LES ANTI-Ro52 ONT ENFIN LEUR MALADIE !

René Louis Humbel

GEAI Octobre 2021

ANTI-Ro52 AUTOANTIBODIES

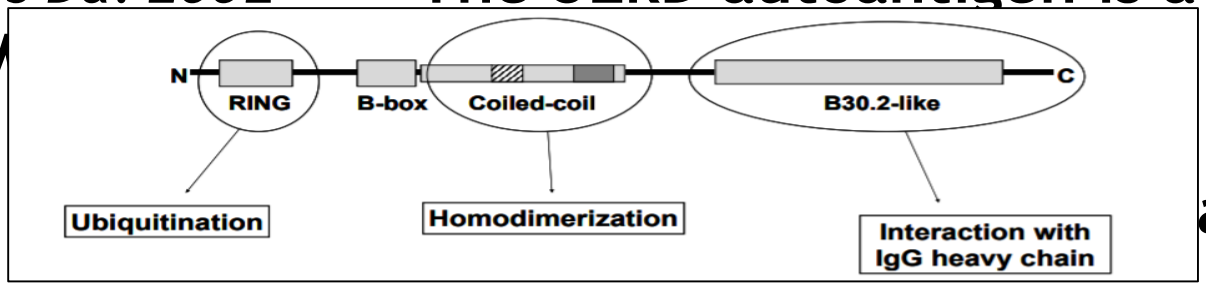
Ben-Chetrit , 1988 Antibodies to a 52kD SSA-Ro Particle Antigen

Chan EK, 1991 Molecular Design of the 52kD Antigen

Itoh K. 1991 52 kD and 60kD Ro Antigens encoded by separate Genes

Boire G. 1995 The 52kD Antigen is not a component of the SSA/Ro complex

Rhodes Da. 2002 The 52kD autoantigen is a TRIM Protein (TRIM



Wada ase

Ann Rheum Dis. 2002 Oct; 61(10): 929–933.

Anti-Ro52 reactivity is an independent and additional serum marker in connective tissue disease

I Peene, L Meheus, S De Keyser, R Humbel, E Veys, and F De Keyser

In conclusion, anti-Ro52 positive sera without anti-Ro60 and anti-La/SSB reactivity can be considered as an independent group, missed by classic anti-SSA/Ro detection methods: precipitin negative, not retrieved by SSA/Ro ELISAs based on natural SSA/Ro, and no specific ANA fluorescence pattern. Their expression is mostly associated with connective tissue diseases, although their precise clinical significance is under study.

Front. Immunol., 06 September 2021 |

TRIM21/Ro52 - Roles in Innate Immunity and Autoimmune Disease

Esther L. Jones, Stephen M. Laidlaw[†] *and Lynn B. Dustin*[*]

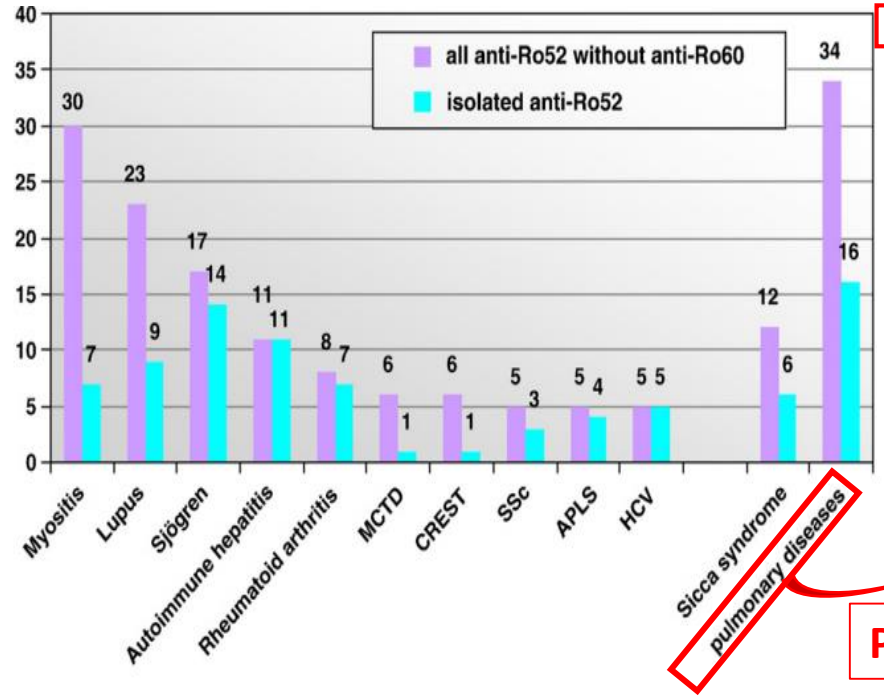
Autoimmun Rev. 2011 Jul;10(9):509-13.

Clinical significance of anti-Ro52 (TRIM21) antibodies non-associated with anti-SSA 60kDa antibodies: results of a multicentric study

P Ghillani [1], C André, C Toly, A M Rouquette, D Bengoufa, P Nicaise, C Goulvestre, A Gleizes, M A Dragon-Durey, M A Alyanakian, P Chretien, S Chollet-Martin, L Musset, B Weill, C Johanet

247 cases : 155 Ro52 no SSA60 + ENA (63%)

89 Ro52 isolated (36%)



Pulmonary manifestations in 34 patients.

	Isolated anti-Ro52 (n = 16)	Associated anti-Ro52 Ab (n = 18)
Interstitial lung disease	6 (37.5%)	5 (27.7%)
Pulmonary fibrosis	5 (31%)	5 (27.7%)
Pulmonary arterial Hypertension	2 (12.5%)	3 (16%)
Lung cancer	1 (6%)	0
BOOP[a]	0	1 (5%)

[a] Bronchiolitis obliterans with organizing pneun

PULMONARY DISEASES

Front. Immunol., 07 June 2021 |

Interstitial Lung Disease in Connective Tissue Disease: A Common Lesion With Heterogeneous Mechanisms and Treatment Considerations

Tihong Shao[1,2†], Xiaodong Shi[3†], Shanpeng Yang[4], Wei Zhang[5], Xiaohu Li[6], Jingwei Shu[6], Shehabaldin Alqalyoobi[7], Amir A. Zeki[8], Patrick S. Leung[2*] and Zongwen Shuai[1*]

Manifestation	RA	SSc	SS	SLE	PM/DM	MCTD
Airways disease	15%	70%	40%	10%	60%	30%
ILD **Interstitial Lung Disease**	++	+++	++	+	+++	++
NSIP **Non Specific Int. Pneum.**	++	+++	++	++	+++	++
UIP **Unspecific Int. Pneum.**	+++	+	+	+	+	+
OP **Organizing Pneumomia**	++	+	+	+	+++	+
DAD/AIP	+	+	+	++	++	+
LIP	+	–	++	+	–	–
DAH	+	+		++	+	+
Pleural disease	++	–	+	+++	–	+
Vascular disease	+	+++	+	+	+	++
Pulmonary hypertension	+	+++	+	+	+	+
Parenchymal nodules	+	–	–	–	–	–
Respiratory muscle disease	–	–	–	+	++	+
Aspiration pneumonia	–	+++	–	–	+	+

Ro52 and INTERSTITIAL LUNG DISEASE

Authors		Nb Tested		Nb Anti-Ro52		ILD
Ghillani	2011	247	CDT	89	isolated	37.5%
				155	associated	27.7%
Ferreira	2012	41	CDT	35		74.4%
Hudson	2012	963	SScl	194		44.2%
Wodkowski	2015	1574	SScl	103	isolated	57.0%
				320	associated	38.0%
Gunnarson	2016	113	MCTD	33		54.0%
Sabbagh	2019	371	Myos	53		36.0%
Xing	2020	153	DM	82		68.8%
Buvry	2020	68	Sjögren	31		41.9%
Decker	2021	408	CTD	113		48.7%
Kujinovic	2021	165	Myos.	52		56.5%
Wu	2021	4782	CTD	635	isolated	55.4%
				686	+ SSA60	20.1%

Ann Rheum Dis: -eular.3810 on 19 May 2021. I

SUBCLINICAL INTERSTITIAL LUNG DISEASE IS FREQUENT AND PROGRESSES ACROSS DIFFERENT CONNECTIVE TISSUE DISEASES

A. M. Hoffmann-Vold [1], H. Andersson [1], S. Reiseter [2], H. Fretheim [1], I. Barua [1], T. Garen [1], Ø. Midtvedt [1], R. Gunnarsson [1], M. Durheim [3], T. M. Aaløkken [4], Ø. Molberg [1]

525 Patients CTD

		Progression Lung Fibrosis
ILD	**231 (44%)**	**72 (51%)**
Subclinical ILD	**67 (13%)**	**20 (38%)**

Am J Respir Crit Care Med. 2007 Oct 1;176(7):691-7.

Idiopathic nonspecific interstitial pneumonia: lung manifestation of undifferentiated connective tissue disease?

Brent W Kinder [1], Harold R Collard, Laura Koth, David I Daikh, Paul J Wolters, Brett Elicker, Kirk D Jones, Talmadge E King Jr

Characteristics	Patients with UCTD* (*n* = 28)	Patients with other IIP† (*n* = 47)
Age at first lung symptom, yr, mean (range)	50 (31–68)	65 (41–86)
Age at first enrollment, yr, mean (range)	54 (33–69)	69 (46–90)
Sex, n (%)		
Men	9 (32)	36 (77)
Women	19 (68)	11 (23)
Symptoms and signs at presentation, n (%)		
Lung related		
Dyspnea	28 (100)	47 (100)
Cough	23 (82)	46 (98)
Wheeze	2 (7)	1 (2)
Systemic		
Arthralgias/joint swelling	18 (64)	6 (13)
GERD Gastroesophageal	18 (65)	16 (34)
Raynaud's phenomenon	17 (61)	0 (0)
Dysphagia	10 (36)	2 (4)
Sicca symptoms	8 (29)	6 (13)
Recurrent fever	7 (25)	2 (4)
Skin changes (rash)	7 (25)	1 (2)
Morning stiffness	5 (18)	0 (0)
Unintentional weight loss	3 (11)	5 (11)
Proximal muscle weakness	3 (11)	0 (0)
Oral ulcerations	1 (4)	0 (0)
Photosensitivity	0	0
Alopecia (nonandrogenic)	0	0

Int J Clin Pract. 2021 Mar;75(3):e13679.

Anti-Ro52 antibodies in clinical practice: A single-centre experience

Si Wu [1], Xiaojun Tang [1], Liping Wu [2], Liangjing Lu [3], Xuebing Feng [1]

4782 Ro52 positive cases

CTD	3185 (66.6%)
UCTD	1473 (30.8%)
Normal	124 (2.6%)

	Ro52	Ro52+SSA60
CTD	54.7%	85.5%
NON CTD	42.5%	12.3%
INTERSTITIAL LUNG DISEASE		
ILD	55.4%	20.1%

TABLE 3 Specific manifestations related to anti-Ro52 in CTD inpatients

Manifestation	$Ro52^+Ro60^-$ (n = 635)	$Ro52^+Ro60^+$ (n = 686)
Leucopenia	96 (15.1%)	166 (24.2%)****
Thrombocytopenia	127 (20.0%)	216 (31.5%)****
Anaemia	22 (3.5%)	37 (5.4%)
Proteinuria	133 (20.9%)	251 (36.6%)****
Hematuria	174 (27.4%)	265 (38.6%)****
Renal insufficiency	83 (13.1%)	133 (19.4%)**
Liver dysfunction	182 (28.7%)	216 (31.5%)
Live cirrhosis	24 (3.8%)	43 (6.3%)*
Arthritis/arthralgia	174 (27.4%)	320 (46.6%)****
Muscle weakness	129 (20.3%)	171 (24.9%)*
ILD	352 (55.4%)	138 (20.1%)****
Pulmonary infection	100 (15.7%)	80 (11.7%)*
PAH	39 (6.1%)	57 (8.3%)
Skin rash	111 (17.5%)	193 (28.1%)****
Oral ulcer	26 (4.1%)	54 (7.9%)**
Raynaud's phenomenon	63 (9.9%)	82 (12.0%)

Chest. 2011 Nov;140(5):1292-1299.

Autoimmune-featured interstitial lung disease: a distinct entity

Rekha Vij [1], Imre Noth [2], Mary E Strek [1]

200 Patients ILD

63 Autoimmune

58 Idiopathic

37 CTD

Symptoms	AIF-ILD (n = 63)	IPF (n = 58)	CTD-ILD (n = 37)
Dry eyes/dry mouth	36 (57.1)	9 (15.5)	23 (62.2)
Gastroesphageal Reflux	28 (44.4)	10 (17.2)	19 (51.4)
Leg/foot swelling	23 (36.5)	4 (6.9)	10 (27.0)
Weight loss	23 (36.5)	6 (10.3)	7 (18.9)
Joint pain/swelling	17 (27.0)	5 (8.6)	23 (62.2)
Rash	6 (9.5)	3 (5.2)	10 (27.0)
Raynaud phenomenon	6 (9.5)	0 (0)	19 (51.4)
Sensitivity to light	6 (9.5)	2 (3.4)	6 (16.2)
Dysphagia	6 (9.5)	2 (3.4)	6 (16.2)
Hand ulcers	1 (1.6)	0 (0)	5 (13.5)
Mouth ulcers	1 (1.6)	1 (1.7)	3 (8.1)
Morning stiffness	1 (1.6)	0 (0)	5 (13.5)
Proximal muscle weakness	0 (0)	0 (0)	4 (10.8)
Usual Interstitial Pneumonia	**62%**	**92%**	**38%**

AUTOIMMUNE INTERSTITIAL LUNG DISEASEIN CTD

INTERSTITIAL PNEUMONIA

ILD as First Manifestation of CTD

Lung Dominant CTD (ILD-CTD)

Subclinical/Preclinical Forms ILD

CONNECTIVE TISSUE DISEASE

Moderate Manifestations of CTD

- **Occult- *Forme Fruste* CTD**
- **Pseudo-Lupus**
- **Amyopoathic Dermatomyositis**
- **Systemic Sclerosis *sine Sclerosis***

Unclassifiable/Undifferentiated CTD (UCTD)

Eur Respir J. 2015 Oct;46(4):976-87.

An official European Respiratory Society/American Thoracic Society research statement: interstitial pneumonia with autoimmune features

IPAF

Aryeh Fischer [1], Katerina M Antoniou [2], Kevin K Brown [3], Jacques Cadranel [4], Tamera J Corte [5], Roland M du Bois [6], Joyce S Lee [7], Kevin O Leslie [8], David A Lynch [9], Eric L Matteson [10], Marta Mosca [11], Imre Noth [12], Luca Richeldi [13], Mary E Strek [14], Jeffrey J Swigris [15], Athol U Wells [16], Sterling G West [17], Harold R Collard [18], Vincent Cottin [19], "ERS/ATS Task Force on Undifferentiated Forms of CTD-ILD"

This ERS/ATS research statement proposes that the name "interstitial pneumonia with autoimmune features" (IPAF) be used to identify individuals with interstitial pneumonia and features suggestive of a CTD that do not meet established classification criteria for a characterisable CTD.

Respiratory Research (2019) 20:256

Presentations and outcomes of interstitial lung disease and the anti-Ro52 autoantibody

A. Sclafani[1*], K. M. D'Silva[2], B. P. Little[3], E. M. Miloslavsky[2], J. J. Locascio[4], A. Sharma[3] and S. B. Montesi[1]

73 patients with ILD and Ro52

ELISA SSA Mix

Ro52 isolated (no SSA60/ENA): 50 (68%)
44 (60%)
Ro52 + Myositis Spec.Ab: 23 (32%)
19 (14%)
No Prior Diag. CTD : 78%
IPAF criteria 30.1 %

Testing for anti-Ro52 may help to phenotype unclassifiable ILD patients, particularly as part of the serologic criteria for IPAF.

Research Square, 01 Mar 2021

Serum Anti-Ro52/Tripartite Motif-containing 21, A Novel Criterion of Interstitial Pneumonia With Autoimmune Features

Tahara M, Sakamoto N, Satoh M, Ishimoto H, Yura H, Yamasaki K, Kido T, Fujino Y, Hasegawa T, Tanaka S, Yatera K, Mukae H

IDIOATHIC INTERSTITIAL PNEUMONIAS	Anti-Ro52 positive	Anti-Ro52 negative
Subjects	n = 20	n = 268
Age (years)	67.5 [63–74]	70 [63–75]
Male, n (%)	11 (55)	182 (68)
Smoking (Pack-years)	19 [0–42]	23 [0–49]
Fulfilled IPAF criteria, n (%)	10 (50)	45 (17)
Clinical Domain, n (%)	4 (20)	22 (8)
Serological Domain, n (%)	15 (75)	71 (26)
Morphological Domain, n (%)	8 (40)	119 (44)

Conclusion: Anti-Ro52-positive IIP patients have clinical features consistent with IPAF. Adding anti-Ro52 in IPAF criteria may be considered in the future.

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INTERSTITIAL PNEUMONIA

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IPAF

ANTI-Ro52