SOCIETAT CATALANOBALEAR DE MEDICINA INTERNA

L'Acadèmia

Congrés de la Societat Catalano-Balear de Medicina Interna

- XVII Edició -

4 i 5 de maig de 2017

Casa Convalescència. Barcelona

Congrés de la Societat Catalano-Balear
de Medicina Interna
- XVII Edició -
4 i 5 de maig de 2017
Casa Convalescència. Barcelona

SINDROMES AUTOINFLAMMATORIS DE L'ADULT

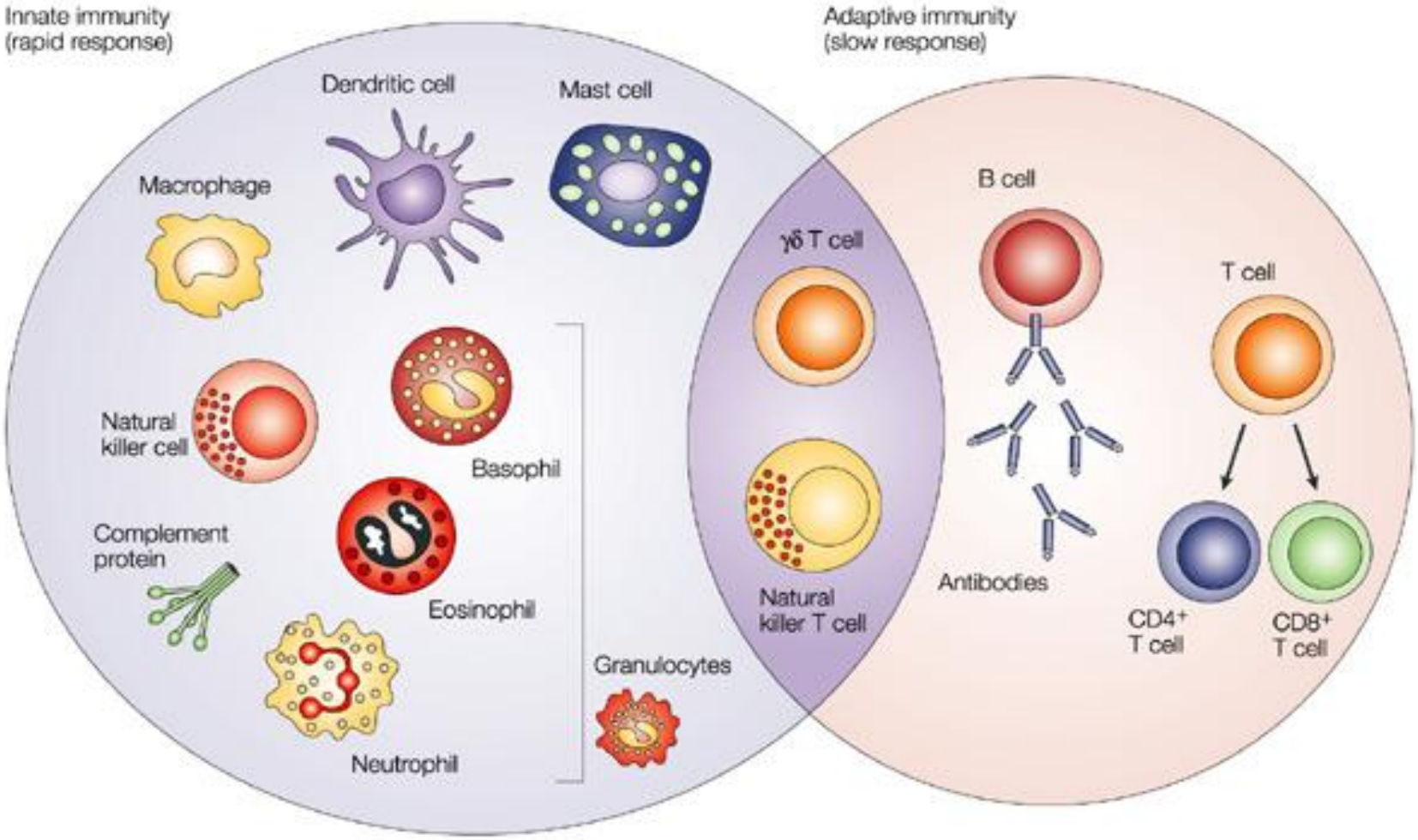
Dr. S. Buján
Unitat de Malalties Sistèmiques i Autoimmunes
Hospital Universitari VH

ISSAID

The International Society of Systemic Auto-Inflammatory Diseases

Autoinflammatory diseases are defined as illnesses caused by primary dysfunction of the innate immune system. This new concept includes a broad number of diseases, initially focusing on **Hereditary recurrent fevers** such as the prototype FMF, Familial Mediterranean Fever.

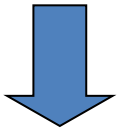
Until recently, these conditions were defined only by phenotypic features, including recurrent attacks of fever, abdominal pain, arthritis or cutaneous signs, which sometimes overlap and may obscure accurate diagnosis. However, this disease classification has expanded due to the recent advances in our understanding of disease pathogenesis with the discovery of the molecular basis of these disorders. Additional disorders which are now regarded as autoinflammatory diseases include **hereditary** disorders such as Blau disease and **complex** disorders such as Crohn's or Behcet's disease.


Innate immunity
(rapid response)
Adaptive immunity
(slow response)
Dendritic cell
Mast cell
Macrophage
γδ T cell
B cell
T cell
Natural
killer cell
Basophil
Complement
protein
Eosinophil
Natural
killer T cell
Antibodies
CD4+
T cell
CD8+
T cell
Granulocytes
Neutrophil

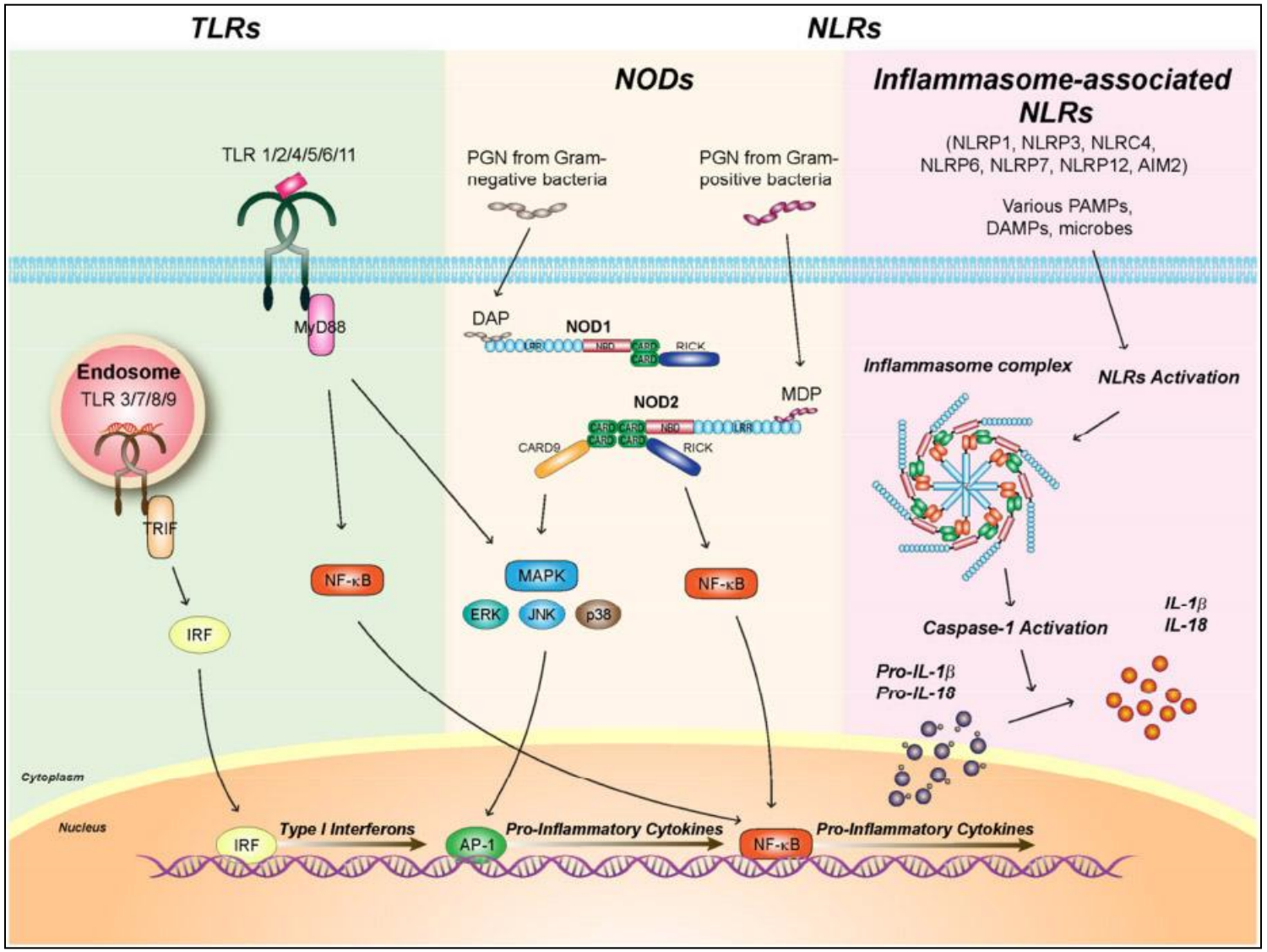
- Innate immune system cells

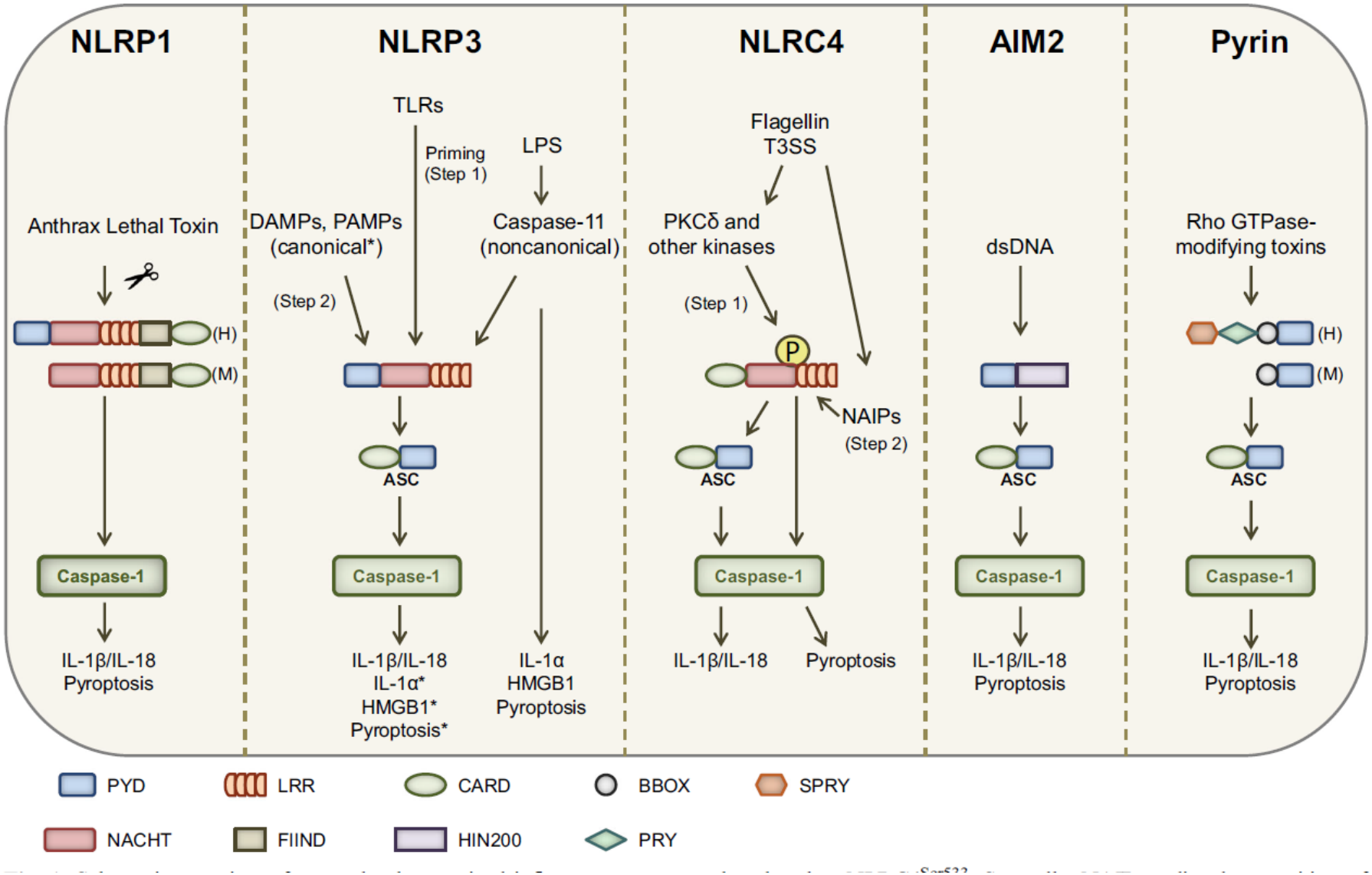
- Pattern recognition receptors (PRR)

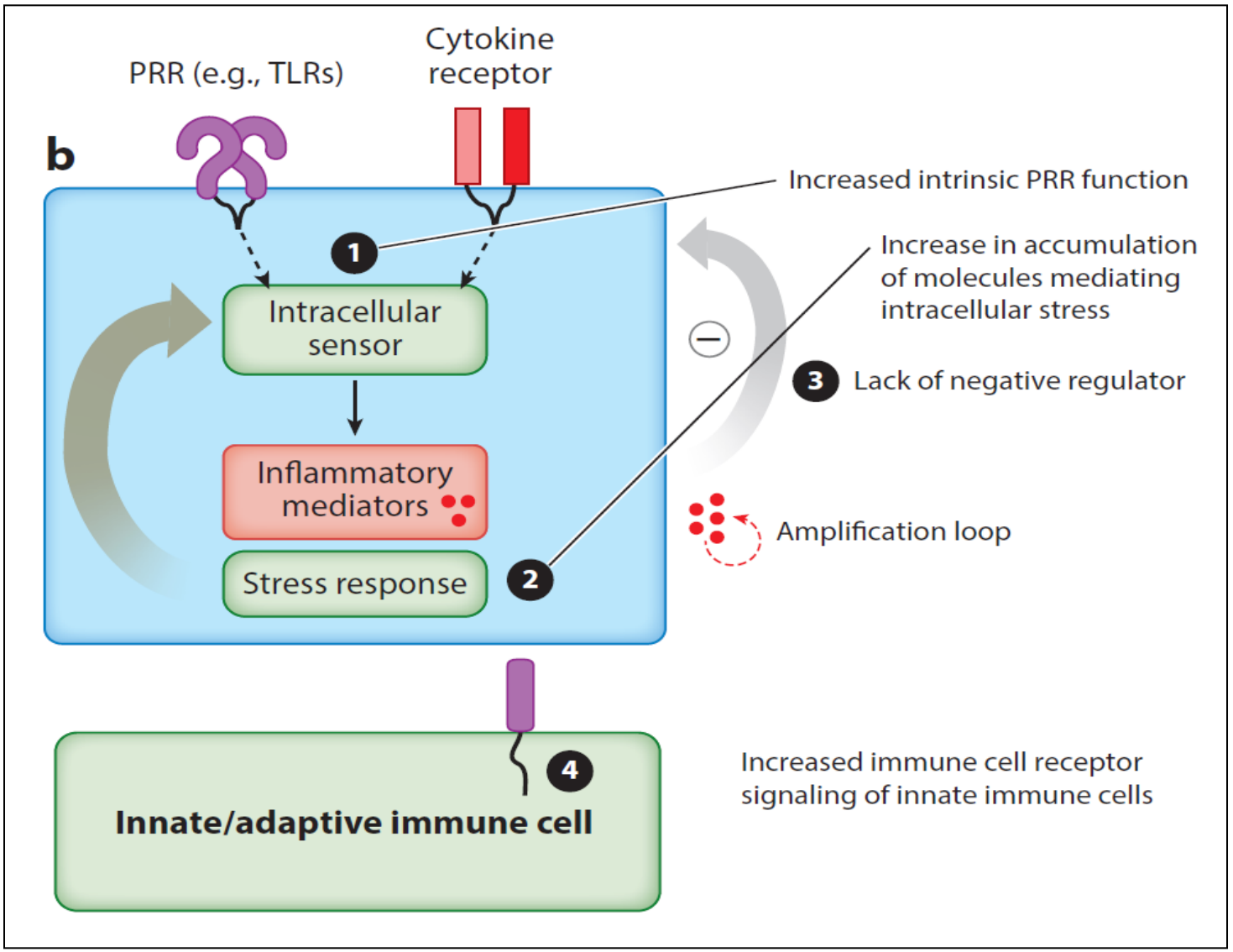
- Pathogen-associated molecular patterns (PAMPs) / Danger-associated molecular patterns (DAMPS)

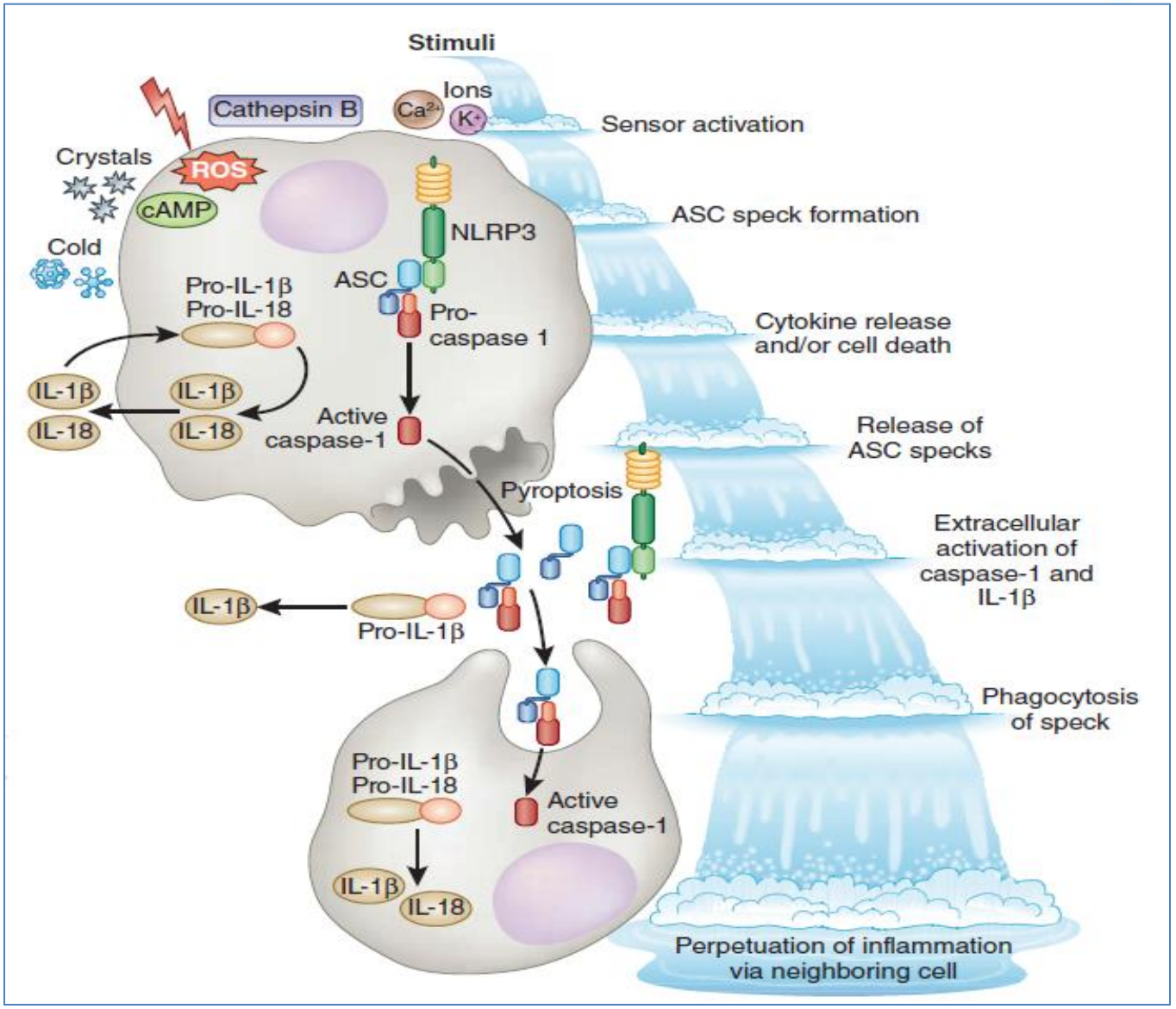


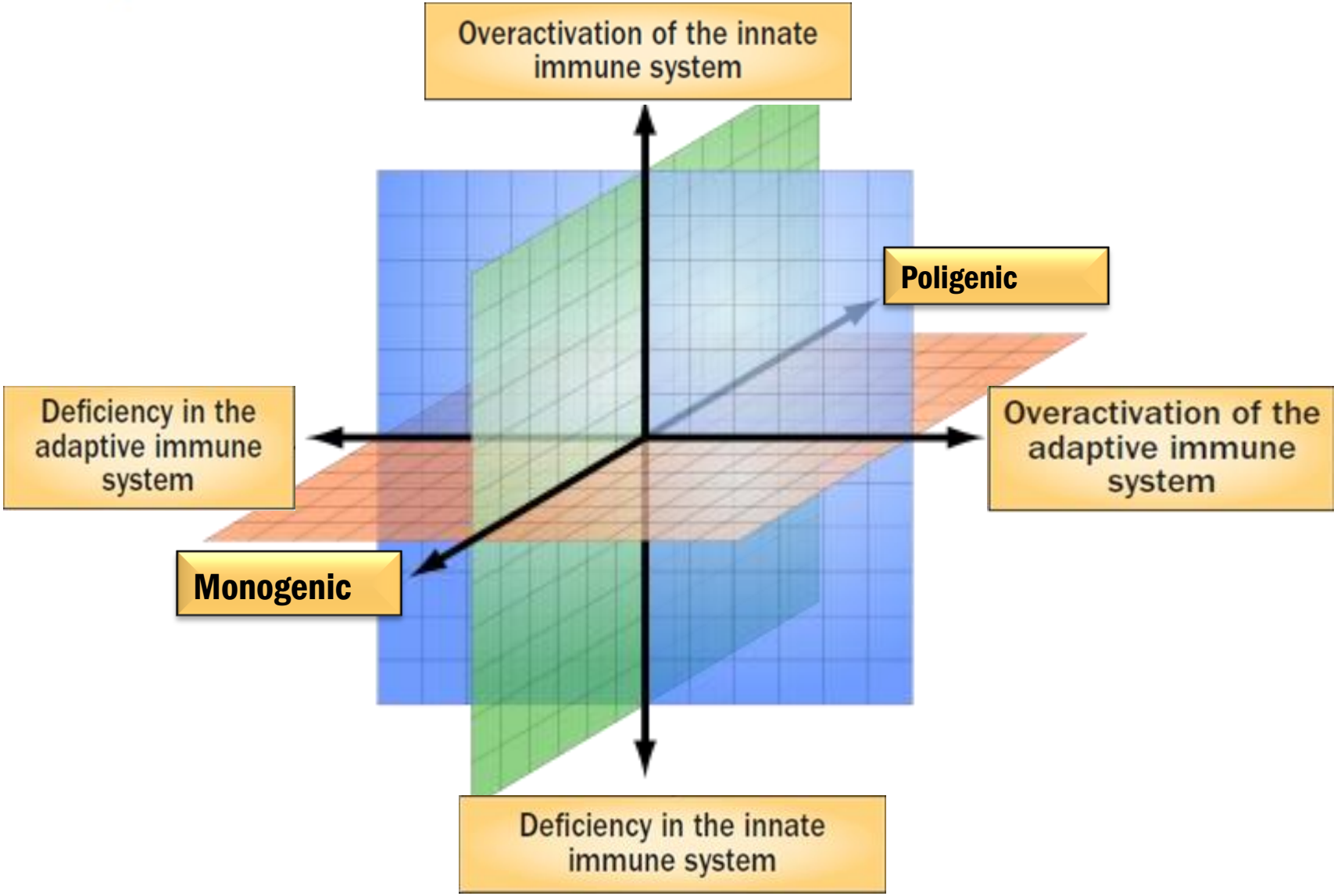
- Proinflammatory cytokines release / intracellular activation of proinflammatory pathways


TLRs
NLRs
NODs
Inflammasome-associated NLRs
(NLRP1, NLRP3, NLRC4, NLRP6, NLRP7, NLRP12, AIM2)
TLR 1/2/4/5/6/11
PGN from Gram-negative bacteria
PGN from Gram-positive bacteria
Various PAMPs, DAMPs, microbes
MyD88
DAP
NOD1
RICK
Endosome
TLR 3/7/8/9
TRIF
NOD2
MDP
CARD9
Inflammasome complex
NLRs Activation
NF-κB
MAPK
ERK
JNK
p38
NF-κB
IRF
Caspase-1 Activation
IL-1β
IL-18
Pro-IL-1β
Pro-IL-18
Cytoplasm
Nucleus
IRF
Type I Interferons
AP-1
Pro-Inflammatory Cytokines
NF-κB
Pro-Inflammatory Cytokines


NLRP1
Anthrax Lethal Toxin
(H)
(M)
Caspase-1
IL-1β/IL-18
Pyroptosis
NLRP3
TLRs
Priming
(Step 1)
LPS
DAMPs, PAMPs
(canonical*)
Caspase-11
(noncanonical)
(Step 2)
ASC
Caspase-1
IL-1β/IL-18
IL-1α*
HMGB1*
Pyroptosis*
IL-1α
HMGB1
Pyroptosis
NLRC4
Flagellin
T3SS
PKCδ and
other kinases
(Step 1)
P
NAIPs
(Step 2)
ASC
Caspase-1
IL-1β/IL-18
Pyroptosis
AIM2
dsDNA
ASC
Caspase-1
IL-1β/IL-18
Pyroptosis
Pyrin
Rho GTPase-
modifying toxins
(H)
(M)
ASC
Caspase-1
IL-1β/IL-18
Pyroptosis
PYD
LRR
CARD
BBOX
SPRY
NACHT
FIIND
HIN200
PRY


b
PRR (e.g., TLRs)
Cytokine receptor
1
Intracellular sensor
Inflammatory mediators
Stress response
2
Increased intrinsic PRR function
Increase in accumulation of molecules mediating intracellular stress
3
Lack of negative regulator
Amplification loop
4
Innate/adaptive immune cell
Increased immune cell receptor signaling of innate immune cells


Stimuli
Ions
Cathepsin B
Sensor activation
Crystals
ROS
cAMP
NLRP3
ASC speck formation
Cold
ASC
Pro-IL-1β
Pro-IL-18
Pro-
caspase 1
Cytokine release
and/or cell death
IL-1β
IL-1β
IL-18
IL-18
Active
caspase-1
Release of
ASC specks
Pyroptosis
Extracellular
activation of
caspase-1 and
IL-1β
IL-1β
Pro-IL-1β
Phagocytosis
of speck
Pro-IL-1β
Pro-IL-18
Active
caspase-1
IL-1β
IL-18
Perpetuation of inflammation
via neighboring cell


Overactivation of the innate immune system
Poligenic
Deficiency in the adaptive immune system
Overactivation of the adaptive immune system
Monogenic
Deficiency in the innate immune system

Congrés de la Societat Catalano-Balear de Medicina Interna

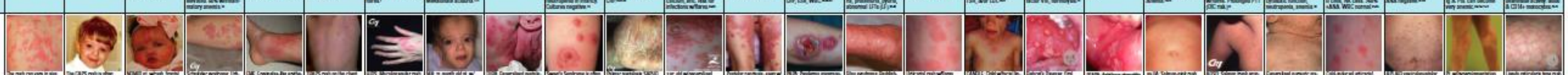
- XVII Edició -

4 i 5 de maig de 2017
Casa Convalescència. Barcelona

Comparison Chart of Systemic Autoinflammatory Diseases (SAID)

	Cryopyrin-Associated Periodic Syndromes (CAPS)				Pyrin	Protein Folding	Mevalonate Kinase Deficiencies		Inflammatory Bone Diseases			Pyogenic Diseases	
	Familial Cold Autoinflammatory Syndrome*	Muckle-Wells Syndrome*	Neonatal-Onset Multisystem Autoinflammatory Disease—aka Chronic Infantile Neurological Cutaneous Articular Syndrome (CINCA)*	Schnitzler Syndrome	Familial Mediterranean Fever*	Tumour Necrosis Factor (TNF)-Associated Periodic Sydrome—aka Familial Hibernian Fever*	Hyperimmuno-globulinemia D with Periodic Fever Syndrome (HIDS)*	Mevalonate Aciduria (MA) (Mevalonate Kinase Deficiencies, such as HIDS & MA are also referred to as MKD)	Deficiency of Interleukin-1β (IL-1β) Receptor Antagonist (DIRA)—aka Osteomyelitis, Sterile Multifocal w/Periostitis Pustulosis	Majeed Syndrome—aka Chronic Recurrent Multifocal Osteomyelitis, Congenital Dyserythropoietic Anemia, & Neutrophilic Dermatosis	Chronic Recurrent Multifocal Osteomyelitis—aka Synovitis, Acne, Pustulosis, Hyperostosis, Osteitis Syndrome	Deficiency of Interleukin-36-Receptor Antagonist (DITRA)—aka Generalized Pustular Psoriasis (GPP)	Familial Psoriasis (PSORS2)—aka CARD14-Mediated Pustular Psoriasis
ACRONYM	FCAS	MWS	NOMID/CINCA	SCHNITZLER	FMF	TRAPS	HIDS	MA	DIRA/OMPP	MAJEED	CRMO/SAPHO	DITRA/PSORP	CAMPS/PSORS2
GENE	NLRP3	NLRP3	NLRP3	Currently unknown (Some pts. w/somatic NLRP3 mutations)*	MEFV	TNFRSF1A	MVK	MVK	IL1RN	LPIN2	Currently unknown	IL36RN	CARD14
INHERITANCE	Autosomal Dominant. Large familial groups, some spontaneous mutations	Autosomal Dominant. Spontaneous mutations, some familial groups	Autosomal Dominant. Spontaneous mutations, few familial cases	Unknown	Autosomal Recessive. Some cases are gene-dosage-dependent autosomal dominant	Autosomal Dominant. Spontaneous mutations, some familial groups	Autosomal recessive. Some cases w/only one mutation found	Autosomal recessive	Autosomal recessive	Autosomal recessive	Currently unknown	Autosomal recessive	Autosomal Dominant. Spontaneous mutations, some familial groups
ETHNICITY	Affects all races, but many are of European descent	Affects all races, but many are of European descent	Any-present in all races	Affects all races, but most cases are in Europe [illegible]	Turk, Armenian, Arab, Sephardic Jew, Italian [illegible]	Affects all races. 2nd most common inherited SAID after FMF	Mostly of Dutch descent, or Northern European	Mostly of Dutch descent, or Northern European	[illegible]	Currently, the only documented cases are of Middle Eastern ancestry	[illegible]	[illegible]	[illegible]
FREQUENCY IN THE WORLD	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
TIMING OF SYMPTOMS OR ATTACKS	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
AGE OF ONSET	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
SYSTEMIC FINDINGS:													
SKIN/CUTANEOUS	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
NEUROLOGIC	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
AUDITORY	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
OPHTHALMIC	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
CARDIO-PULMONARY	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
ABDOMINAL	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
LYMPHATIC	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
JOINTS/BONES MUSCLES & CARTILAGE	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
VASCULITIS	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
AMYLOIDOSIS	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
ABNORMAL LABS	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

	Pyogenic Diseases	Granulomatous	Monarch-1	Proteasome	Idiopathic		Macrophage Activation Diseases			PLCG2-associated		SLC29A3 related	ADA2 deficiency
	Pyogenic Sterile Arthritis, Pyoderma Gangrenosum, & Acne Syndrome	Juvenile Systemic Granulomatosis—aka Blau syndrome, Pediatric Granulomatous Arthritis (PGA), Early Onset Sarcoidosis, or Jabs Syndrome	NLRP12-Associated Periodic Fever Syndrome—aka Familial Cold Autoinflammatory Syndrome 2, or Guadeloupe Periodic Fever	Chronic Atypical Neutrophilic Dermatosis w/ Lipodystrophy & Elevated Temperature—aka Nakajo-Nishimura Syndrome	Behçets Disease	Periodic Fever, Aphthous Stomatitis, Pharyngitis, & Cervical Adenitis (PFAPA)—aka Marshall Syndrome	Systemic-Onset Juvenile Idiopathic Arthritis—aka Still's, Systemic Juvenile Idiopathic Arthritis	Adult-Onset Stills Disease—aka Adult Still's, Wissler-Fanconi Syndrome	(Primary) Familial Hemophagocytic Lymphohistiocytosis—aka Familial Erythrophagocytic Lymphohistiocytosis	PLCG2-associated Antibody Deficiency & Immune Dysregulation, (PLAID)—aka Familial Atypical Cold Urticaria (FACU) or FCAS3	Autoinflammation & PLCG2-associated Antibody Deficiency & Immune Dysregulation (APLAID)	SLC29A3 Spectrum Disorder—aka H syndrome; Pigmented Hypertrichosis w/IDDM; Faisalabad Histiocytosis & Sinus Histiocytosis w/Massive Lymphadenopathy	Deficiency of Adenosine Deaminase 2 (DADA2)—aka Fever w/Early Onset Stroke (FEOS)
ACRONYM	PAPA	BLAU/PGA/EOS	NLRP12/FCAS2	CANDLE/PRAAS	BEHÇETS/BD	PFAPA	soJIA/sJIA	AOSD	1° HLH/FHL	PLAID/FCAS3	APLAID	SLC29A3	DADA2
GENE	PSTPIP1	NOD2	NLRP12	PSMB8; also PSMB4, PSMB9, PSMA3, POMP	ERAP1 (with HLA-B51); also variants near CCR1, KLRC4, STAT4	Currently unknown	Currently unknown. HLA-DRB1 in some pts. w/European ancestry*	Currently unknown	PRF1, STX11, STXBP2, UNC13-4, RAB27A, X-link: SH2D1A, BIRC4	Heterozygous genomic deletions within the PLCG2 gene*	PLCG2 mutation	SLC29A3	CECR1
INHERITANCE	Autosomal Dominant. Spontaneous mutations, some familial groups	Autosomal Dominant	Autosomal Dominant. Spontaneous mutations, some familial groups	Autosomal recessive	Complex	Currently unknown	Complex	Currently unknown	Autosomal recessive, [illegible]	Autosomal Dominant	Autosomal Dominant	Autosomal recessive	Autosomal recessive
ETHNICITY	[illegible]	Affects all races	[illegible]	[illegible]	[illegible]	Affects all races	Affects all races. [illegible]	Rare. Affects all races	[illegible]	Unknown. [illegible]	Unknown	[illegible]	Unknown
FREQUENCY IN THE WORLD	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
TIMING OF SYMPTOMS OR ATTACKS	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
AGE OF ONSET	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
SYSTEMIC FINDINGS:													
SKIN/CUTANEOUS	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
NEUROLOGIC	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
AUDITORY	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
OPHTHALMIC	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
CARDIO-PULMONARY	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
ABDOMINAL	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
LYMPHATIC	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
JOINTS/BONES MUSCLES & CARTILAGE	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
VASCULITIS	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
AMYLOIDOSIS	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
ABNORMAL LABS	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]



[illegible]

List of abbreviations: [illegible]

*These noted diseases are also referred to as "Classic" Hereditary Periodic Fever Syndromes (CAPS, FMF, HIDS, & TRAPS)

All Cited References & Full Image Credits are Listed on the Back Side of this Chart. [illegible]

NOMID ALLIANCE

Table 1 | Clinical features and management of FMF, TRAPS and MKD

Syndrome feature	FMF	TRAPS	MKD	
			HIDS	Mevalonic aciduria
Mode of inheritance	Autosomal recessive	Autosomal dominant	Autosomal recessive	Autosomal recessive
Age at onset (years)	<20	<20	<1	<1
Duration of attack (days)[a]	<2	>14	4–6	4–5
Musculoskeletal features	Monoarthritis, myalgia	Severe myalgia, monoarthritis	Arthralgia, occasional oligoarthritis	Arthralgia
Abdominal features	Sterile peritonitis	Severe pain	Splenomegaly, severe pain	Splenomegaly, pain might occur
Cutaneous features	Erysipelas-like erythema, often on the shins and dorsum of foot	Centrifugal rash starting on trunk and migrating to extremities	Maculopapular rash	Morbilliform rash
Ocular features	Uncommon	Conjunctivitis, periorbital edema	Uncommon	Uncommon
Distinguishing clinical symptoms	Erysipelas-like erythema	Migratory myalgia and rash	Cervical lymphadenopathy	Dysmorphic features, neurological symptoms
Gene	*MEFV*	*TNFRSF1A*	*MVK*	*MVK*
Protein	Pyrin	TNFRSF1A	Mevalonate kinase	Mevalonate kinase
Estimated incidence of amyloidosis	~50% (precolchicine era)	10–20%	<10%	Unknown
Standard therapy	Colchicine	Corticosteroids	NA	NA
Therapies or treatment approaches requiring additional study	IL-1-blocking drugs, TNF inhibitors	Etanercept, anakinra	Anakinra, TNF inhibitors	NA

[a]Duration is variable; values given here are typical. Abbreviations: FMF, familial Mediterranean fever; HIDS, hyper-IgD syndrome; IL, interleukin; MKD, mevalonate kinase deficiency; NA, not applicable; TNF, tumor necrosis factor; TRAPS, TNF-receptor-associated periodic syndrome.

Table 2 | Clinical features and management of CAPS and PFAPA

Syndrome feature	CAPS			PFAPA
	FCAS	MWS	NOMID	
Mode of inheritance	Autosomal dominant	Autosomal dominant	Autosomal dominant	None
Age at onset (years)	<1	<20	<1	<5
Duration of attack (days)[a]	<2	1–2	Unknown	3–5
Musculoskeletal features	Arthralgia, occasional myalgia	Limb pain, arthralgia, arthritis	Epiphyseal bone formation	Uncommon
Abdominal features	None	Might occur	Hepatomegaly Splenomegaly	Uncommon
Cutaneous features	Cold-induced generalized urticaria-like rash	Generalized urticaria-like rash	Generalized urticaria-like rash	Uncommon
Ocular features	Conjunctivitis	Conjunctivitis	Papilledema, uveitis	Uncommon
Distinguishing clinical symptoms	Cold-induced episodes	Sensorineural hearing loss	Chronic aseptic meningitis, sensorineural hearing loss, arthropathy	Aphthous ulcers, lymphadenopathy, pharyngitis
Gene	*NLRP3*	*NLRP3*	*NLRP3*	None
Protein	Cryopyrin	Cryopyrin	Cryopyrin	None
Estimated incidence of amyloidosis	<10%	~25%	Unknown	None
Standard therapy	Anakinra, rilonacept	Anakinra, rilonacept	Anakinra	Single-dose corticosteroid (limited use)
Therapies or treatment approaches requiring additional study	Canakinumab	Canakinumab	Canakinumab, thalidomide	Colchicine, cimetidine, montelukast, tonsillectomy

[a]Duration is variable; values given here are typical. Abbreviations: CAPS, cryopyrin-associated periodic syndrome; FCAS, familial cold autoinflammatory syndrome; MWS, Muckle–Wells syndrome; NOMID, neonatal-onset multisystem inflammatory disease; PFAPA, periodic fever adenitis pharyngitis and aphthous stomatitis.

SIGNES GUIA:

- **Febre periòdica + / - manifestacions comunes "atípiques":**

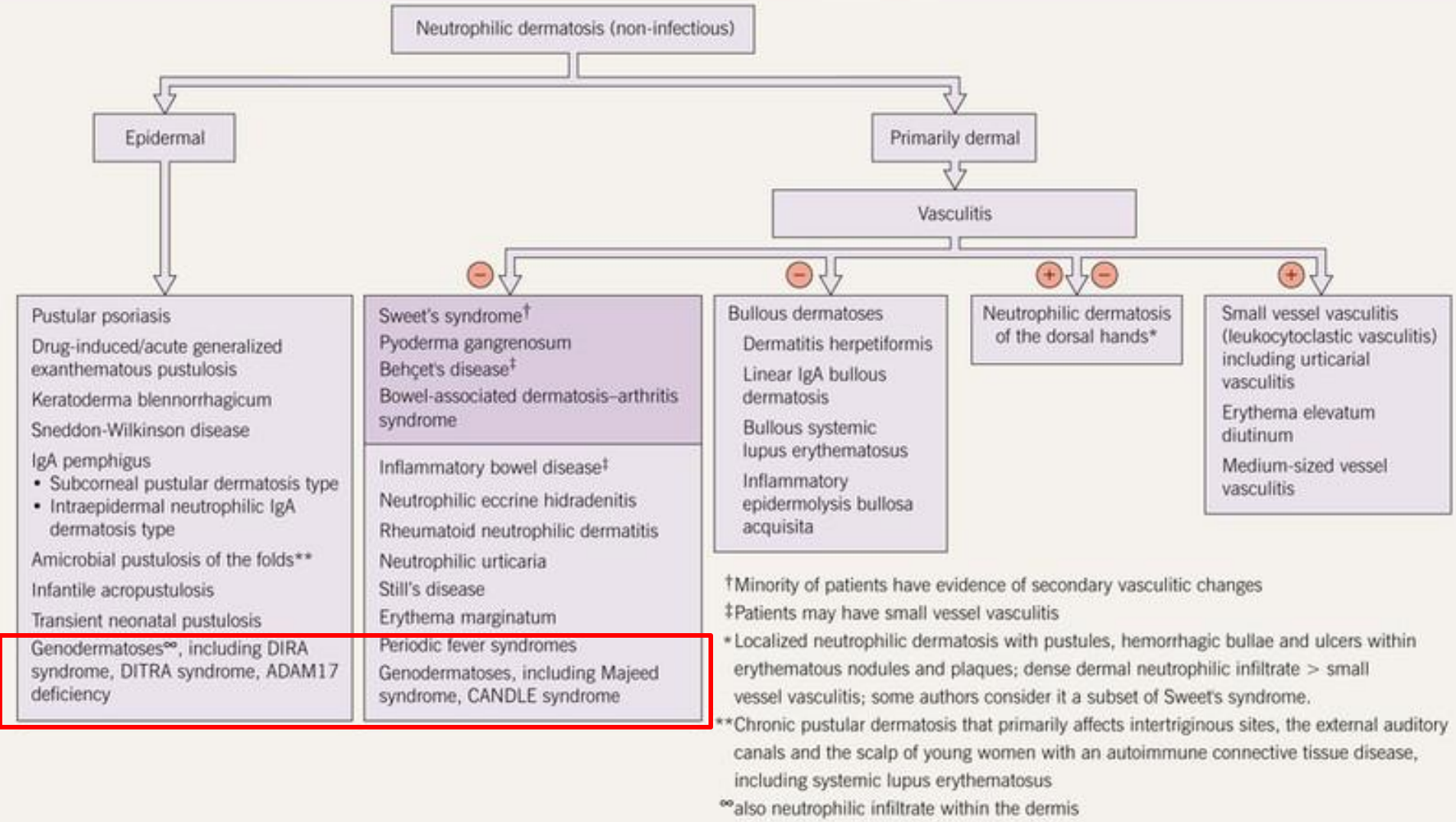
  - Dermatològiques
  - Alergològiques
  - Reumatològiques
  - Neurològiques
  - Oftalmològiques
  - Abdominals
  - Amiloidosi 2ª

- Manifestacions comunes “atípiques”:

  - Dermatològiques
    - Pioderma gangrenòs
    - Pitiriasi rubra
    - Psoriasi pustular d’inici neonatal / infantil precoç
    - Lipodistròfia
    - Erisipela- like
    - Dermatosi neutrofílica Sweet – like
    - Vasculitis PAN-like infantil / precoç
    - Eritema malar “lupus-like” infantil

  - Alergològiques
    - Urticària desencadenada per fred NO a frígore
    - Urticària – vasculitis idiopàtica refractària

NON-INFECTIOUS NEUTROPHILIC DERMATOSES



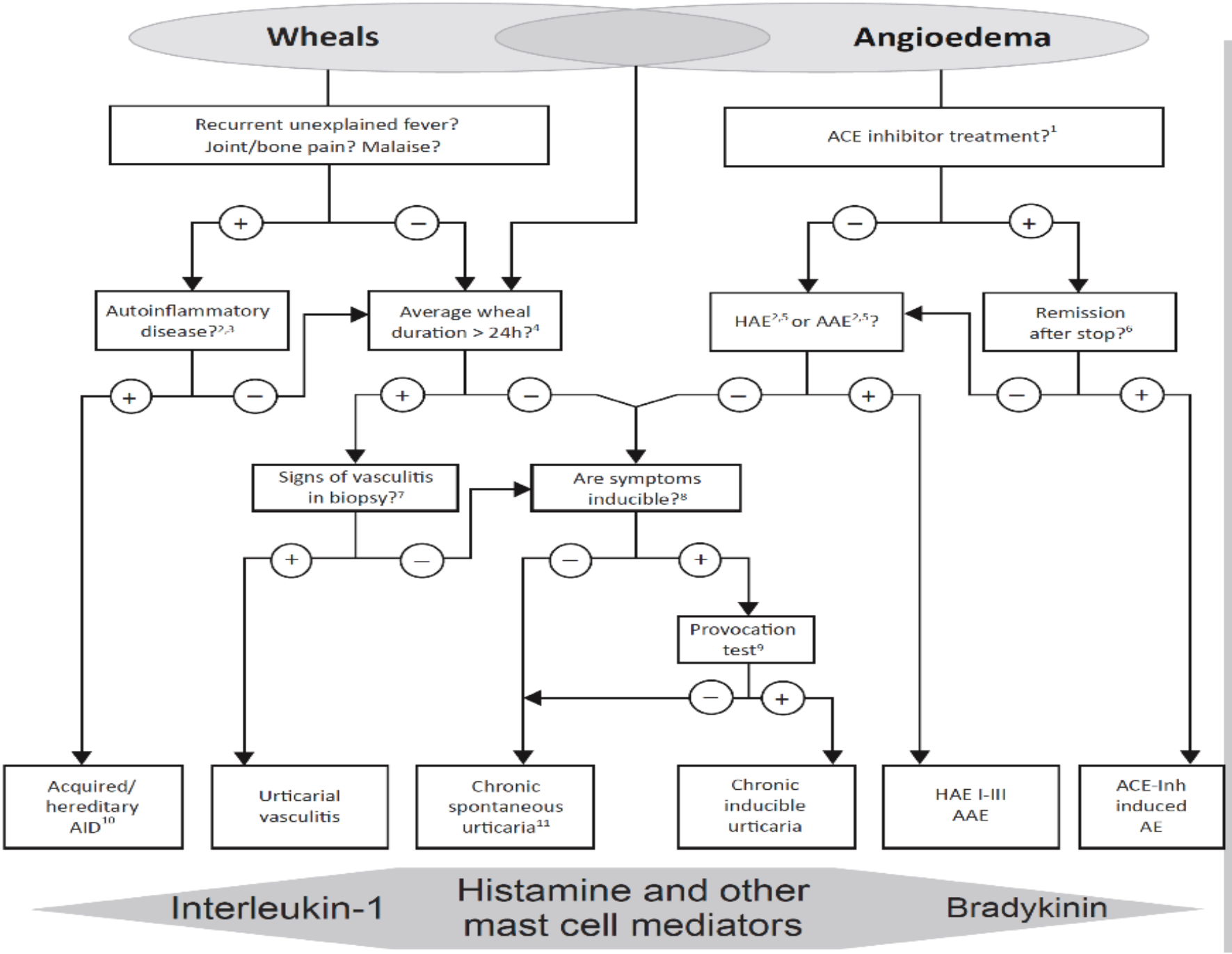
†Minority of patients have evidence of secondary vasculitic changes

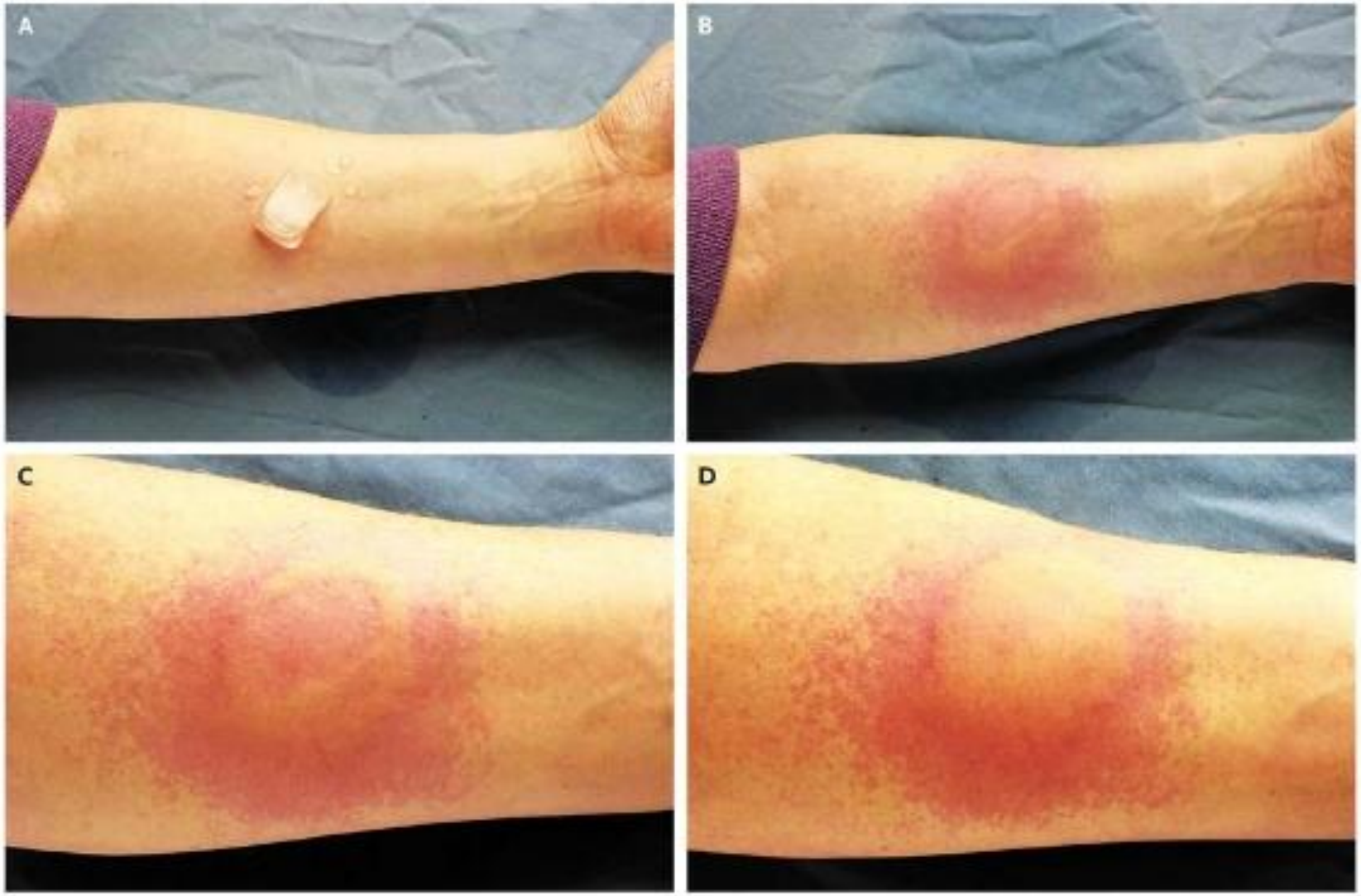
‡Patients may have small vessel vasculitis

*Localized neutrophilic dermatosis with pustules, hemorrhagic bullae and ulcers within erythematous nodules and plaques; dense dermal neutrophilic infiltrate > small vessel vasculitis; some authors consider it a subset of Sweet's syndrome.

**Chronic pustular dermatosis that primarily affects intertriginous sites, the external auditory canals and the scalp of young women with an autoimmune connective tissue disease, including systemic lupus erythematosus

∞also neutrophilic infiltrate within the dermis


Wheals
Angioedema
Recurrent unexplained fever? Joint/bone pain? Malaise?
ACE inhibitor treatment?[1]
Autoinflammatory disease?[2,3]
Average wheal duration > 24h?[4]
HAE[2,5] or AAE[2,5]?
Remission after stop?[6]
Signs of vasculitis in biopsy?[7]
Are symptoms inducible?[8]
Provocation test[9]
Acquired/ hereditary AID[10]
Urticarial vasculitis
Chronic spontaneous urticaria[11]
Chronic inducible urticaria
HAE I-III AAE
ACE-Inh induced AE
Interleukin-1
Histamine and other mast cell mediators
Bradykinin
History
Diagnostic tests
Treatment


A
B
C
D

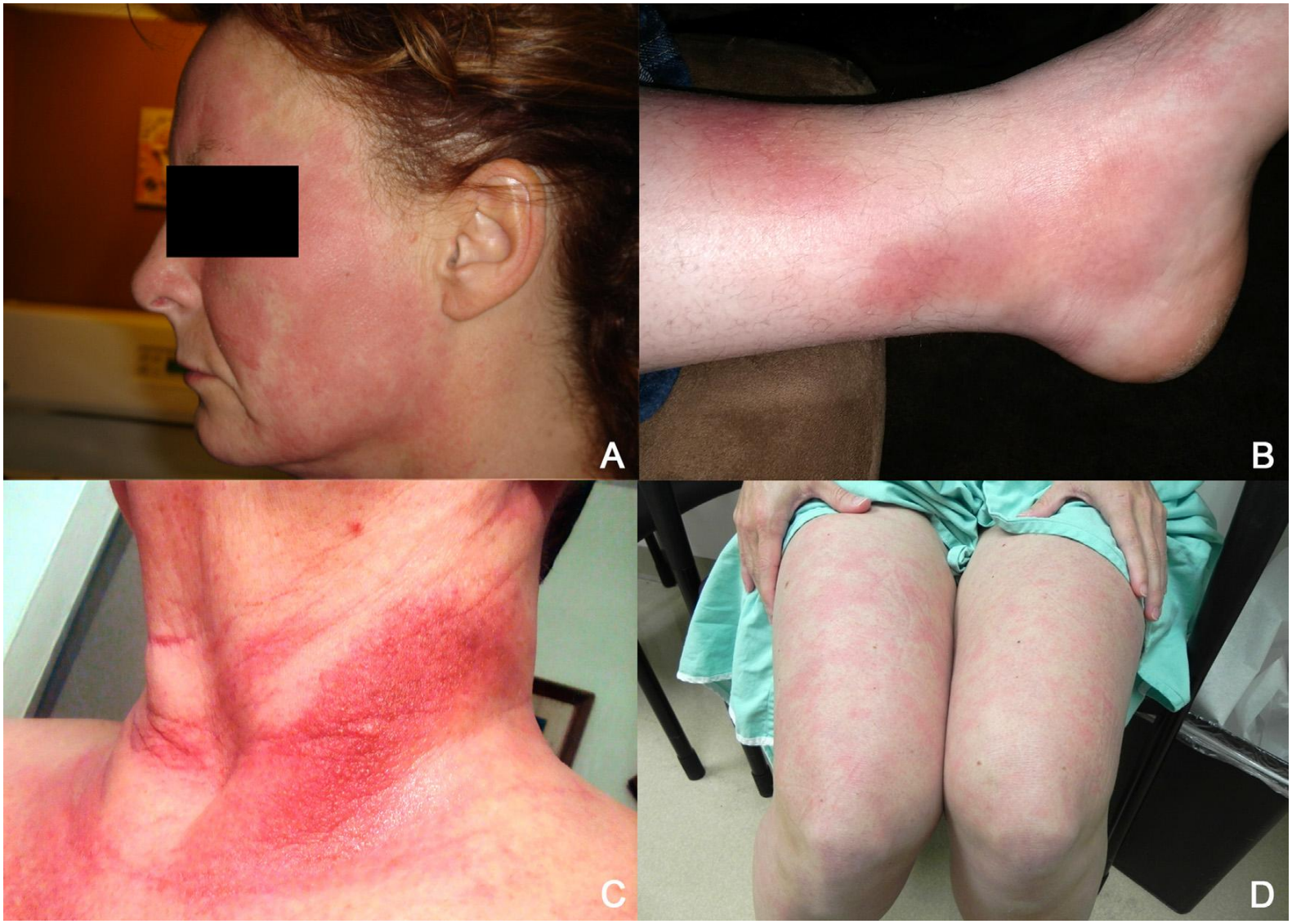
- Manifestacions comunes “atípicas”:
  - Reumatològiques
    - Hidrartros recidivant
    - Mono /òligo / poliartritis seronegatives refractàries
    - Remodelació / sobrecreixement patelar
  - Neurològiques
    - HTEC
    - Edema de papila
    - Meningitis asèptica (de repetició)
  - Oftalmològiques
    - Edema palpebral
    - Conjuntivitis de repetició
    - Uveitis granulomatosa

- XVII Edició -
4 i 5 de maig de 2017
Casa Convalescència. Barcelona

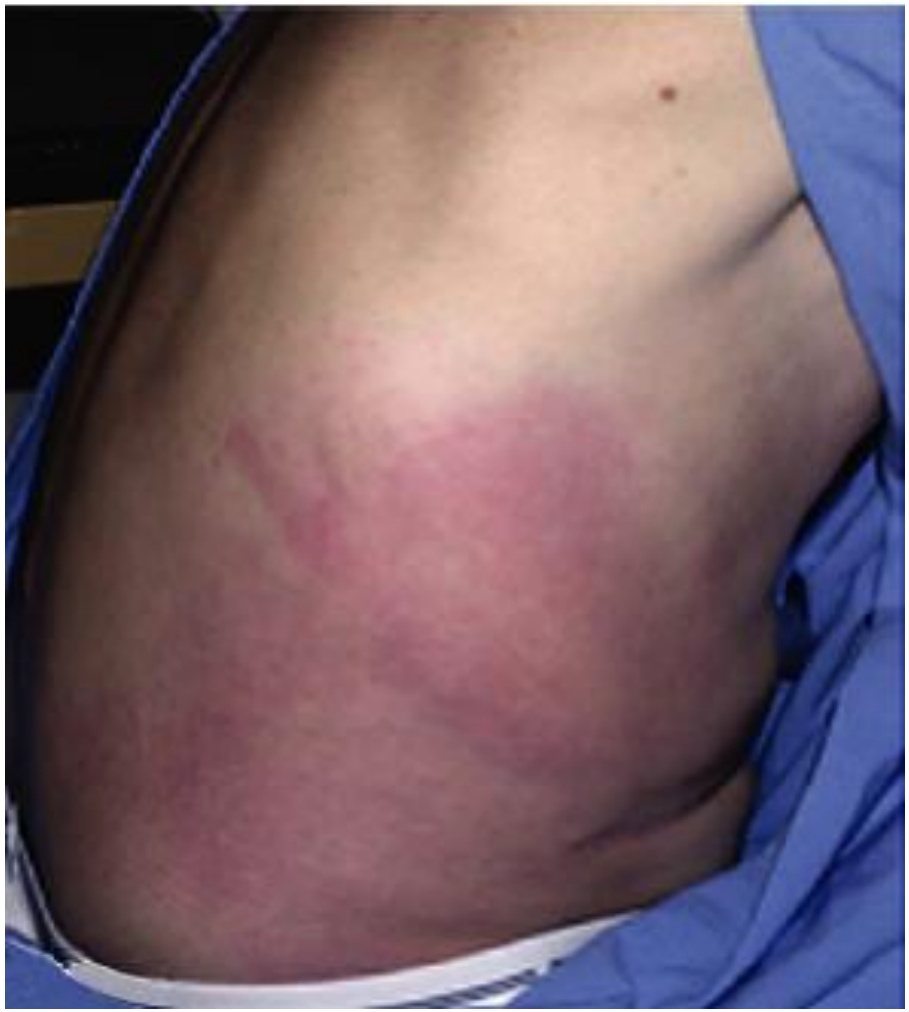
- Manifestacions comunes “atípiques”:

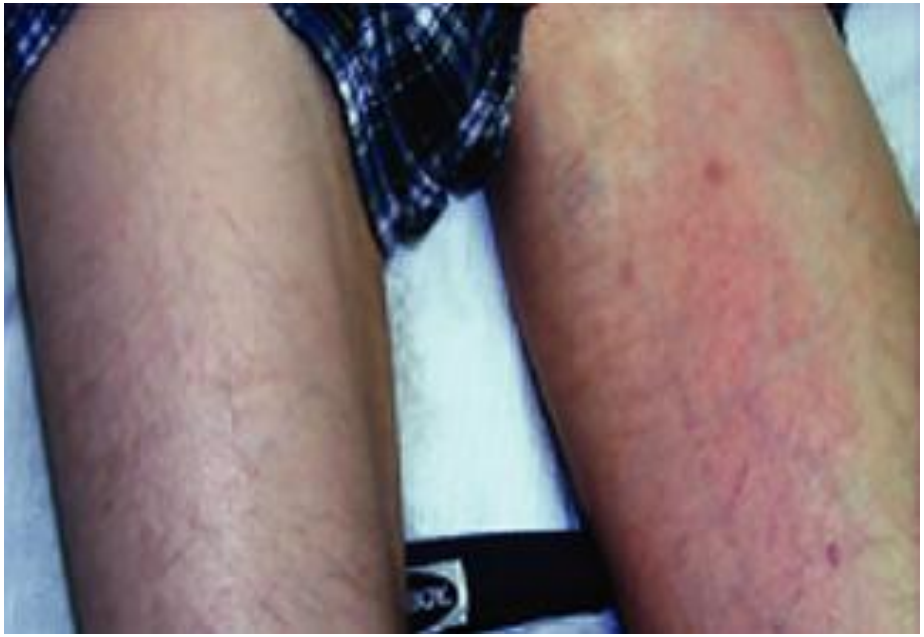
  - Otorrinolaringológiques:
    - Aftosi
    - Faringitis
    - Adenitis cervical
    - Hipoacusia neurosensorial

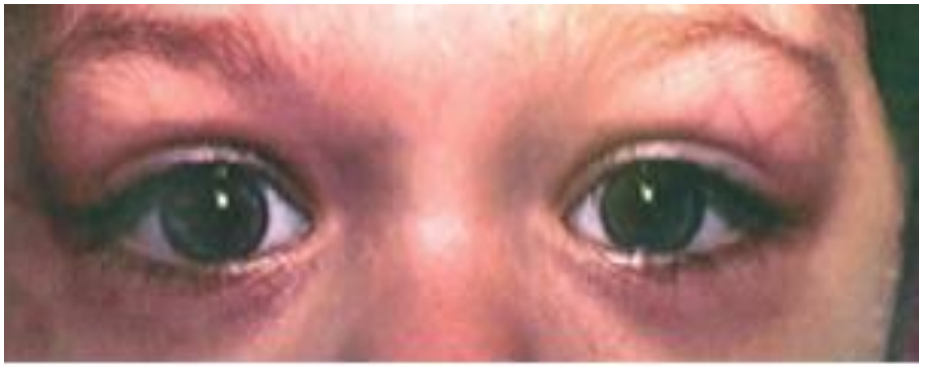
  - Amiloidosi 2ª

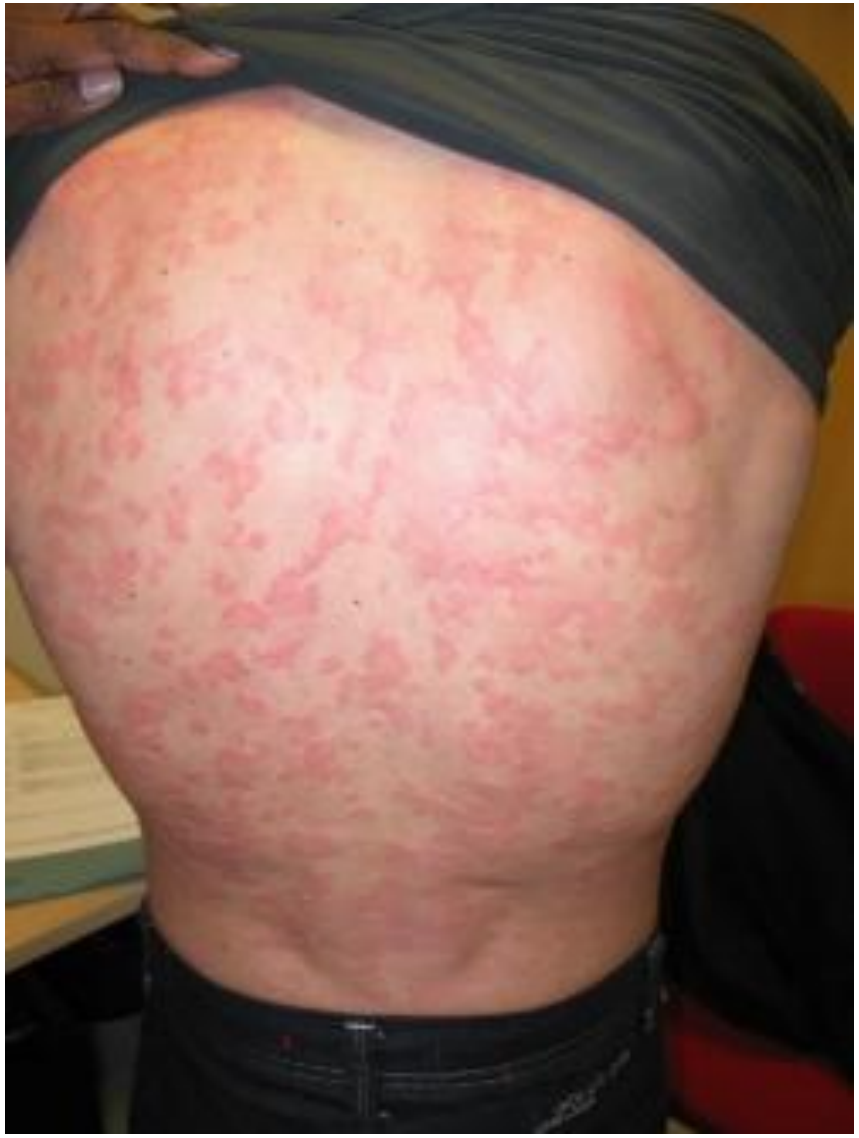


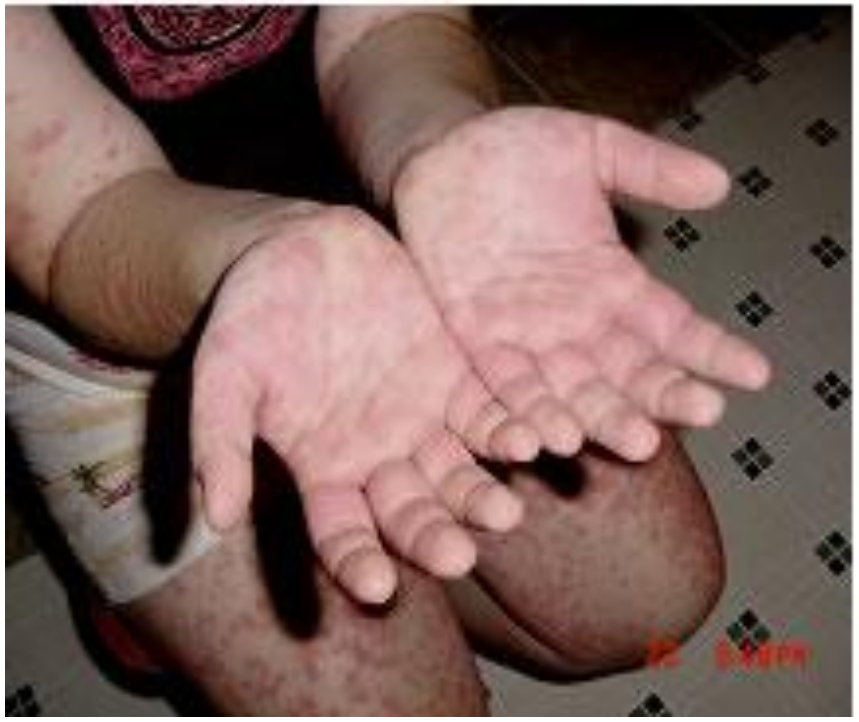
Yao Q. Et al. Seminars inArthritis and Rheumatism (2015)

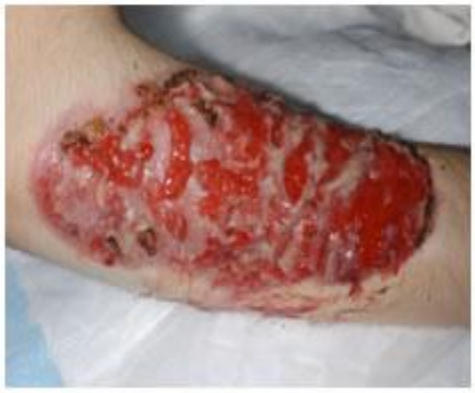


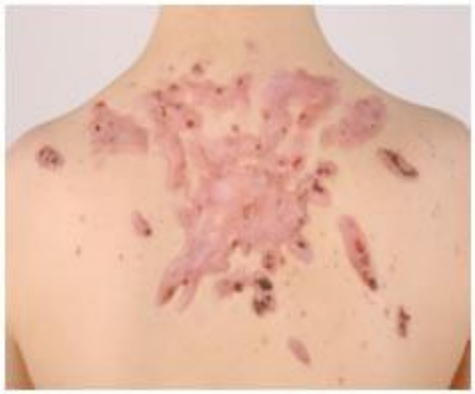


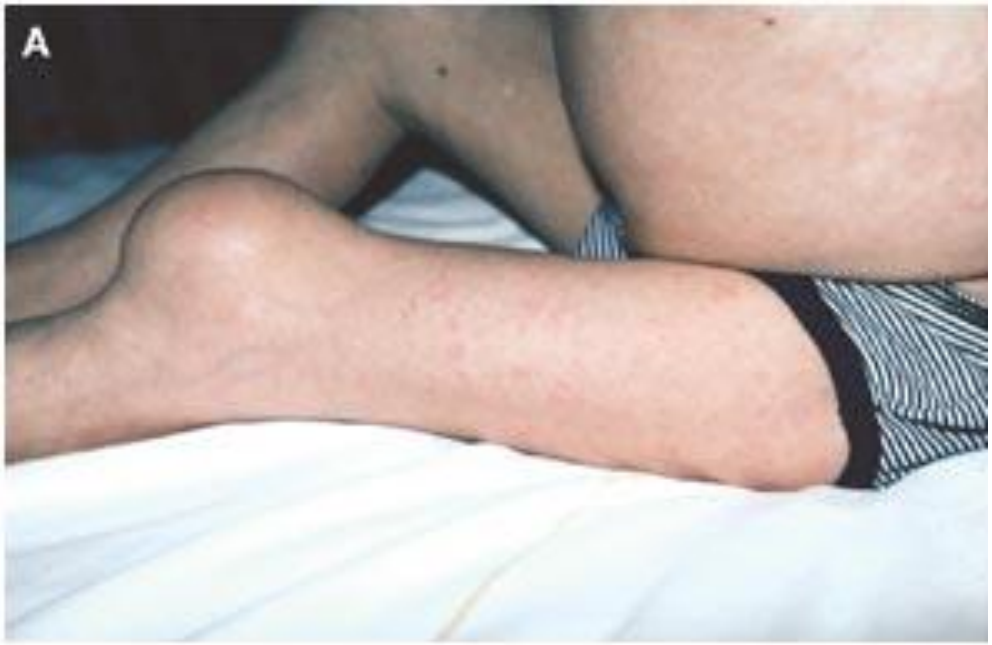


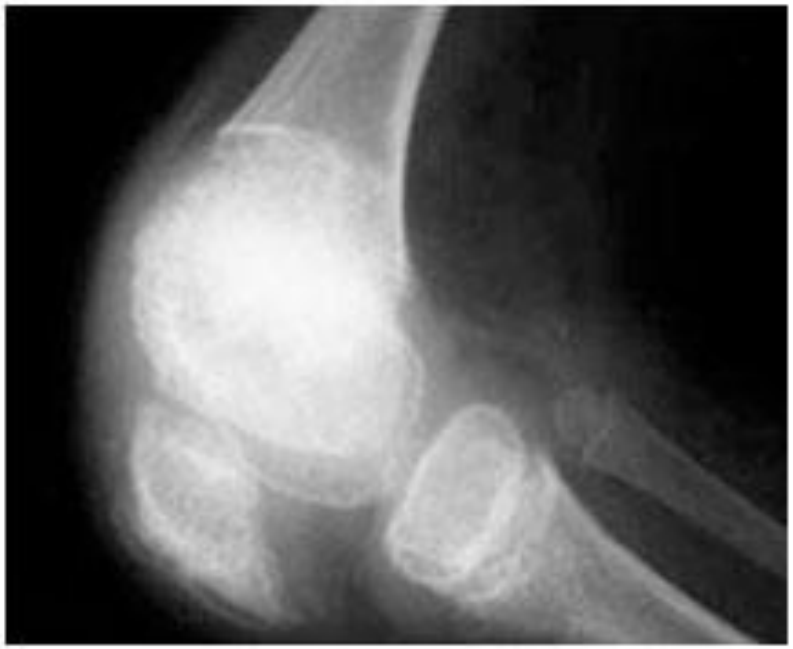




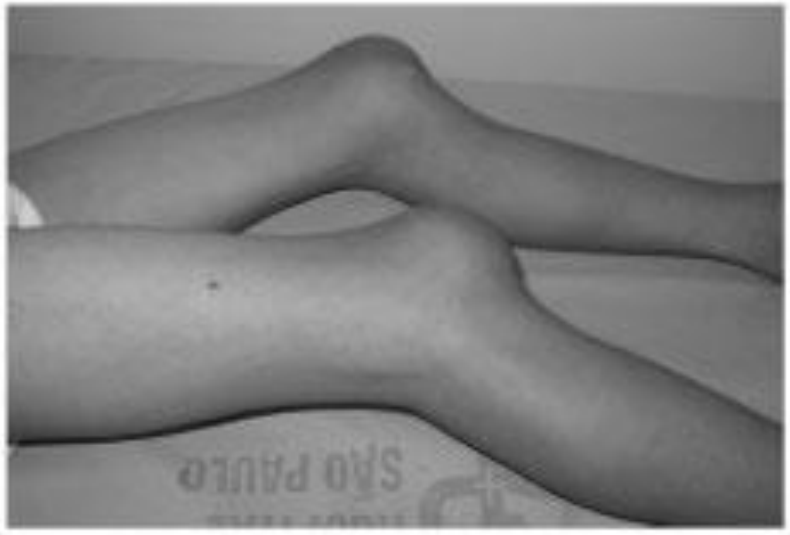


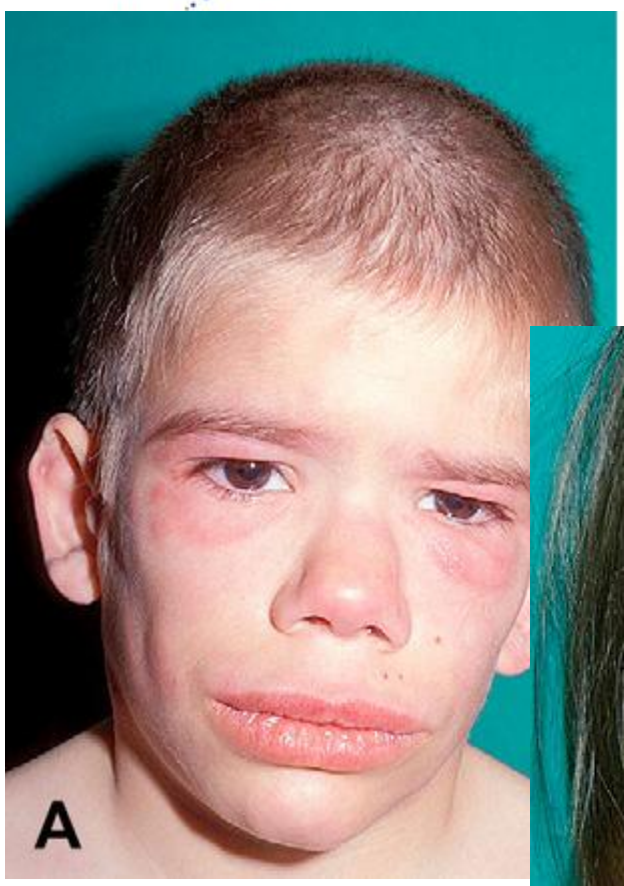


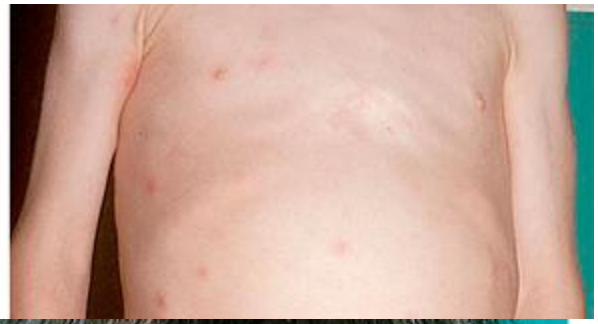




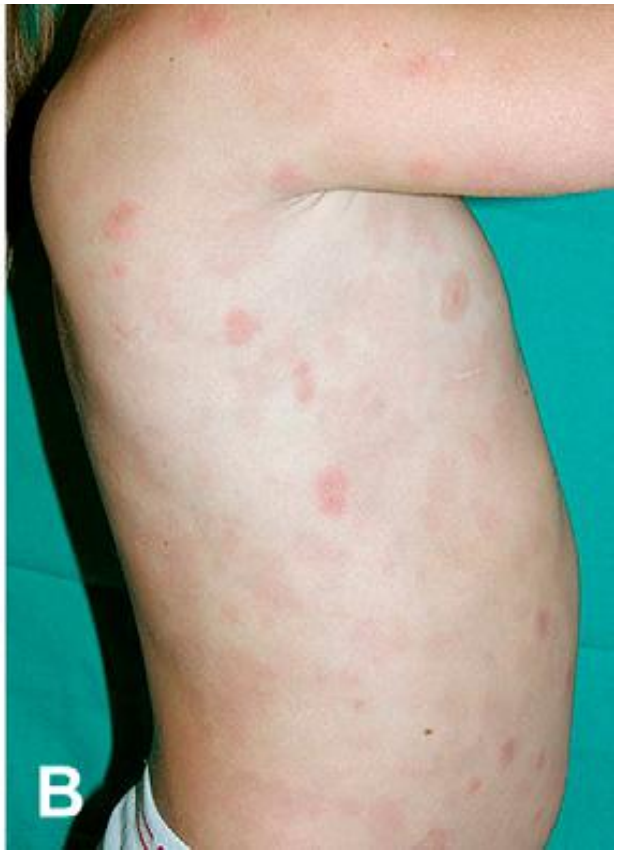
Nature Clinical Practice Rheumatology (2008) **4**, 481-489



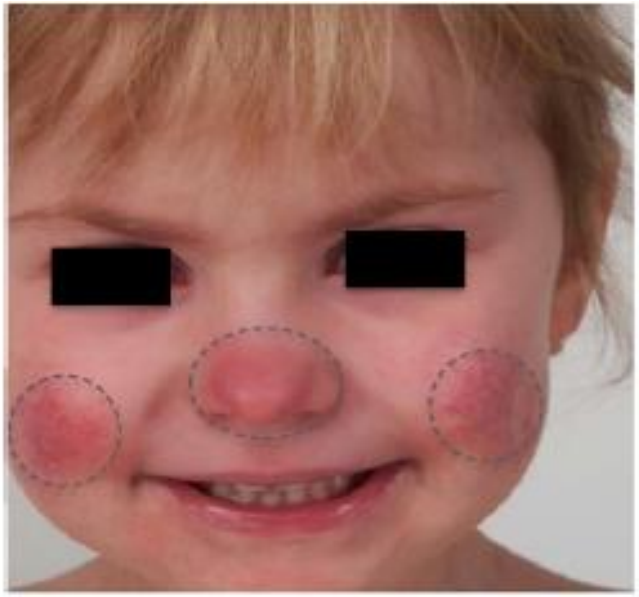

A

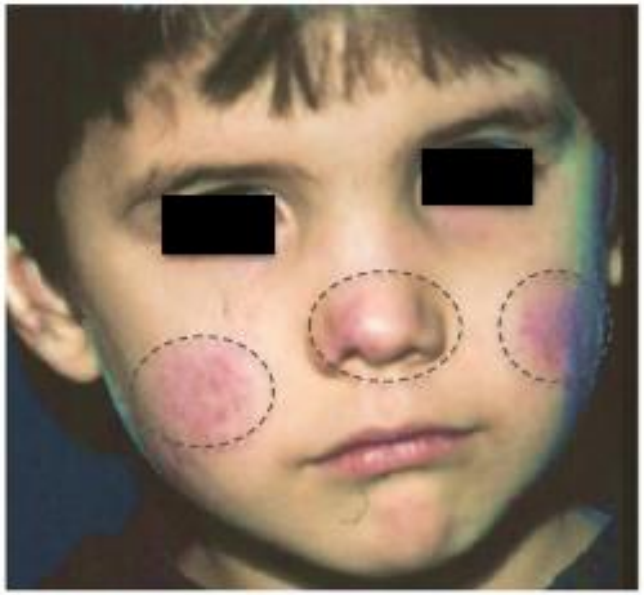



A

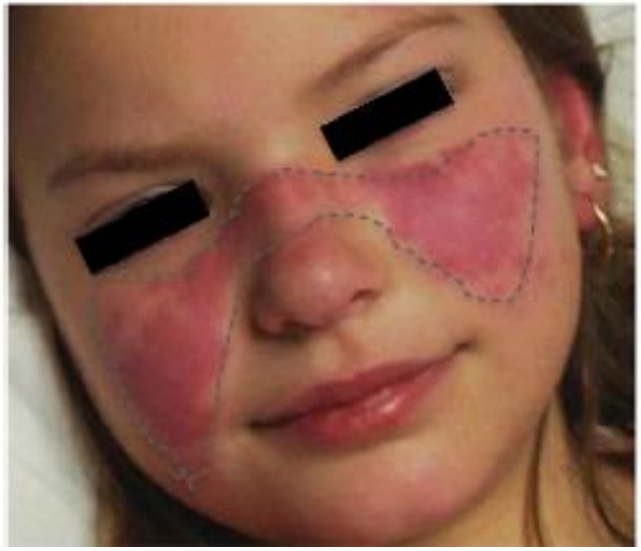

B

SAVI

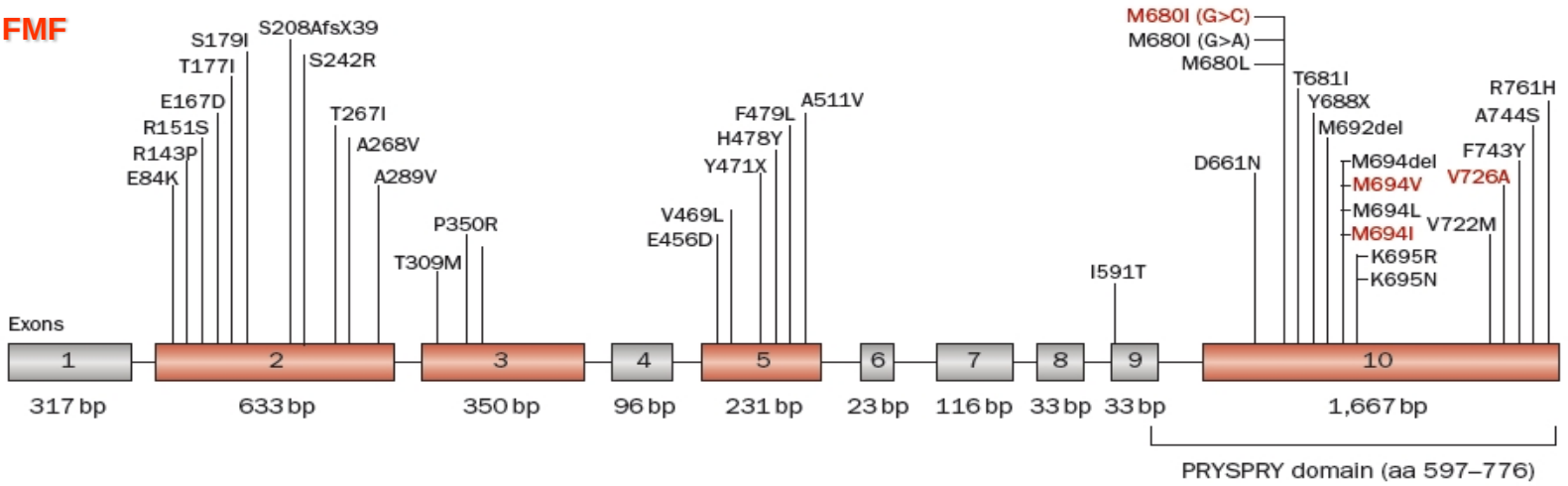




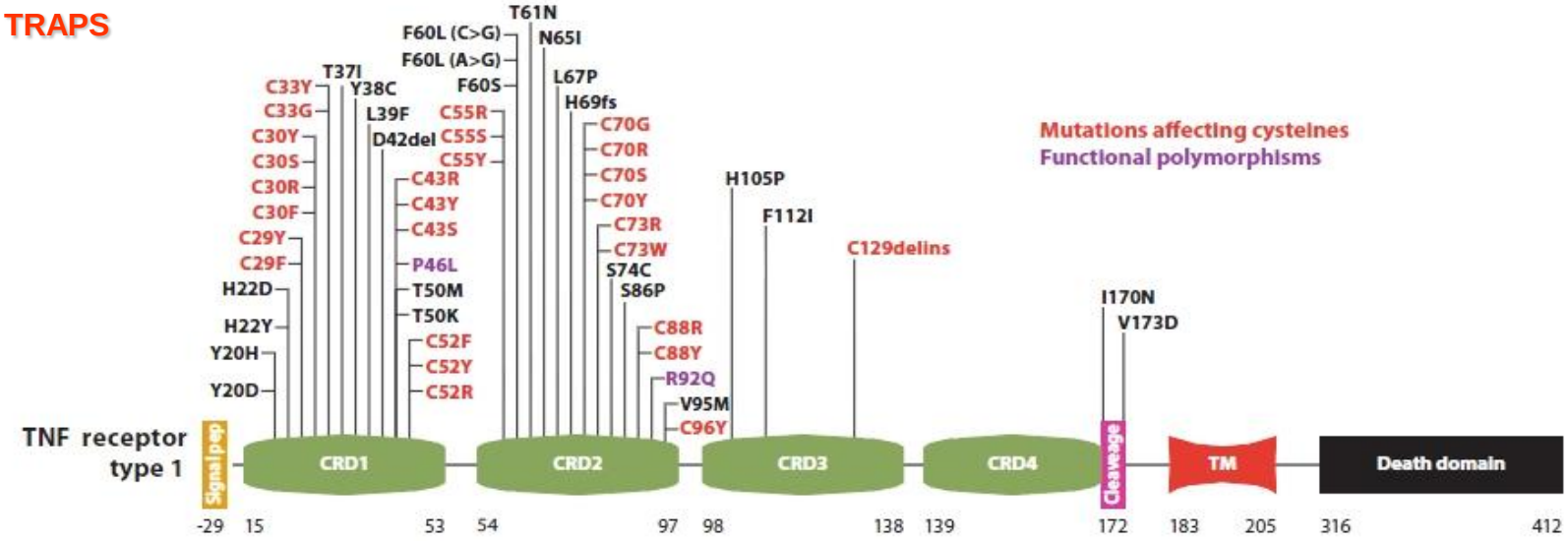
SLE

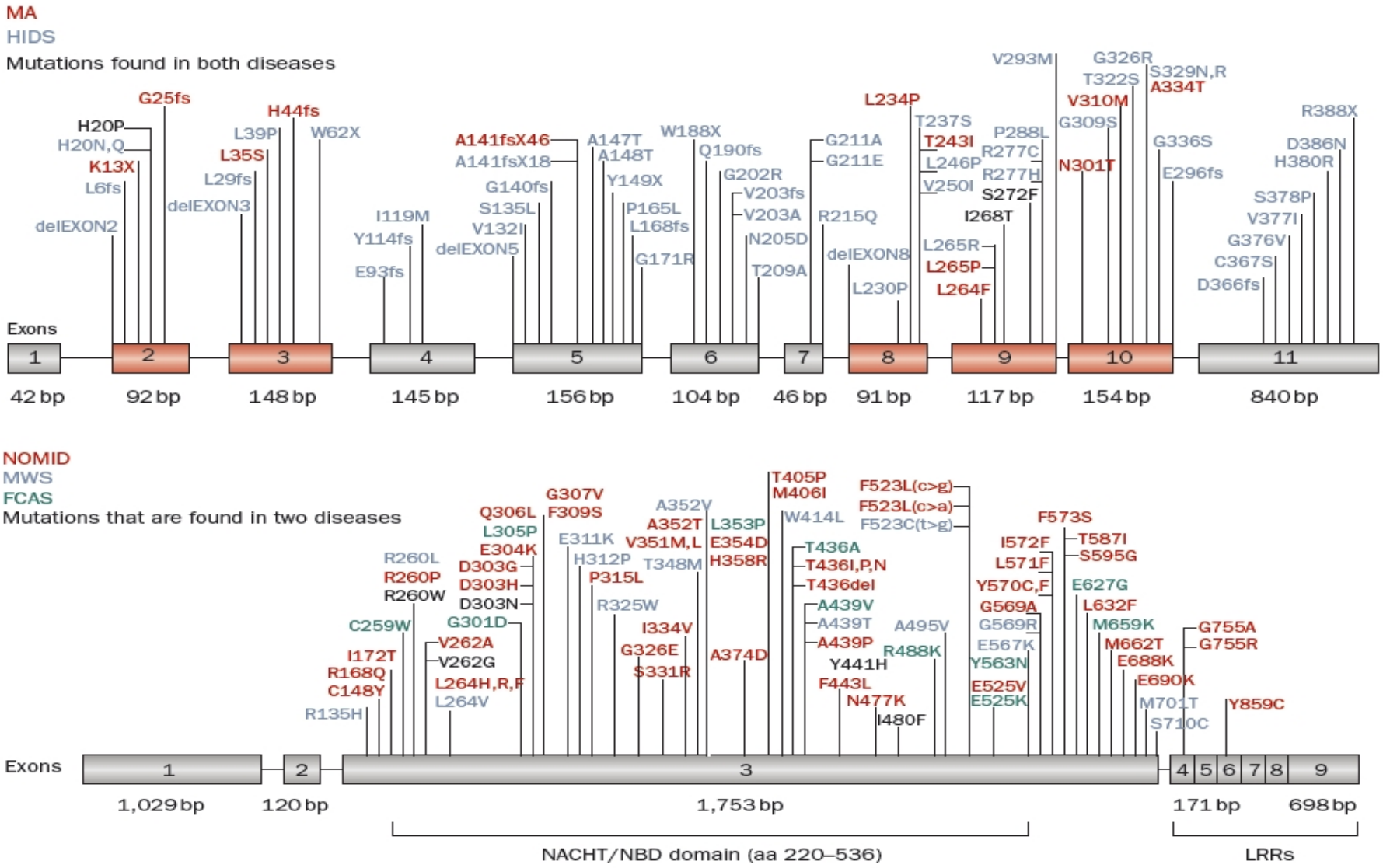


FMF


M680I (G>C)
M680I (G>A)
M680L
T681I
Y688X
M692del
R761H
A744S
F743Y
V726A
M694del
M694V
M694L
M694I
V722M
K695R
K695N
D661N
S179I
S208AfsX39
T177I
S242R
E167D
T267I
R151S
A268V
R143P
A289V
E84K
P350R
T309M
F479L
A511V
H478Y
Y471X
V469L
E456D
I591T
Exons
1
2
3
4
5
6
7
8
9
10
317 bp
633 bp
350 bp
96 bp
231 bp
23 bp
116 bp
33 bp
33 bp
1,667 bp
PRYSPRY domain (aa 597–776)

TRAPS


T61N
F60L (C>G)
N65I
F60L (A>G)
T37I
F60S
L67P
C33Y
Y38C
H69fs
C33G
L39F
C55R
C70G
C30Y
D42del
C55S
C70R
C30S
C55Y
C70S
C30R
C43R
C70Y
C30F
C43Y
C73R
C29Y
C43S
C73W
C29F
P46L
S74C
H22D
T50M
S86P
H22Y
T50K
C88R
Y20H
C52F
C88Y
Y20D
C52Y
R92Q
C52R
V95M
C96Y
H105P
F112I
C129delins
I170N
V173D
Mutations affecting cysteines
Functional polymorphisms
TNF receptor type 1
Signal pep
CRD1
CRD2
CRD3
CRD4
Cleavage
TM
Death domain
-29
15
53
54
97
98
138
139
172
183
205
316
412


MA
HIDS
Mutations found in both diseases
G25fs
H20P
H20N,Q
K13X
L6fs
delEXON2
H44fs
L39P
L35S
L29fs
delEXON3
W62X
I119M
Y114fs
E93fs
A141fsX46
A141fsX18
G140fs
S135L
V132I
delEXON5
A147T
A148T
Y149X
P165L
L168fs
G171R
W188X
Q190fs
G202R
V203fs
V203A
N205D
T209A
G211A
G211E
R215Q
delEXON8
L230P
L234P
T237S
T243I
L246P
V250I
V293M
P288L
R277C
R277H
S272F
I268T
L265R
L265P
L264F
G326R
T322S
S329N,R
A334T
V310M
G309S
N301T
G336S
E296fs
R388X
D386N
H380R
S378P
V377I
G376V
C367S
D366fs
Exons
1
2
3
4
5
6
7
8
9
10
11
42 bp
92 bp
148 bp
145 bp
156 bp
104 bp
46 bp
91 bp
117 bp
154 bp
840 bp
NOMID
MWS
FCAS
Mutations that are found in two diseases
T405P
M406I
W414L
F523L(c>g)
F523L(c>a)
F523C(t>g)
A352V
A352T
V351M,L
T348M
L353P
E354D
H358R
A374D
G307V
F309S
Q306L
L305P
E304K
D303G
D303H
D303N
E311K
H312P
P315L
R325W
G301D
I334V
G326E
S331R
R260L
R260P
R260W
C259W
V262A
V262G
I172T
R168Q
C148Y
L264H,R,F
L264V
R135H
T436A
T436I,P,N
T436del
A439V
A439T
A439P
Y441H
F443L
N477K
I480F
A495V
R488K
F573S
I572F
L571F
Y570C,F
G569A
G569R
E567K
Y563N
E525V
E525K
T587I
S595G
E627G
L632F
M659K
M662T
E688K
E690K
M701T
S710C
G755A
G755R
Y859C
Exons
1
2
3
4
5
6
7
8
9
1,029 bp
120 bp
1,753 bp
171 bp
698 bp
NACHT/NBD domain (aa 220–536)
LRRs

- Aparició asincrònica de la simptomatología
- Absència d'alteració analítica
- Absència d'història familiar
- Estudi genètic negatiu

SINDROME AUTOINFLAMATORIO = INFLAMACION

DATOS INFLAMATORIOS OBJETIVOS:

- VSG
- PCR
- SAA
- CALPROTECTINA (S100A12)

- Limitacions dels estudis genètics i proteòmics:
  - Mutacions vs. polimorfismes
  - Polimorfismes funcionals
  - Manca d'identificació de la mutació
  - Coexistència de > 1mutació (gens iguals / diferents)
  - Mutacions germinals vs. mutacions somàtiques
  - Mutacions somàtiques en mosaïcisme
  - Efecte de la mutació genètica sobre la proteïna codificada:
    - Guany / pèrdua de l'efecte de la proteïna codificada
    - Guany / pèrdua de l'efecte regulador sobre les vies efectores

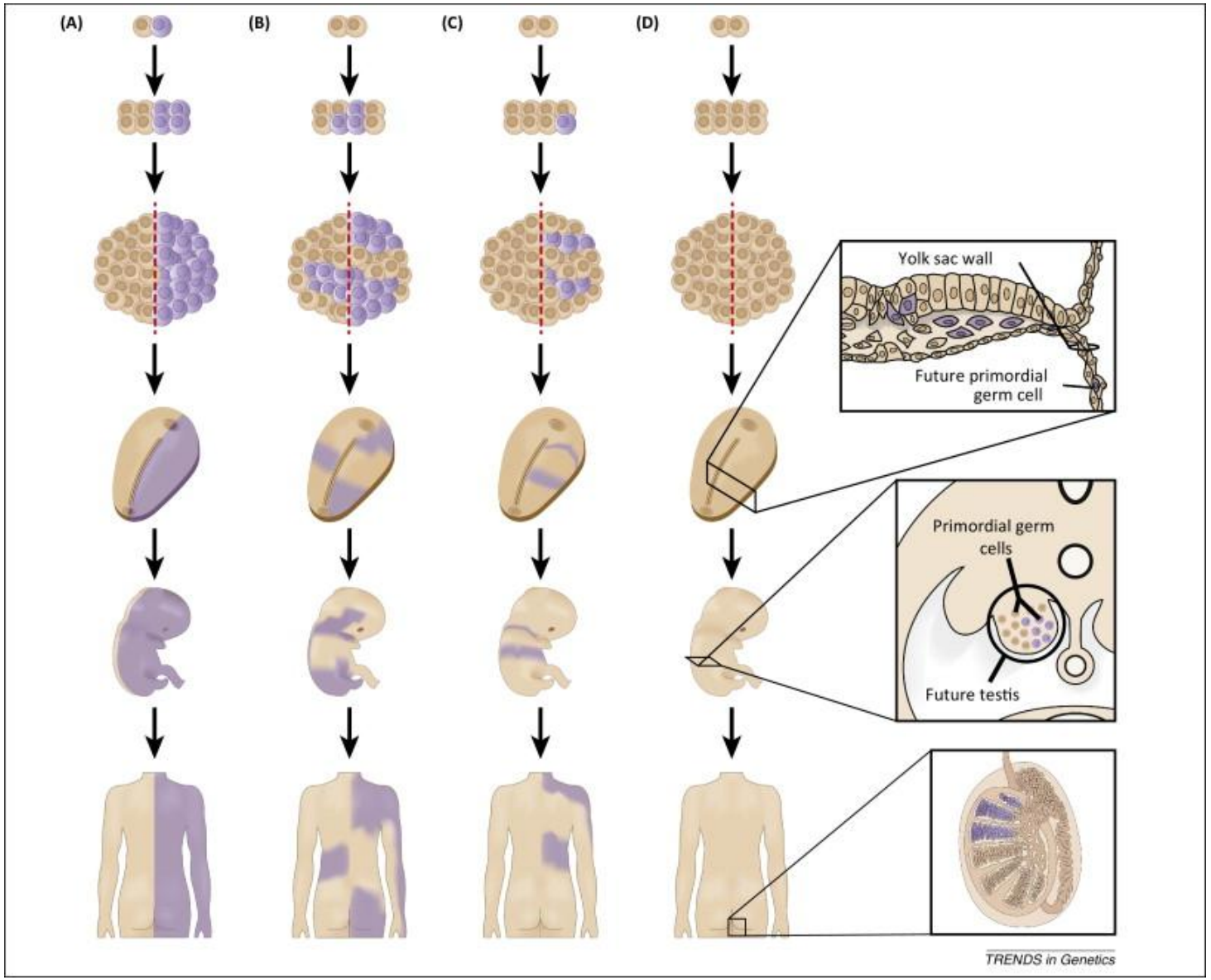
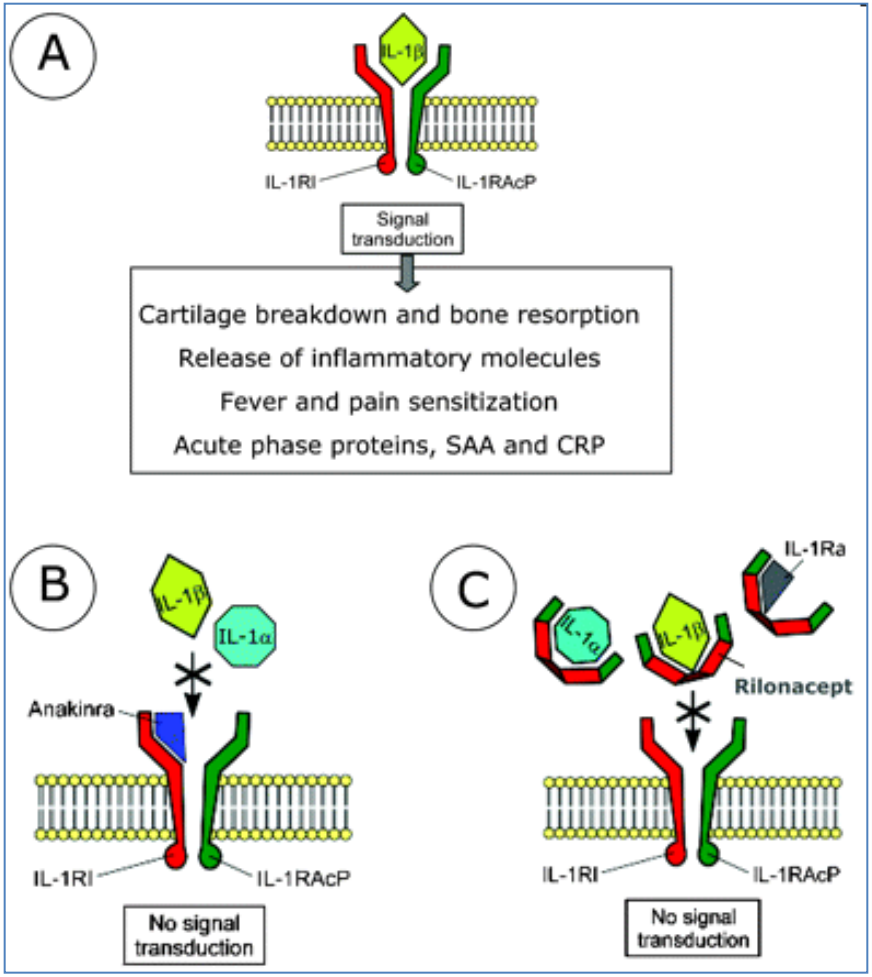
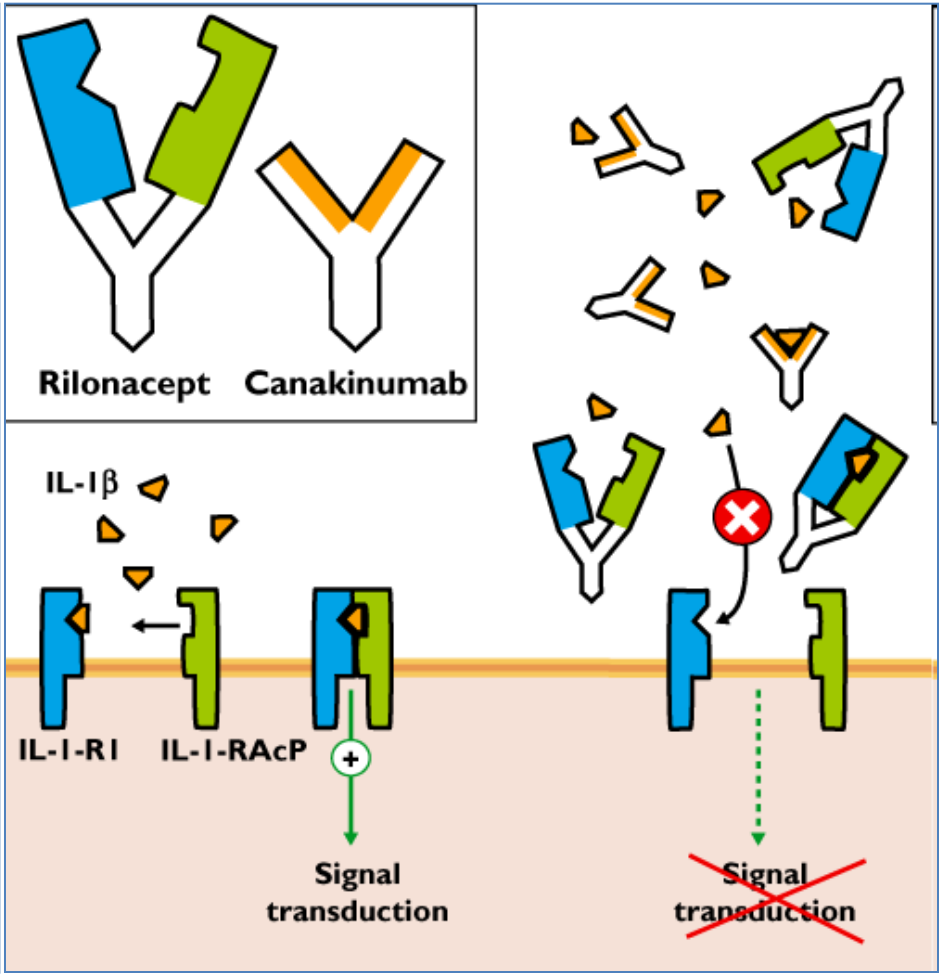

(A)
(B)
(C)
(D)
Yolk sac wall
Future primordial germ cell
Primordial germ cells
Future testis
TRENDS in Genetics

Table 2 Summary of evidence for treatments of choice

Disease	Level of evidence*	Treatments
FMF	1b	Colchicine
Colchicine resistant	2b	Corticosteroids
	2b†	Interferon-α
	4	Anakinra, etanercept, infliximab
CAPS	1b	Canakinumab, rilonacept
	2b	Anakinra
TRAPS	4	Corticosteroids
	2b	Anakinra, etanercept
MKD	4	NSAIDs, corticosteroids
	2b	Anakinra
	4	Etanercept
PAPA	4	Corticosteroids, anakinra, etanercept, infliximab, adalimumab
DIRA	1c	Anakinra
NLRP12	4	NSAIDs, corticosteroids
PFAPA	1a	(Adeno)tonsillectomy
	2b	Corticosteroids
	4	Anakinra

*Levels of evidence according to Oxford criteria:[4] 1a, systematic review of randomised controlled trials (RCTs); 1b, RCT; 1c, all-or-none effect; 2a, systematic review of cohort studies; 2b, cohort study; 2c, outcomes; 3a, systematic review of case-control studies; 3b, case-control study; 4, case series; 5, expert opinion.


A
IL-1β
IL-1RI
IL-1RAcP
Signal transduction
Cartilage breakdown and bone resorption
Release of inflammatory molecules
Fever and pain sensitization
Acute phase proteins, SAA and CRP
B
IL-1β
IL-1α
Anakinra
IL-1RI
IL-1RAcP
No signal transduction
C
IL-1Ra
IL-1α
IL-1β
Rilonacept
IL-1RI
IL-1RAcP
No signal transduction


Rilonacept
Canakinumab
IL-1β
IL-1-R1
IL-1-RAcP
+
Signal transduction
Signal transduction

Identificar símptomes

Descartar causes més prevalents

Història familiar

Evaluació objectiva d'inflamació

Consultar