



Autoanticorpi nelle miopatie infiammatorie idiopatiche



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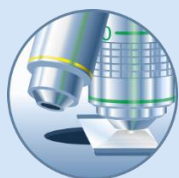
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- ▶ La **letteratura** citata è segnata con numeri **rossi**: cliccandoli si va agli autori alla fine del documento. Cliccando il simbolo della mano (☞) si ritornerà all'inizio della tabella rispettiva.
- ▶ I nomi degli **autoanticorpi** oppure le loro abbreviazioni elencati nelle tabelle sono collegate con le descrizioni, che si aprono cliccando i nomi rispettivi.
- ▶ Le **sensibilità** e **specificità** indicate dipendono decisamente sia dai metodi di dosaggio, sia dalle variabilità genetiche ed etno-geografiche sia dai gruppi di pazienti e dai controlli esaminati, tutto ciò si riflette in risultanze considerabilmente divergenti. Di conseguenza i numeri indicati trasmettono solo un riferimento approssimativo per la selezione di un'indagine adatta alle questioni cliniche. Per questo tante volte sono state indicate valutazioni qualitative quali "bassa", "media" oppure "alta".



Autoanticorpi nelle miopatie infiammatorie idiopatiche

Dermatomiosite (DM)

Autoanticorpi	Sens [%]	Spec [%]	Malattie associate
● ANA- IFI (test di screening)	50 - 80	bassa	molteplici
Anticorpi miosite specifici (MSA) *7			
● TIF1-γ *1	14 - 31	alta *2	DMg, DMa, MAC 58
● MDA5 (CADM-140)	11 - 35 *4	alta *2	CADM, ILD, LCM 17, 45, 28, 32
● NXP2 (MJ)	fino a 30 *5	alta *2	DMg, DMa, (MAC?) 28
● SAE	fino a 8 *6	alta *2	DMa 64
● Mi-2	5 - 30	> 95	DM (PM, MCI) 6, 33, 62, 64
● alanil-tRNA sintetasi (PL12)	fino a 6	alta *3	PM, DM, ILD 6, 25
● asparaginil-tRNA sintetasi (KS)	< 1	alta *3	PM, DM, ILD 6
● glicil-tRNA sintetasi (EJ)	< 1	alta *3	PM, DM, ILD 23a
● istidil-tRNA sintetasi (Jo-1)	9 - 20	> 95 *3	PM, DM, ILD, OM 6, 33, 25, 64
● isoleucil-tRNA sintetasi (OJ)	< 1	alta *3	PM, DM, ILD 6
● fenilalanil-tRNA sintetasi (ZO)	non nota	non nota	PM, DM, ILD
● treonil-tRNA sintetasi (PL7)	< 3	alta *3	PM, DM, ILD 6, 25
● tirosil-tRNA sintetasi (Ha, YRS)	non nota	non nota	PM, DM, ILD
● SRP	0 - 3	alta *3	PM, DM, NAM 6, 33, 64

*1 Gli anticorpi anti-TIF1-γ (150 kDa), -β (100 kDa), -α (140 kDa) possono presentarsi in combinazioni diverse. La radioimmunoprecipitazione rileva il 98,8 % degli anti-TIF1, tranne anti-TIF1-β solitari (20). La loro prevalenza nella DM giovanile (DMg) è del 23 - 29 % (22, 57), nella DM dell'adulto (DMa) del 13 - 30 % (22, 19, 57, 56); il 50 - 75 % dei pazienti anti-TIF1 positivi presenta neoplasie (20, 19).

*2 Questi anticorpi vengono considerati specifici di DM.

*3 La specificità si riferisce alle miopatie infiammatorie idiopatiche complessive (DM, PM, DM/PM-overlap).

*4 Le indicazioni delle sensibilità si riferiscono soprattutto a studi su campioni asiatici. Uno studio americano (17) ne rivela del 13 % e accenna lesioni cutanee e mucocutanee spiccate ("dermato-pulmonary syndrome").

*5 Le sensibilità riferite sono del 18 - 29 % in DM giovanile, la quale si manifesta con debolezza muscolare pronunciata, calcinosi, contratture articolari e necrosi muscolari (14, 25, 23). Anti-NXP2 sono stati riscontrati nel 17 - 30 % dei giovani adulti affetti da DM nei Stati Uniti e in Europa (17, 9), nel 1,6 % in Giappone (28). Nella forma adulta alcuni anti-NXP2 sono risultati associati a neoplasie ed nel 8 % a PM (9).

*6 Sensibilità più basse (< 2 %) rivelate in studi giapponesi.

*7 A seconda di Troyanov (59) gli MSA e MAA, esclusi anti-Mi-2, anti-SS-A/Ro e anti-SS-B/La, vengono chiamati „anticorpi di overlap" e classificati in tre gruppi:

1. anti-sintetasi: anti-Jo1, -OJ, -EJ, -KS, -PL7, -PL12.

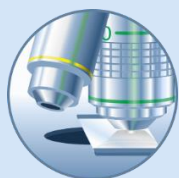
2. anticorpi associati a SSc: anti-centromeri, -Scl 70, -Th/To, -RNA-polimerasi, -PM/Scl, -U1snRNP, -U2-snRNP, -U3-snRNP, -U5snRNP, -Ku.

3. altri anticorpi di overlap: anti-SRP, -nucleoporina.

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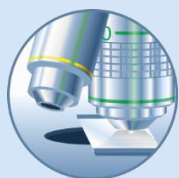
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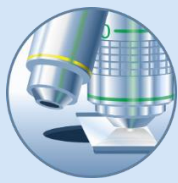
Dermatomiosite (DM)				
Autoanticorpi	Sens [%]	Spec [%]	Malattie associate	
Anticorpi miosite specifici (MSA) *7				
● PMS1	8	non nota	DM, PM, aplA	8
● PMS2	4	non nota	DM, PM	8
● MLH1	4	non nota	DM, PM	8
● DNA-PC _{CS}	2	non nota	DM, PM	8
● Mas	1	non nota	DM, PM, AIH	6
Anticorpi miosite associati (MAA) *7				
● PM/Scl	fino a 13	intermedia	DM, PM, OM	61, 48, 5, 6, 33
● Ku	1	intermedia	DM, PM, OM	6, 64
● fibrillarina	4	intermedia	DM, PM, OM	33
● U1-snRNP (U1-70K)	4	bassa	MCTD, LES, SS	6, 33, 10, 64
● SS-A/Ro 60	4	bassa	LES, SS	6, 64
● SS-A/Ro 52	22 - 24	bassa	SS, LES	6, 33
● SS-B/La	3 - 13	bassa	SS, LES	6, 33
Altri anticorpi				
● istoni (H1)	17	bassa	LES	34
● argonate 2 (Su)	4 - 9	bassa	PM, DM, SLE, MCDT, SS	53
● cellule endoteliali	36	bassa	multiplici	12
● proteasoma (20S; αC9)	62	bassa	DM, LES	15
● ADAM 10	casistica	bassa	DM, ILD	21
● proteina di membrana muscolare	15 - 20 *8	bassa	DM, PM, SSc, LES, AR	54
● Myo22/25	8	bassa	DM, PM	35
● 56 kDa proteina del nucleo	85 - 90	bassa	DMg, DMa, PM	2, 7, 13
*8 Elisa con cellule del rhabdomyosarcoma (TE671).				
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Autoanticorpi nelle miopatie infiammatorie idiopatiche



Polimiosite (PM)			
Autoanticorpi	Sens [%]	Spec [%]	Malattie associate
Anticorpi miosite specifici (MSA)			
● SRP	7	alta *	PM, NAM, ASRPS, (DM) 6, 33
● Mi-2	0 - 9	alta *	DM, PM, IBM 6, 33, 62
● alanil-tRNA sintetasi (PL12)	fino all'8	alta *	PM, DM, ILD 6, 25
● asparaginil-tRNA sintetasi (KS)	< 1	alta *	PM, DM, ILD 6
● glicil-tRNA sintetasi (EJ)	< 1	alta *	PM, DM, ILD
● istidil-tRNA sintetasi (Jo-1)	19 - 33	> 95 *	PM, DM, ILD 6, 33, 25
● isoleucil-tRNA sintetasi (OJ)	< 1	alta *	PM, DM, ILD 6
● fenilalanil-tRNA sintetasi (ZO)	non nota	non nota	PM, DM, ILD
● treonil-tRNA sintetasi (PL7)	< 3	alta *	PM, DM, ILD 6, 25
● tirosil-tRNA sintetasi (Ha, YRS)	non nota	non nota	PM, DM, ILD
● PMS1	8	non nota	DM, PM, aplA 8
● PMS2	4	non nota	DM, PM 8
● MLH1	4	non nota	DM, PM 8
● DNA-PC _{CS}	2	non nota	DM, PM 8
● Wa	casistica	non nota	PM, ILD 30, 43
● KJ	casistica	non nota	PM, ILD 55
● Mas	1	non nota	DM, PM, AIH 6
Anticorpi miosite associati (MAA) vedi Dermatomiosite			
● PM/Scl	fino al 7	intermedia	DM, PM, OM 61, 48, 5, 6, 33
Altri anticorpi vedi Dermatomiosite			
* La specificità si riferisce alle miopatie infiammatorie idiopatiche complessive (DM, PM, DM/PM-overlap).			
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Autoanticorpi nelle miopatie infiammatorie idiopatiche

Sindrome antisintetasi

Autoanticorpi	Sens [%]	Spec [%]	Malattie associate
● istidil-tRNA sintetasi (Jo-1)	35,5	*	DM, PM, CADM, ILD 6 , 33 , 25
● glicil-tRNA sintetasi (EJ)	22,8	*	DM, PM, ILD, CADM
● treonil-tRNA sintetasi (PL7)	17,5	*	DM, PM, ILD, CADM 6 , 25
● alanil-tRNA sintetasi (PL12)	10,8	*	ILD, CADM, DM 6 , 25
● asparaginil-tRNA sintetasi (KS)	7,8	*	ILD, CADM 6
● isoleucil-tRNA sintetasi (OJ)	4,5	*	ILD, PM, DM 6
● fenilalanil-tRNA sintetasi (ZO)	non nota	*	PM, DM, ILD
● tirosil-tRNA sintetasi (Ha, YRS)	non nota	*	PM, DM, ILD
● SS-A/Ro 52	18,6	*	
● SS-B/La	2,4	*	
● centromero	2,4	*	
● U1-snRNP	1,2	*	
● Scl-70	< 1	*	
● Th/To	< 1	*	
● U3-snRNP	< 1	*	
● Sm	< 1	*	

* La sindrome anti-sintetasi si definisce attraverso la presenza di un anticorpo anti-sintetasi, quindi riferimenti alla specificità degli anticorpi sono superflui. Sono indicate le prevalenze degli anticorpi anti-sintetasi specifici e degli altri anticorpi associati in pazienti con sindrome antisintetasi ([23a](#)).

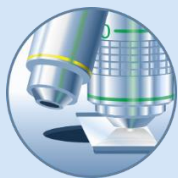
L'esordio e le manifestazioni della sindrome variano a seconda della specificità dell'anticorpo anti-sintetasi.

Sintomi: esordio acuto, febbre, interstiziopatia polmonare (ILD, 80 %), "mani da meccanico" (ipercheratosi della cute) (70 %), fenomeno di Raynaud (40 %), artrite (60 %), occasionalmente di forma erosiva. La manifestazione clinica della miosite può mancare innanzitutto nello stadio evolutivo e in presenza di anti-PL7 o anti-PL12 (forma amiotopica) ([25](#)).

A seconda di Troyanov ([59](#)) è stata classificata "miosite di *overlap*".

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Autoanticorpi nelle miopatie infiammatorie idiopatiche



Miopatia necrotizzante immuno-mediata (NAM)

Autoanticorpi	Sens [%]	Spec [%]	Malattie associate
● SRP 54 kDa * ¹	3	alta	PM, DM, NAM 6, 33
● SRP 68 kDa	< 1	alta	PM, DM, NAM 24
● SRP 72 kDa	< 1	alta	PM, DM, NAM 24
● 7 SL-RNA * ²	non nota	non nota	DP, PM 52
● HMG-CoA-reduttasi * ³	bassa	alta	assunzione di statine 39, 40

*¹ Anticorpi anti-SRP possono essere associati ad una forma di miopatia immuno-mediata rapidamente progressiva con necrosi muscolari, fibre muscolari degenerate e rigeneranti, con scarsa infiltrazione di cellule infiammatorie, a volte con lesioni vascolari somiglianti alla dermatomiosite, che si presentano mediante riduzione e allargamento dei capillari, in alcuni casi con deposizioni del complemento e talvolta con interessamento del miocardio (**sindrome anti-SRP**). La miopatia necrotizzante può essere concomitante a neoplasie e infezioni virali (HIV) (39).

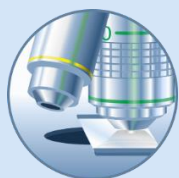
A seconda di Troyanov (59) è stata classificata "miosite di *overlap*".

*² Anticorpi anti-7SL-RNA vengono rivelati prevalentemente in pazienti giapponesi anti-SRP positivi.

*³ Spesso associato all'assunzione precedente di statine. Da segnalare, che la maggioranza prevalente dei pazienti in terapia con statine, anche in casi di modesta incompatibilità, non sviluppa anticorpi anti-HMG-CoA-reduttasi (63). Gli anticorpi sono abbinati a DRB1*1101.

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Autoanticorpi nelle miopatie infiammatorie idiopatiche

Connettiviti overlap miosite-sclerosi sistemica

Autoanticorpi	Sens [%]	Spec [%]	Malattie associate
● PM/Scl	15 - 36	alta	OM 61, 48, 5, 6, 33, 16
● esosomi * ¹	non nota	non nota	OM 5
● Ku * ²	4 - 25	alta	OM, DM, PM 13, 33, 49, 18, 16
● fibrillarina	22	alta	OM 33
● U5-snRNP	casistica	non nota	OM 36
● istidil-tRNA sintetasi (Jo-1)	10 - 25	alta	PM, DM, OM, ILD 33, 64
● Mi-2	0 - 5	alta	PM, DM 33, 64
● SRP	3	alta	PM, DM 33
Altri anticorpi *³			
● ANA- IFI	fino al 60	bassa	molteplici
● Scl-70	30 - 38	alta	SSc, OM 33
● centromeri	60 - 80	alta	SSc, OM
● RNA-polimerasi	22 - 30	alta	SSc, OM
● Th/To	fino al 13	alta	SSc, OM
● U1-snRNP (U1-70K)	fino al 21 *	bassa	MCTD, LES, SS 6, 33, 10
● U2-snRNP	fino al 15 *	bassa	11, 42
● SS-A/Ro 60	4 *	bassa	LES, SS 6
● SS-A/Ro 52	fino al 37 *	intermedia	SS, LES 13, 6, 33
● SS-B/La	fino al 16 *	bassa	SS, LES 6, 33
● ds-DNA	< 2 *	bassa	LES
● CCP	14 *	bassa	AR

Sindromi di *overlap*: la sindrome più frequente è la sindrome da sovrapposizione di DM/PM con la sclerosi sistemica nel 40 - 50 % dei casi (59, 60), più rare sono sovrapposizioni con lupus eritematoso (LES), connettivite mista (MCTD), artrite reumatica e le sindromi anti-sintetasi o anti-SRP.

*¹ Principalmente in pazienti anti-PM/Scl positivi. Proteine bersaglio sono hRp4p, hRp40p, hRp41p, hRp42p, hR46p, hCsl4p (5).

*² Presenza in miositi *overlap* in associazione a sclerosi sistemica, sindrome di Sjögren, lupus eritematoso sistemico (49, 18). Necrosi muscolari e interstiziopatia polmonare sono stati riferiti nel 75 % dei casi. Anticorpi vengono riscontrati anche senza miosite in LES, SSc, AR, SS. L'8 % circa dei pazienti anti-Ku positivi si presenta con DM/PM (38).

*³ Gli autoanticorpi di seguito elencati in prima linea sono considerati marcatori delle diverse connettiviti indicate (malattie associate). Con varia frequenza essi sono riscontrati anche in pazienti con sindromi di DM/PM-*overlap*. Le loro specificità si riferiscono alla sclerosi sistemica progressiva, quelle segnalate con * alla sindrome DM/PM-*overlap*.

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Miopatia associata a neoplasia

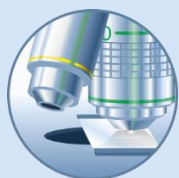
Autoanticorpi	Sens [%]	Spec [%]	Malattie associate
● TIF1- γ * ¹	13 - 30	alta	DMg, DMa, MAC
● NXP2 (MJ) * ²	fino al 30	alta	DMg, DMa (MAC?)

*¹ Neoplasie vengono rivelate nel 50 - 75 % dei pazienti. Anticorpi sono anche presenti in pazienti con DM giovanile (in questi casi non associati a neoplasie), e rarissime in PM. Tumori accompagnanti sono carcinomi della mammella, del polmone, pancreas e colon (USA, 1), oppure tumori nasofaringei, del polmone, della mammella e cervice (Taiwan, 27).

*² Nella forma adulta (DMa) alcuni anti-NXP2 sono risultati associati a neoplasie (9, 17, 25).

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Autoanticorpi nelle miopatie infiammatorie idiopatiche



Miopia da corpi inclusi (MCI)

Autoanticorpi	Sens [%]	Spec [%]	Malattie associate
● 5'-nucleosidasi citosolica 1A (cN1A)	34	98	MCI 37, 47
● istidil-tRNA sintetasi (Jo-1)	2 - 5 ^{*1}		PM, DM 6, 51
● alanil-tRNA sintetasi (PL12)	4 ^{*1}		PM, DM 51
● SRP	0 - 3 ^{*1}		PM, DM 6, 51
● Mi-2	2 - 8 ^{*1}		DM, PM 6, 51
Altri anticorpi			
● ANA-IIFT	29 ^{*2}		molteplici 51
● ds-DNA	2		LES 51
● fattori reumatoidi	casistica ^{*2}		AR 31
● mitocondri (AMA)	casistica ^{*2}		PBC 31
● SS-A/Ro 52	16 - 25 ^{*2}		SS, LES 6, 31, 51
● SS-A/Ro 60	4 - 6		LES, SS 6, 31, 51
● SS-B/La	5 ^{*2}		SS, LES 6, 31, 51
● U1-snRNP	4 - 6		MCTD, LES, SS 6, 51

^{*1} Livelli sierici non sono aumentati significativamente in paragone a campioni di controllo di soggetti sani (51).

^{*2} Anche nell'accostamento di sindrome di *overlap*, di sindrome di Sjögren con MCI (31, 50).

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Autoanticorpi nelle miopatie infiammatorie idiopatiche



Abbreviazioni

Sens	sensibilità
Spec	specificità

malattie

AIH	epatite autoimmune
aplA	anemia aplastica
AR	artrite reumatoide
ASRPS	sindrome anti-SRP
CADM	dermatomiosite clinicamente amiopatica
DM, DMg, DMa	dermatomiosite, - giovanile, - dell'adulto
ILD	interstiziopatia polmonare (interstitial lung disease)
LCM	lesioni cutanee e mucocutanee
LES	lupus eritematoso sistemico
MAC	miosite associata a neoplasia
MCI	miopatia da corpi inclusi
MCTD	connettivite mista, mixed connective tissue disease
NAM	miopatia necrotizzante immuno-mediata
OM	DM/PM-overlap
PBC	cirrosi biliare primitiva
PM	polimiosite
SS	sindrome di Sjögren
SSc	sclerosi sistemica progressiva

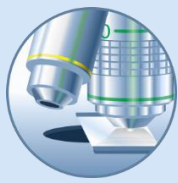
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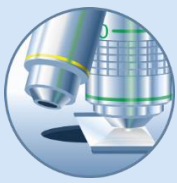
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