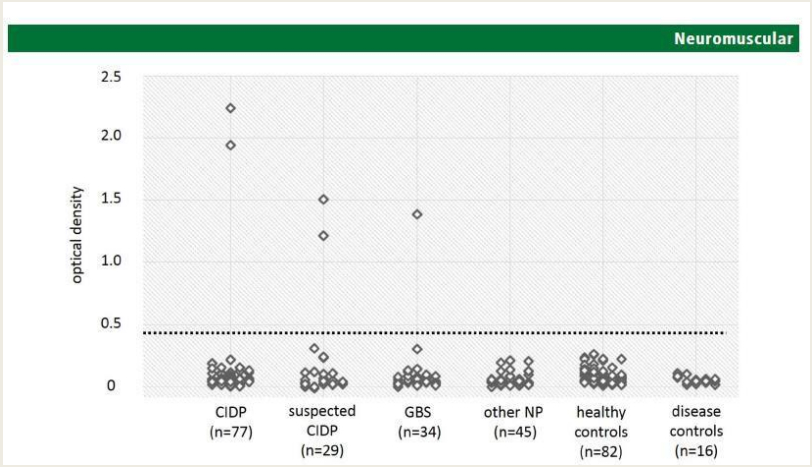
Neuromuscular

RESEARCH PAPER

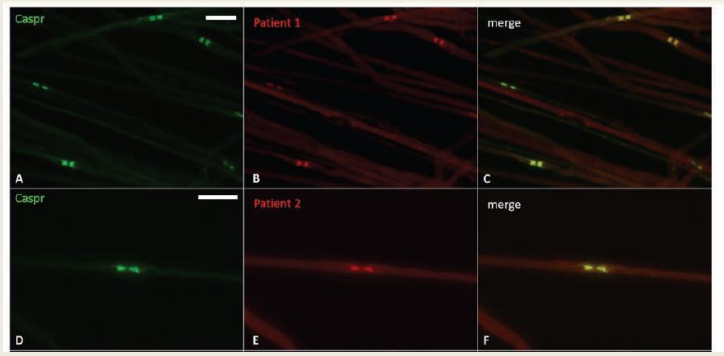
Neurofascin-155 IgM autoantibodies in patients with inflammatory neuropathies

Kathrin Doppler,[1] Helena Stengel,[1] Luise Appeltshauser,[1] Julian Grosskreutz,[2] Judy King Man Ng,[3] Edgar Meinl,[3] Claudia Sommer[1]

Neuromuscular



CNTN1/CASPR1 COMPLEX



CNTN1/CASPR1 COMPLEX PATIENTS

CBA	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8
CNTN1	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative
Caspr1	Negative	Positive	Positive	Positive	Positive	Negative	Negative	Positive
CNTN1/Caspr1	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive

CNTN1/CASPR1 COMPLEX PATIENTS

Clinical features	
Sex Age	5 male; 3 females 40-75
Onset	3 acute; 3 subacute; 2 chronic
Initial diagnosis	GBS 5; CIDP 3
CIDP category	Typical 7; DADS 1
Median mRs (blood sampling)	4
First symptoms	Pain 2; Sensory-motor 6
Weakness and sensory	Symmetric 6; Asymmetric 2 Proximal and distal weakness 6; distal 2 Altered sensation in all limbs 8
Tremor	5
Ataxia	5
Cranial nerves	Ophthalmoparesis 2; facial weakness 1
Pain	4
Nephropathy	Nephrotic syndrome 1; Mild proteinuria 1

CNTN1/CASPR1 COMPLEX PATIENTS

Neurophysiological studies	
EFNS/PNS definite diagnostic criteria for CIDP	8
Demielinating	8
Acute denervation	4
Investigations	
CSF Protein levels	Elevated 7; NA 1
MRI lumbar roots	Nerve root enhancement 3; NA 5
Nerve biopsy	Moderate axonal loss, rare inflammatory cells 2; NA 6

Treatment Response	No response	Partial	Good	Not done
IVIG	2	6	0	0
Steroids	3	3	1	1
Plasma Exchange	2	3	0	3
Rituximab	0	2	5	1
Cyclophosphamide	2	0	0	6
ASCT	0	1	0	7

ASCT: Autologous stem-cell transplantation; CMAPs: Compound Muscle Action Potential; **IVIG: Intravenous Immunoglobulin;** NA: Not Available; NR: No Response; SNAP: sensory nerve action potential

NODAL NEUROFASCIN

NF140/NF186

PAN-NEUROFASCIN

NERVE IHC IN NF140/NF186 ANTIBODIES

Table 1 Clinical features of patients with anti-Nfasc140/186 IgG

	CIDP1	CIDP2	CIDP3	CIDP4	CIDP5
Gender	M	F	M	M	F
Age at onset	61	70	2	75	50
Previous infection	Sore throat and bronchitis	Infection	No	No	No
Other dysimmune disease	Anti Ro/SSA	RPF	No	FSGS	FSGS
Onset	Subacute	Subacute	Subacute	Chronic	Subacute
Sensory ataxia	Yes	Yes	No	Yes	Yes
Neuropathic pain	No	No	No	No	No
Cranial nerve involvement	Yes	No	No	No	Yes
Modified Rankin Scale	5	4	4	4	5
Tremor	No	No	No	No	No
Respiratory failure	Yes	No	No	No	Yes
Intensive care unit	Yes	No	No	No	Yes

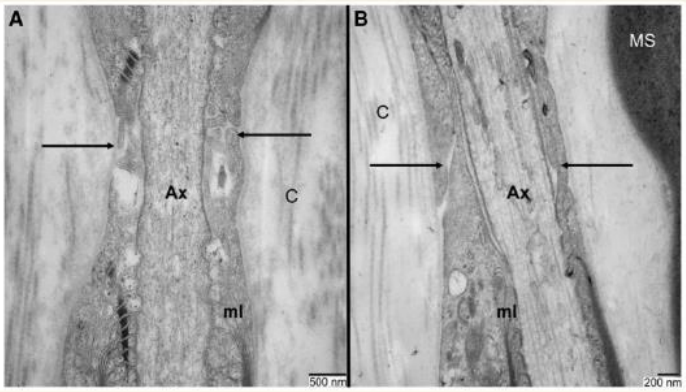
doi:10.1093/brain/awy134 BRAIN 2018: 0; 1–4 | e1

BRAIN
A JOURNAL OF NEUROLOGY

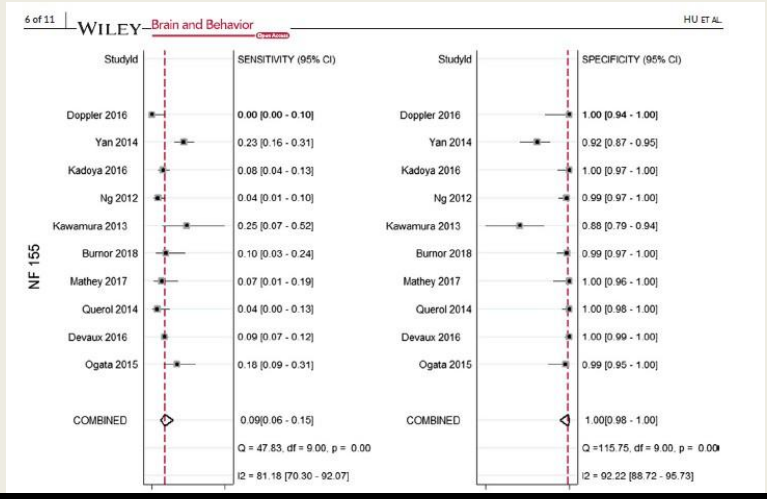
LETTER TO THE EDITOR

Subacute nodopathy with conduction blocks and anti-neurofascin 140/186 antibodies: an ultrastructural study

Jean-Michel Vallat,[1] Stéphane Mathis,[2] Laurent Magy,[1] Pierre Bounolleau,[3] Marie Skarzynski,[4] Anne Heitzmann,[5] Constance Manso,[6] Jérôme Devaux[7] and Antonino Uncini[8]



CONTROVERSIAL ISSUES



	NF155	NF 186	CNTN1
Sensitivity (95% CI)	0.09 (0.06–0.15)	0.01 (0–0.05)	0.05 (0.03–0.08)
Specificity (95% CI)	1.00 (0.98–1.00)	1.00 (0.91–1.00)	1.00 (0.93–1.00)
PLR (95% CI)	21.5 (5.5–83.8)	5.2 (0.3–94.4)	26.3 (0.5–1,260.9)
NLR (95% CI)	0.91 (0.87–0.95)	0.99 (0.98–1.00)	0.96 (0.93–0.98)
DOR (95% CI)	8.21 (3.57–18.89)	0.86 (0.06–13.24)	4.63 (2.01–10.71)
AUC (95% CI)	0.41 (0.37–0.45)	0.10 (0.08–0.13)	0.17 (0.14–0.21)
Publication bias	0.07	0.74	0.21

nti

G

O.D. value (450 nm)

NEUROFASCIN-155 AS A PUTATIVE ANTIGEN IN COMBINED CENTRAL AND PERIPHERAL DEMYELINATION

Andrea Cortese, MD
Jérôme J. Devaux, PhD
Elisabetta Zardini, MSc
Constance Manso, BSc
Guillaume Taieb, MD
Clarisse Carra Dallière, MD
Philippe Merle, MD
Cecilia Osera, PhD
Silvia Romagnolo, BSc
Nicolò Visigalli, MD
Giuseppe Piscosquito, MD
Ettore Salsano, MD
Enrico Alfonsi, MD
Arrigo Moglia, MD
Davide Pareyson, MD
Enrico Marchioni, MD
Diego Franciotta, MD

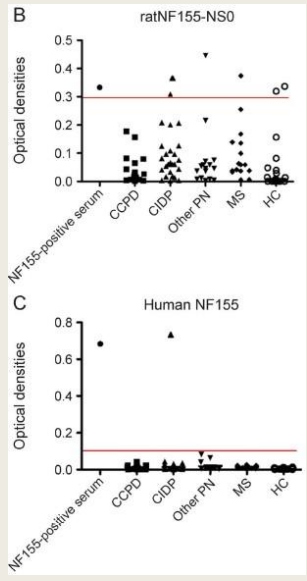


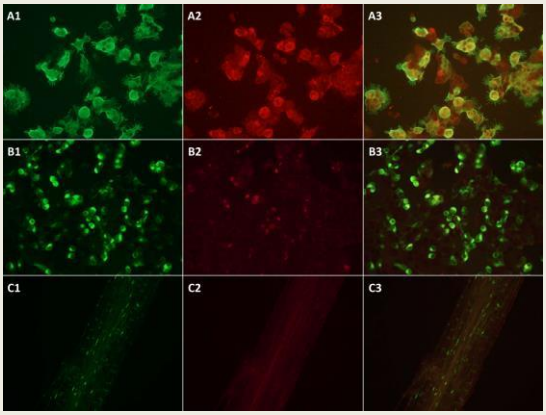
Table 2 IgG1 through IgG4 subclasses of IgG-positive patients

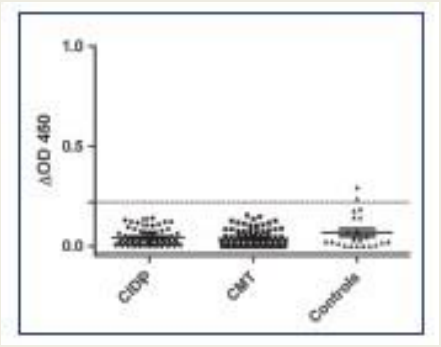
Case	Diagnosis	Isoform reactivity and titer	IgG subtype (if IgG present and strong enough to subtype)
1	CIDP	NF155 IgG and IgM 1:200	Predominantly IgG4; also detected IgG1 and IgG2
2	CIDP	NF155 IgG 1:800; NF186 IgG 1:1,600	Predominantly IgG4; also detected IgG1 and IgG2
3	CIDP	NF155 IgG 1:1,600	Predominantly IgG4; also detected minimal IgG1 and IgG2
4	CIDP	NF155 IgG 1:3,200	Detected IgG1, IgG2, and IgG4
5	CIDP	NF186 IgM 1:1,600	—
6	GBS	NF155 IgM 1:3,200	—
7	AMAN	NF186 IgM 1:1,600	—
8	GBS	NF186 IgM 1:3,200	—
9	Idiopathic neuropathy	NF155 IgM 1:400	—
10	Idiopathic Neuropathy	NF186 IgG 1:800	Detected minimal IgG4
11	Idiopathic neuropathy	NF186 IgM 1:800	—
12	CMT	NF155 IgM 1:200	—
13	CMT	NF155 IgG 1:3,200	Predominantly IgG1, No IgG2, IgG3, or IgG4 detected
14	CMT	NF155 IgM 1:100	—

Detection of IgG and IgM antibodies against nodo-paranodal proteins in CMT and CIDP

Lorena Martín-Aguilar[1], Elba Pascual-Goñi[1], Cinta Lleixà[1], Marina Frasquet[3], Herminia Argente[3], Angel Cano-Abascal[4], Jordi Diaz-Manera[1,2], Elena Cortés-Vicente[1], Ricard Rojas-García[1,2], Ana Lara Pelayo[4], Teresa Sevilla[3], Luis Querol[1,2]

HOSPITAL DE LA SANTA CREU I SANT PAU
UNIVERSITAT AUTÒNOMA DE BARCELONA





Contents lists available at ScienceDirect

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journal homepage: www.elsevier.com/locate/ensci

Case report

Presence of both anti-contactin 1 and anti-neurofascin 140 antibodies in a case of chronic inflammatory demyelinating polyneuropathy

Hsin-Pin Lin, Kwo Wei David Ho, Miguel Chuquilin*

Department of Neurology, University of Florida, Gainesville, FL 32610, United States

Neurofascin 140 and 155 antibodies in an atypical case of POEMS syndrome

Torge Rempe, MD[1]†, Kwo Wei David Ho, MD, PhD[1]†, Mohammad Shahid, MBBS, MD[2], Li-Jun Yang, MD[2], Miguel Chuquilin, MD[1]*

[1]Dept. of Neurology, [2]Pathology, Immunology and Laboratory Medicine

University of Florida, 1600 SW Archer Rd, Gainesville, FL 32610

OTHER AUTOANTIBODIES

GM1
MAG
CRMP5

Patient ID	Results
7	sulfatides IgM 1/31356
	sulfatides IgG 1/832
22	IgM aGM1 1/500
24	sulfatides IgM 1/592
31	IgG GM1 1/6160
	IgM GM1 1/2314
	IgM aGM1 1/1442
	IgM GD1b1/500
32	IgG aGM1 1/580
36	IgM GM1 1/2154
39	IgG aGM1 1/528
	IgG GD1a 1/528
	IgM aGM1 1/2559
	sulfatides IgM 1/3245
	sulfatides IgG 1/831
55	sulfatides IgM 1/800
	IgM aGM1 1/500
56	IgG aGM1 1/1000
	IgM GM1 1/500
64	IgM GM1 > 1/12500
	IgM aGM1 > 1/12500
	IgM GD1b > 1/12500
65	IgM GM1 1/7829
	IgM aGM1 1/2359
	IgM GD1b 1/2868

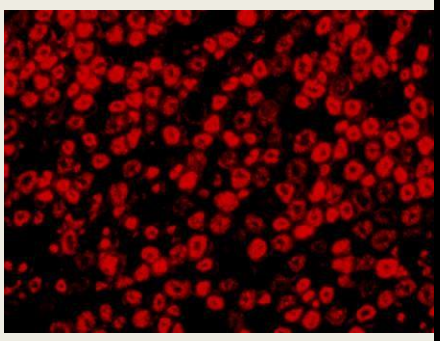
SCIENTIFIC REPORTS

OPEN

Clinical and laboratory features of anti-MAG neuropathy without monoclonal gammopathy

ived: 31 January 2019
pted: 2 April 2019
ished online: 16 April 2019

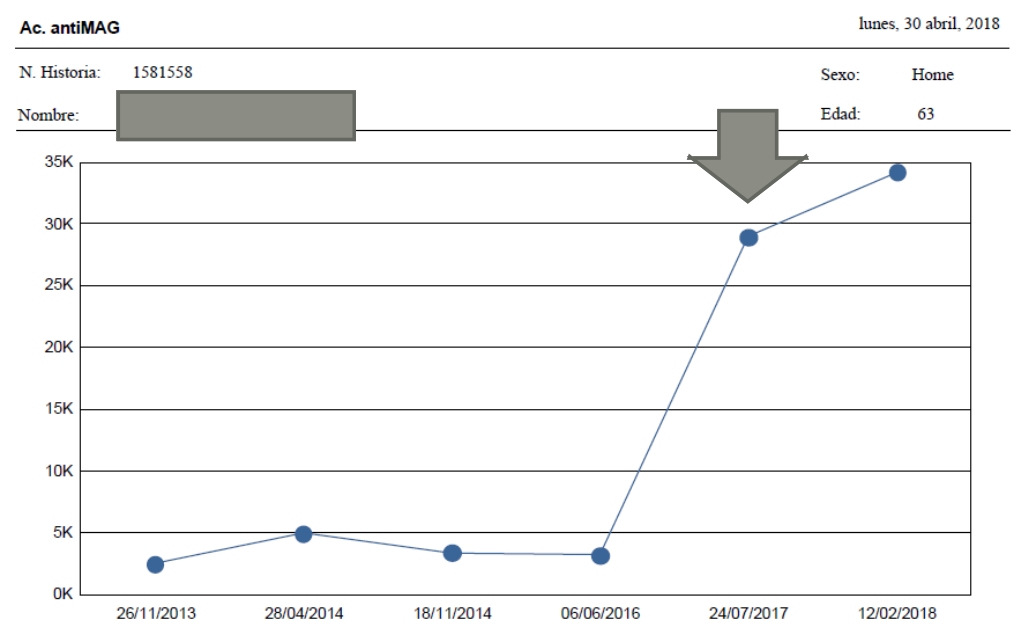
Elba Pascual-Goñi[1], Lorena Martín-Aguilar[1], Cinta Lleixà[1], Laura Martínez-Martínez[1], Manuel J. Simón-Talero[3], Jordi Díaz-Manera[1,2], Elena Cortés-Vicente[1,2], Ricard Rojas-García[1,2], Esther Moga[1], Cándido Juárez[1], Isabel Illa[1,2] & Luis Querol[1,2]



CONTROL

PRE
(1800 BU)

POST



- 43 years old woman
- Neuropathy fulfilling CIDP diagnostic criteria
- Invasive thymoma
- Multiple autoinmune syndromes
  - *Alopecia*
  - *Hashimoto*
  - *Lupus (with nephropathy)*
- Autoantibodies (in the absence of symptoms)
  - *Anti-AChR*
  - *Anti-CASPR2*

- 50 years old male
- Initially diagnosed as GBS (one month progression of weakness)
- Response to IVIg and relapse
  - *CIDP*
- Anti-CRMP5 antibodies detected in our screening
- Thymoma

2.8%

5.7%

1.4%

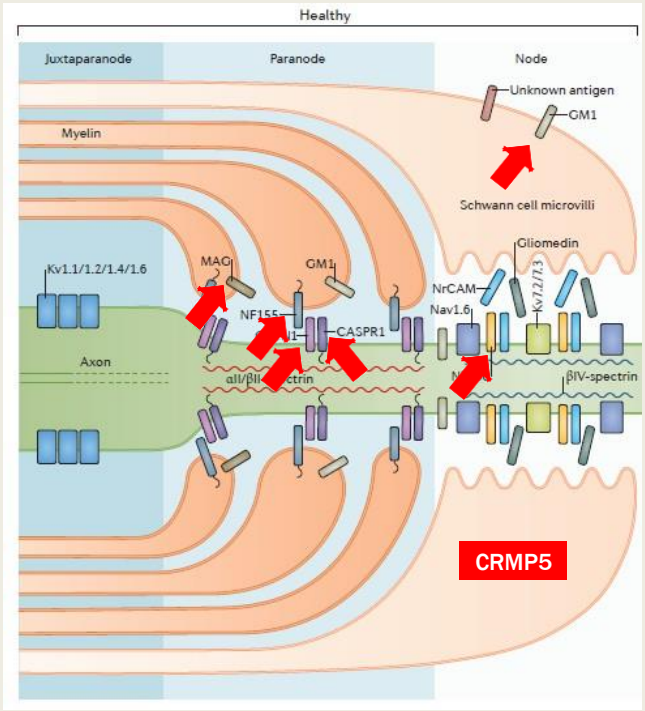
1.4%

5.7%

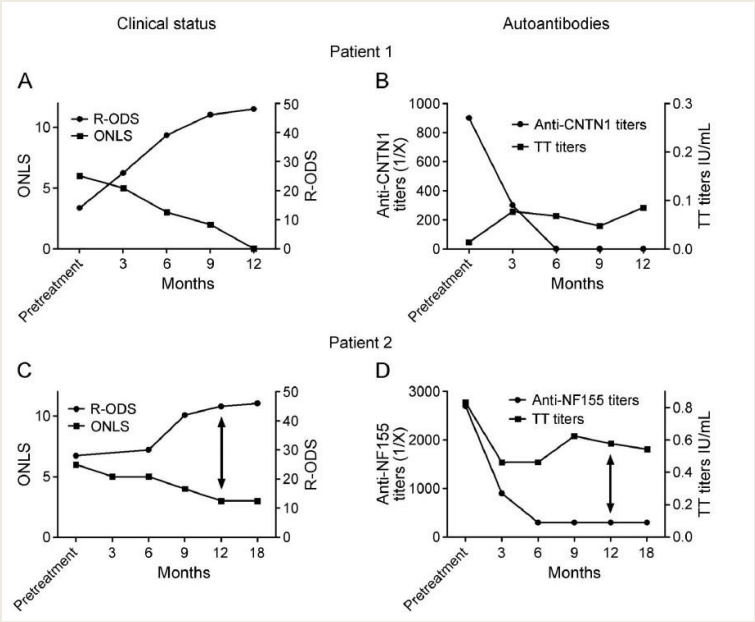
5.7%

2.8%

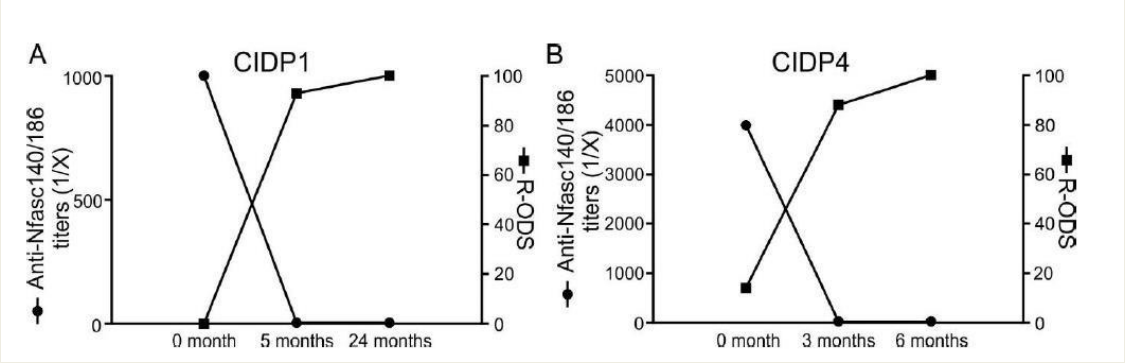
25%

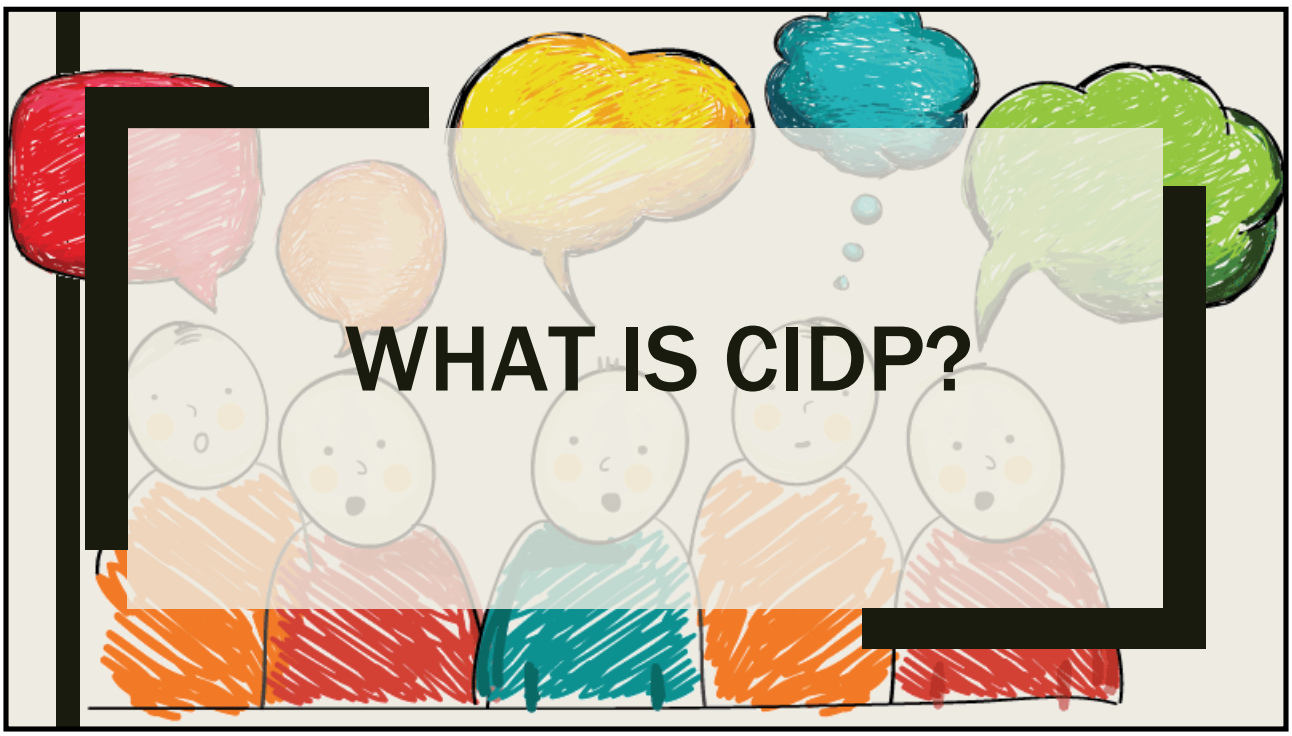


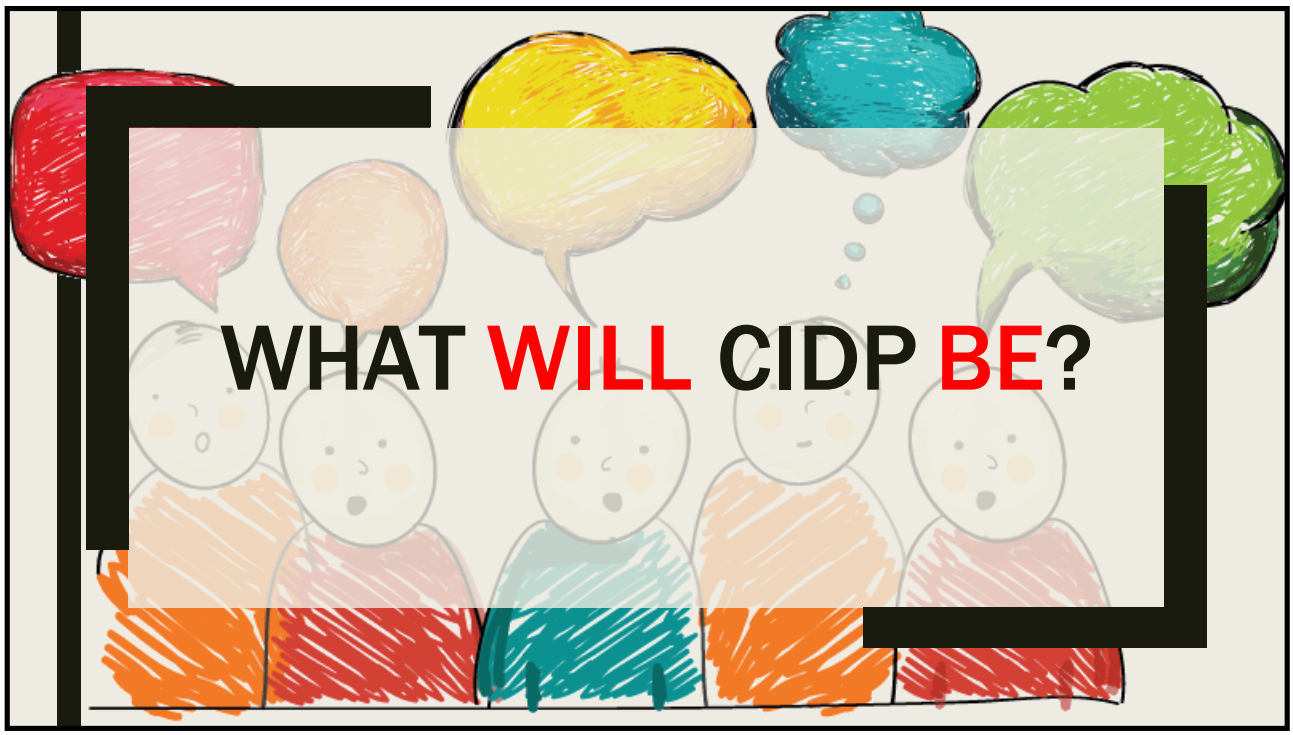
IMPLICATIONS FOR THERAPY

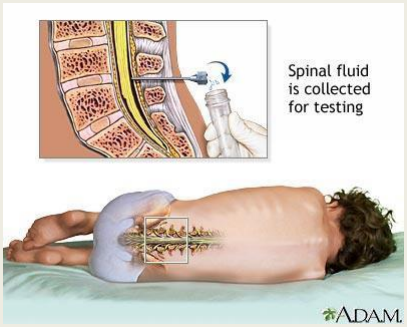

Clinical status
Autoantibodies
Patient 1
A
B
R-ODS
ONLS
Anti-CNTN1 titers
TT titers
Anti-CNTN1 titers (1/X)
TT titers IU/mL
Pretreatment
Months
Patient 2
C
D
Anti-NF155 titers
TT titers
Anti-NF155 titers (1/X)

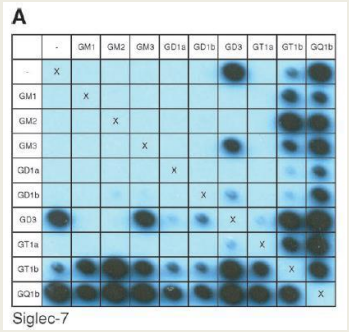
NF140


A
CIDP1
B
CIDP4
Anti-Nfasc140/186 titers (1/X)
R-ODS
0 month
5 months
24 months
3 months
6 months


WHAT IS CIDP?


WHAT WILL CIDP BE?


Spinal fluid
is collected
for testing
A.D.A.M.


A
-
GM1
GM2
GM3
GD1a
GD1b
GD3
GT1a
GT1b
GQ1b
Siglec-7

INC BASE

IN SUMMMARY…

- Inflammatory neuropathies are frequently caused by pathogenic autoantibodies
- Autoantibody detection has led to the discovery of novel syndromes, risk factors or pathological features
- Testing these autoantibodies has diagnostic, prognostic and therapeutic implications
- Technical precision and the use of confirmatory assays is crucial to avoid insensitive or unspecific findings that may lead to diagnostic errors or poor therapeutic choices

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