



«Συστηματική αυτοάνοση νόσος από τύπου I IFNs»

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Παθολογικής Φυσιολογίας

Ιατρική Σχολή ΕΚΠΑ

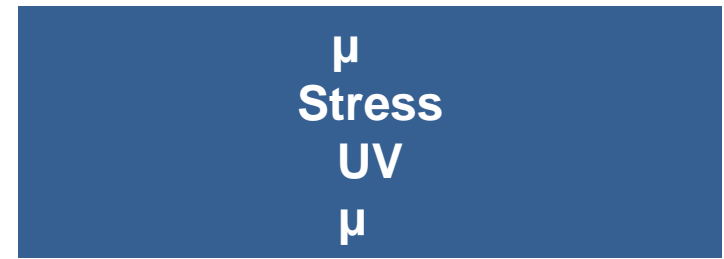
02.11.2019

Αυτοάνοσα Νοσήματα- Γενικά χαρακτηριστικά

- Αυτοάνοσες αποκρίσεις κατά εαυτού
- Αντισώματα κατά ενδογενών νουκλεϊκών οξέων ή οργανοειδικών αντιγόνων
- Βλάβη ιστών-οργάνων
- Προσβολή κατεξοχήν γυναικών
- Οικογενή προδιάθεση
- Απουσία φλεγμονώδους αντίδρασης



μ - A

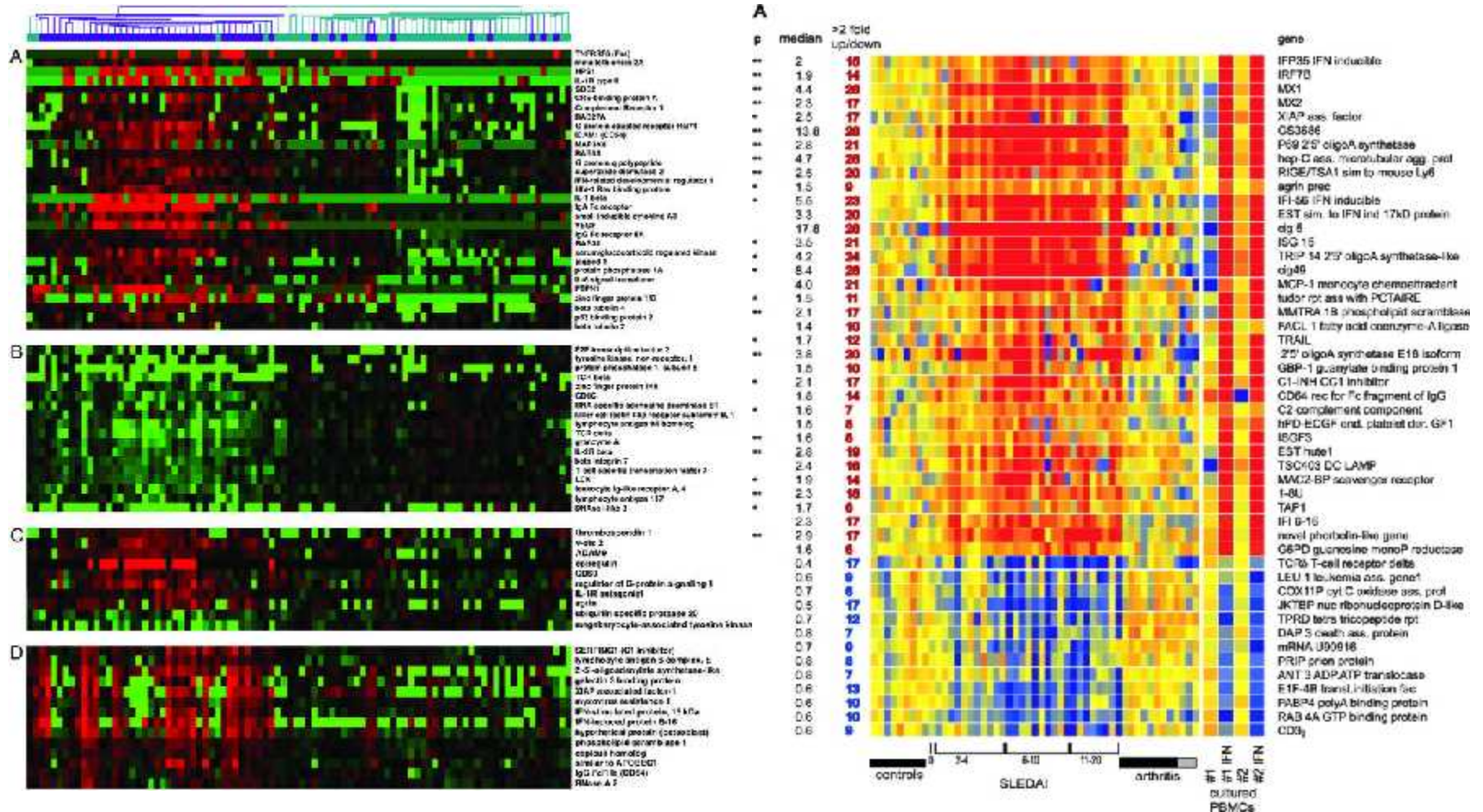


μ

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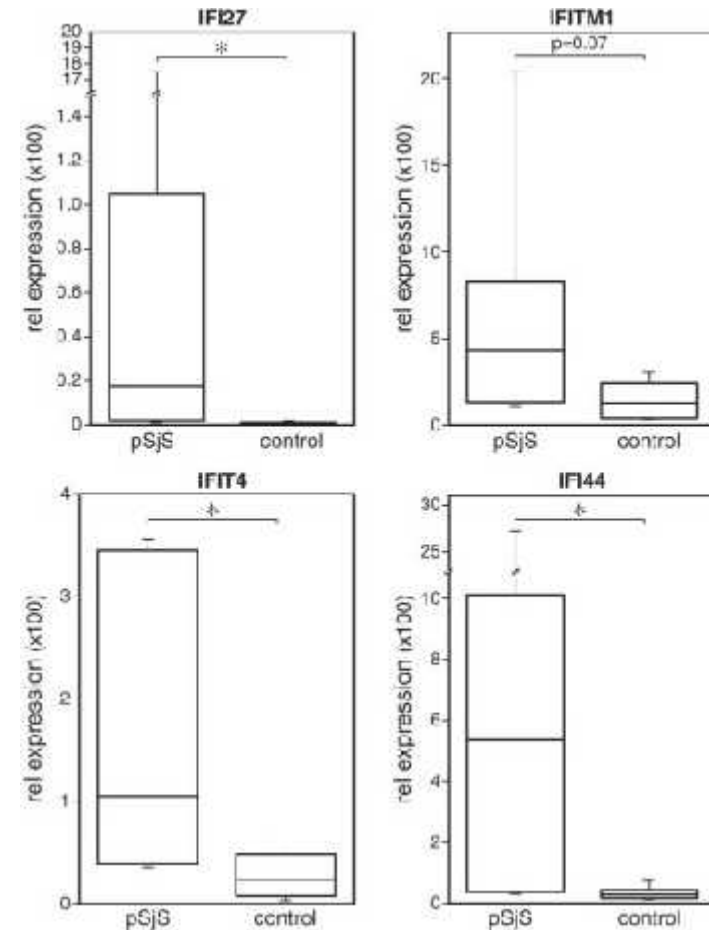
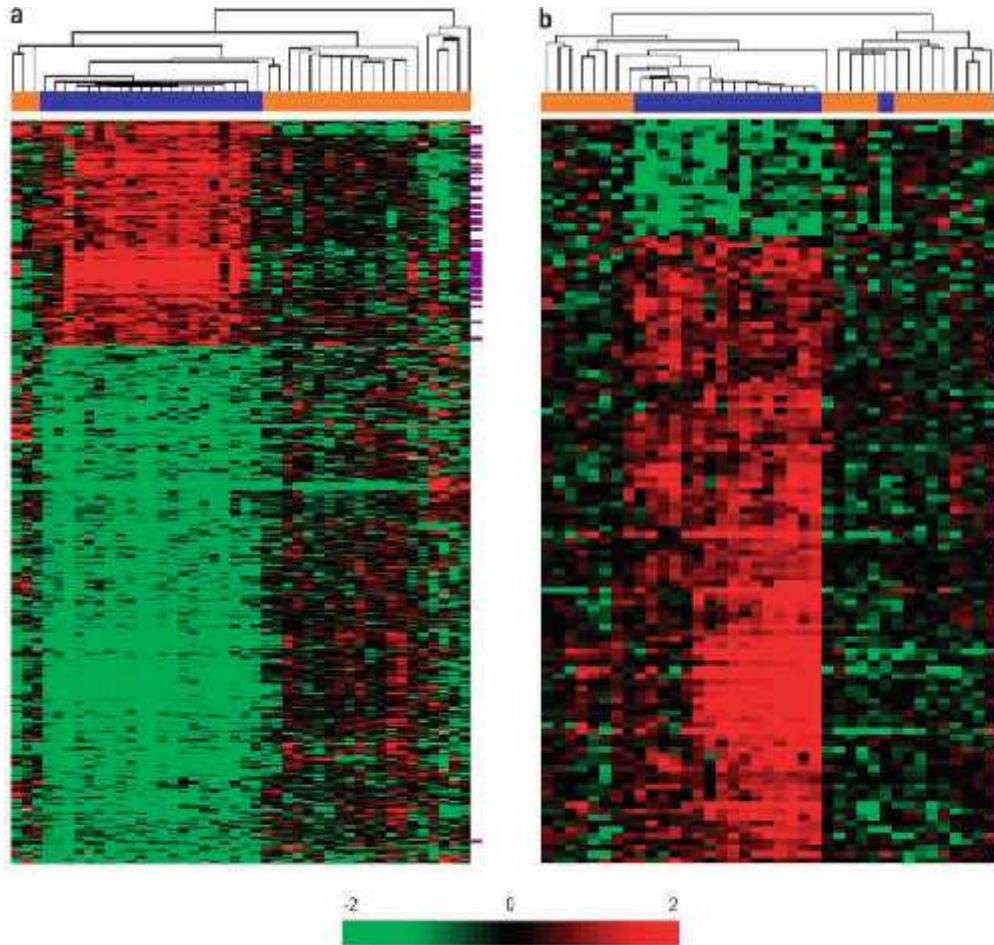


Crow et al, Arthritis Res Ther, 2003

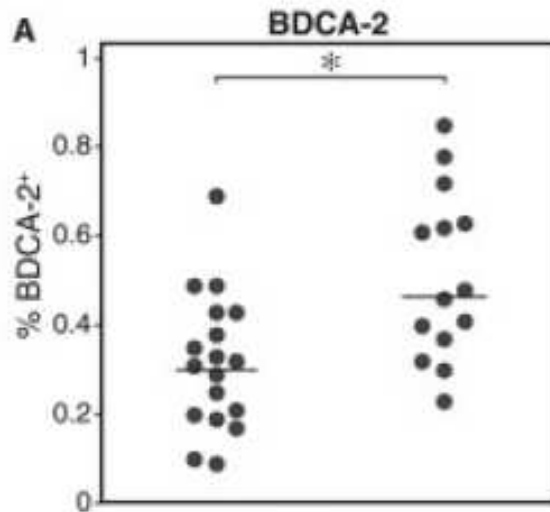
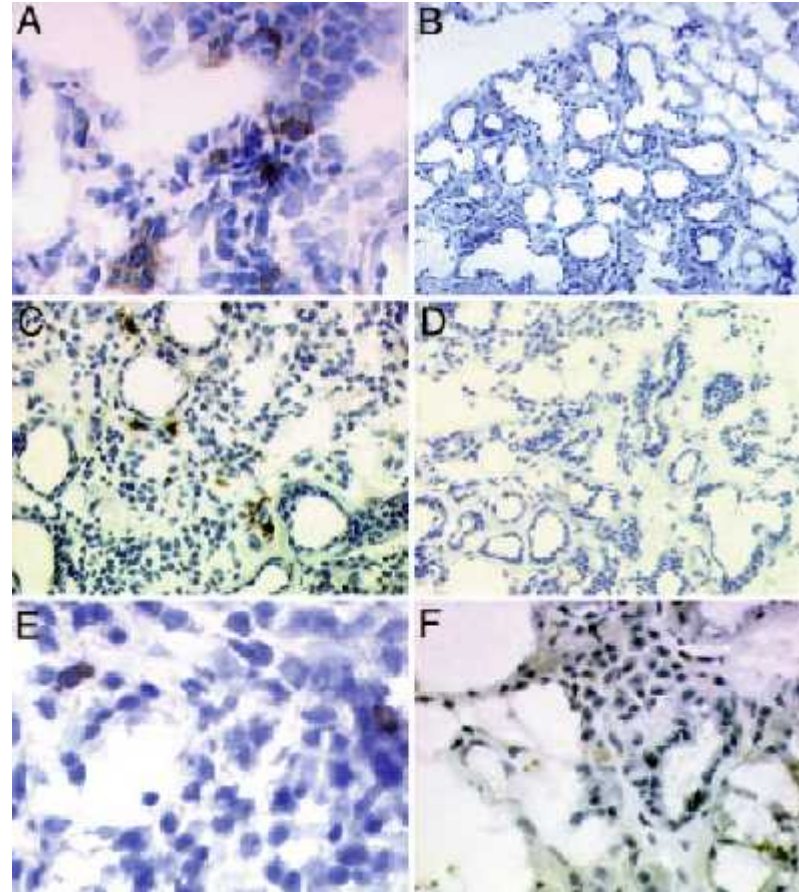
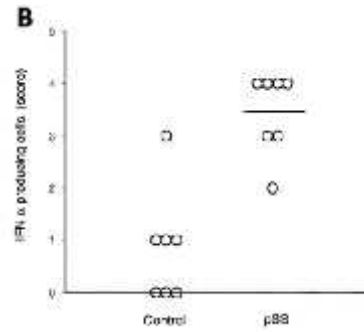
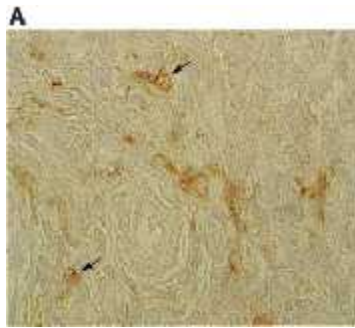
ennett et al, J Exp Med, 2003

aechler et al, Proc Natl Acad Sci U S A, 2003

Αυξημένη έκφραση γονιδίων επαγόμενων από ιντερφερόνη τύπου I σε περιφερικά μονοκύτταρα από ασθενείς με σύνδρομο Sjogren



Ιντερφερόνη τύπου I και σύνδρομο Sjogren

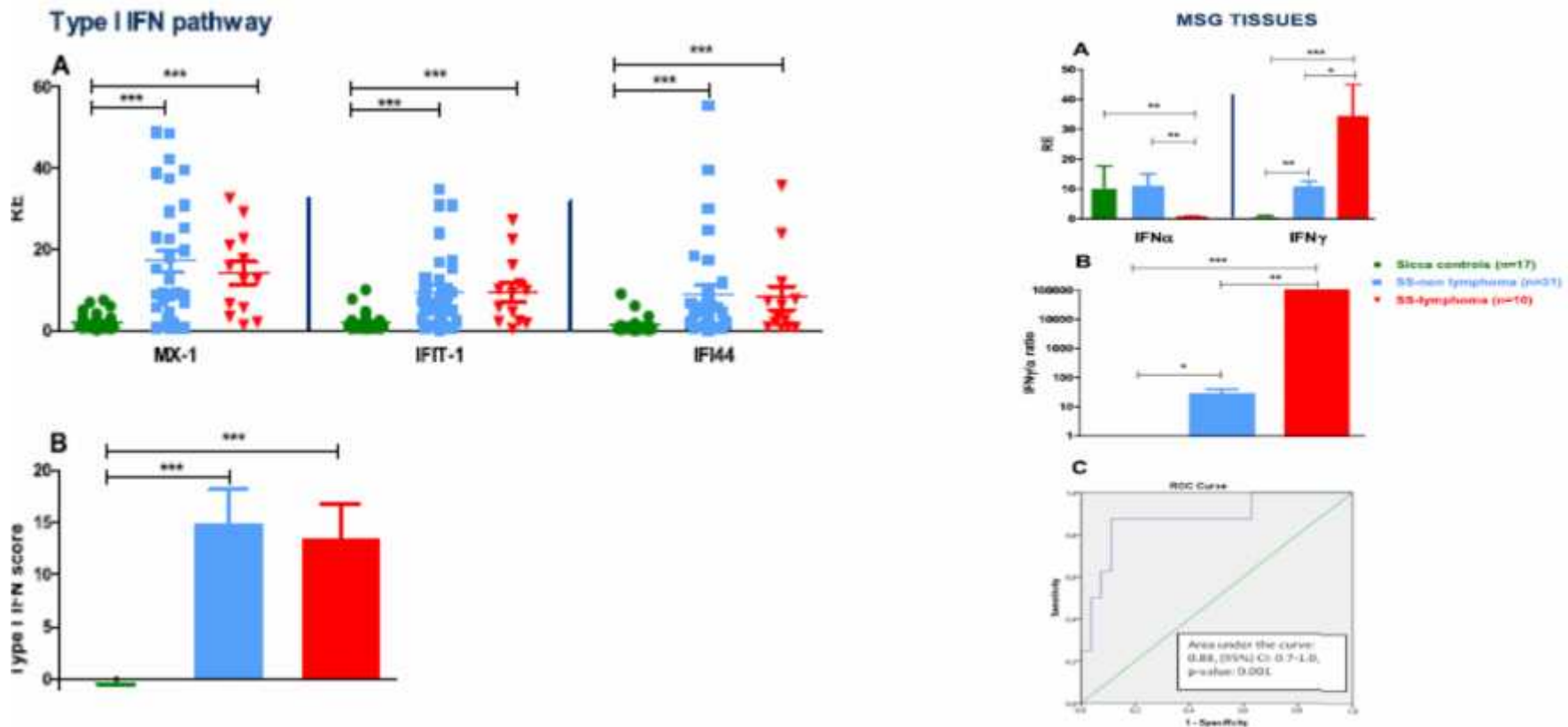


Båve U, Arthritis Rheum. 2005 ;52:1185-95

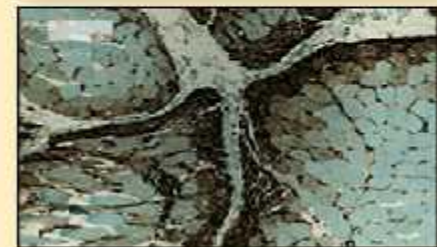
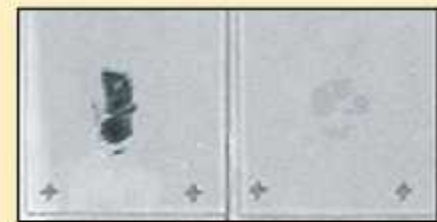
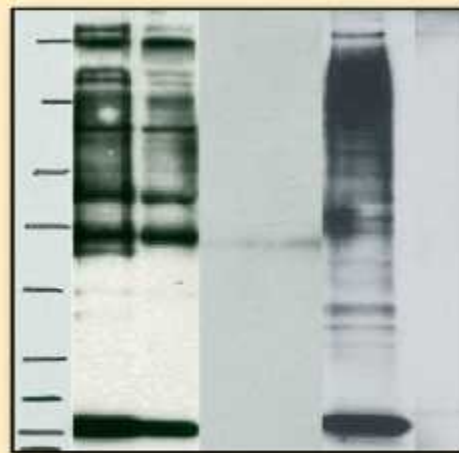
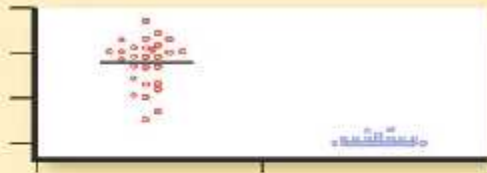
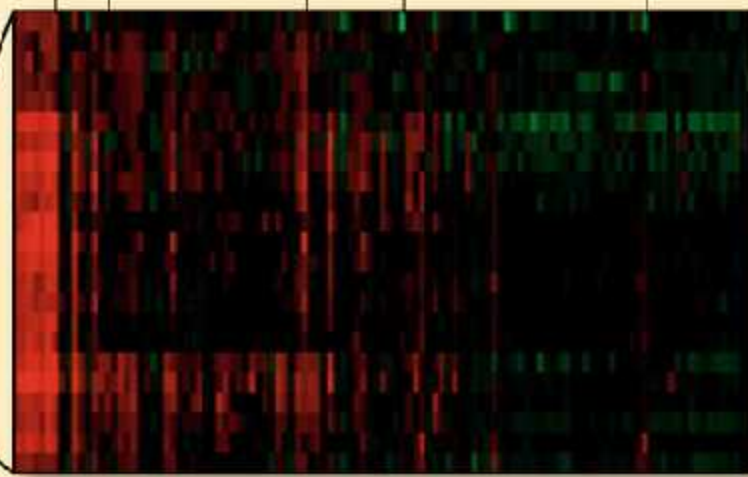
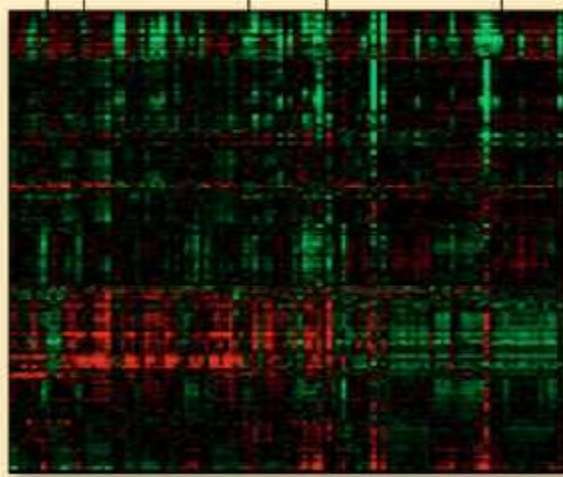
Gottenberg JE, Proc Natl Acad Sci U S A. 2006 Feb 21;103(8):2770-5.

Type I and II interferon signatures in Sjogren's syndrome pathogenesis: Contributions in distinct clinical phenotypes and Sjogren's related lymphomagenesis

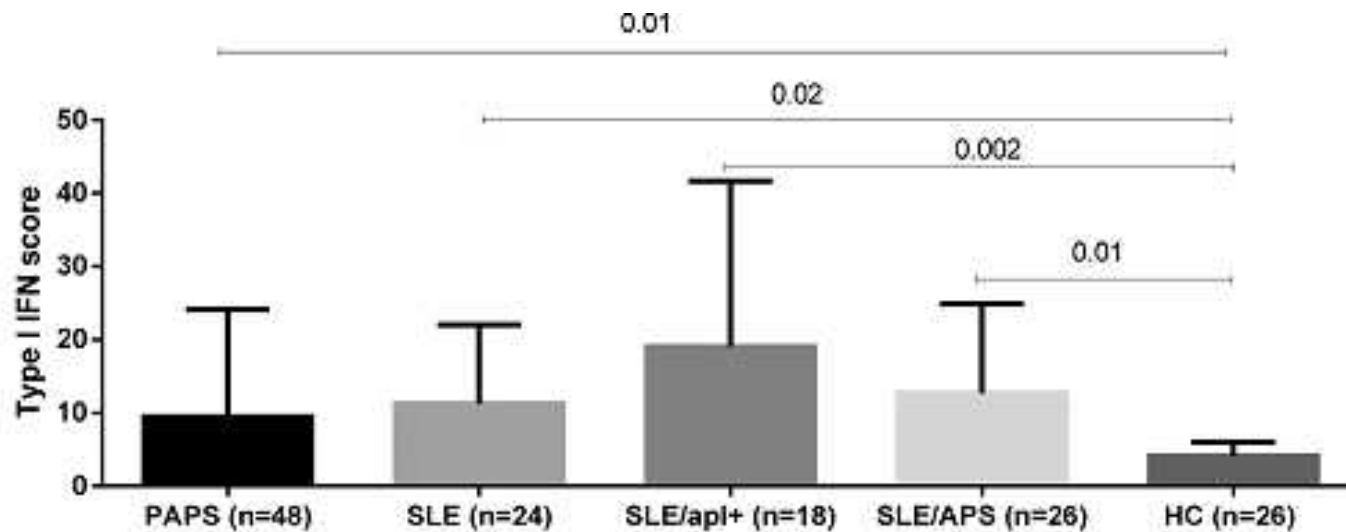
Adrianos Nezos ^a, Fotini Gravani ^b, Anna Tassidou ^c, Efstathia K. Kapsogeorgou ^d, Michael Voulgarelis ^d, Michael Koutsilieris ^a, Mary K. Crow ^{e,1}, Clio P. Mavragani ^{a, d, 1, *}



Αυξημένη έκφραση γονιδίων επαγόμενων από τύπου I ιντερφερόνη σε ασθενείς με δερματομυοσίτιδα



Αυξημένη έκφραση γονιδίων επαγόμενων από τύπου I ιντερφερόνη σε ασθενείς με αντιφωσfolιπιδικό σύνδρομο



A μ

μ

Immune interferon in the circulation of patients with autoimmune disease.

Hooks JJ, Moutsopoulos HM, Geis SA, Stahl NI, Decker JL, Notkins AL.

N Engl J Med. 1979 Jul 5;301(1):5-8.

μ

- 1982: .
- 1990: μ μ μ IFN- μ .
- 1999: in vitro μ FN- « μ μ »
- 1999: μ

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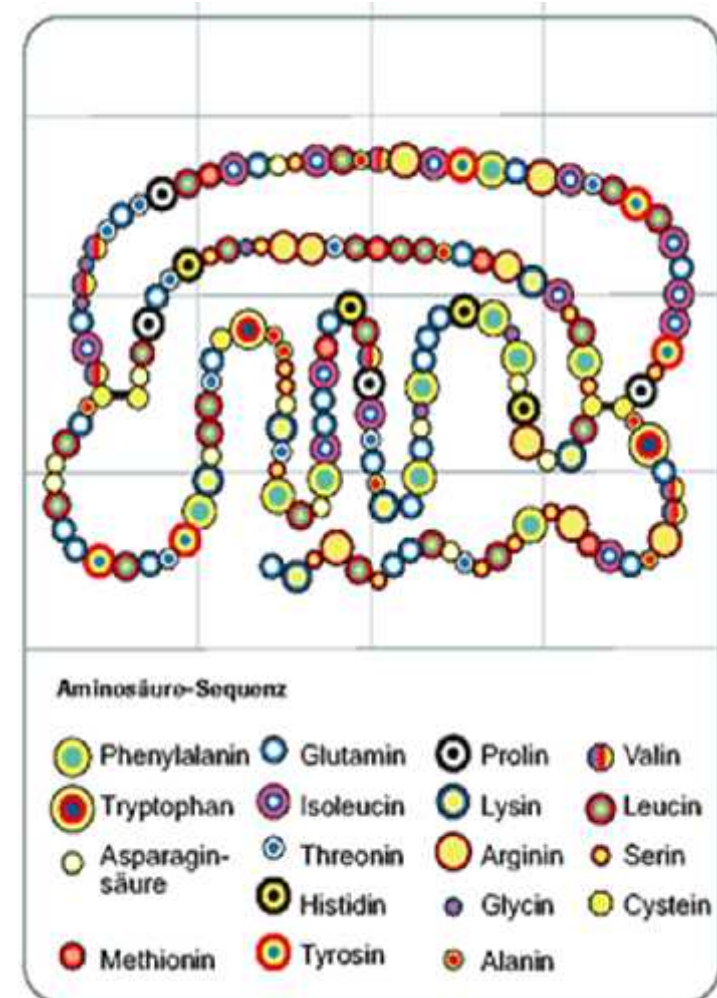
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- 1957 (Isaacs and Lindenmann)
- Ουσίες που «παρεμβαίνουν» (interfere) στον πολλαπλασιασμό των ιών σε κυτταρικές καλλιέργειες
- Φυσικές πρωτεΐνες και γλυκοπρωτεΐνες
- Εκκρίνονται από τα ευκαρυωτικά κύτταρα σε απάντηση σε ιογενείς λοιμώξεις, νεοπλασίες
- Μέρος της ελικοειδούς οικογένειας των κυτταροκινών

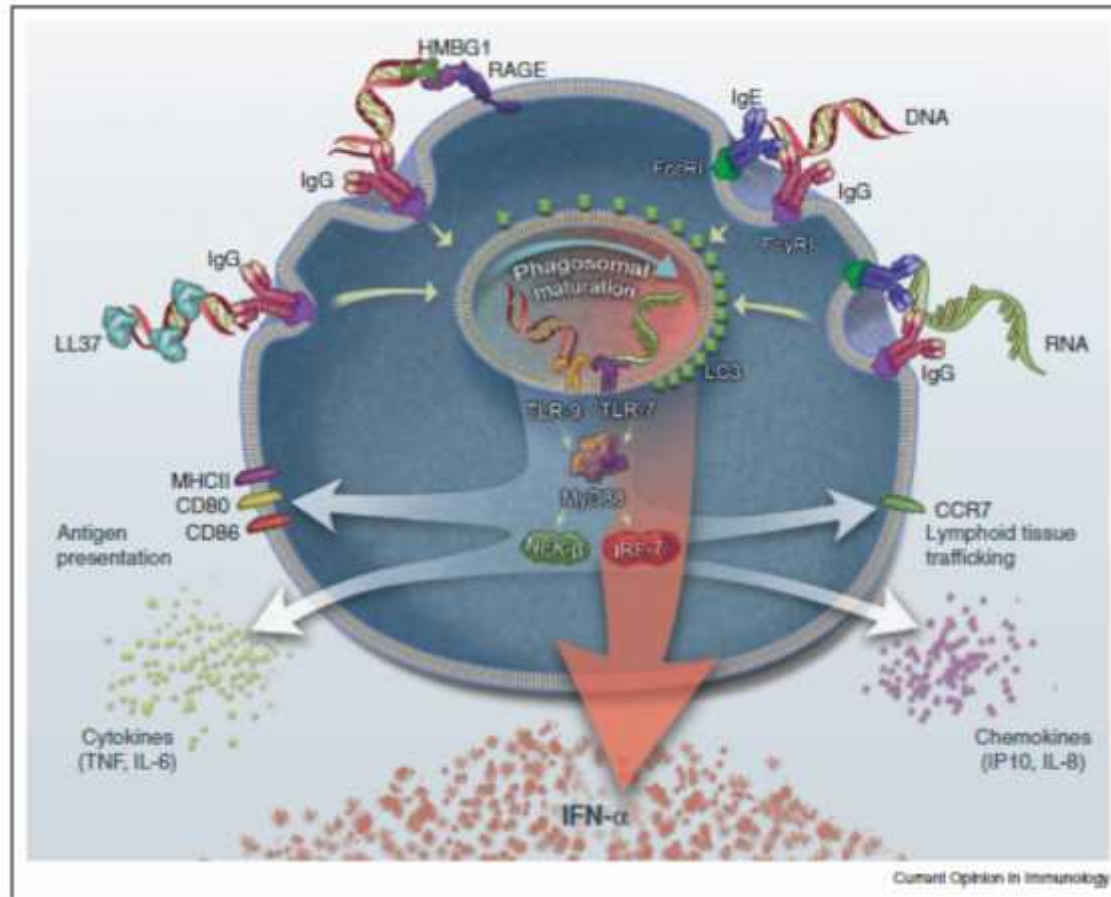


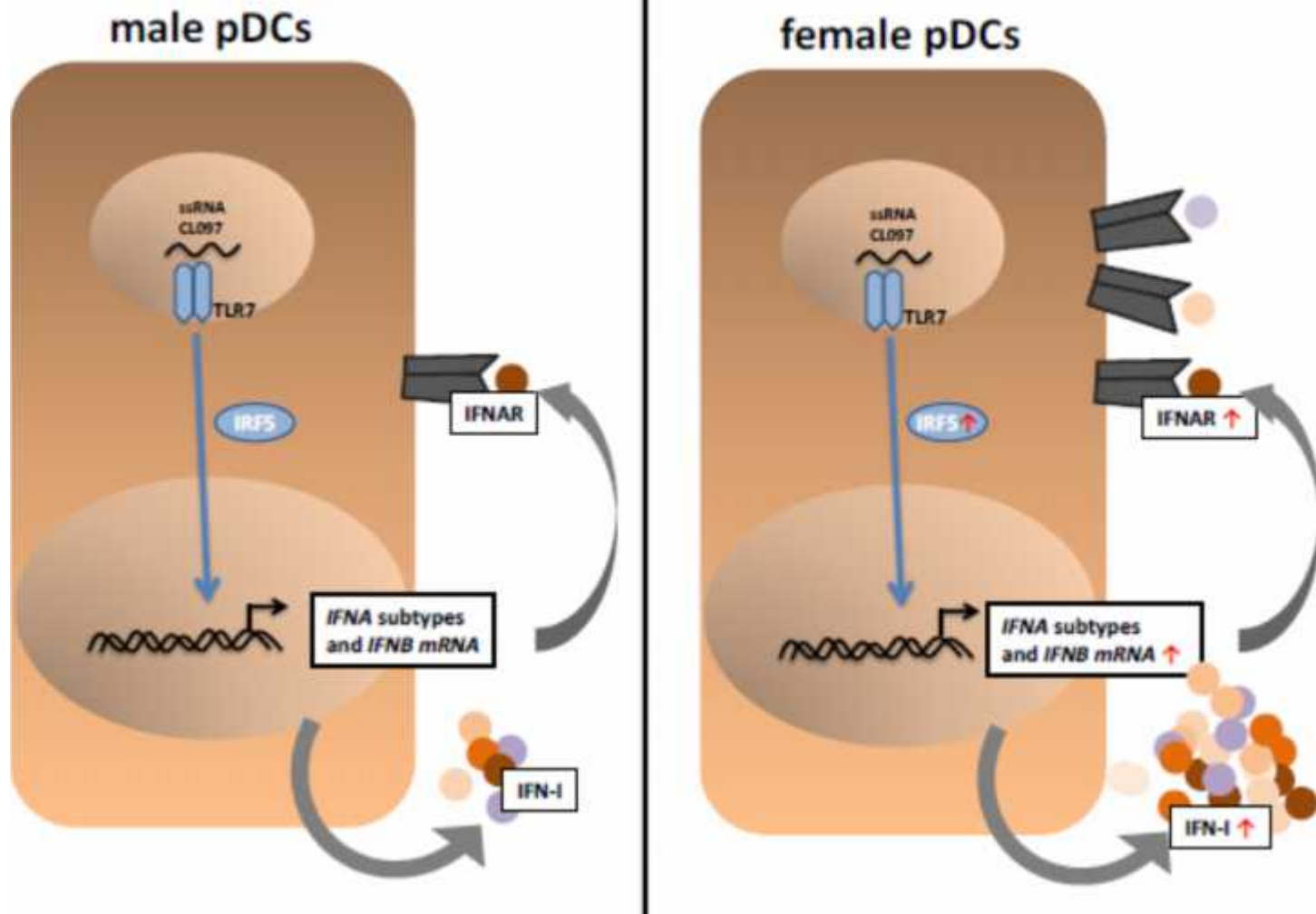
	T	
13 IFN 's, IFN₁, IFN₂, IFN_V, IFN₃	IFN_X	IFN}s (IL-28 and , IL-29)
μ μ 9	μ μ 12	
μ μ -		μ , μ
μ , μ	, μ , μ , μ	μ

μ

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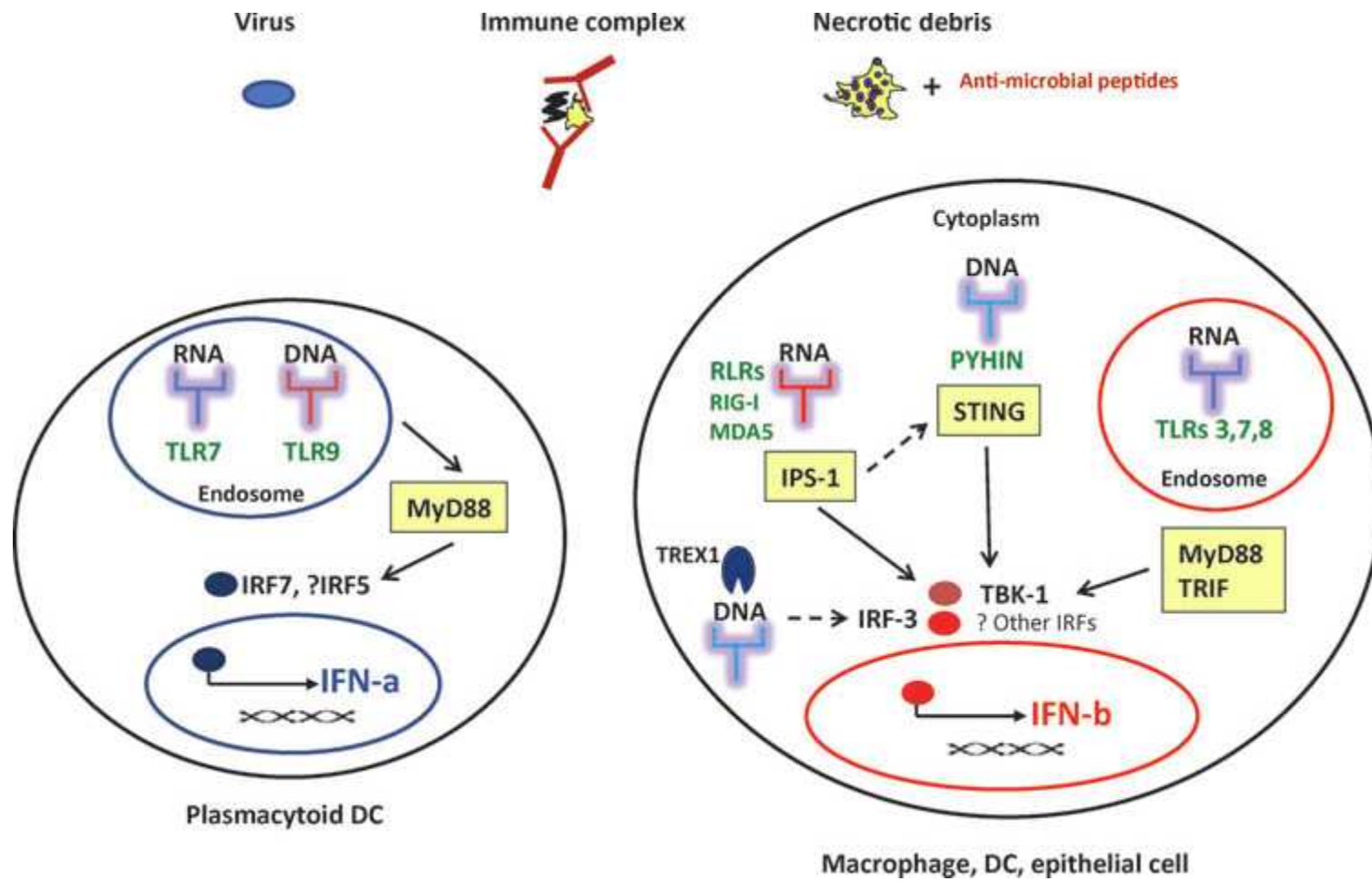




μ

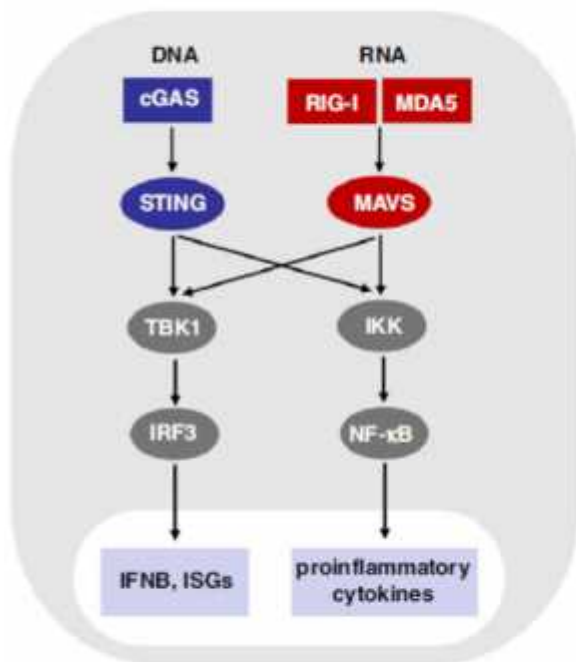
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- μ ;

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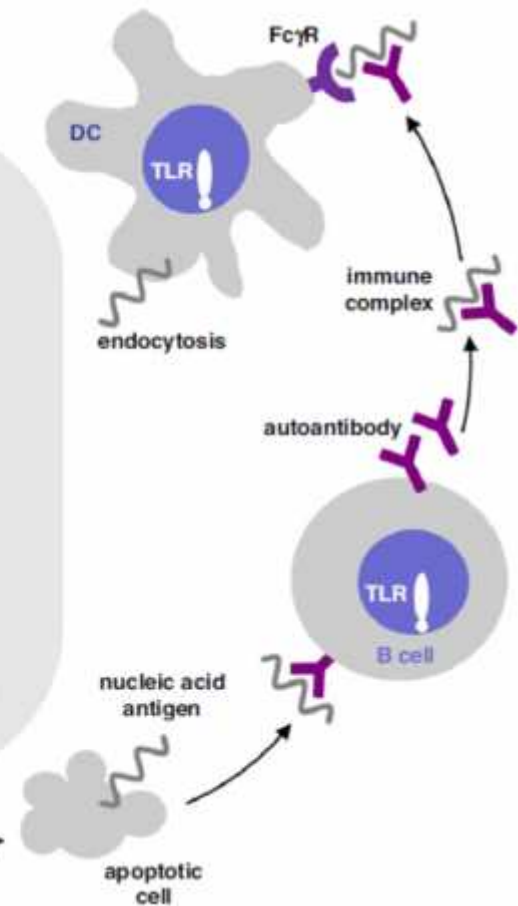
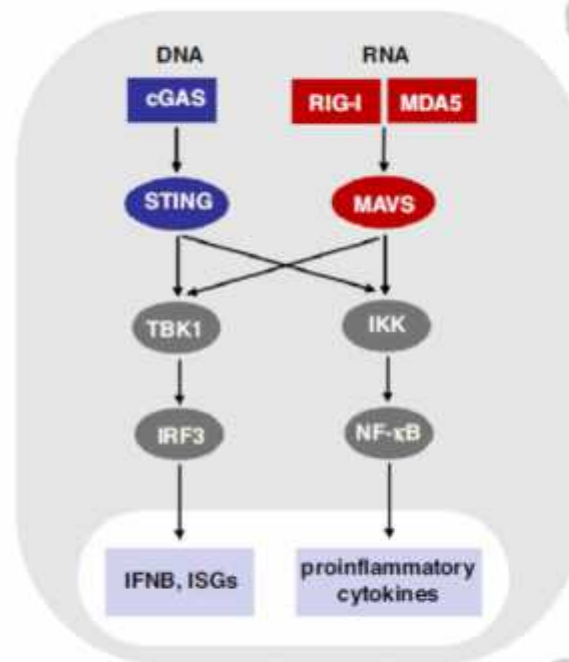


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cell-intrinsic type I IFN activation



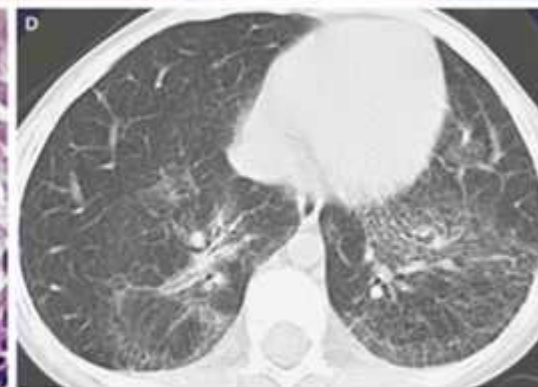
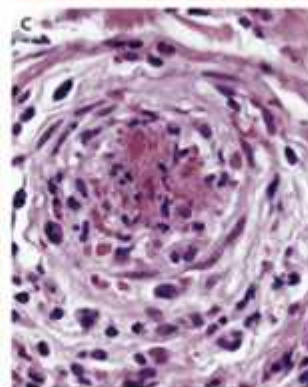
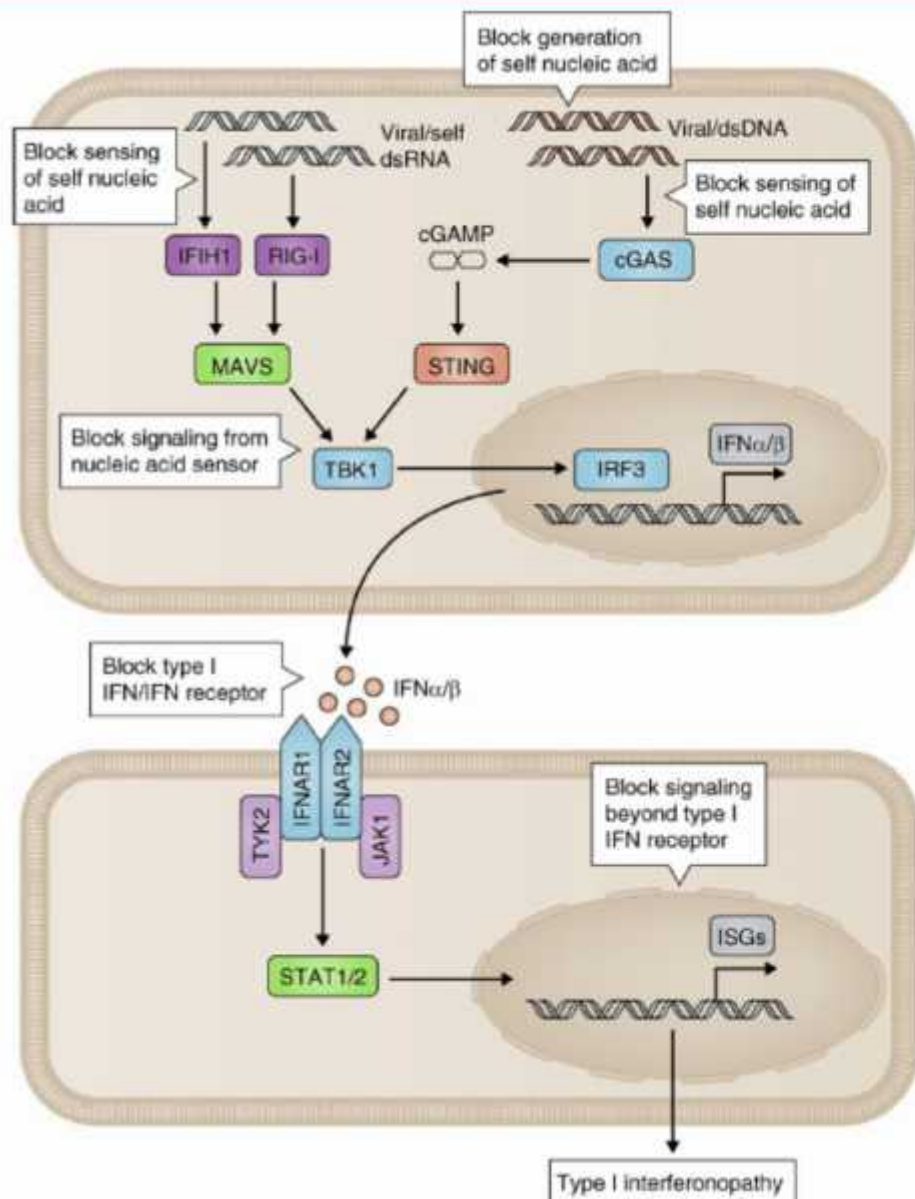
cell-extrinsic type I IFN activation



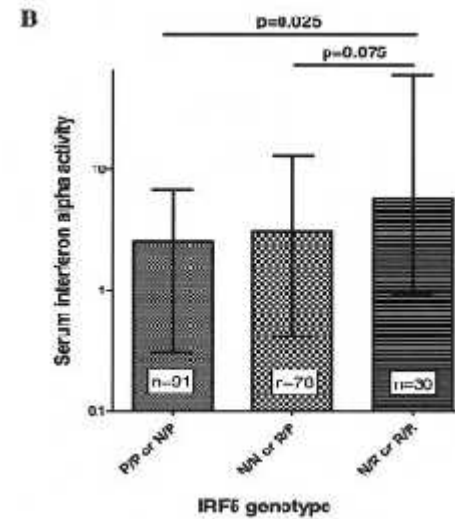
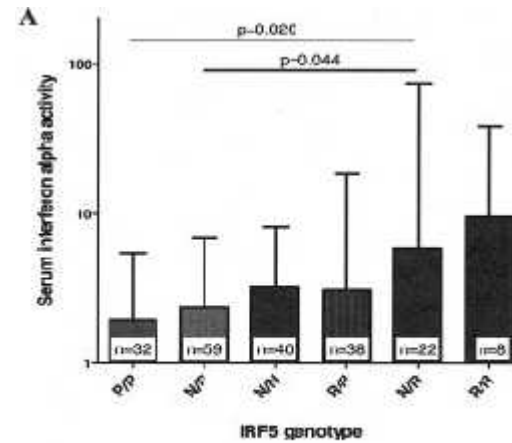
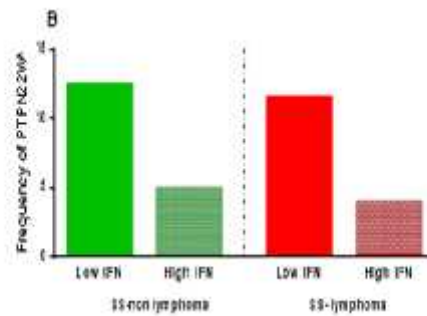
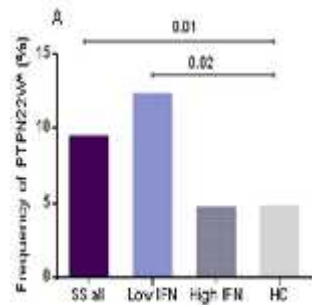
μ

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Ιντερφερονοπάθειες τύπου I

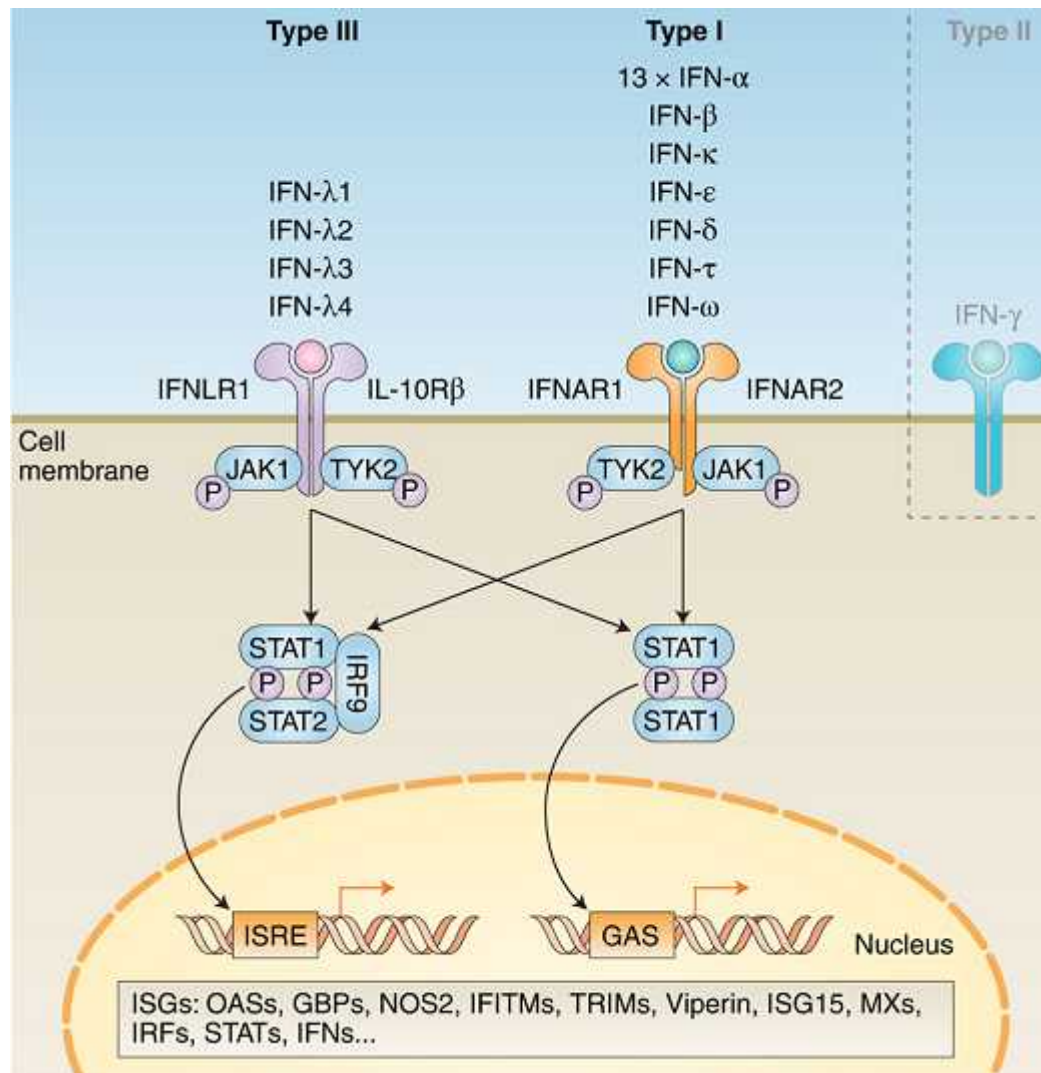


- Πολυγονιδιακές
IRF5, STAT4, PTPN22

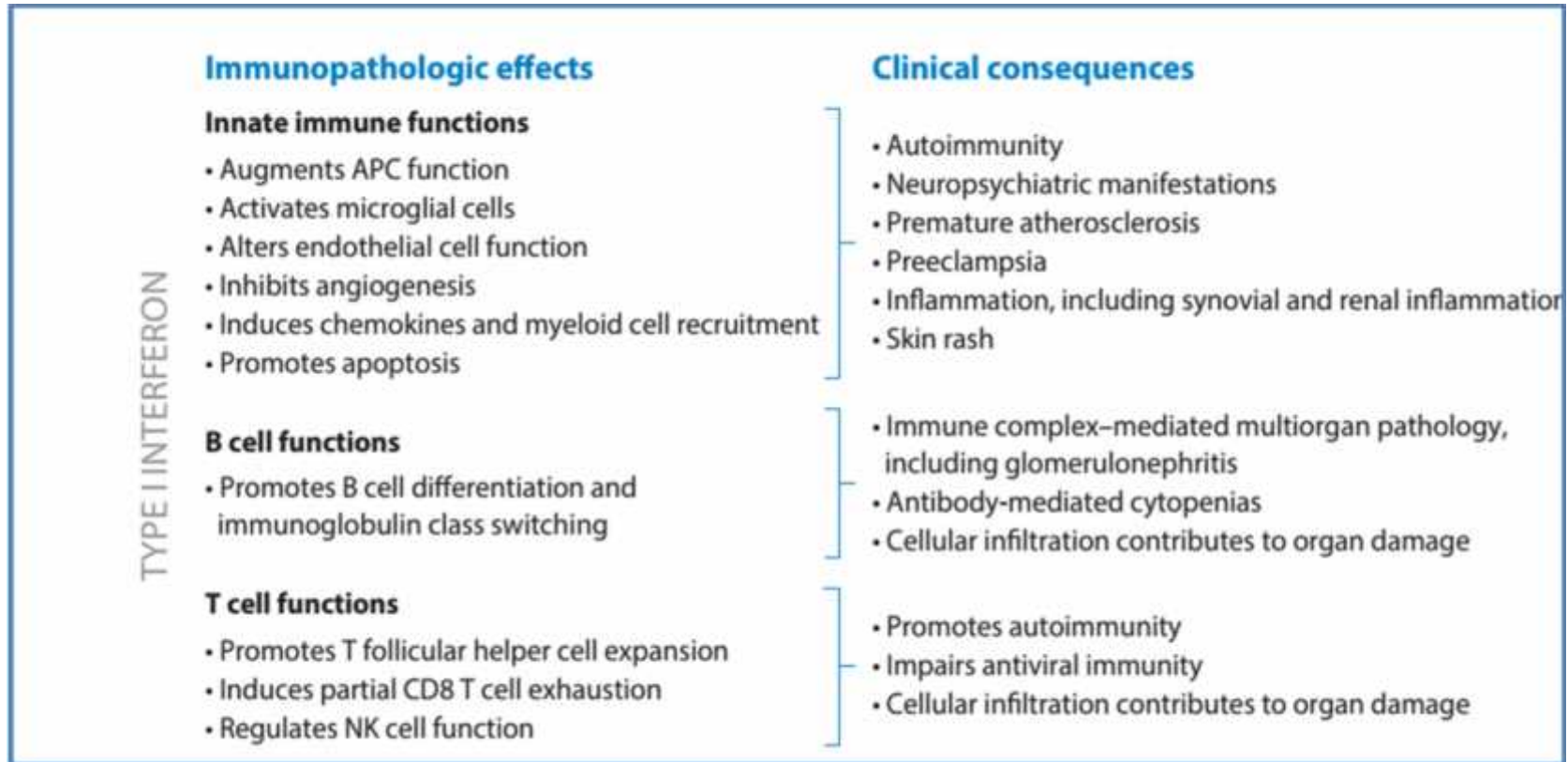


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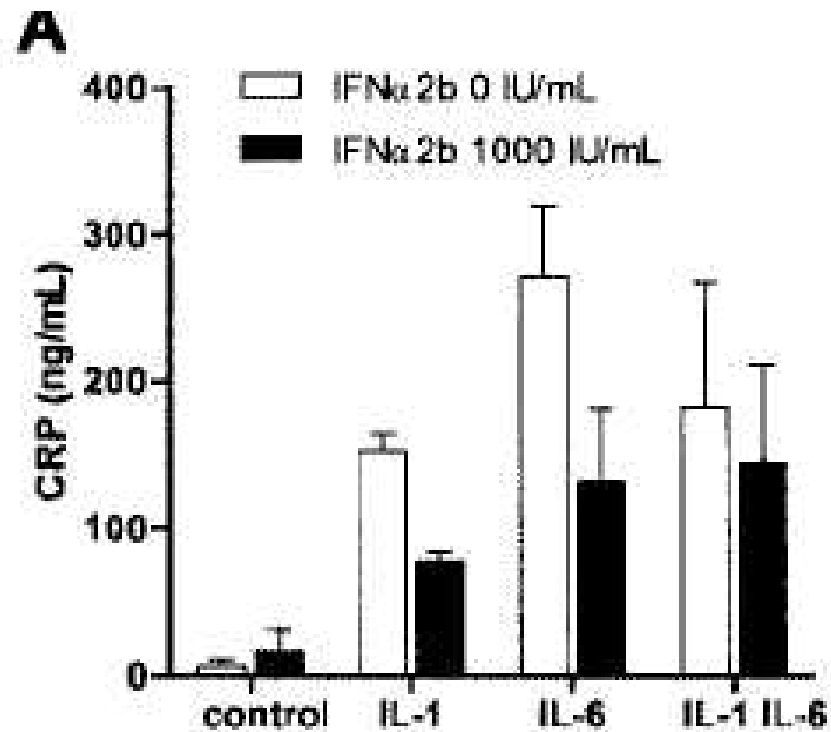
,
μ
μ



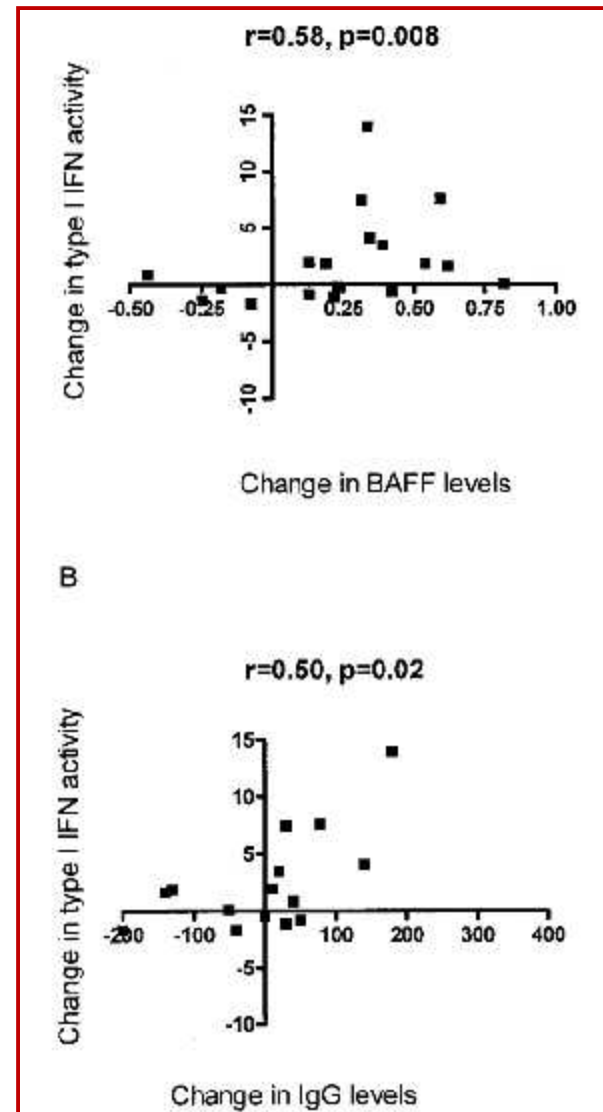
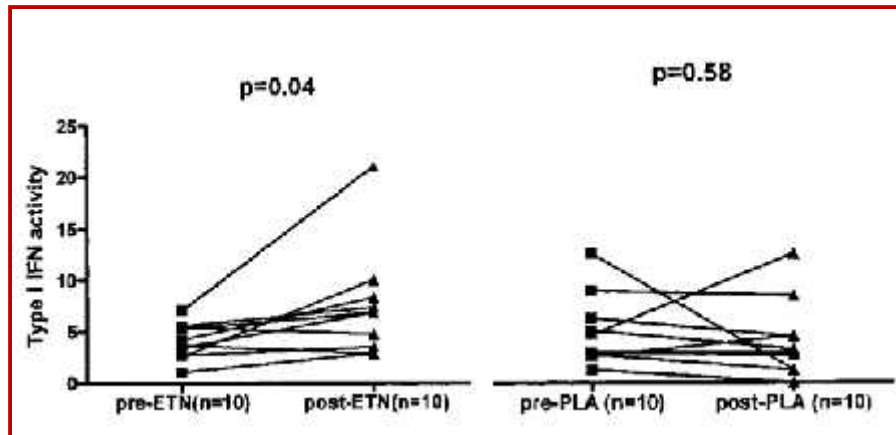
Jaccoud's arthropathy?

Interferon- α Mediates Suppression of C-Reactive Protein

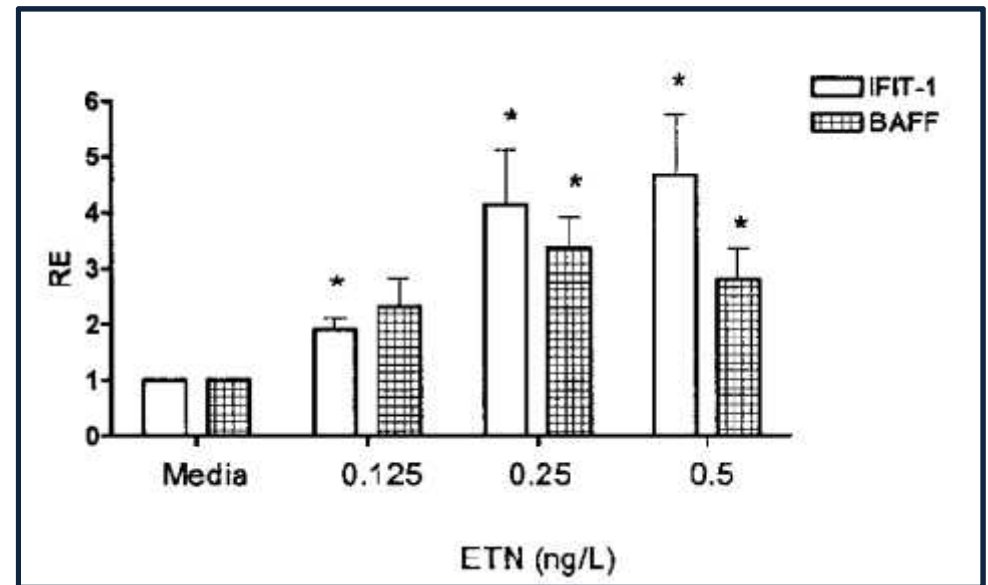
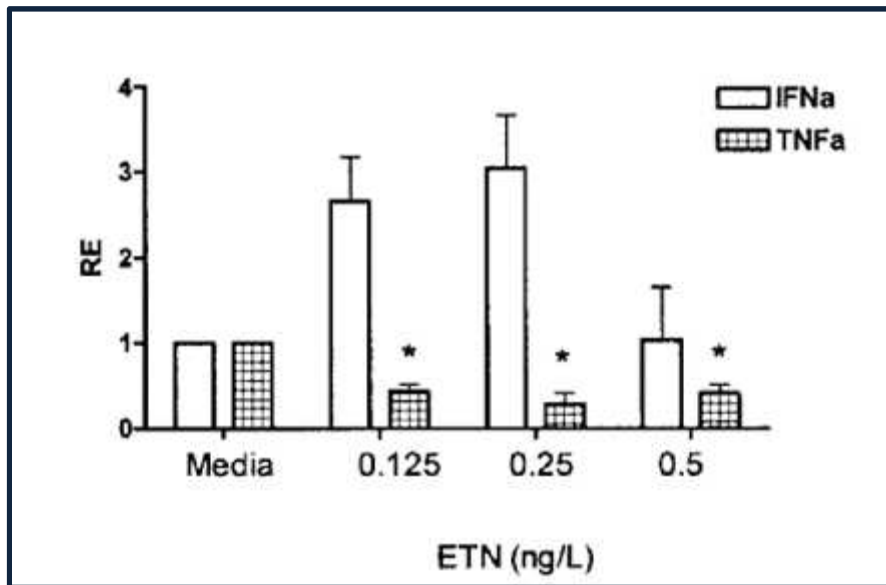
Explanation for Muted C-Reactive Protein Response in Lupus Flares?



- F in vivo

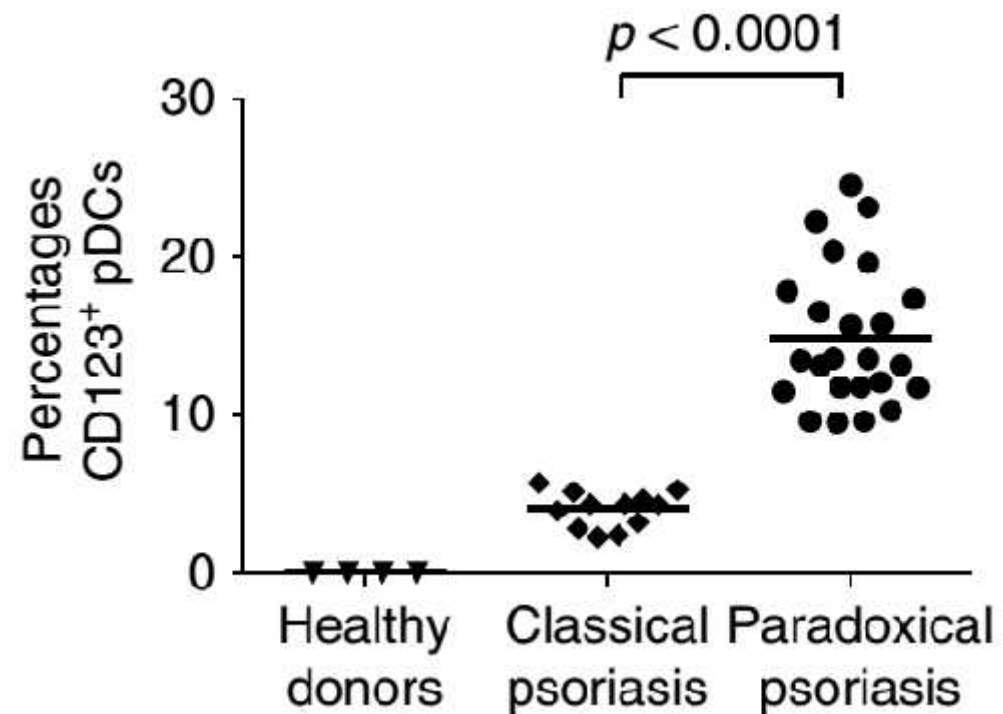


- F in vitro



TNF blockade induces a dysregulated type I interferon response without autoimmunity in paradoxical psoriasis

Curdin Conrad¹, Jeremy Di Domizio¹, Alessio Mylonas¹, Cyrine Belkhodja¹, Olivier Demaria¹, Alexander A. Navarini², Anne-Karine Lapointe¹, Lars E. French², Maxime Vernez¹ & Michel Gilliet¹



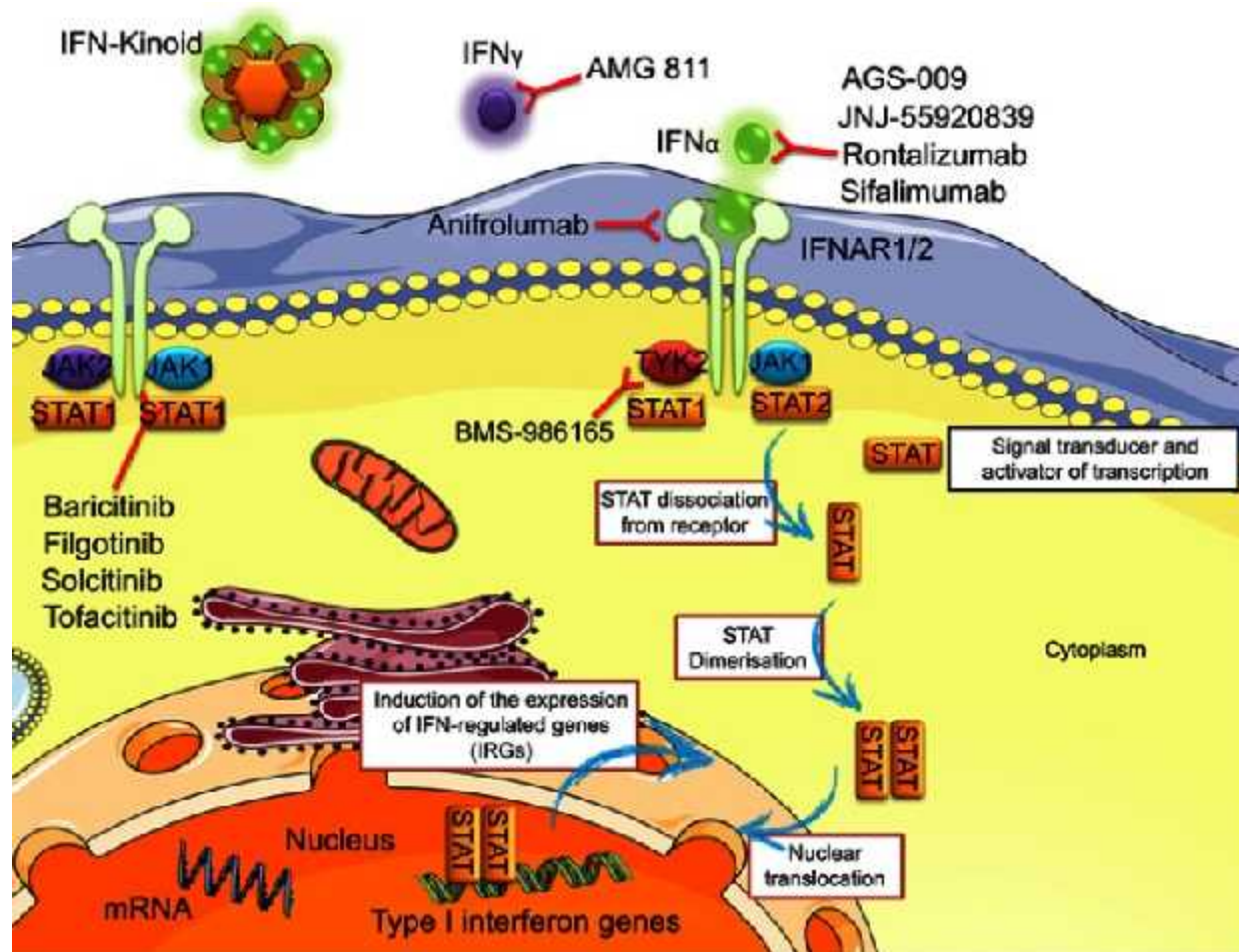
Τύπου I και III ιντερφερόνες στο αντιφωσφολιπιδικό σύνδρομο

- Συσχέτιση αυξημένου λόγου τύπου I IFN/IFNλ με τριπλή θετικότητα στα αντιφωσφολιπιδικά αντισώματα
- Συσχέτιση χαμηλών επιπέδων ιντερφερόνης λ με μαιευτικές επιπλοκές του συνδρόμου

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HCQ

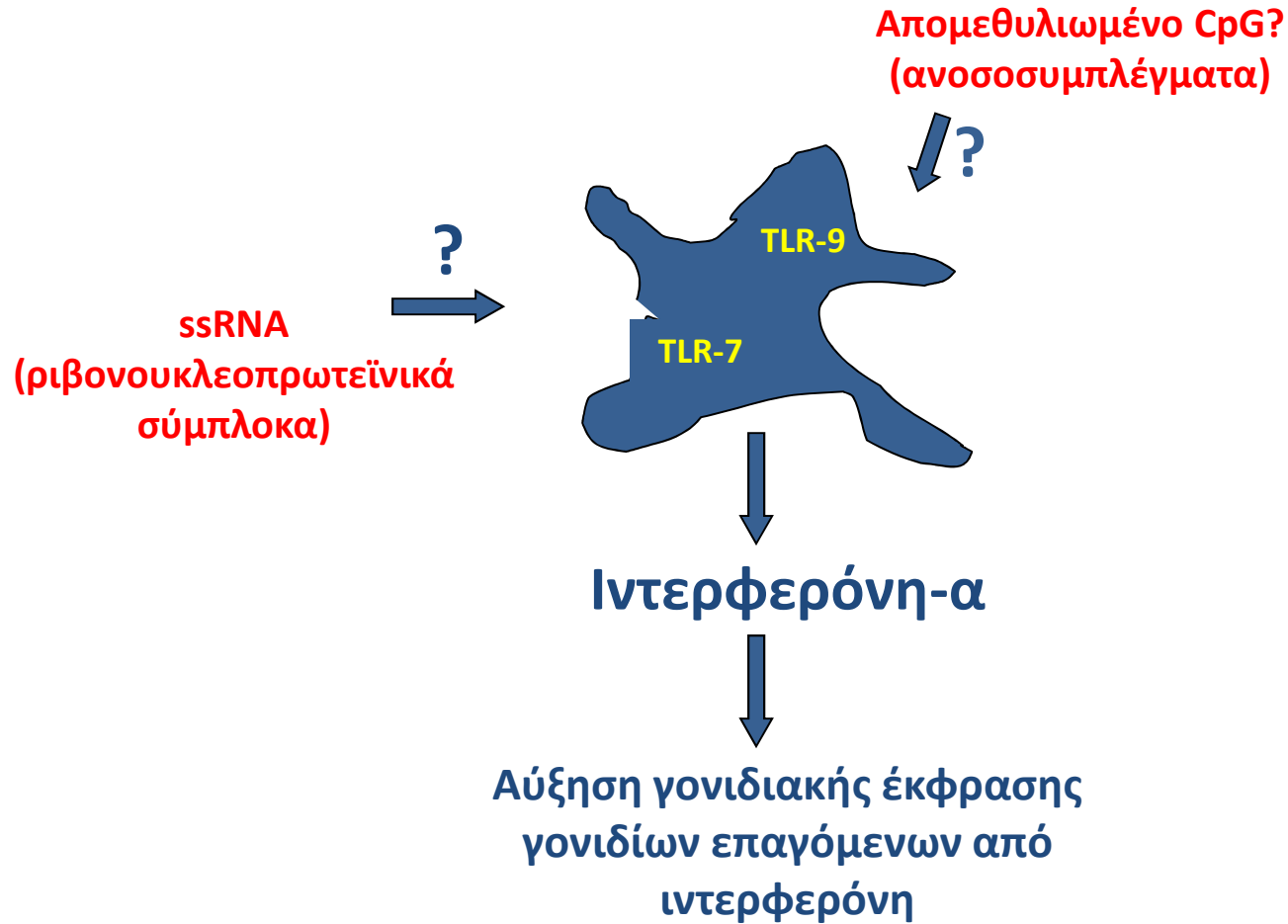


μ

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μ

μ



μ μ μ μ μ

Evidence demonstrated by molecular analysis of nucleic acids from SLE patients' plasma.

Are retroviruses involved in the pathogenesis of SLE?

Krapf FE et al. Rheumatol Int. 1989;9:115-21.

- DNA CpG μ μ
- μ μ μ μ

Plasma DNA in systemic lupus erythematosus. Characterization of cloned base sequences. Li JZ and Steinman CR. Arthritis Rheum. 1989;32:726-33.

- DNA μ μ DNA μ DNA (55% vs 13%) DNA

μ

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μ

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μ

μ

μ

, μ

μ

CpG

μ

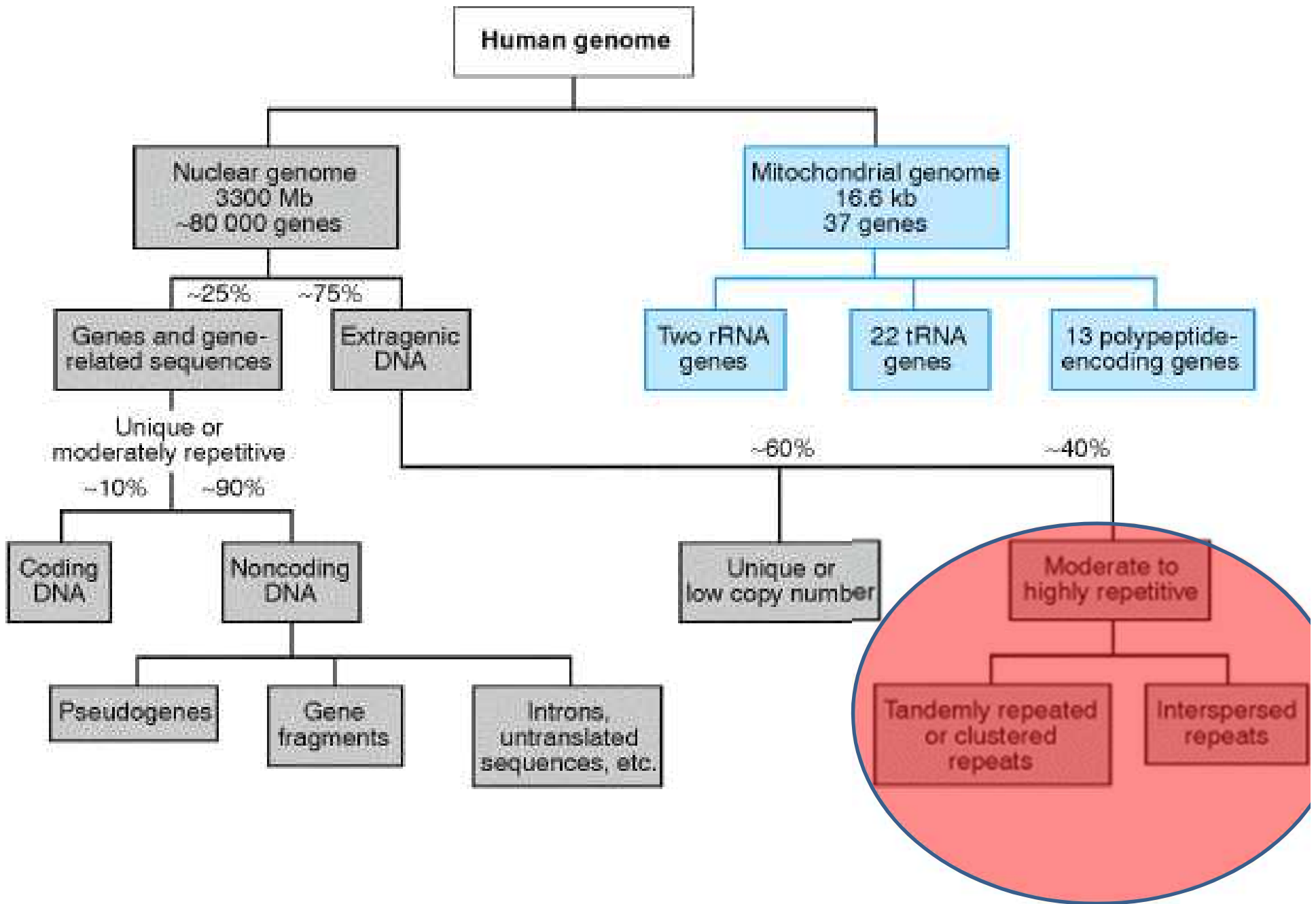
μ

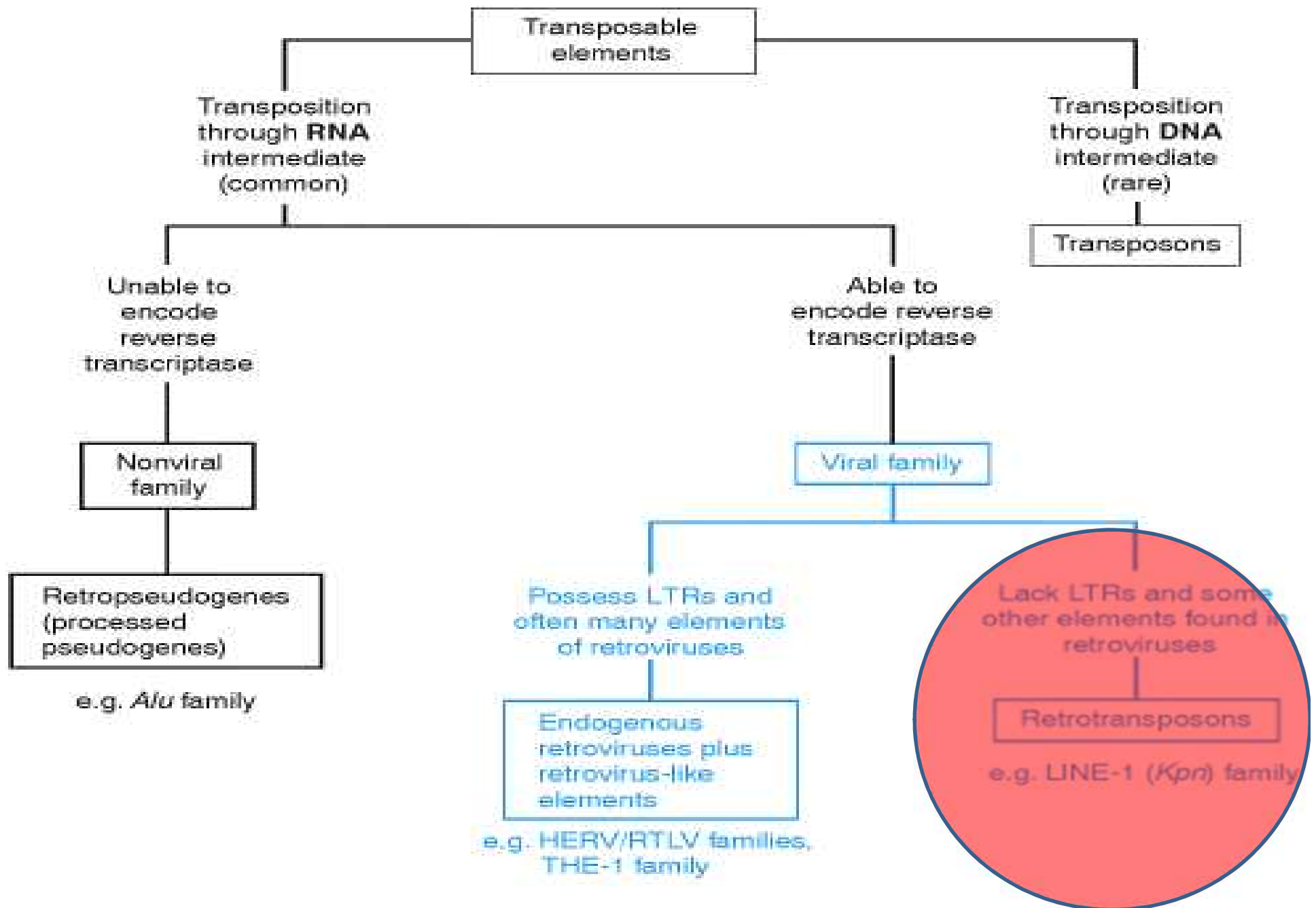
μ

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TLR-7

/ 9

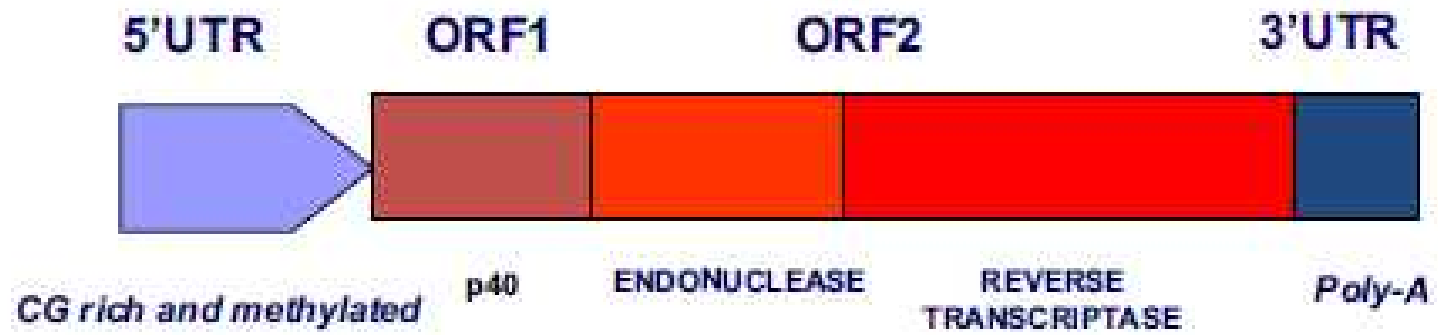




LINE-1

μ : μ μ μ ,
 μ μ

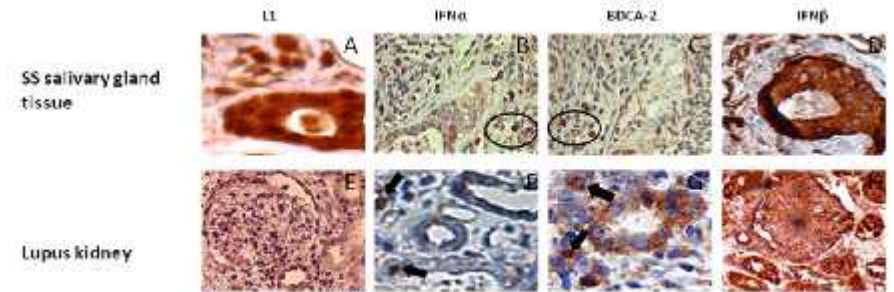
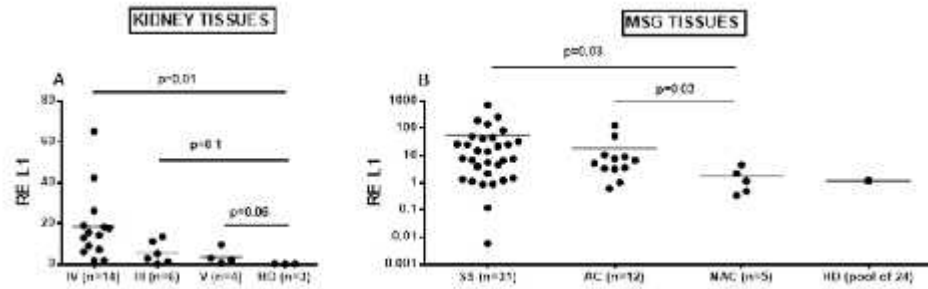
L1 structure





μ μ L1 μ
 μ TLR

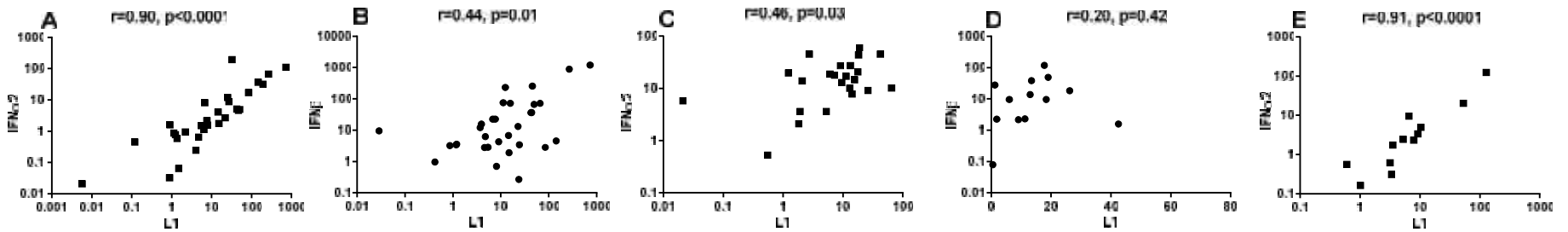
L1 μ IFN- mRNA μ Sjogren



SS MSG TISSUES

SLE KIDNEY TISSUES

AC MSG TISSUES



In vitro

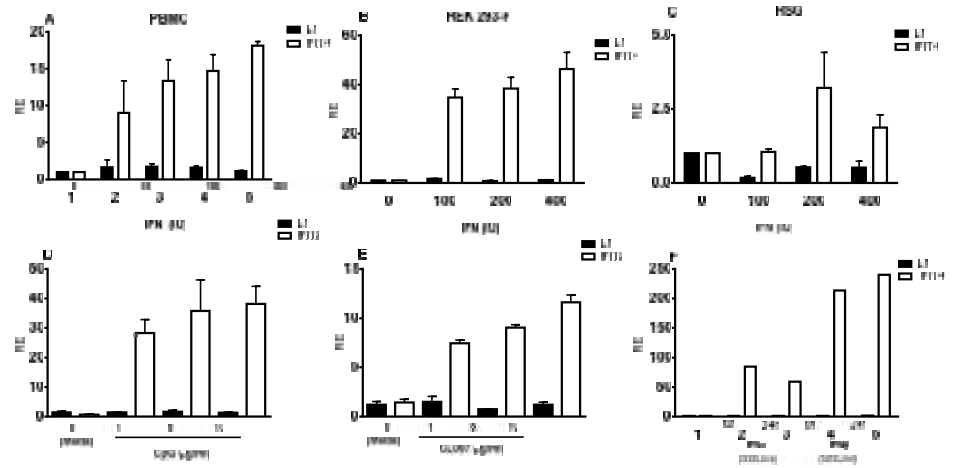
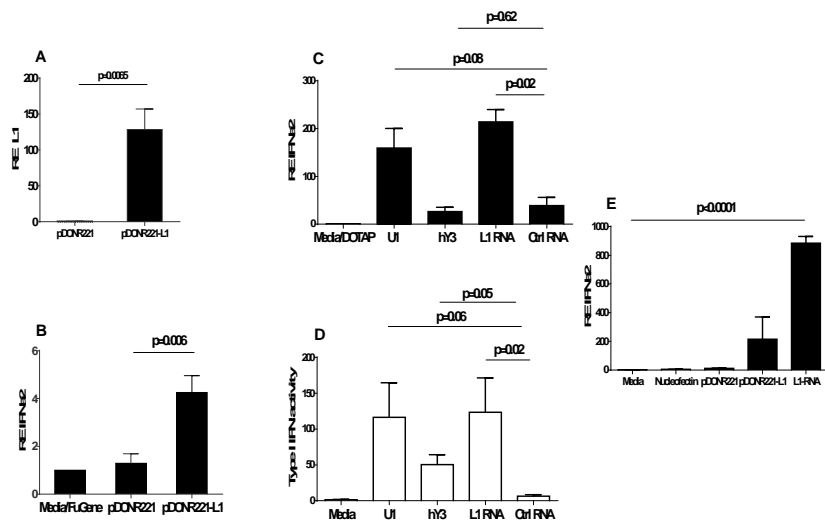
FN

L1

IFN

LR 7/9

L1



A

μ

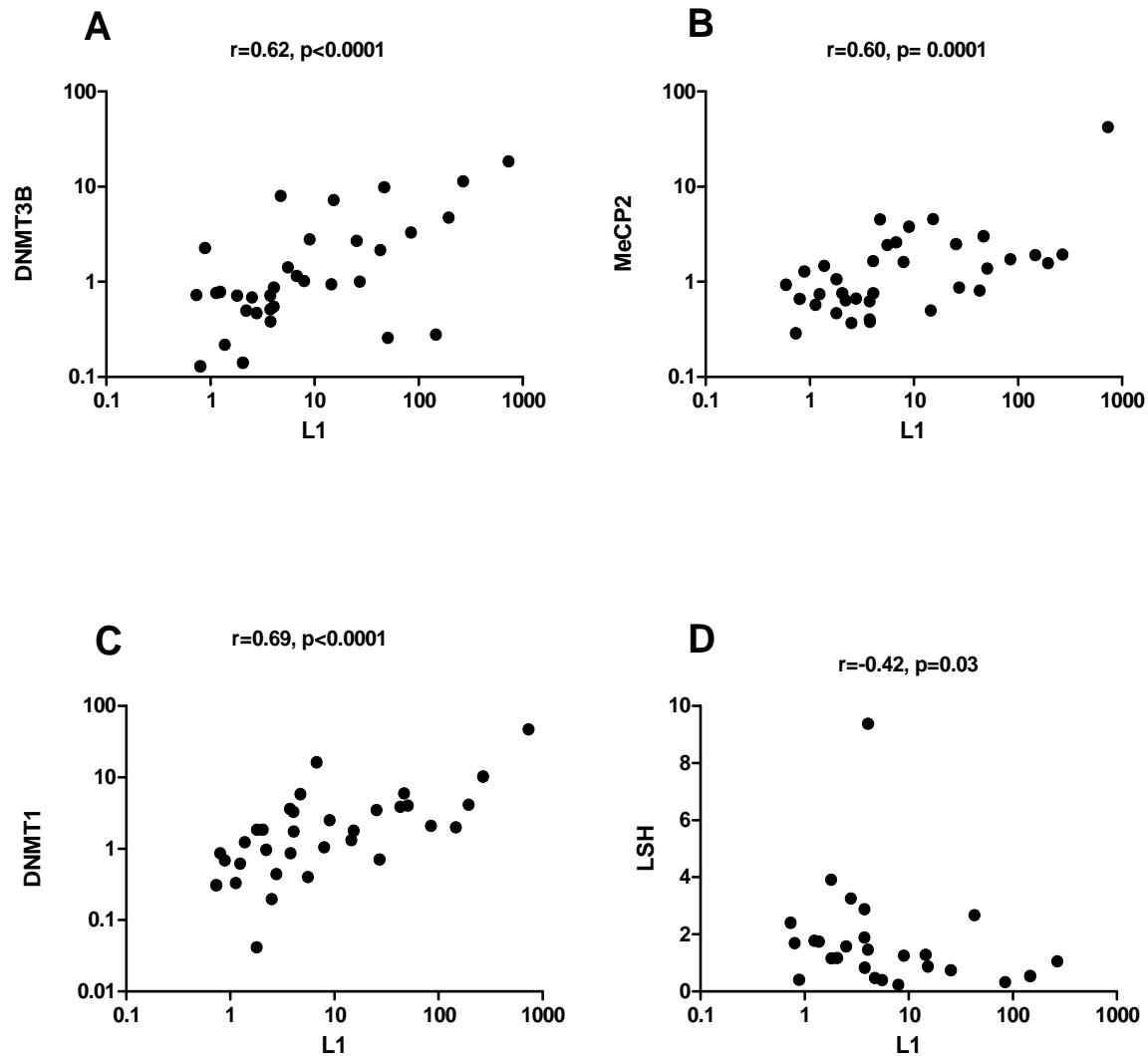
L1 μ

μ

L1

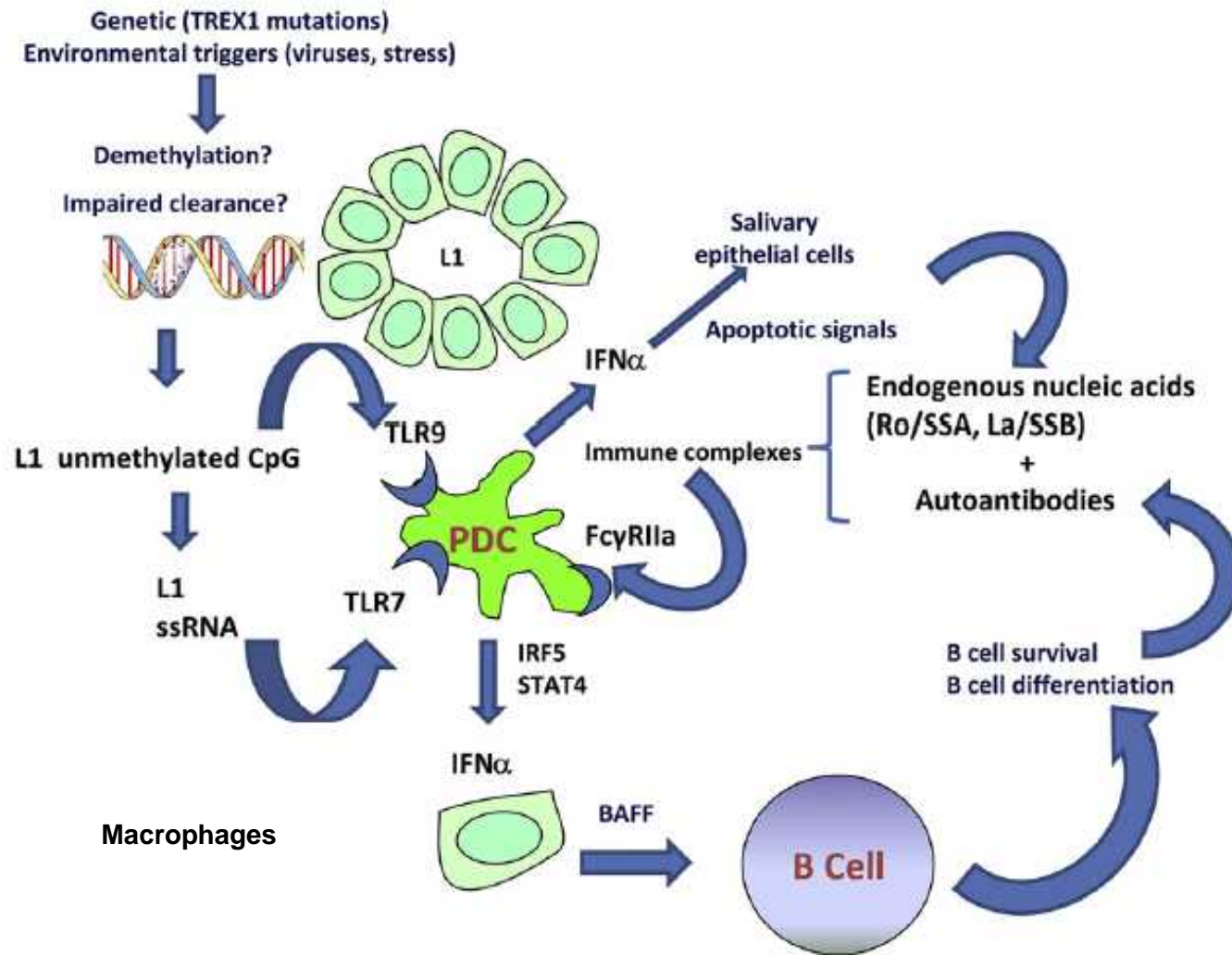
Methylation levels (%)	Spearman's rho	
	L1 mRNA expression	
	r	p-values
CpG pos #1	-0.674	0.003
CpG pos #2	-0.617	0.008
CpG pos #3	-0.674	0.003
CpG pos #4	-0.621	0.008
CpG pos #5	-0.278	0.41
CpG pos #7	-0.664	0.004
CpG pos #8	-0.496	0.09
CpG pos #9	-0.462	0.112
Mean	-0.598	0.011

Αντίστροφη συσχέτιση μεταξύ L1 και LSH



μ μ LINE-1

μ



Θερμές ευχαριστίες

Sagalovskiy I
Guo Q
Kirou KA
Crow MK



Nezos A
Vlachoyiannis N
Kapsogeorgou E
Moutsopoulos HM



**National and Kapodistrian
University of Athens**

ΙΣΝ / ΣΝΦ
ΙΔΡΥΜΑ ΣΤΑΥΡΟΣ ΝΙΑΡΧΟΣ
STAVROS NIARCHOS
FOUNDATION



