II Simposio Multidisciplinar

Enfermedades Autoinmunes Sistémicas

#multiEAS

Madrid

20-21 enero 2023

NH COLLECTION EUROBUILDING

AEDV Academia Española de Dermatología y Venereología

SEMI Sociedad Española de Medicina Interna

SEI Sociedad Española de Inmunología

Sociedad Española de Nefrología

Sociedad Española de Neumología y Cirugía Torácica SEPAR

Sociedad Española de Reumatología

SEPD Sociedad Española de Patología Digestiva

Papel del TIF-1γ en la relación entre autoinmunidad y cáncer en dermatomiositis

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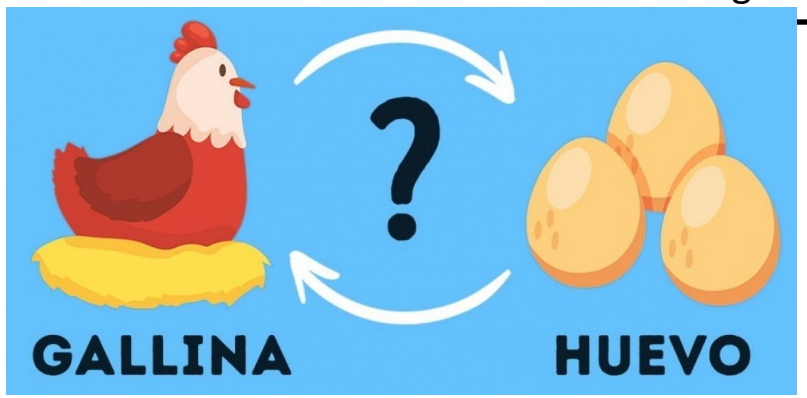
HOSPITAL DE LA SANTA CREU I SANT PAU
UNIVERSITAT AUTÒNOMA DE BARCELONA

Declaración conflictos de intereses

Declaro no tener conflictos de intereses para la realización de esta presentación

AUTOINMUNIDAD Y CÁNCER

ENFERMEDAD AUTOINMUNE	CÁNCER ASOCIADO	STANDARIZED INCIDENCE RATIOS
Dermatomiositis (DM)	Ovario, estómago, pulmón, páncreas, colorectal, mama, linfomas…	3 – 7.7
Esclerosis sistémica (ES)	Pulmón, mama, hematológicos, esófago, orofaringe, piel, cérvix, hígado, vejiga.	1.4 – 3.2
Artritis reumatoide (AR)	Leucemias, linfomas.	1.9 – 2.7
Lupus eritematoso (LES)	Linfoma no Hodking Hematológicos	3.64 2.75



En un proceso autoinmune, la **inflamación crónica** puede desencadenar una **transformación maligna**.

Una **respuesta inmunitaria antitumoral** puede originar una respuesta cruzada y generar un **proceso autoinmune**.

Shah et al. Arthritis and Rheumatology **2015** 67(2) 317-326
Hashefi et al. *Rheum. Dis. Clin. North Am.* **2018**, *44*, 405–418

MIOSITIS ASOCIADA A CÁNCER (CAM)

1. Dermatomiositis High
2. Polimiositis Moderate
3. Miopatía necrotizante inmunomediada Moderate
4. Miositis por cuerpos de inclusión Low
5. Síndrome antisintetasa Low

Factores de riesgo

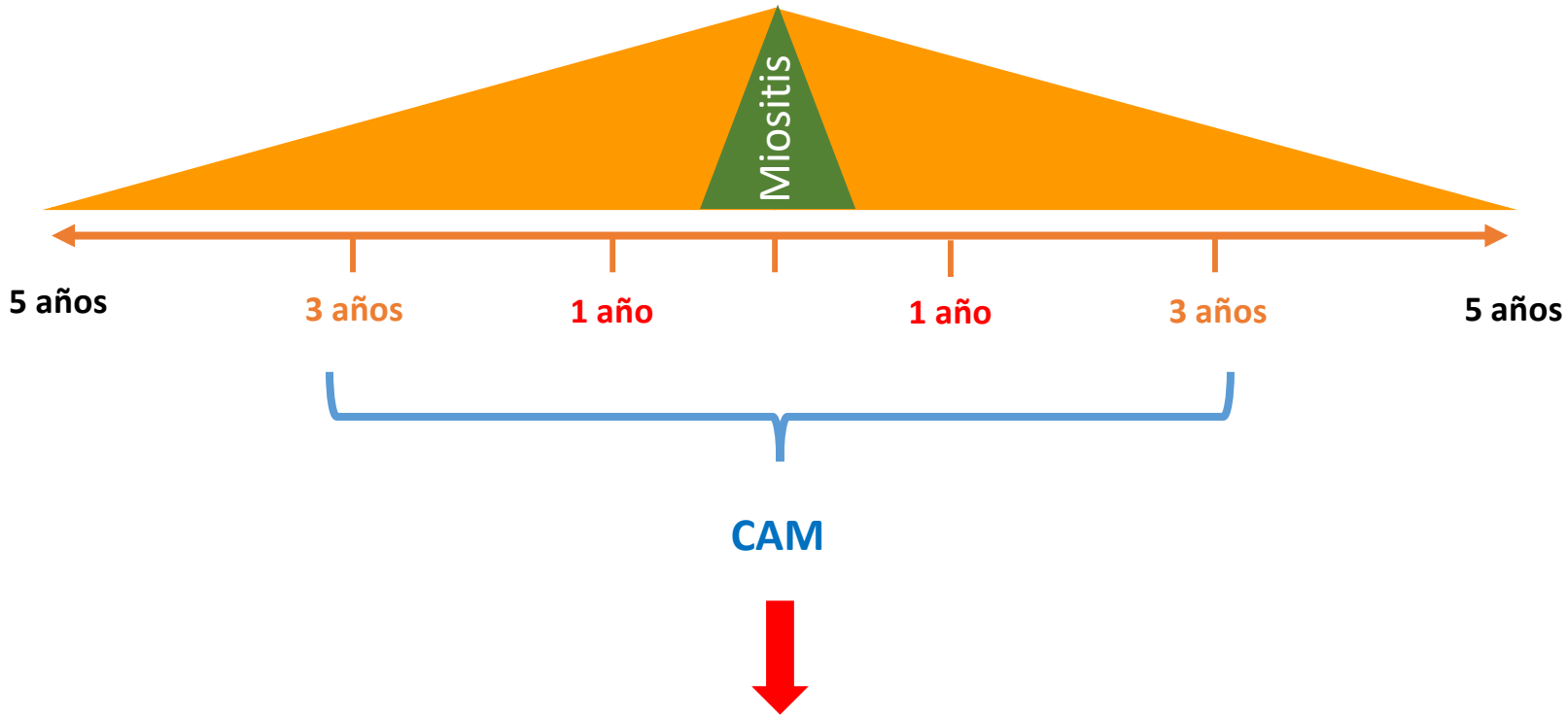
- Mayor edad de aparición de la miositis.
- Sexo varón.
- Necrosis cutánea, ulceración y vasculitis leucocitoclástica.
- Disfagia.
- Enfermedad grave y refractaria.

Factores protectores

- EPI.
- Fenómeno de Raynaud.
- Artritis/artralgia.
- CK y LDH elevadas.

Kardes et al. *Best Practice and Research: Clinical Rheumatology*, **2022**, *36*(2), 101771.

MIOSITIS ASOCIADA A CÁNCER (CAM)



El cáncer es la **principal causa de muerte** en adultos con dermatomiositis → **identificar biomarcadores** para CAM

Kardes et al. *Best Practice and Research: Clinical Rheumatology*, **2022** *36*(2), 101771.

ARTHRITIS & RHEUMATISM
Vol. 54, No. 11, November 2006, pp 3682–3689
DOI 10.1002/art.22164
© 2006, American College of Rheumatology

A Novel Autoantibody to a 155-kd Protein Is Associated With Dermatomyositis

Ira N. Targoff,[1] Gulnara Mamyrova,[2] Edward P. Trieu,[3] Osvaldo Perurena,[4] Bhanu Koneru,[2] Terrance P. O'Hanlon,[2] Frederick W. Miller,[2] and Lisa G. Rider,[2] for the Childhood Myositis Heterogeneity and International Myositis Collaborative Study Groups

2006 2007 2012

Rheumatology 2007;46:25–28
Advance Access publication 25 May 2006
doi:10.1093/rheumatology/kel161

Concise Report

Identification of a novel autoantibody reactive with 155 and 140 kDa nuclear proteins in patients with dermatomyositis: an association with malignancy

K. Kaji, M. Fujimoto, M. Hasegawa, M. Kondo, Y. Saito, K. Komura, T. Matsushita, H. Orito, Y. Hamaguchi, K. Yanaba[1], M. Itoh[1], Y. Asano[2], M. Seishima[3], F. Ogawa[4], S. Sato[4] and K. Takehara

ARTHRITIS & RHEUMATISM
Vol. 64, No. 2, February 2012, pp 523–532
DOI 10.1002/art.33379
© 2012, American College of Rheumatology

Usefulness of Anti-p155 Autoantibody for Diagnosing Cancer-Associated Dermatomyositis

A Systematic Review and Meta-Analysis

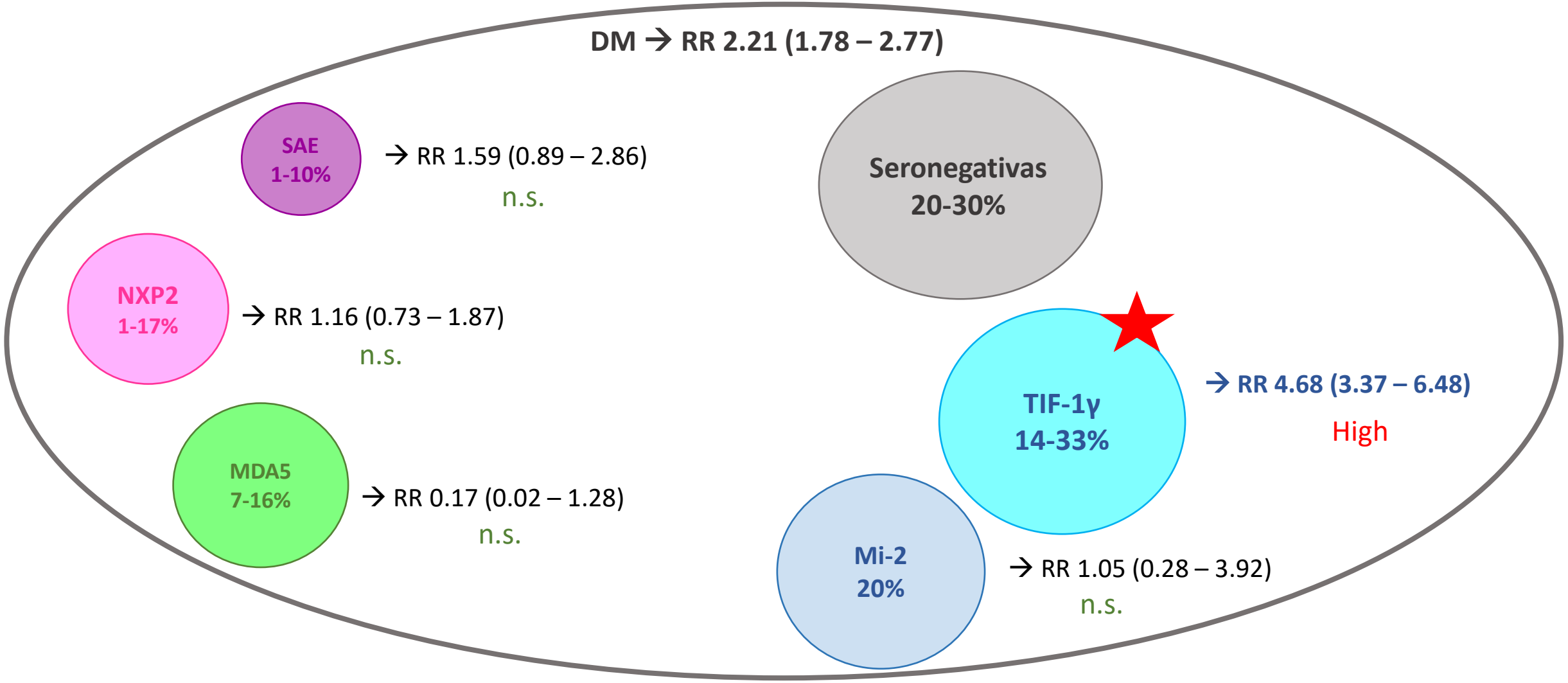
Ernesto Trallero-Araguás,[1] Jose Ángel Rodrigo-Pendás,[2] Albert Selva-O'Callaghan,[2] Xavier Martínez-Gómez,[2] Xavier Bosch,[3] Moisés Labrador-Horrillo,[2] Josep Maria Grau-Junyent,[3] and Miquel Vilardell-Tarrés[2]

ARTHRITIS & RHEUMATISM
Vol. 64, No. 2, February 2012, pp 513–522
DOI 10.1002/art.33403
© 2012, American College of Rheumatology

Myositis-Specific Anti-155/140 Autoantibodies Target Transcription Intermediary Factor 1 Family Proteins

Manabu Fujimoto,[1] Yasuhito Hamaguchi,[1] Kenzo Kaji,[1] Takashi Matsushita,[1] Yuki Ichimura,[2] Masanari Kodera,[3] Naoko Ishiguro,[4] Ikuko Ueda-Hayakawa,[5] Yoshihide Asano,[6] Fumihide Ogawa,[7] Keita Fujikawa,[7] Takuya Miyagi,[8] Eriko Mabuchi,[9] Kenji Hirose,[10] Narihiro Akimoto,[11] Naohito Hatta,[12] Kiyohiro Tsutsui,[13] Akira Higashi,[14] Atsuyuki Igarashi,[15] Mariko Seishima,[16] Minoru Hasegawa,[1] and Kazuhiko Takehara[1]

DERMATOMIOSITIS – Anticuerpos como marcadores de CAM



Trallero-Araguás et al. *Arthritis and Rheumatism*, **2012** 64(2), 523–532
Oldroyd et al. *Rheumatology*, **2021** *60*(6), 2615–2628.

BRIEF PAPER

Distinct dermatomyositis populations are detected with different autoantibody assay platforms

D.F. Fiorentino[1], L. Gutierrez-Alamillo[2], D. Hines[2], Q. Yang[2], L. Casciola-Rosen[2]

Anti-TIF1γ antibodies (anti-p155) in adult patients with dermatomyositis: comparison of different diagnostic assays

Moises Labrador-Horrillo,[1] Maria Angeles Martínez,[2] Albert Selva-O'Callaghan,[1] Ernesto Trallero-Araguás,[1] Eva Balada,[1] Miquel Vilardell-Tarrés,[1] Candido Juarez[2]

Comparison of autoantibody specificities tested by a line blot assay and immunoprecipitation-based algorithm in patients with idiopathic inflammatory myopathies

RHEUMATOLOGY

Rheumatology 2022;61:4991–499
https://doi.org/10.1093/rheumatology/keac28
Advance access publication 17 May 202

Concise report

ELISA, protein immunoprecipitation and line blot assays for anti-TIF1-gamma autoantibody detection in cancer-associated dermatomyositis

Sandra Selickaja [1,2], Angeles S. Galindo-Feria [3,4], Lara Dani[3,5], Tsuneyo Mimori[6,7], Johan Rönnelid [8], Marie Holmqvist [5,9], Ingrid E. Lundberg [3,4,5,*] and Paulius Venalis[5,10,*]

TIF-1γ
14-33%

Anti-TIF-1γ Antibody Detection Using a Commercial Kit vs In-House Immunoblot: Usefulness in Clinical Practice

Anaís Mariscal[1], Milena Milán[2], Andrés Baucells[1], Maria Angeles Martínez[1], Andrea Garcia Guillen[2], Ernesto Trallero-Araguás[3], Marcelo Alvarado-Cardenas[4], Laura Martínez-Martínez[1,5], Leticia Alserawan[1], Teresa Franco-Leyva[1], María Teresa Sanz-Martínez[6], Laura Viñas-Giménez[6], Hector Corominas[2], Cándido Juárez[1,5], Iván Castellví[2,5] and Albert Selva-O'Callaghan[4,5]*

Research paper

Evaluation of a novel particle-based assay for detection of autoantibodies in idiopathic inflammatory myopathies

I. Cavazzana[a], M. Richards[b], C. Bentow[b,*], A. Seaman[b], M. Fredi[a,c], M.G. Giudizi[d], B. Palterer[d], F. Pratesi[e], P. Migliorini[e], F. Franceschini[a,c], M. Satoh[f], A. Ceribelli[g], M. Mahler[b]

INMUNOPRECIPITACIÓN

ELISA

INMUNOBLOT

PARTICLE-BASED ASSAY

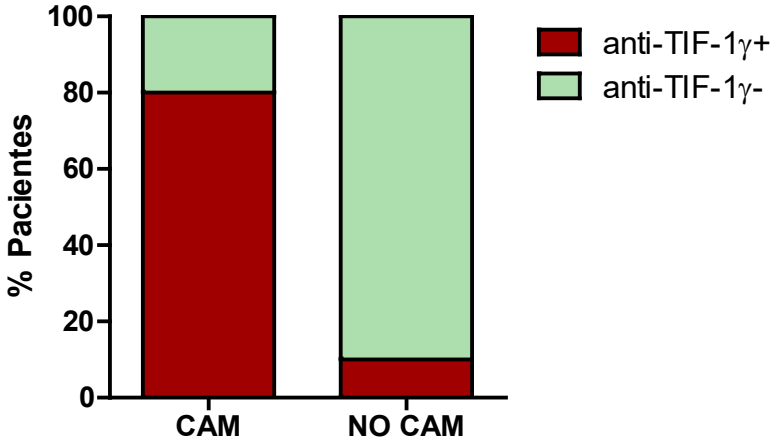
The reliability of immunoassays to detect autoantibodies in patients with myositis is dependent on autoantibody specificity

Sarah L. Tansley[1], Danyang Li[1], Zoe E. Betteridge[1] and Neil J. McHugh [1]

DERMATOMIOSITIS – Anticuerpos como marcadores de CAM

TIF-1γ
14-33%
DM

68-84% CAM



- Los anticuerpos anti-TIF-1γ permiten detectar a un grupo de pacientes con una alta probabilidad de desarrollar cáncer con una **sensibilidad del 78%** y una **especificidad del 89%,** y así realizar las pruebas de cribado y seguimiento pertinentes.

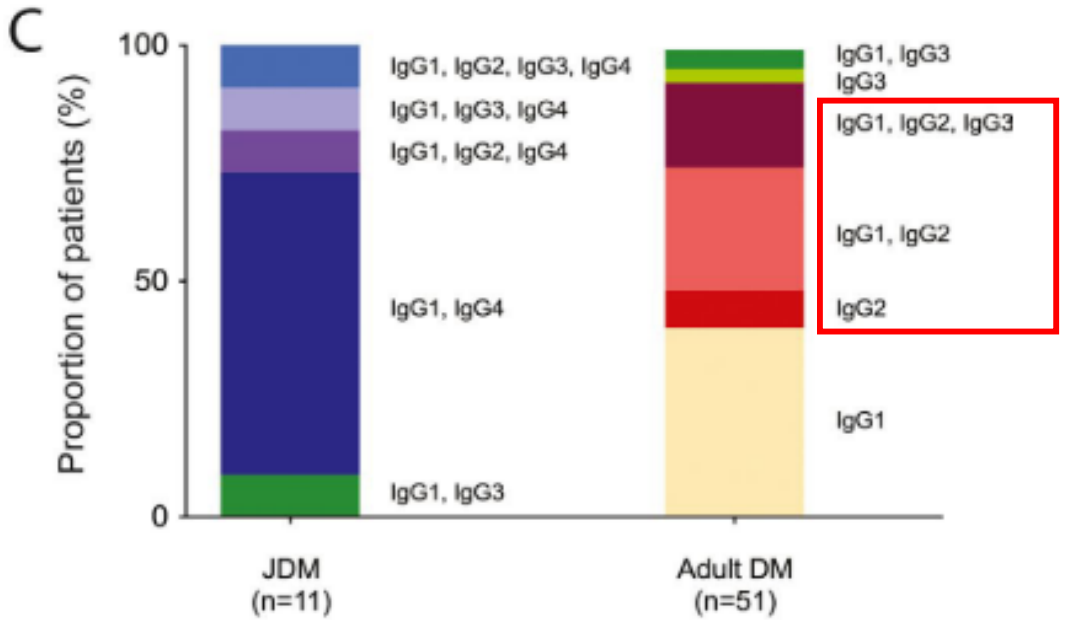
Trallero-Araguás et al. *Arthritis Rheum.* **2012**, *64*, 523–532.

American College of Rheumatology
Empowering Rheumatology Professionals

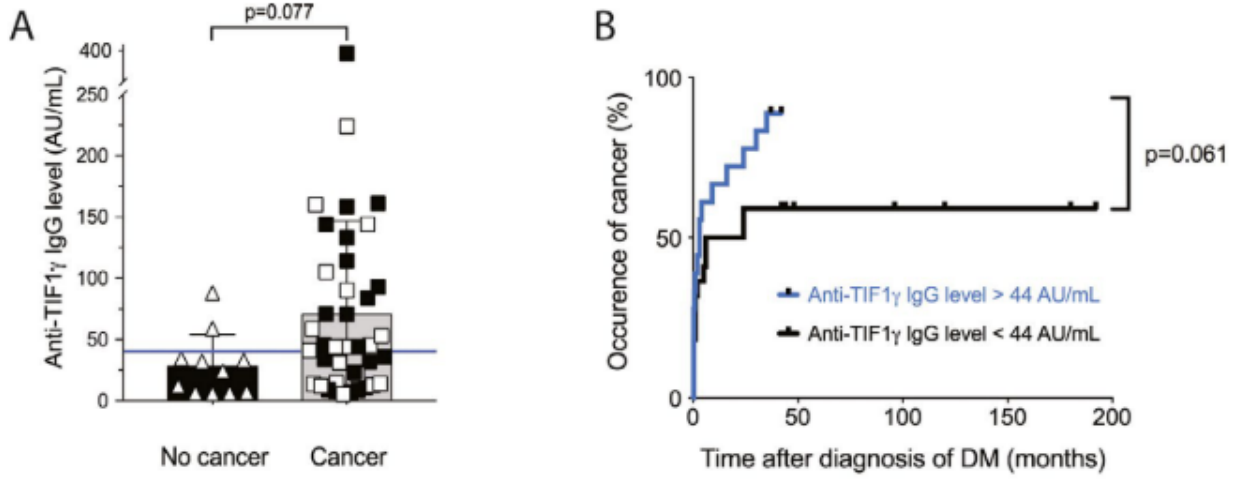
Arthritis & Rheumatology
Vol. 71, No. 8, August 2019, pp 1360–1370
DOI 10.1002/art.40895
© 2019, American College of Rheumatology

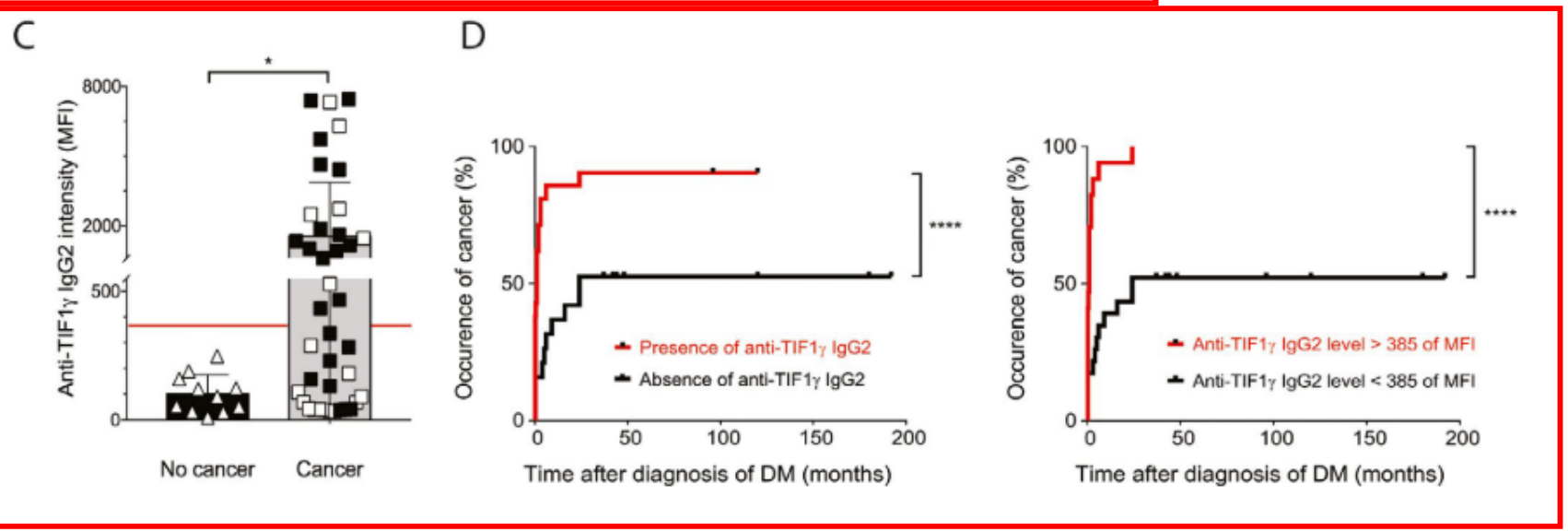
The IgG2 Isotype of Anti–Transcription Intermediary Factor 1γ Autoantibodies Is a Biomarker of Cancer and Mortality in Adult Dermatomyositis

Audrey Aussy,[1] Manuel Fréret,[1] Laure Gallay,[2] Didier Bessis,[3] Thierry Vincent,[4] Denis Jullien,[5] Laurent Drouot,[1] Fabienne Jouen,[1] Pascal Joly,[1] Isabelle Marie,[1] Alain Meyer,[6] Jean Sibilia,[6] Brigitte Bader-Meunier,[7] Eric Hachulla,[8] Mohammed Hamidou,[9] Sophie Huë,[10] Jean-Luc Charuel,[11] Nicole Fabien,[2] Pierre-Julien Viailly,[12] Yves Allenbach,[13] Olivier Benveniste,[13] Nadège Cordel,[14] Olivier Boyer,[1] and the OncoMyositis Study Group



55%





La detección de IgG2 es de utilidad:

- Marcador de **alto riesgo de desarrollar cáncer** en aquellos que no lo tengan en el momento del diagnóstico de DM.
- Identificar pacientes con **alto riesgo de mortalidad** entre aquellos con cáncer.

Aussy et al. *Arthritis Rheumatol.* **2019**, *71*, 1360–1370.

Rheumatology, 2022, **00**, 1–5
https://doi.org/10.1093/rheumatology/keac577
Advance access publication 17 October 2022
Concise report

British Society for Rheumatology
RHEUMATOLOGY
OXFORD

Basic science

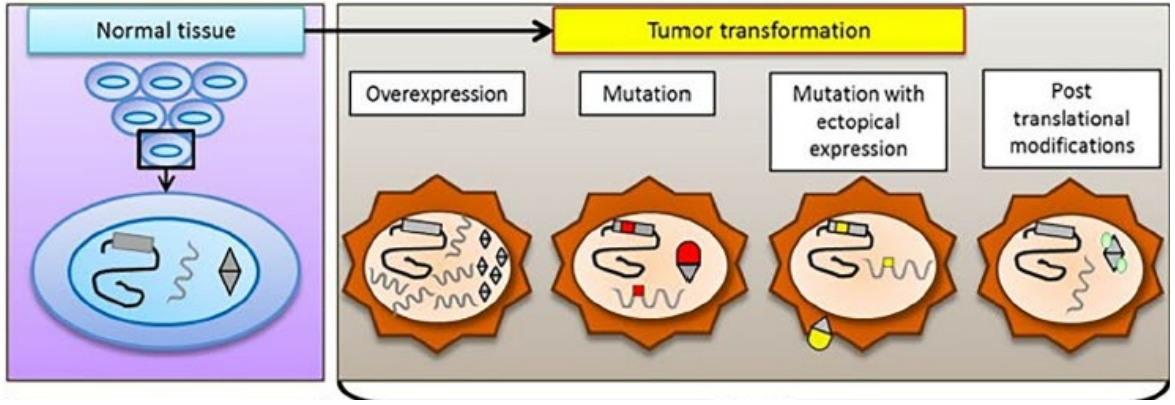
Anti-transcription intermediary factor 1-gamma IgG2 isotype is associated with cancer in adult dermatomyositis: an ENMC multinational study

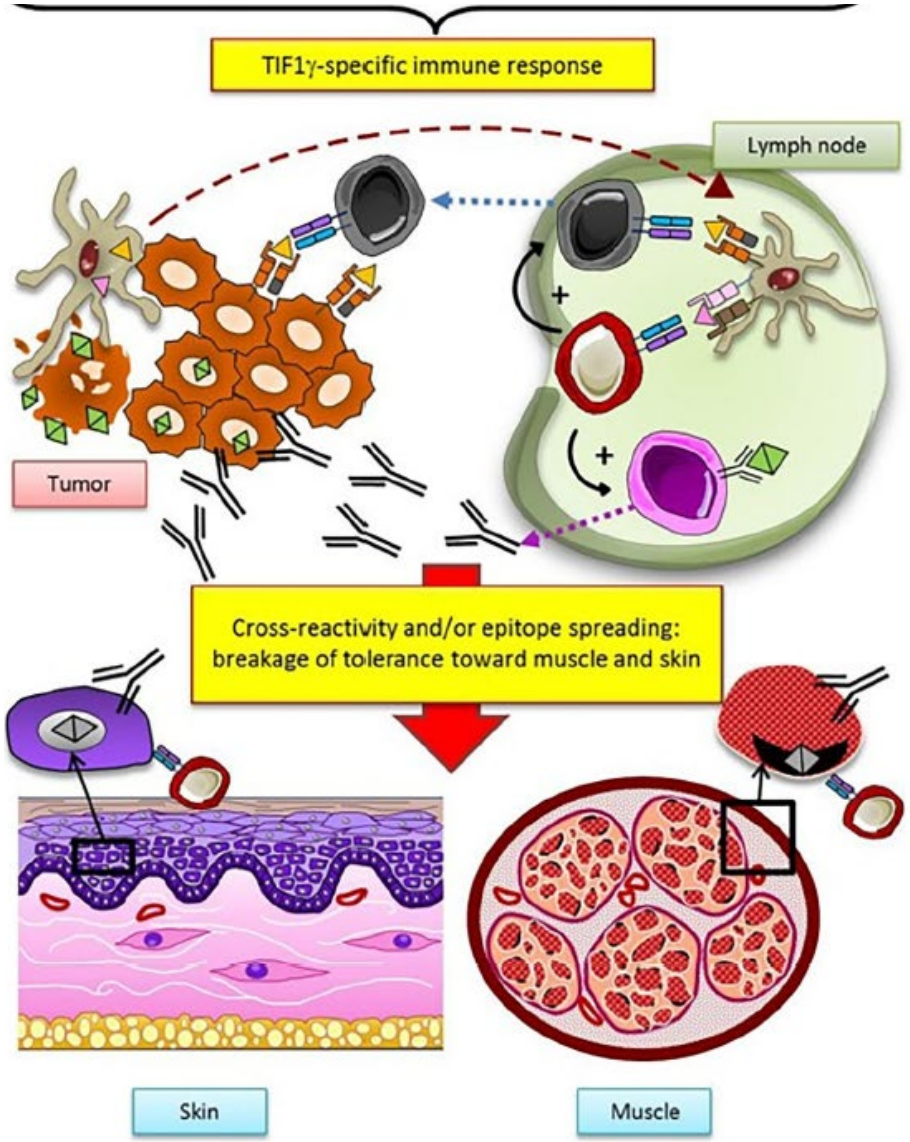
Nadège Cordel [1,2,*,†], Benoît Dechelotte[2,3,†], Fabienne Jouen[2,3], Janine A. Lamb[4], Hector Chinoy [5,6], Paul New[7], Jiri Vencovsky[8,9], Herman Mann[8,9], Angeles S. Galindo-Feria [10,11], Lara Dani[10,11], Albert Selva-O'Callaghan [12], Victoria P. Werth[13], Adarsh Ravishankar[13], Océane Landon-Cardinal[14,15], Benoit Tressières[16], Olivier Boyer[2,3]

- Riesgo incrementado de cáncer en dermatomiositis
- Tumores de diferente origen se asocian a dermatomiositis
- Estrecha relación temporal entre malignidad y aparición de la clínica de miositis

¿Son las dermatomiositis con cáncer un fenómeno paraneoplásico?

¿Son las dermatomiositis con cáncer un fenómeno paraneoplásico?





Patasova et al. *Arthritis Rheumatol.* **2022**, *0*, 1–11, doi:10.1002/art.42345.

¿Son las dermatomiositis con cáncer un fenómeno paraneoplásico?

RHEUMATOLOGY

Rheumatology 2018;57:388–396
doi:10.1093/rheumatology/kex413
Advance Access publication 14 November 2017

Original article

Tumour *TIF1* mutations and loss of heterozygosity related to cancer-associated myositis

Iago Pinal-Fernandez[1,2,3], Berta Ferrer-Fabregas[4], Ernesto Trallero-Araguas[1], Eva Balada[1], Maria Angeles Martínez[5], Jose César Milisenda[6], Gloria Aparicio-Español[7], Moises Labrador-Horrillo[1], Vicente Garcia-Patos[2,7], Josep M. Grau-Junyent[6,*] and Albert Selva-O'Callaghan[1,2,*]

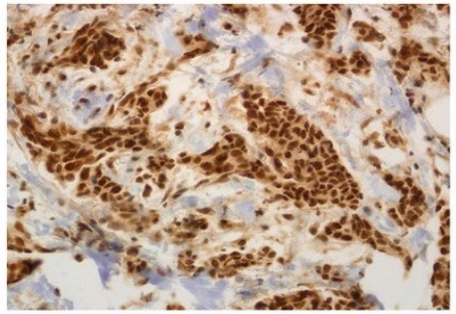
¿Son las dermatomiositis con cáncer un fenómeno paraneoplásico?

Tumores de pacientes con DM y CAM

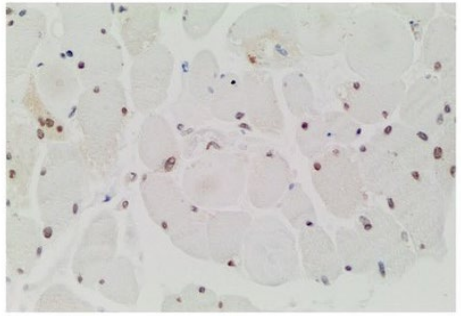
- **Anti-TIF-1γ+** → **71.4%** mutaciones de pérdida de heterocigosidad (LOH)
- **Anti-TIF-1γ-** → **16%** mutaciones LOH

La presencia de mutaciones en los tumores de pacientes con CAM y anti-TIF-1γ+ apoya la hipótesis de una **respuesta inmune dirigida al tumor**.

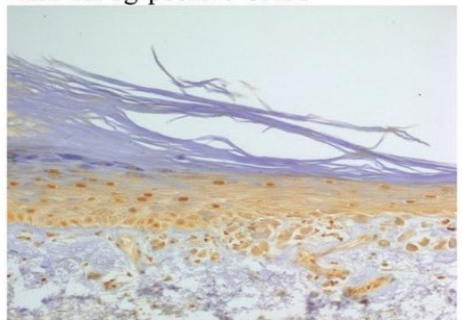
a) Breast adenocarcinoma (IHQ 290)
anti-TIF1g positive CAM



b) Muscle biopsy (IHQ 150)
anti-TIF1g positive CAM



c) Skin biopsy (IHQ 300)
anti-TIF1g positive CAM



Hay **expresión de TIF-1γ en tumores, músculo y piel**. Esta expresión es mayor en pacientes con DM en el tejido tumoral y muscular.

Pinal-Fernandez et al. *Rheumatology (United Kingdom)*, **2018** *57*(2), 388–396.

¿Son las dermatomiositis con cáncer un fenómeno paraneoplásico?

Japanese Dermatological Association
The Journal of Dermatology
doi: 10.1111/1346-8138.15526
Journal of Dermatology 2020; **47**: 1395–1402

ORIGINAL ARTICLE

Clinical features of anti-transcription intermediary factor 1γ (TIF1γ)-positive dermatomyositis with internal malignancy and investigation of the involvement of TIF1γ expression in tumors in the pathogenesis of cancer-associated dermatomyositis

Sei-ichiro MOTEGI,[1,*] Akiko SEKIGUCHI,[1,*] Hidekazu IKEUCHI,[2] Toru SAKAIRI,[2] Hiroomi OGAWA,[3] Takaaki FUJII,[3] Makoto SOHDA,[3] Toshiki YAJIMA,[3] Shota IDA,[4] Yukihiro TAKAYASU,[4] Yuki SHIMODA,[5] Keiju HIROMURA,[2] Hiroshi SAEKI,[3] Ken SHIRABE,[3] Kazuaki CHIKAMATSU,[4] Hideaki YOKOO,[6] Tetsunari OYAMA,[5] Osamu ISHIKAWA[1]

Departments of [1]Dermatology, [2]Nephrology and Rheumatology, [3]General Surgical Science, [4]Otolaryngology-Head and Neck Surgery, [5]Diagnostic Pathology, [6]Human Pathology, Gunma University Graduate School of Medicine, Maebashi, Japan

Más expresión de TIF-1γ en tumores.

RHEUMATOLOGY
Rheumatology 2021;60:5863–5867
doi:10.1093/rheumatology/keab260
Advance Access publication 25 March 2021

Concise report

TRIM33 gene somatic mutations identified by next generation sequencing in neoplasms of patients with anti-TIF1γ positive cancer-associated dermatomyositis

Nadège Cordel[1,2], Céline Derambure[3,*], Sophie Coutant[3,*], Xavier Mariette[4], Denis Jullien[5], Sébastien Debarbieux[6], Olivier Chosidow[7,8], Alain Meyer[9], Didier Bessis[10], Pascal Joly[2,11], Alexis Mathian[12], Hervé Levesque[13], Jean-Christophe Sabourin[3,14], Isabelle Tournier[3], Olivier Boyer[2,15] and the OncoMyositis Study group[†]

Mutaciones en el gen del TIF-1γ en tumores de pacientes con DM, CAM y anticuerpos anti-TIF-1γ.

¿Son las dermatomiositis con cáncer un fenómeno paraneoplásico?

Concise report

CED
Clinical and Experimental Dermatology

Expression of the autoantigen TRIM33/TIF1γ in skin and muscle of patients with dermatomyositis is upregulated, together with markers of cellular stress

B. Scholtissek,[1] S. Ferring-Schmitt,[1] J. Maier[1] and J. Wenzel[1]

[1]*Department of Dermatology and Allergy, University Hospital, Bonn, Germany*

doi:10.1111/ced.13180

Mayor expresión de TIF-1γ en piel y músculo de pacientes con DM.

Received: 26 April 2018 | Revised: 26 July 2018 | Accepted: 28 September 2018

DOI: 10.1111/1756-185X.13424

ORIGINAL ARTICLE

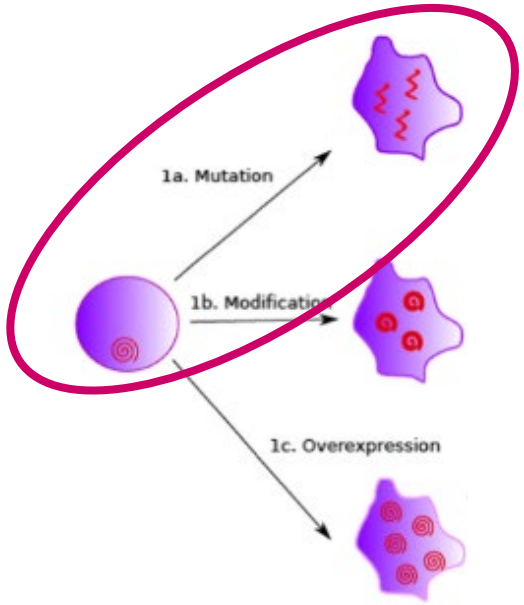
WILEY International Journal of Rheumatic Diseases

Anti-TIF1γ antibody and the expression of TIF1γ in idiopathic inflammatory myopathies

Young Kim[1] | Kyu Sang Song[2] | Eun Hee Sohn[3] | Seong Wook Kang[4] | In Seol Yoo[4] | Seung-Cheol Shim[4] | Su-Jin Yoo[4] | Jinhyun Kim[4]

La expresión de TIF-1γ en músculo de pacientes con miositis se asocia a la presencia de anticuerpos anti-TIF1γ.

¿Son las dermatomiositis con cáncer un fenómeno paraneoplásico?



Mutación del gen TIF-1γ (neoantígeno)

Respuesta inmune (anticuerpos anti-TIF-1γ)

Daño en tejidos que expresan TIF-1γ

++
+

Deleción del gen TIF-1γ (pérdida de heterocigosidad)

Crecimiento del tumor

Selva-O'callaghan et al. *Neuromuscular Disorders*, **2019** Nov;29(11):819-825

Sin embargo, un **16-32%** de pacientes con **DM TIF-1γ⁺ no** desarrollan **cáncer**…

Ausencia de cáncer

Eliminación del cáncer por el sistema inmune

¿Marcadores para diferenciar estos pacientes?

The Journal of Clinical Investigation

CLINICAL MEDICINE

Immune responses to CCAR1 and other dermatomyositis autoantigens are associated with attenuated cancer emergence

David F. Fiorentino,[1] Christopher A. Mecoli,[2] Matthew C. Rosen,[3] Lorinda S. Chung,[4] Lisa Christopher-Stine,[2] Antony Rosen,[2] and Livia Casciola-Rosen[2]

[1]Department of Dermatology, Stanford University School of Medicine, Redwood City, California, USA. [2]Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA. [3]Department of Neurobiology, The University of Chicago, Chicago, Illinois, USA. [4]Division of Immunology and Rheumatology, Stanford University School of Medicine, Palo Alto, California, USA.

Published: January, 2022.

Myositis

CLINICAL SCIENCE

Coexisting autoantibodies against transcription factor Sp4 are associated with decreased cancer risk in patients with dermatomyositis with anti-TIF1γ autoantibodies

Yuji Hosono,[1] Brandon Sie,[2] Iago Pinal-Fernandez ,[1,3] Katherine Pak,[1] Christopher A Mecoli ,[4] Maria Casal-Dominguez,[1,3] Blake M Warner ,[5] Mariana J Kaplan ,[6] Jemima Albayda,[4] Sonye Danoff,[7] Thomas E Lloyd,[3] Julie J Paik ,[4] Eleni Tiniakou ,[4] Rohit Aggarwal,[8] Chester V Oddis,[8] Siamak Moghadam-Kia,[8] Carmelo Carmona-Rivera ,[6] Jose César Milisenda,[9] Josep Maria Grau-Junyent,[9] Albert Selva-O'Callaghan ,[10] Lisa Christopher-Stine,[3,4] H Benjamin Larman,[2] Andrew Lee Mammen [1,3,4]

Published: August, 2022.

The Journal of Clinical Investigation

CLINICAL MEDICINE

Immune responses to CCAR1 and other dermatomyositis autoantigens are associated with attenuated cancer emergence

David F. Fiorentino,[1] Christopher A. Mecoli,[2] Matthew C. Rosen,[3] Lorinda S. Chung,[4] Lisa Christopher-Stine,[2] Antony Rosen,[2] and Livia Casciola-Rosen[2]

[1]Department of Dermatology, Stanford University School of Medicine, Redwood City, California, USA. [2]Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA. [3]Department of Neurobiology, The University of Chicago, Chicago, Illinois, USA. [4]Division of Immunology and Rheumatology, Stanford University School of Medicine, Palo Alto, California, USA.

CCAR1

Table 2. Frequency of antibody specificities (identified in Table 1) across anti-TIF1-γ–positive DM patient cohorts

		Cancer (ever) = Yes			Cancer (ever) = No		
	Autoantigen	Hopkins *n* = 44, *n* (%)	Stanford *n* = 38, *n* (%)	Combined *n* = 82	Hopkins *n* = 98, *n* (%)	Stanford *n* = 72, *n* (%)	Combined *n* = 170
32%	CCAR1	10 (23%)	8 (21%)	18 (22%)	35 (36%)	27 (38%)	62 (36%)
	SOX5	7 (16%)	4 (11%)	11 (13%)	29 (30%)	13 (18%)	42 (25%)
	TBL	3 (7%)	4 (11%)	7 (9%)	18 (18%)	9 (13%)	27 (16%)
	IMMT	2 (5%)	0	2 (2%)	9 (9%)	7 (10%)	16 (9%)
	C1Z1	1 (2%)	1 (3%)	2 (2%)	8 (8%)	3 (4%)	11 (6%)
	NACC	0	1 (3%)	1 (1%)	3 (3%)	2 (3%)	5 (3%)
	NVL	0	1 (3%)	1 (1%)	0	1 (1%)	1 (0.5%)
	GATD	0	0	0	0	1 (1%)	1 (0.5%)
	RCC1	0	0	0	0	1 (1%)	1 (0.5%)
	KDMA	0	0	0	0	1 (1%)	1 (0.5%)

The data are broken down by cancer status in the Johns Hopkins cohort, the Stanford cohort, and in the combined cohorts.

Pacientes con anti-CCAR1 y cáncer → ¿son equivalentes en estadio del tumor y tiempo de aparición del cáncer desde el diagnóstico de DM?

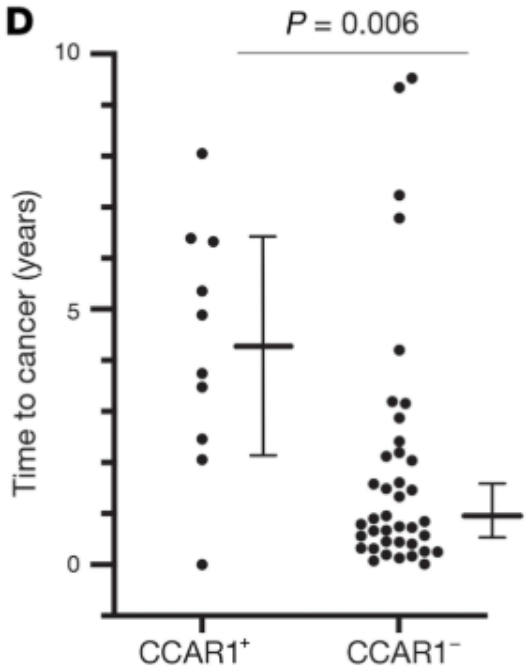
Fiorentino et al. *The Journal of Clinical Investigation*, **2022** *132*(2).

CCAR1

Table 5. Frequency of high- versus low-stage cancers stratified by anti-CCAR1 antibody status

Autoantibody status	TNM stage 0 or 1 at cancer diagnosis	TNM stage 2, 3, or 4 at cancer diagnosis
	n (%)	*n* (%)
Anti-CCAR1–positive	8/9 (89%)	1/9 (11%)
Anti-CCAR1–negative	14/33 (42%)	19/33 (58%)

Analysis is restricted to cancers diagnosed between DM-symptom onset and 10 years follow-up. Patients were included if there was information regarding stage at cancer diagnosis and are pooled from both Stanford and Hopkins cohorts. Significantly higher percentage of cancers at diagnosis were of low stage (stage 0 or 1) in patients with anti-CCAR1 antibodies ($P = 0.02$, Fischer's exact test). TNM, tumor/nodes/metastasis.

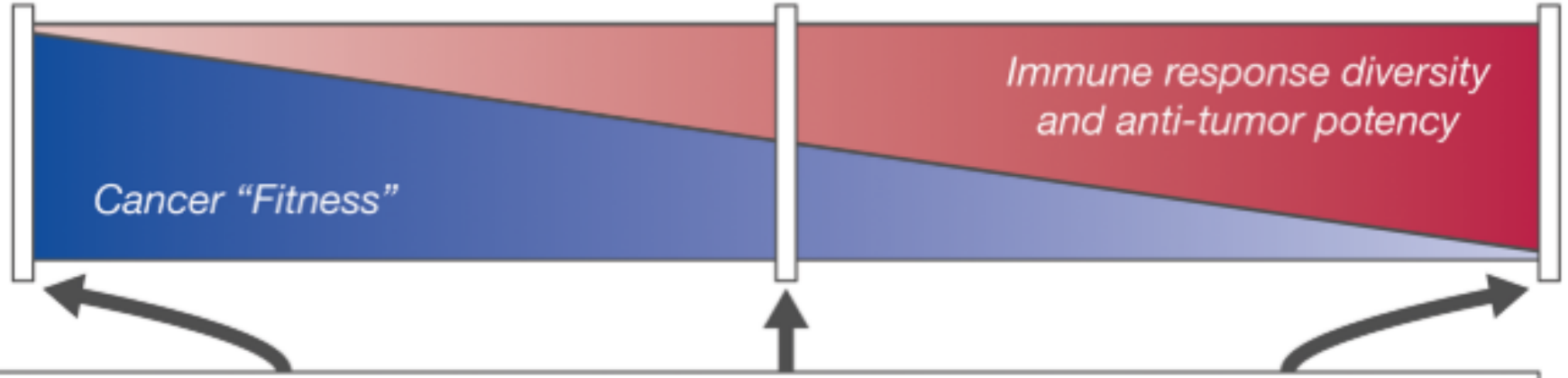


Los pacientes con anti-CCAR1 tienen mayor proporción de tumores que se diagnostican en estadio bajo que los pacientes anti-CCAR1-.

El tiempo de aparición del cáncer tras la DM es mayor en los pacientes con anti-CCAR1+. Mediana **4.3 vs 0.86 años**.

Fiorentino et al. *The Journal of Clinical Investigation*, **2022** *132*(2).

CCAR1



	Scenario A	Scenario B	Scenario C
Autoantibod(ies)	Anti–TIF1-γ alone	Anti–TIF1-γ /CCAR1/Other	Anti–TIF1-γ /CCAR1/Other
Time to cancer emergence	Short interval < 1yr	Interval 1–5 yrs	No cancer emerges
Cancer Stage	More advanced at Dx	Smaller, less advanced	No cancer emerges
Predominating force	Cancer	Changes over time	Immune response
Immunoediting stage	Escape	Equilibrium -> Escape	Elimination/Equilibrium

Fiorentino et al. *The Journal of Clinical Investigation*, **2022** *132*(2).

CLINICAL SCIENCE

Coexisting autoantibodies against transcription factor Sp4 are associated with decreased cancer risk in patients with dermatomyositis with anti-TIF1γ autoantibodies

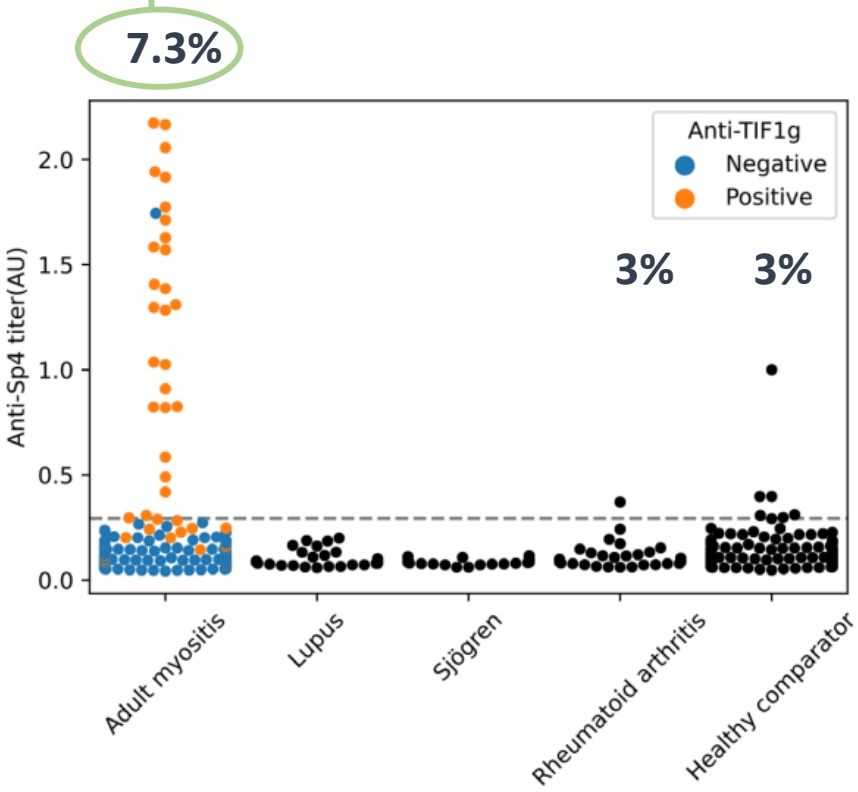
Yuji Hosono,[1] Brandon Sie,[2] Iago Pinal-Fernandez ,[1,3] Katherine Pak,[1] Christopher A Mecoli ,[4] Maria Casal-Dominguez,[1,3] Blake M Warner ,[5] Mariana J Kaplan ,[6] Jemima Albayda,[4] Sonye Danoff,[7] Thomas E Lloyd,[3] Julie J Paik ,[4] Eleni Tiniakou ,[4] Rohit Aggarwal,[8] Chester V Oddis,[8] Siamak Moghadam-Kia,[8] Carmelo Carmona-Rivera ,[6] Jose César Milisenda,[9] Josep Maria Grau-Junyent,[9] Albert Selva-O'Callaghan ,[10] Lisa Christopher-Stine,[3,4] H Benjamin Larman,[2] Andrew Lee Mammen [1,3,4]

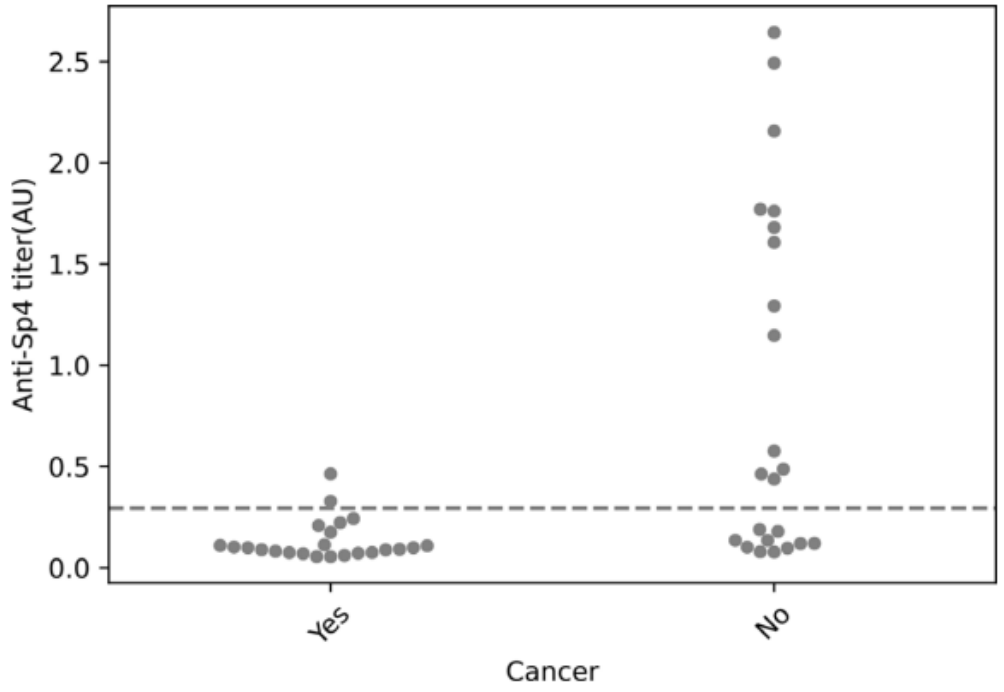
Sp4

- Todos DM: 10.6%
- 96% tienen también Ac anti-TIF-1γ

DM anti-TIF-1γ⁺ → 43% anti-Sp4⁺

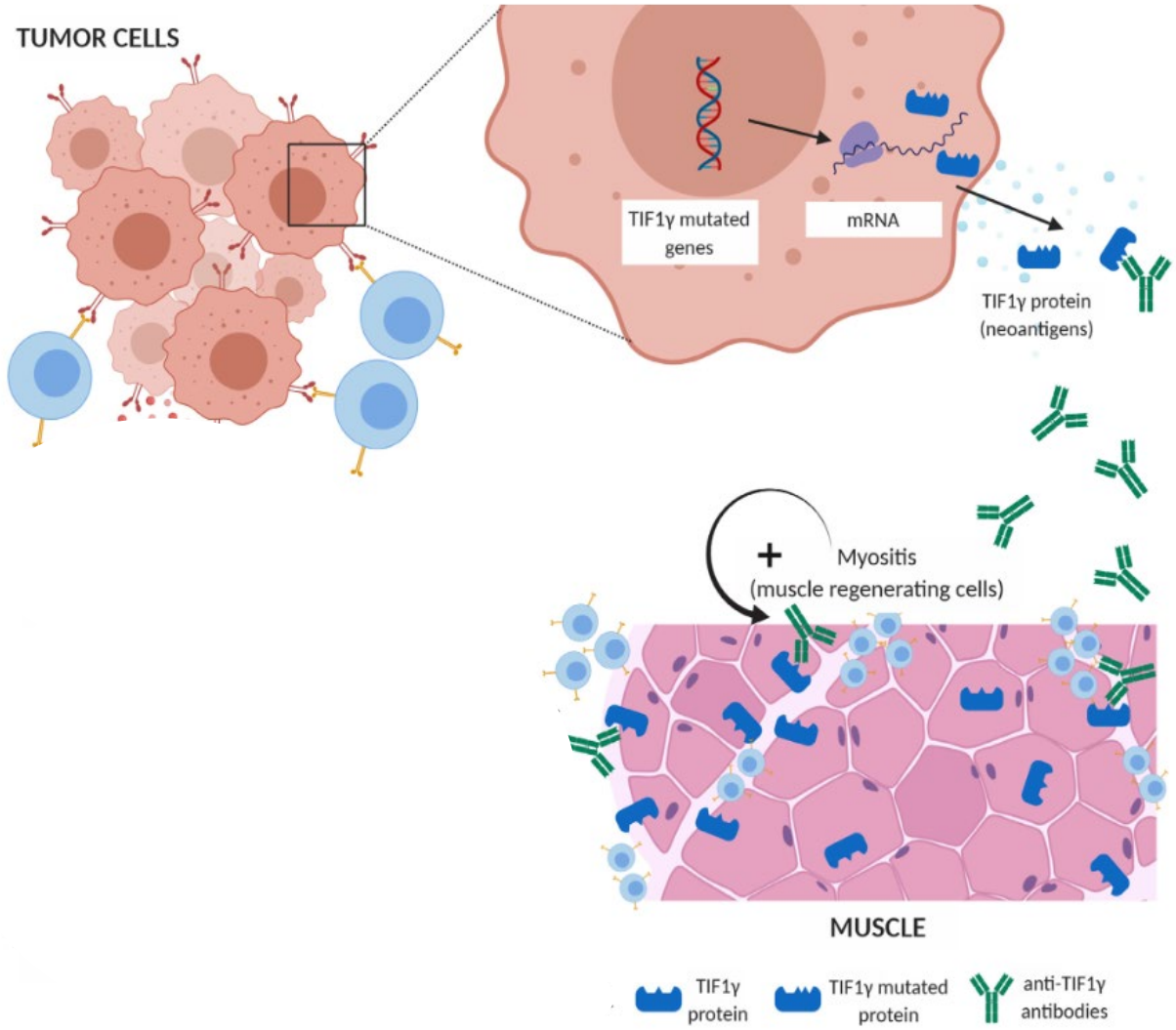
- **13.3%** anti-Sp4+ CAM
- **67.8%** anti-Sp4- CAM

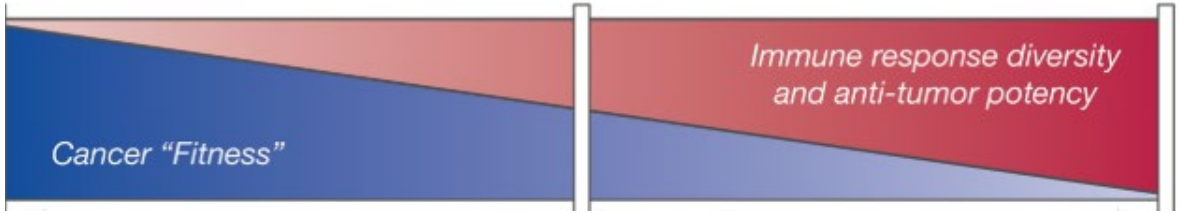




Hosono et al. *Annals of the Rheumatic Diseases*, **2022** *0*, 1–7.

TAKE-HOME MESSAGES





TIF-1γ+ (confirmado)

68-84%	16-32%

CCAR1
Sp4
Otros

Selva-o'Callaghan et al. *Neuromuscul. Disord.* **2019**, Nov;29(11):819-825.

GRACIAS