

XXXI Congreso Nacional de la Sociedad Española de Medicina Interna

II Congreso Ibérico de Medicina Interna

OVIEDO

17-20 Noviembre 2010

**Auditorio-Palacio de Congresos
"Príncipe Felipe"**

**VII Congreso de la Sociedad
Asturiana de Medicina Interna**

**ENFERMEDADES
AUTOINFLAMATORIAS
TRATAMIENTO**

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HOSPITAL DO MEIXOEIRO

¿POR QUÉ TANTO INTERÉS?

- EMERGENTES
- MULTIDISCIPLINARIAS
- MECANISMO PATOGÉNICO
- NUEVOS TRATAMIENTOS

¿RARAS?





Amyloid purpura



This image shows palpebral and periorbital purpura in a patient with amyloidosis.

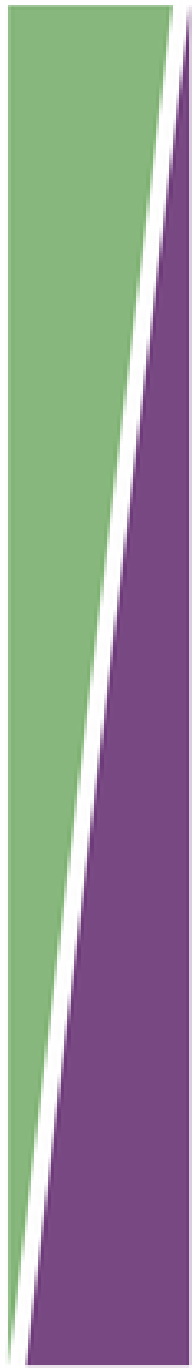
Reproduced with permission from: Eder, L, Bitterman, H. Image in clinical medicine. Amyloid purpura. N Engl J Med 2007; 356: 2406. Copyright ©2008 Massachusetts Medical Society. All rights reserved.

PIODERMA GANGRENOSO



AUTOINFLAMACIÓN VERSUS AUTOINMUNIDAD

- ¿ENFERMEDADES AUTOINMUNES PURAS?
- ¿ENFERMEDADES AUTOINFLAMATORIAS PURAS?
- ¿COMBINACIÓN DE MECANISMOS EN EL MISMO PACIENTE?



**RARE MONOGENIC
AUTOINFLAMMATORY
DISEASES**

FMF, TRAPS, HIDS, PAPA
Blau syndrome (uveitis)

**POLYGENIC
AUTOINFLAMMATORY
DISEASES**

Crohn disease, ulcerative colitis
Degenerative diseases, e.g. osteoarthritis
Gout/pseudogout/other crystal arthropathies
Some categories of reactive arthritis and Psoriasis/psoriatic arthritis (no MHC association)
Self-limiting inflammatory arthritis including diseases clinically presenting as RA
Storage diseases/congenital diseases with associated tissue inflammation
Non-antibody associated vasculitis including giant cell and Takayasu arteritis
Idiopathic uveitis
Acne and acneform associated diseases
Some neurological diseases, e.g. acute disseminated encephalomyelitis
Erythema nodosum associated disease, including sarcoidosis

MIXED PATTERN DISEASES
with evidence of acquired component
(MHC class I associations) and
autoinflammatory components

Ankylosing spondylitis
Reactive arthritis
Psoriasis/psoriatic arthritis
Behcet Syndrome
Uveitis (HLA-B27 associated)

**CLASSIC POLYGENIC
AUTOIMMUNE DISEASES**
(organ-specific and non-specific)

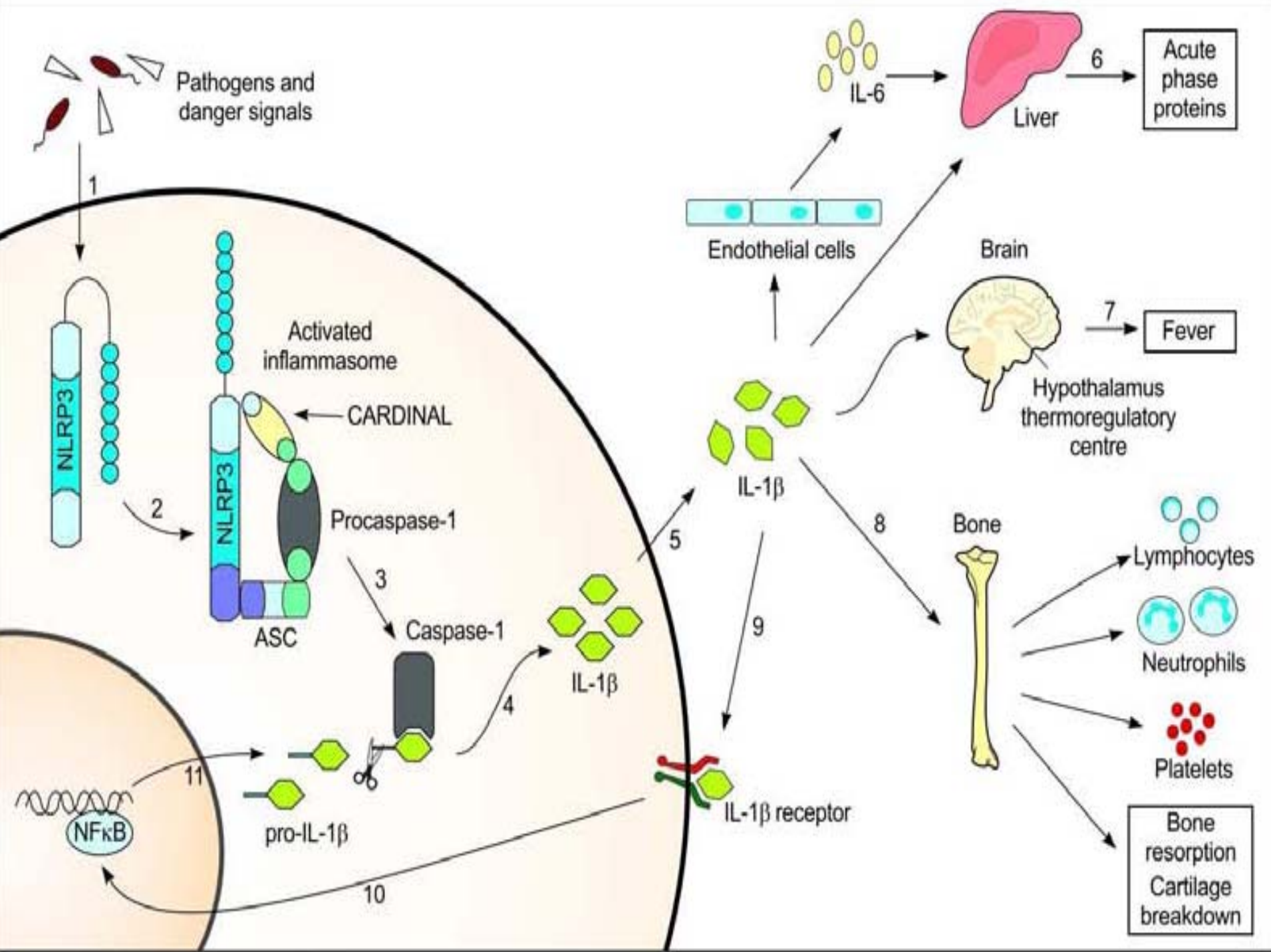
Rheumatoid arthritis
Autoimmune uveitis (sympathetic ophthalmia)
Coeliac disease
Primary biliary cirrhosis
Autoimmune gastritis/pernicious anaemia
Autoimmune thyroid disease
Addison disease
Pemphigus, pemphigoid, vitiligo
Myasthenia gravis
Dermatomyositis, polymyositis, scleroderma
Goodpasture syndrome
ANCA associated vasculitis
Type 1 diabetes
Sjogren syndrome
Systemic lupus erythematosus

**RARE MONOGENIC
AUTOIMMUNE
DISEASES**

ALPS, IPEX, APECED

CLAVES

- NLRP3-INFLAMASOMA
 - COMPLEJO MOLECULAR QUE REGULA LA PRODUCCIÓN DE DIVERSAS CITOQUINAS
 - FUNDAMENTALMENTE:
 - IL-1B



CLAVES

- LOS SÍNDROMES AUTOINFLAMATORIOS MONOGÉNICOS TIENEN DEFECTOS EN LAS PROTEINAS ESENCIALES DEL INFLAMASOMA O DE SUS REGULADORES.

–IL-1B DEPENDIENTES

CLAVES

- EL MISMO MECANISMO FISIOPATOLÓGICO ESTÁ DEMOSTRADO EN UN NÚMERO CADA VEZ MAYOR DE PROCESOS EN LOS CUALES SE PRODUCE ACTIVACIÓN POR «SEÑALES» PROPIAS O EXTERNAS DEL INFLAMASOMA

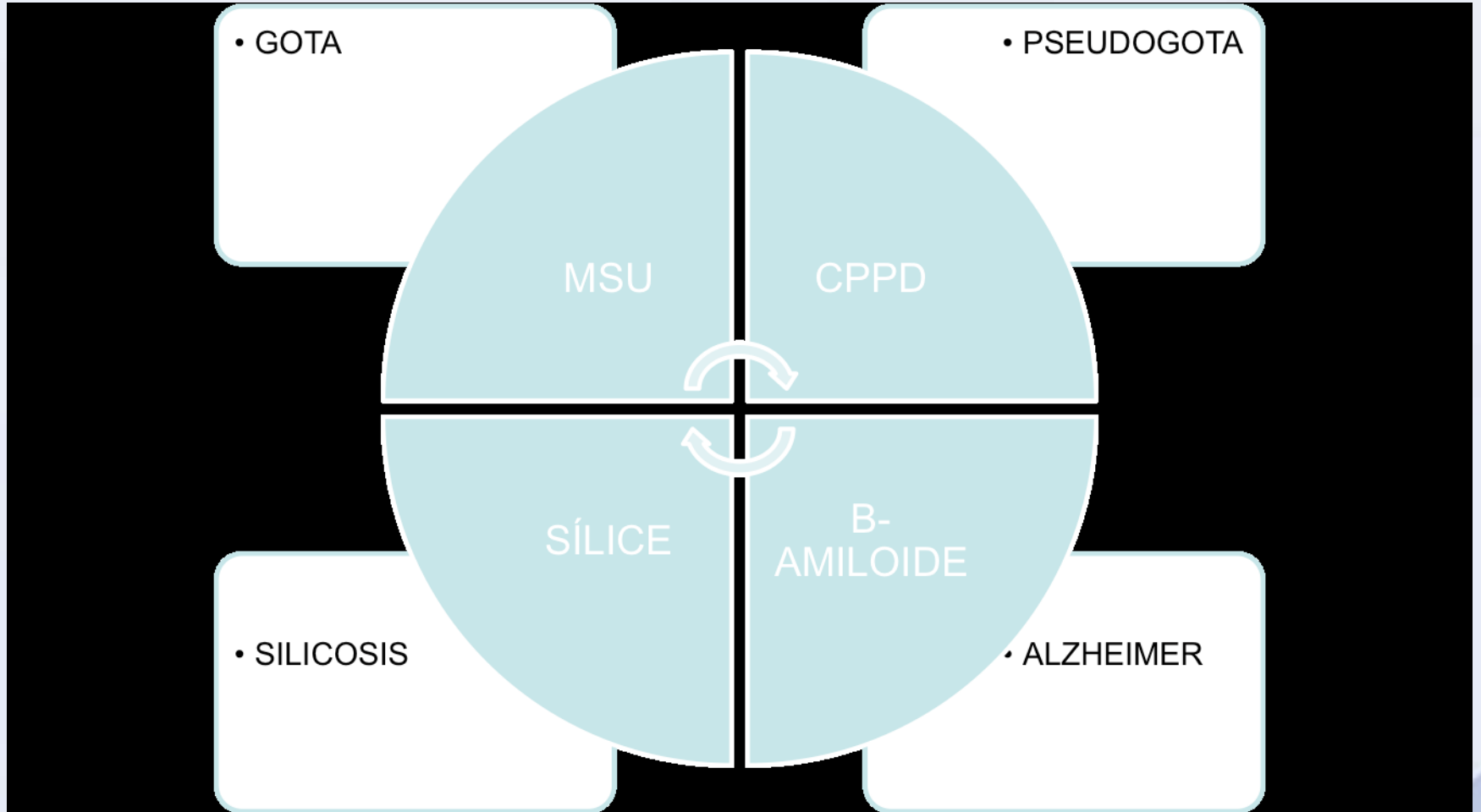
CLAVES

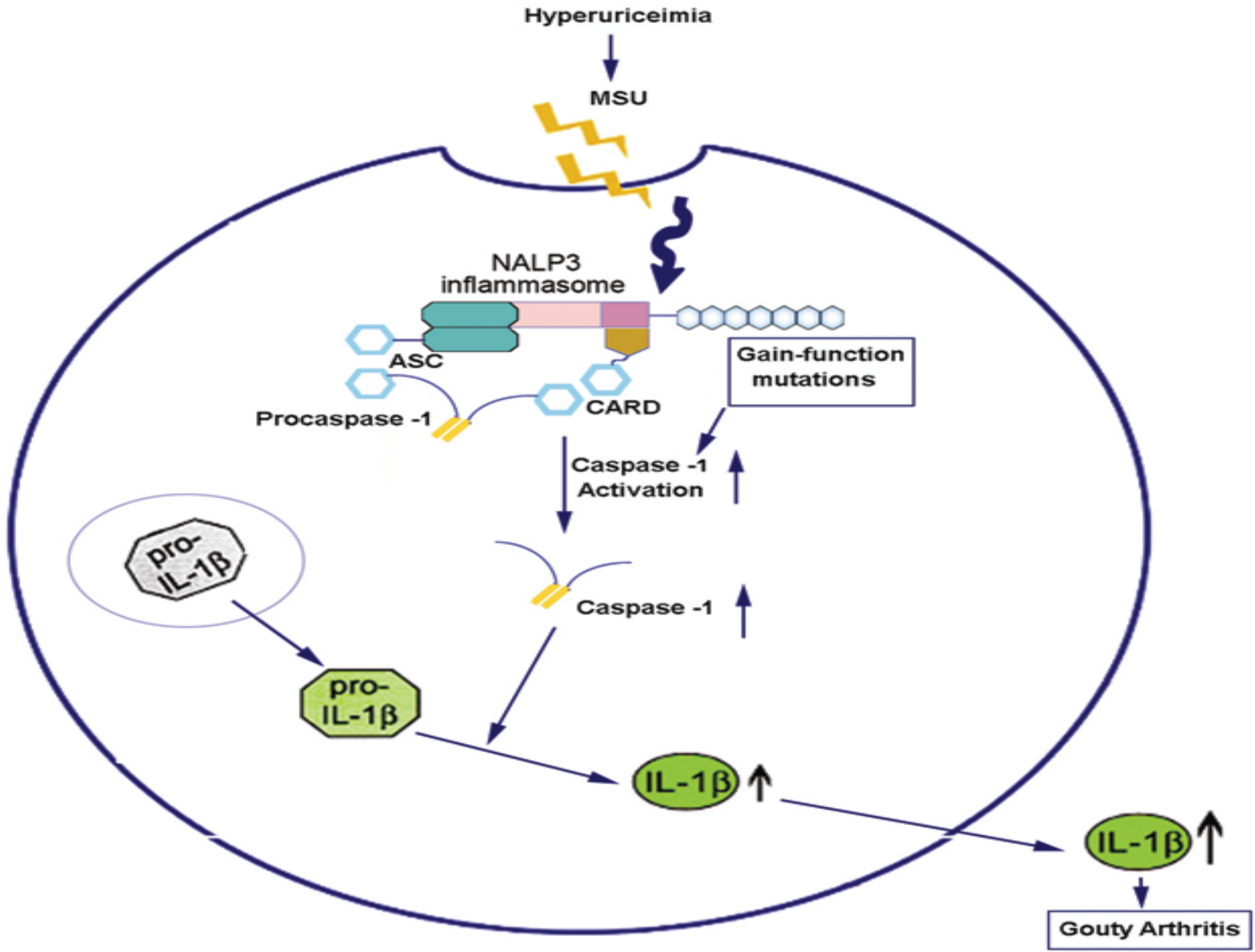
- DISPONEMOS DE TRATAMIENTOS CAPACES DE INHIBIR LA ACTIVIDAD DEL MEDIADOR PRINCIPAL

- **IL-1B**



ACTIVIDAD NLRP3





Intracellular innate immunity in gouty arthritis: role of NALP3 Inflammasome

Ru Liu-Bryan

Immunology and Cell Biology (2010) 88,20-23

**Calcium pyrophosphate deposition disease
mimicking polymyalgia rheumatica:
a prospective followup study of predictive factors
for this condition in patients presenting
with polymyalgia symptoms.**

[Pego-Reigosa JM](#), [Rodriguez-Rodriguez M](#), [Hurtado-Hernandez Z](#), [Gromaz-Martin J](#),
[Taboas-Rodriguez D](#), [Millan-Cachinero C](#), [Hernandez-Rodriguez I](#), [Gonzalez-Gay MA](#).

Arthritis Rheum. 2005 Dec 15;53(6):931-8

Hospital Meixoeiro, Vigo, Spain. jose.maria.pego.reigosa@sergas.es

IL-1R1/MyD88 signaling and the inflammasome are essential in pulmonary inflammation and fibrosis in mice

Pamela Gasse¹, Caroline Mary¹, Isabelle Guenon², Nicolas Noulin^{1,3}, Sabine Charron¹, Silvia Schnyder-Candrian¹, Bruno Schnyder¹, Shizuo Akira⁴, Valérie F.J. Quesniaux¹, Vincent Lagente², Bernhard Ryffel¹ and Isabelle Couillin¹

¹Laboratory of Molecular Immunology and Embryology, University of Orleans and CNRS, Orleans, France.

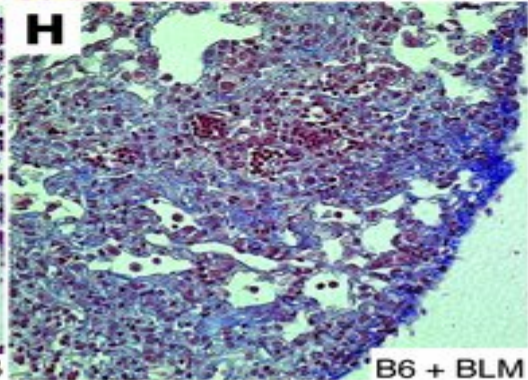
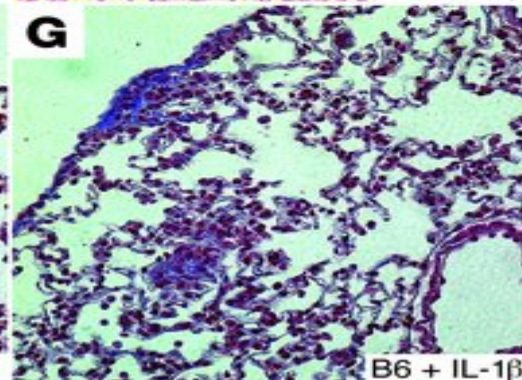
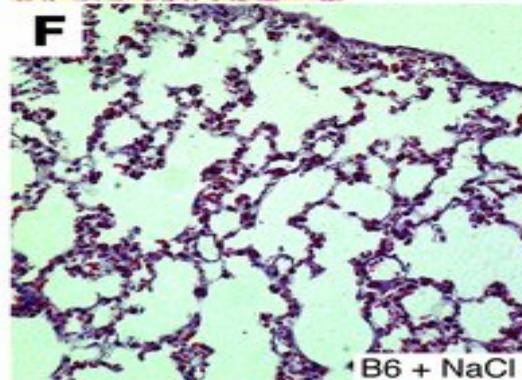
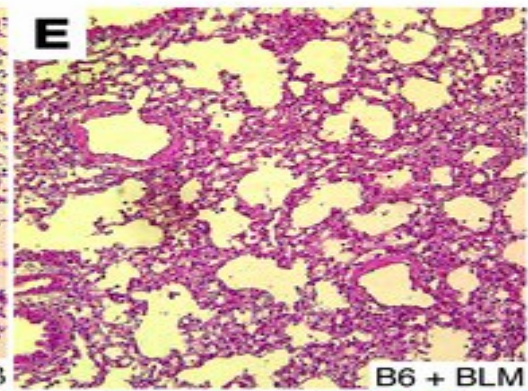
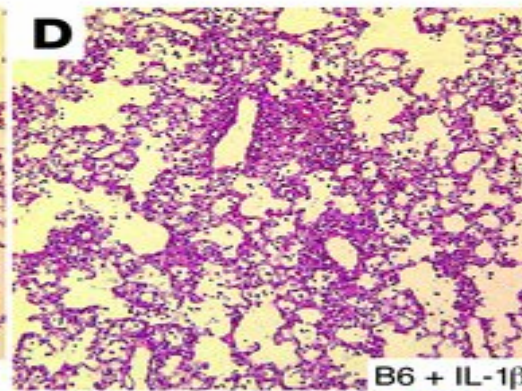
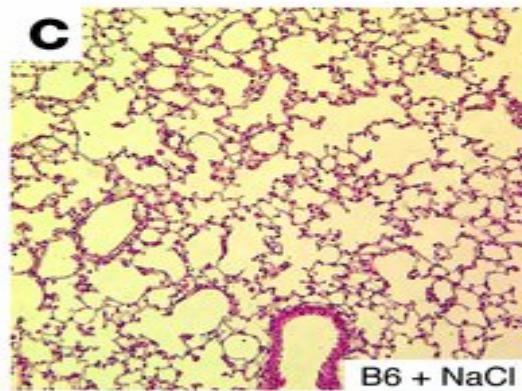
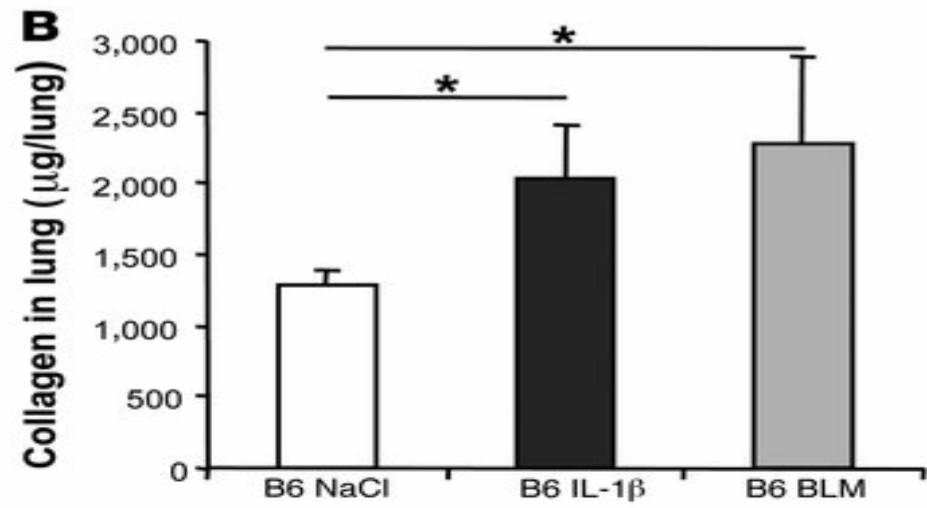
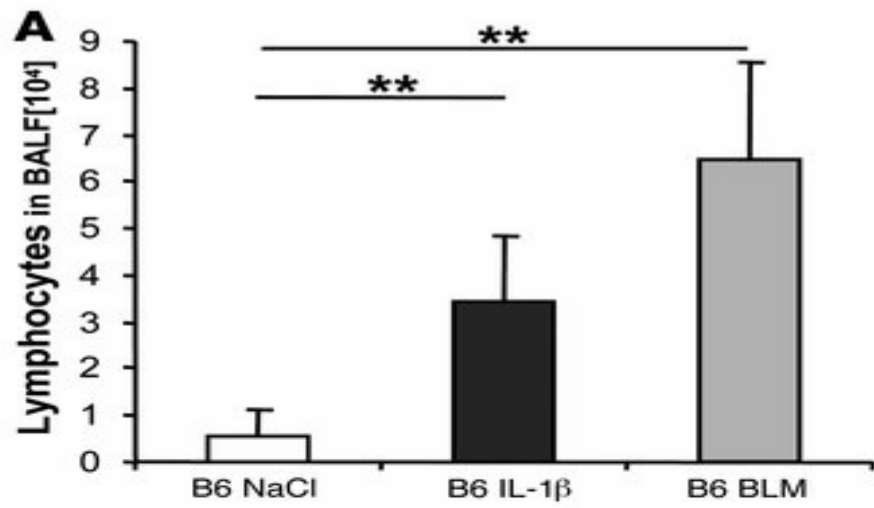
²INSERM U620, Université de Rennes 1, Rennes, France.

³Key-Obs SA, Orleans, France.

⁴Osaka University, Suita, Osaka, Japan.

J Clin Invest. 2007;117(12):3786–3799.

doi:10.1172/JCI32285.



**Cytokine and immunogenetic profiles in Japanese patients with adult-onset Still's disease.
Association with chronic articular disease.**

Fujii T, Nojima T, Yasuoka H, Satoh S, Nakamura K, Kuwana M, et al.

Rheumatology 2001;40:1398–404.

CLAVES

- DISPONEMOS DE TRATAMIENTOS CAPACES DE INHIBIR LA ACTIVIDAD DEL MEDIADOR PRINCIPAL

- **IL-1B**



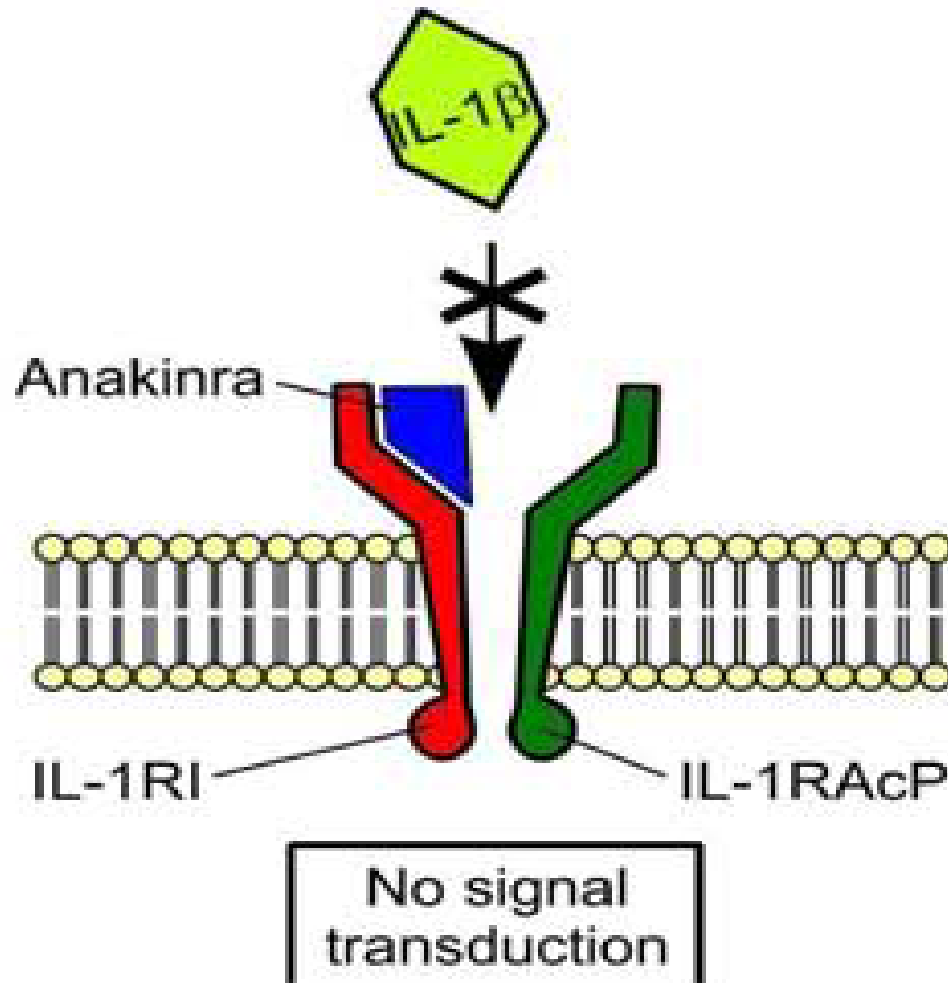
- **Terapia anti-IL-1 β**
- La evidencia de su eficacia y seguridad en determinados Síndromes Autoinflamatorios surge de los estudios clínicos:
 - Anakinra – estudios abiertos
 - Rilonacept – estudios aleatorizados de fase III en adultos
 - Canakinumab – estudios aleatorizados de fase III en niños y adultos

¹Farasat S *et al.* 2008; ²Touitou I, Kone-Paut I. 2008; ³Hawkins PN, Lachmann HJ. 2003; ⁴Glaser RL, Goldbach-Mansky R. 2008; ⁵Hoffman HM *et al.* 2004; ⁶Ross JB *et al.* 2008; ⁷Goldbach-Mansky R *et al.* 2006; ⁸Hoffman HM *et al.* 2008; ⁹Lachmann HJ *et al.* 2008

Therapy

Characteristics

Anakinra



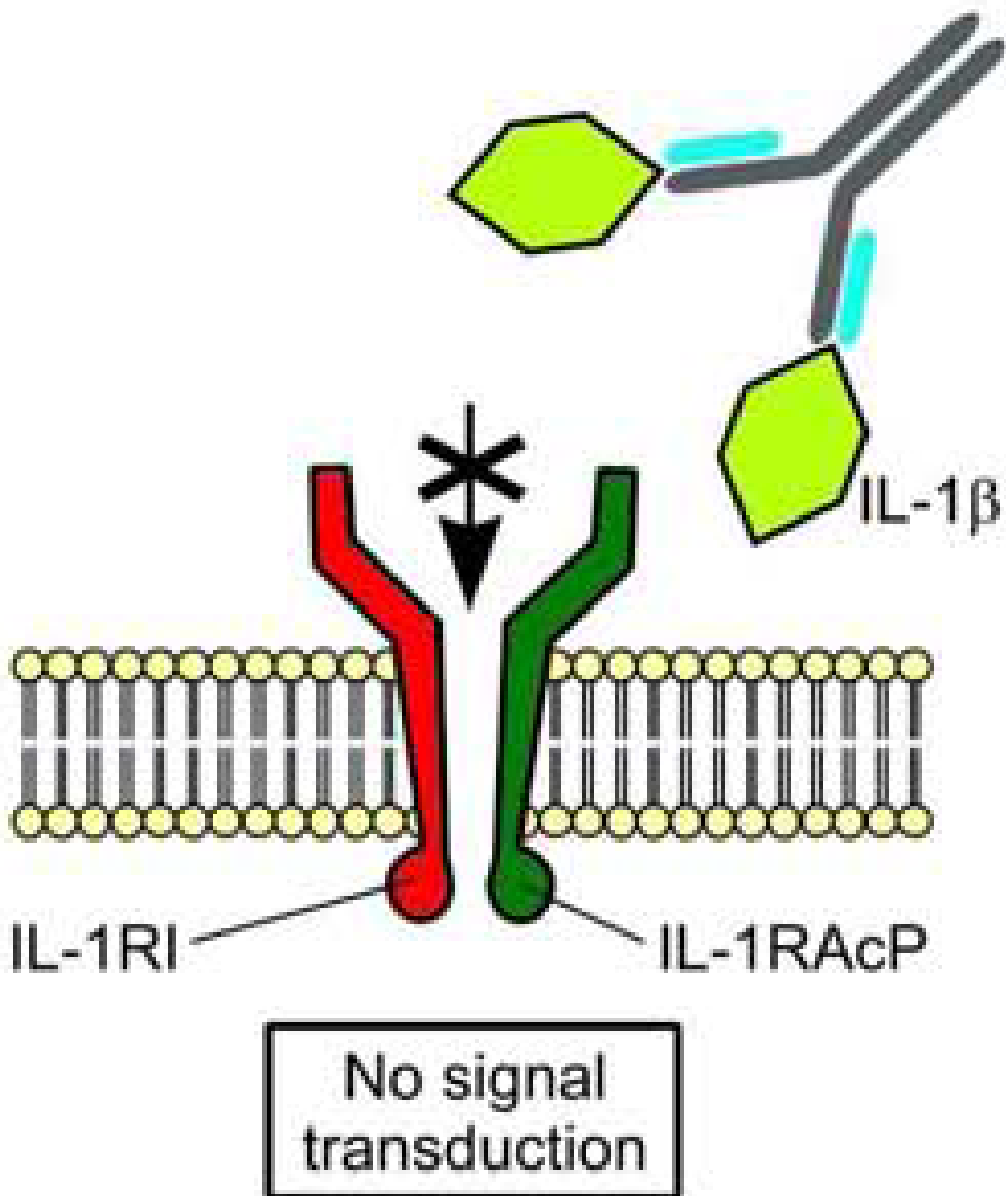
Structure:

Recombinant form of the endogenous IL-1 receptor antagonist, IL-1Ra; mimics IL-1Ra in blocking IL-1 β binding to receptor

Half-life: 4–6 hours

Frequency of administration: daily

Canakinumab

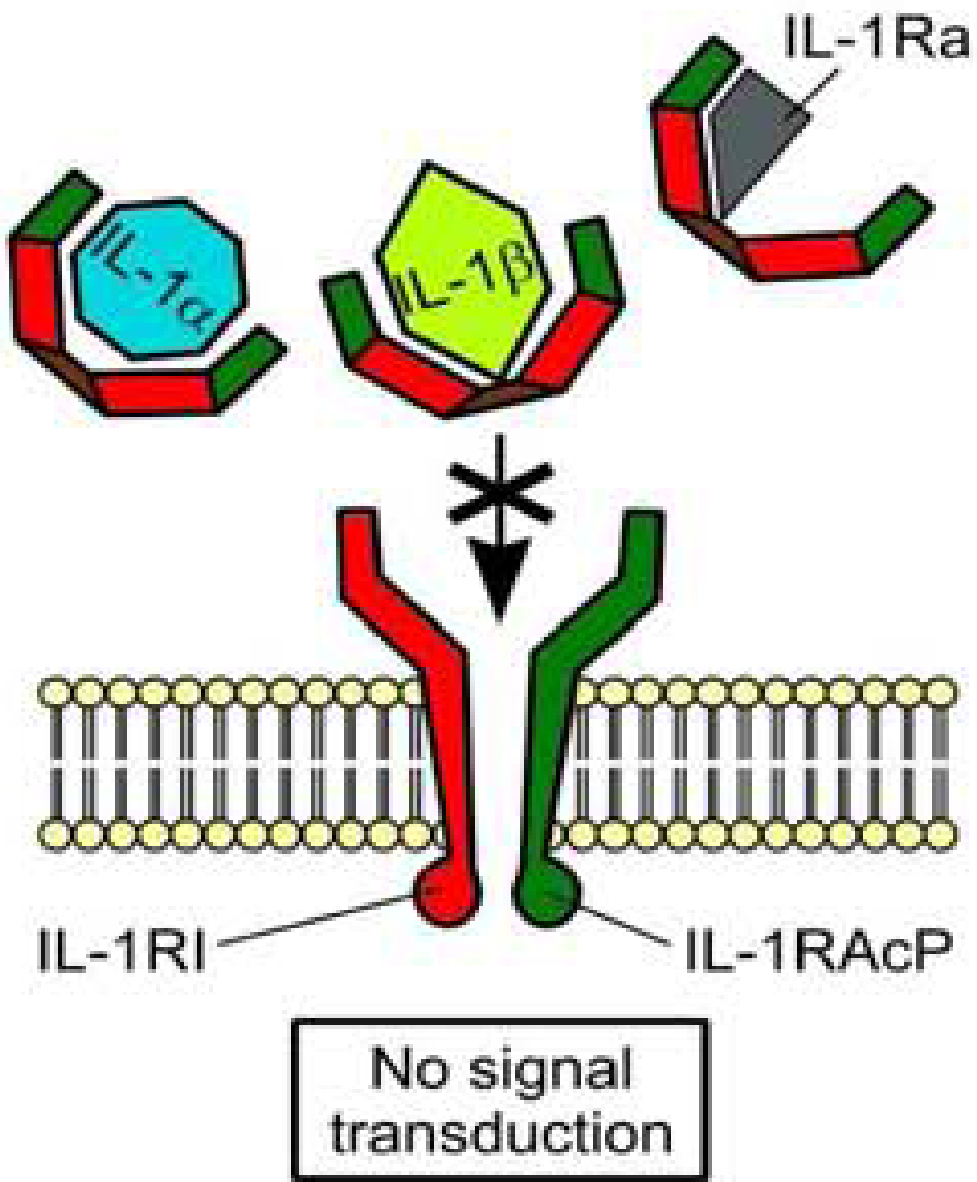


Structure:
Fully human IgG1 anti-IL-1β monoclonal antibody; prevents IL-1β binding to receptor

Half-life: 21–28 days

Frequency of administration: once every 8 weeks for CAPS

Rilonacept



Structure:

Fusion protein comprising the extracellular domains of IL-1RI and IL-1RAcP attached to a human IgG molecule; prevents IL-1 β binding to receptor

Half-life: 8.6 days

Frequency of administration: weekly

Use of canakinumab in the cryopyrin-associated periodic syndrome.

Lachmann HJ, Kone-Paut I, Kuemmerle-Deschner JB, Leslie KS, Hachulla E, Quartier P,

Gitton X, Widmer A, Patel N, Hawkins PN;

Canakinumab in CAPS Study Group.

Collaborators (11)

Madhoo S, Berthelot JM, Jorgensen C, Morell-Dubois S, Mouy R, Marie I, Lacassagne S, Chaturvedi R, Vargas C, Block JA, Smith J.

University College London Medical School, London, United Kingdom.

h.lachmann@medsch.ucl.ac.uk

N Engl J Med. 2009 Jun 4;360(23):2416-25

Role of interleukin-1 (IL-1) in the pathogenesis of systemic onset juvenile idiopathic arthritis and clinical response to IL-1 blockade.

Pascual V, Allantaz F, Arce E, Punaro M, Banchereau J.

J Exp Med 2005;201:1479–86.

Canakinumab for the treatment of acute flares in difficult-to-treat gouty arthritis.

So A, De Meulemeester M, Pikhlak A, et al.

Arthritis Rheum 2010;62 (10):3064-76

Interleukin-1 receptor antagonist (anakinra) treatment in patients with systemic-onset juvenile idiopathic arthritis or adult onset Still disease: preliminary experience in France

T Lequerre¹, P Quartier², D Rosellini², F Alaoui³, M De Bandt⁴, O Mejjad¹, I Kone-Paut⁵, M Michel⁶, E Dernis⁷, M Khellaf⁶, N Limal⁸, C Job-Deslandre⁹, B Fautrel¹⁰, X Le Loe¹, J Sibilia³ on behalf of the Société Francophone pour la Rhumatologie et les Maladies Inflammatoires en Pédiatrie (SOFREMIP) and the Club Rhumatismes et Inflammation

Ann Rheum Dis 2008;67:302–308.

doi:10.1136/ard.2007.076034

Rapid responses to anakinra in patients with refractory adult-onset Still's disease.

Fitzgerald AA, Leclercq SA, Yan A, Homik JE, Dinarello CA.

Arthritis Rheum 2005;52:1794–803.

- **Effective Treatment of Steroid Refractory Adult-onset Still's Disease with Anakinra**
- *The Journal of Rheumatology 2008; 35:5*



Muchas gracias