Psöriatik artrit tedavisinde güncel yolaklar

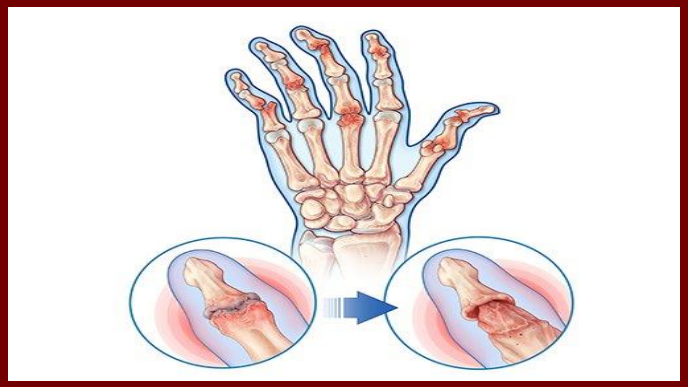
Dr. Songül Çildağ
Adnan Menderes Üniversitesi
İmmünoloji-Romatoloji Bilim Dalı

- Epidemiyoloji
- İmmünopatoloji
- Güncel tedavi yolakları

EPİDEMİYOLOJİ

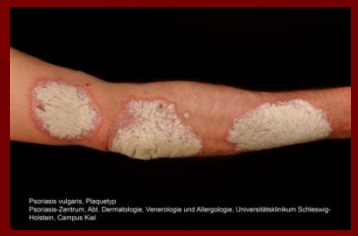
PSÖRİAZİS

- Psöriazis; toplumda %2 sıklıkta
- Hastaların %6-42'de Psöriatik artrit (PsA)
- Psöriazis; 30-50, PsA; 40-50 yaş
- K=E
- Hastaların %40'da aile öyküsü
- Heterojen klinik-hastada hastaya farklı sunum

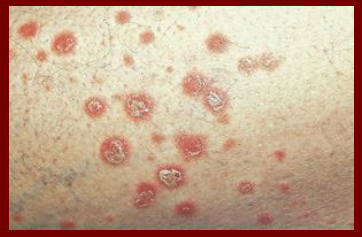


Psöriazis sınıflandırma

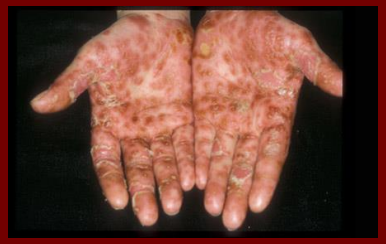
Psöriazis Vulgaris (Plak psöriazis)



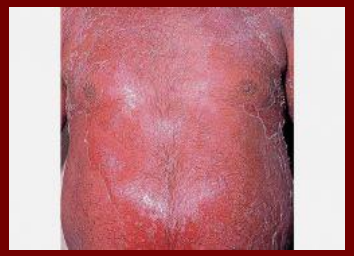
Guttat Psöriazis



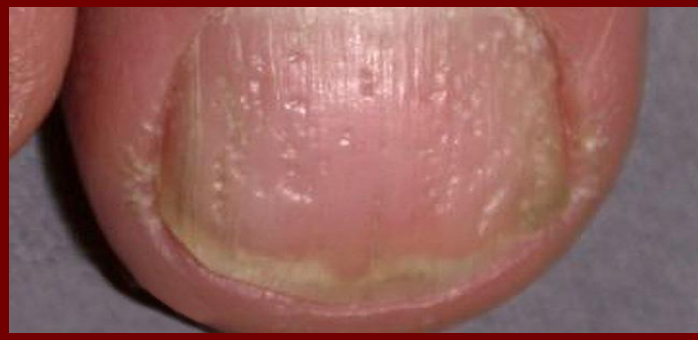
Püstüler psöriazis



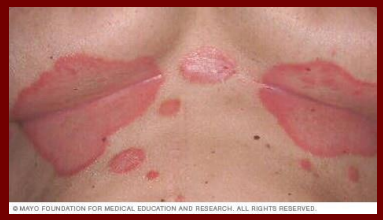
Eritrodermik psöriazis



Tırnak psöriazisi



İnverse psöriazis



Genetik ve Çevresel Faktörler

GENOTİP

PSORS1	*TYK2*
IL-23A	*IL28RA*
IL-23R	*IFIH1*
IL-12B	*ZNF313*
IL-13	*ERAP1*
TRAF3IP2	*HLA-C*

Keratinositler

ÇEVRESEL FAKTÖRLER

Stres Travma
İlaçlar Sigara
Mikroorganizmalar

Proinflamatuar sitokinler

HLA-CW6 en sık tanımlanmış alel

Psöriatik Artrit

- %70 cilt lezyonları sonrası artrit
  %15 artrit sonrası cilt lezyonları
  %15 eş zamanlı
  Artrit
  Spondilit
  Entesit
  Daktilit
  Cilt
  Tırnak

CASPAR (PsA klasifikasyon kriterleri) ≥3

(inflamatuvar eklem hastalığı varlığında-artrit, spondilit, entesit)

- Halihazırda psöriazis (2),
  Psöriazis öyküsü(1),
  Aile öyküsü (1)
- Daktilit (1) (mevcut/öykü)
- RF negatifliği (1)
- Tırnak değişiklikleri (1)
- Juxtaartikuler yeni kemik formasyonu (1)

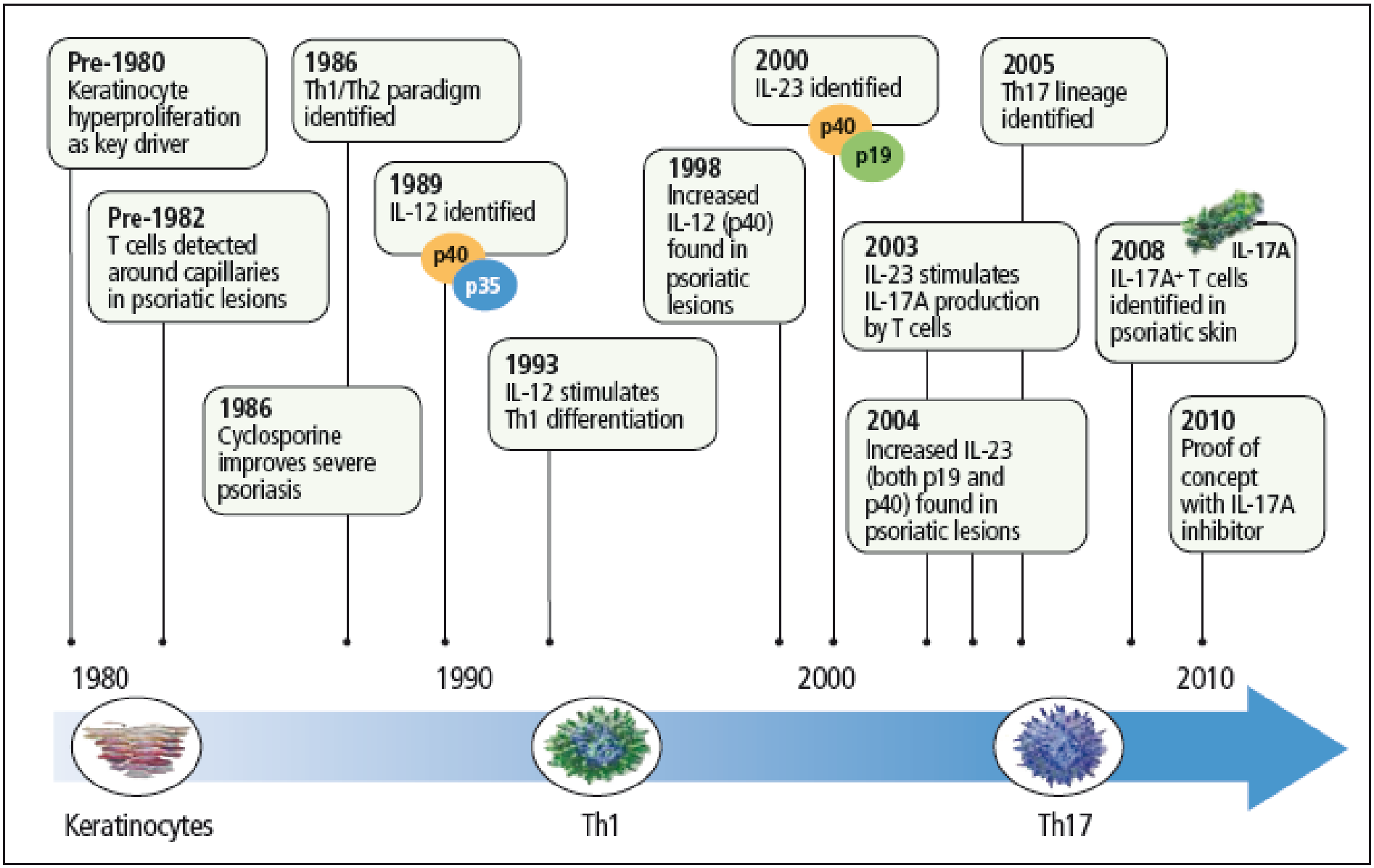
Psöriatik Artrit-genetik

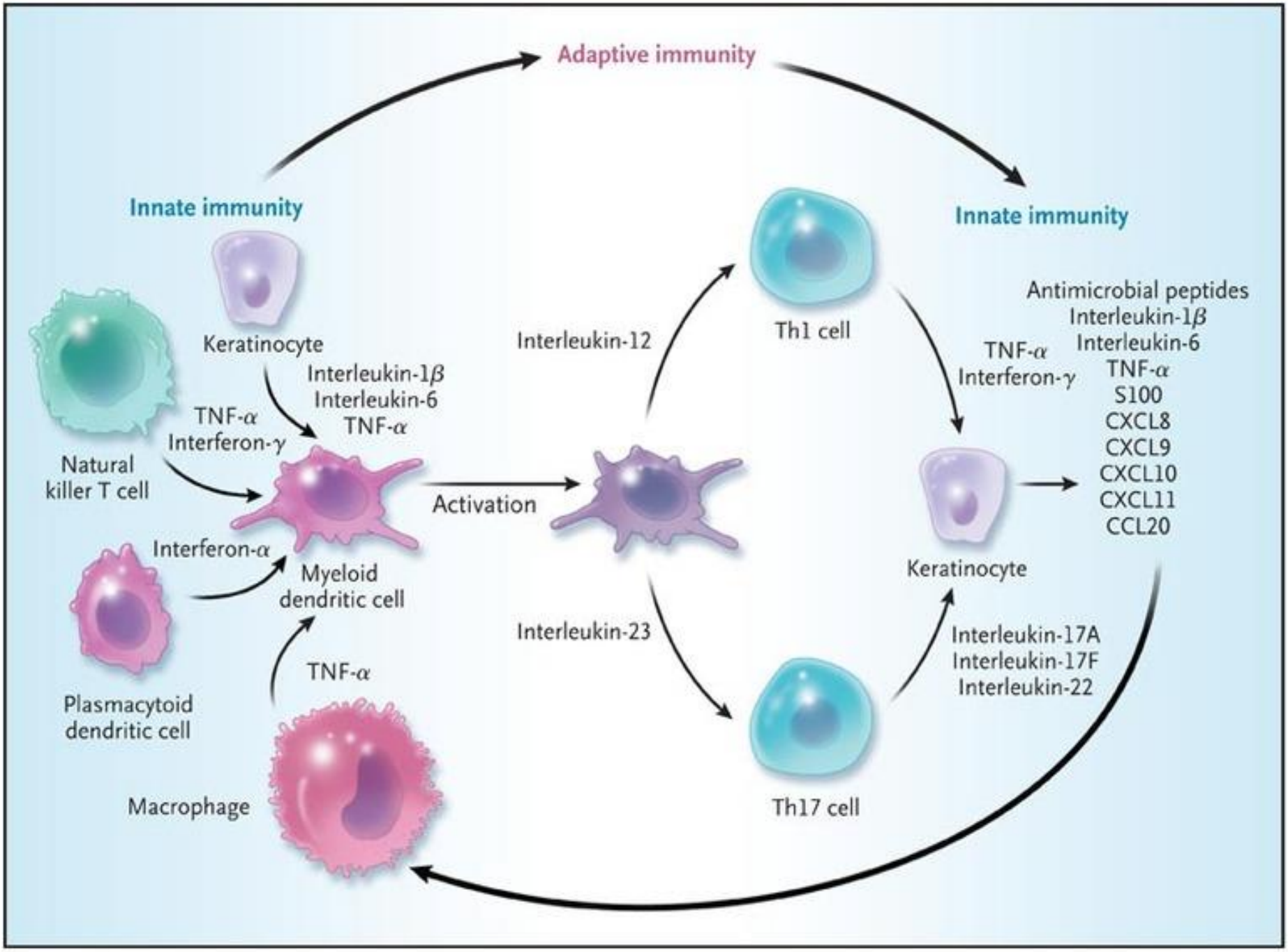
- HLA-CW6; cilt lezyonlarından uzun süre sonra PsA gelişimine
- HLA-B27, HLA-B39; Cilt lezyonları ile eş zamanlı PsA gelişimi
- HLA B27*:05:02: entesit, daktilit, simetrik sakroileit (spondilit için risk faktörü)
- HLA-B*08:01:01-HLAC*07:01:01:eklem füzyonu, deformite, asimetrik sakroileit, daktilit

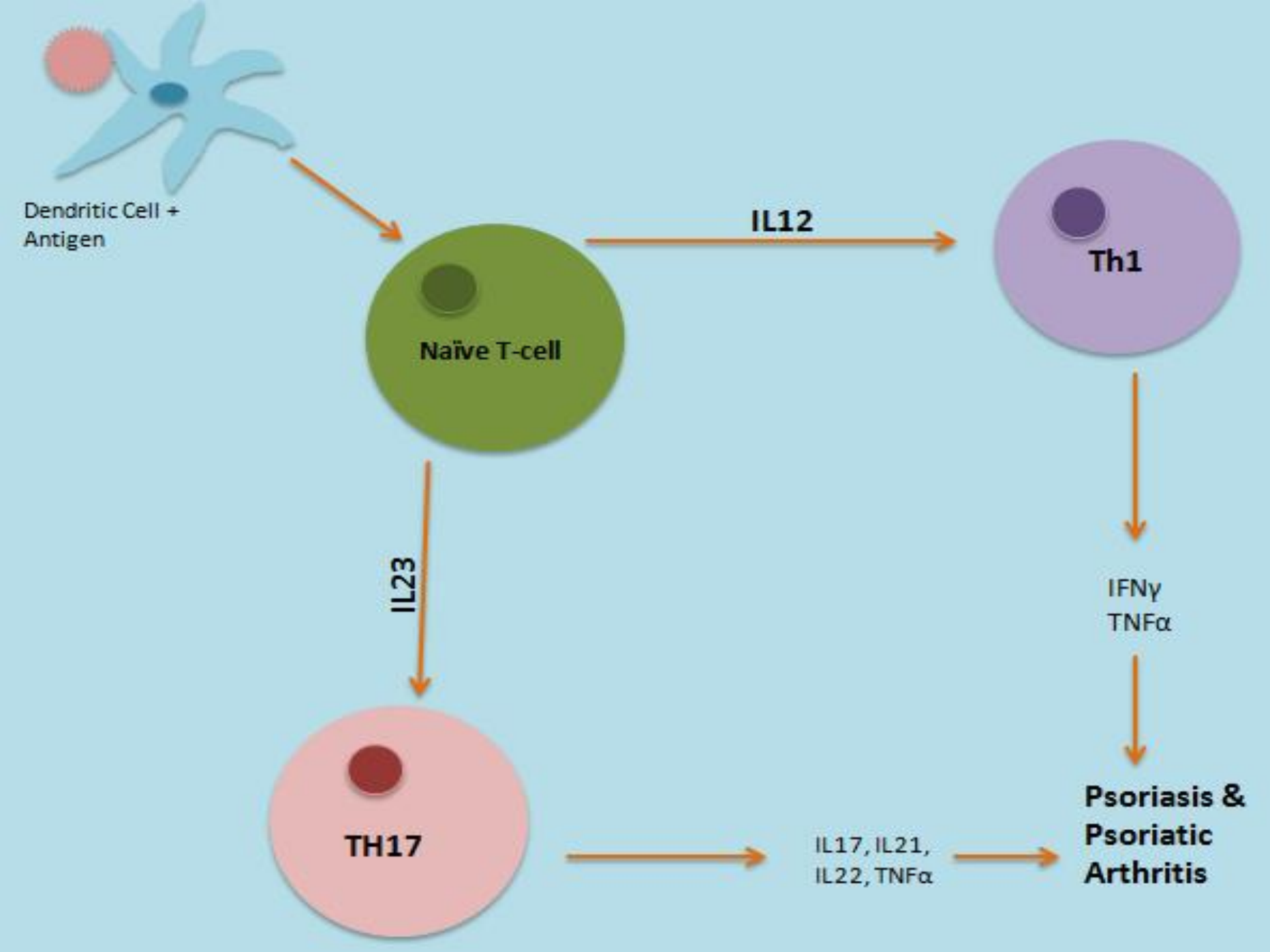
Psöriatik artrit -genetik

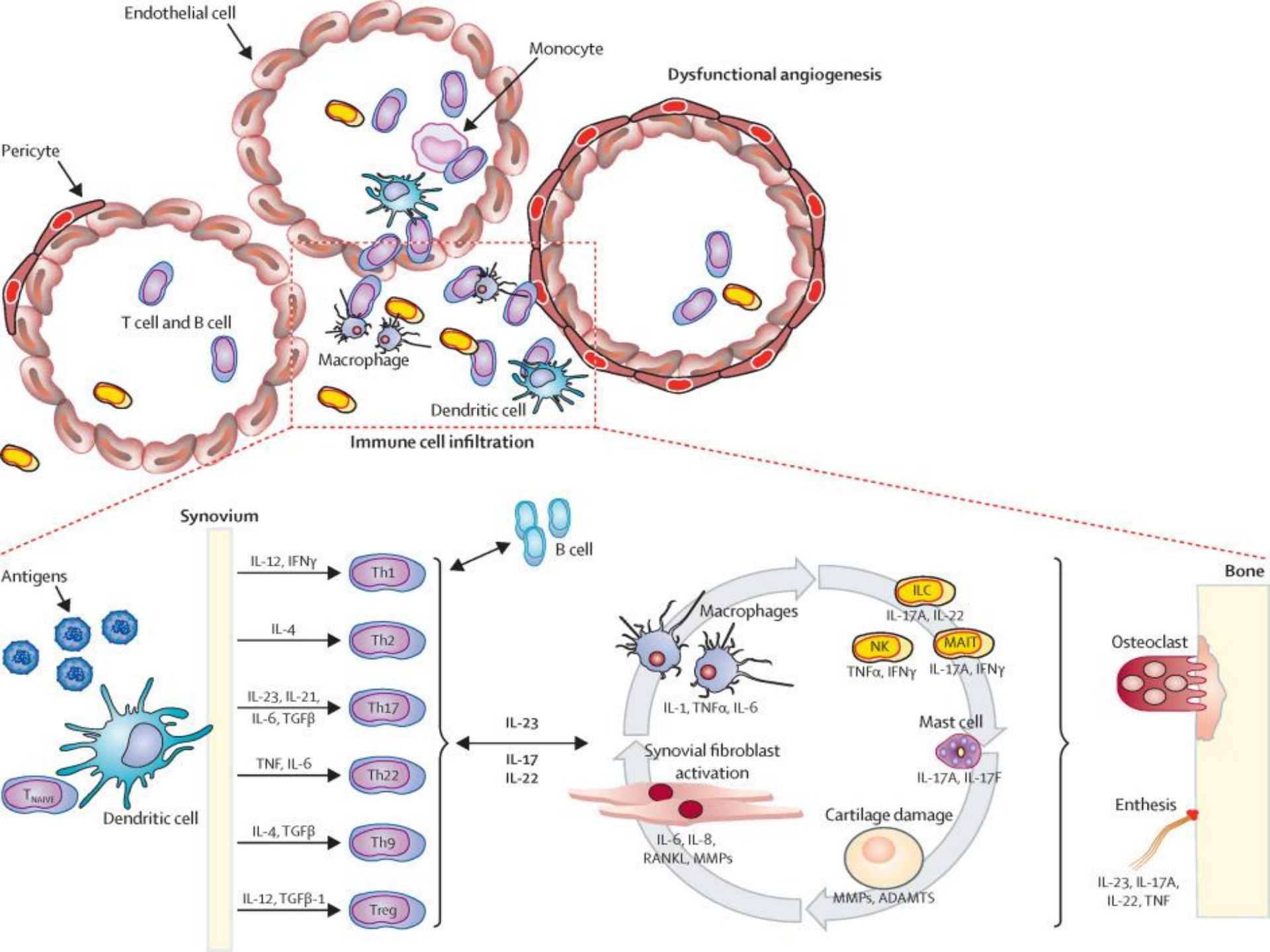
	Lokus	Patojenik fonksiyon
HLA-B	6	Peptidlerin CD8+Th sunumu
HLA-Cw6	6p21.3	Psöriazis için şüpheli
RUNX1	17q25	Th-17 dif için transkripsiyon fak.
IL12B	5q33.3	Aktif makrofaj. salınarak Th-1 gelişimi
TNFAIP3	6	CD4+Th'in yaşam devamı, inflamatuvar otoimmün hst ilişki
PTPN22	1p13	Lenfosit sp. tirozin fosfataz-immün h'in aktivasyonunu düzenler
IL23R	1p32.1–1p31.2	CD8+T, Th17 aktivasyonu ve devamlılığı
IL13	5q31.1	Th2 aracılı immünite; gen-çevre sigara etkileşimi

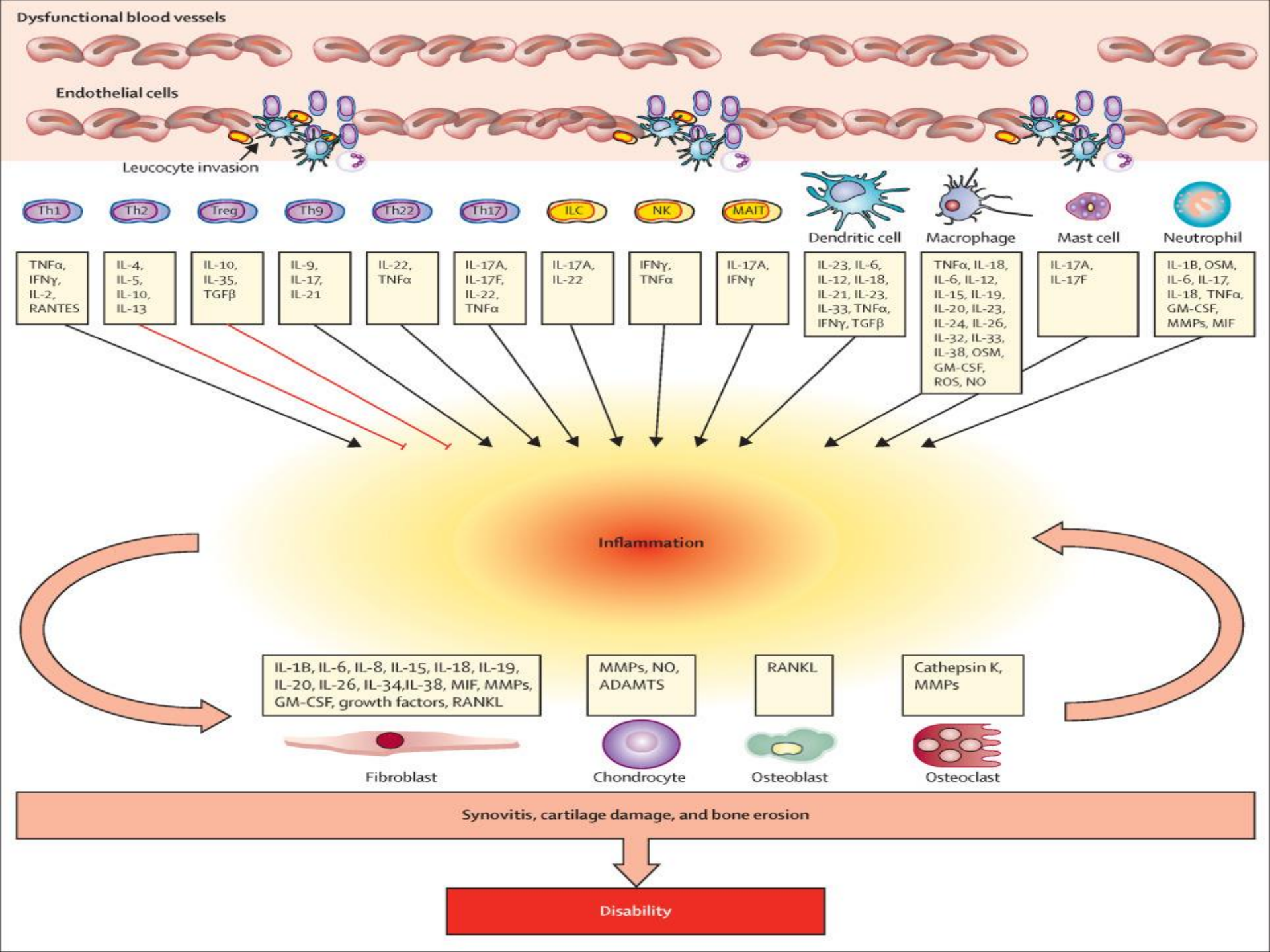
İmmünopatogenez

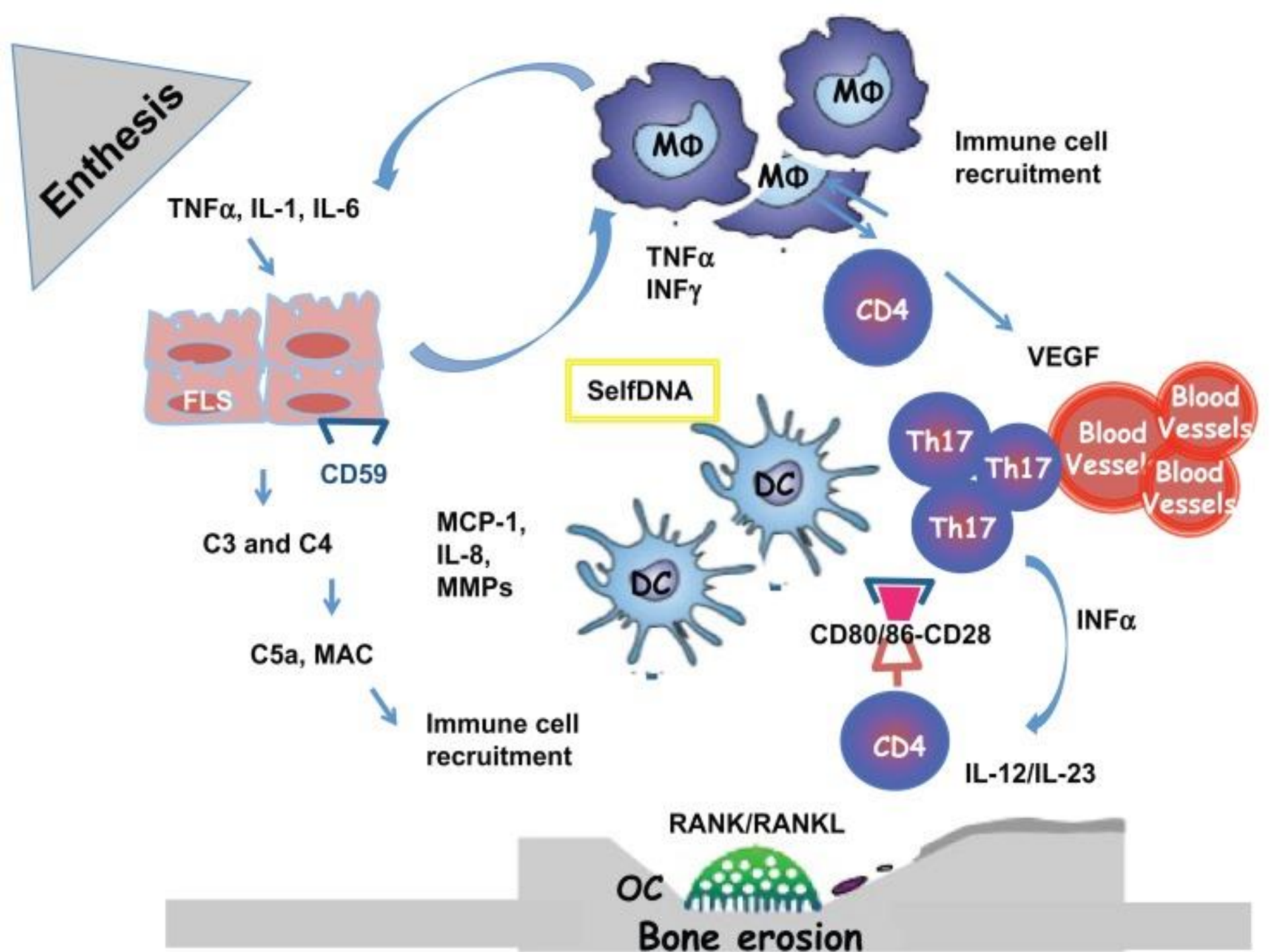

Pre-1980
Keratinocyte hyperproliferation as key driver
Pre-1982
T cells detected around capillaries in psoriatic lesions
1986
Th1/Th2 paradigm identified
1986
Cyclosporine improves severe psoriasis
1989
IL-12 identified
p40
p35
1993
IL-12 stimulates Th1 differentiation
1998
Increased IL-12 (p40) found in psoriatic lesions
2000
IL-23 identified
p40
p19
2003
IL-23 stimulates IL-17A production by T cells
2004
Increased IL-23 (both p19 and p40) found in psoriatic lesions
2005
Th17 lineage identified
2008
IL-17A
IL-17A+ T cells identified in psoriatic skin
2010
Proof of concept with IL-17A inhibitor
1980
1990
2000
2010
Keratinocytes
Th1
Th17


Adaptive immunity
Innate immunity
Innate immunity
Keratinocyte
Interleukin-1β
Interleukin-6
TNF-α
TNF-α
Interferon-γ
Natural killer T cell
Interferon-α
Myeloid dendritic cell
Plasmacytoid dendritic cell
TNF-α
Macrophage
Activation
Interleukin-12
Th1 cell
Interleukin-23
Th17 cell
TNF-α
Interferon-γ
Keratinocyte
Antimicrobial peptides
Interleukin-1β
Interleukin-6
TNF-α
S100
CXCL8
CXCL9
CXCL10
CXCL11
CCL20
Interleukin-17A
Interleukin-17F
Interleukin-22


Dendritic Cell +
Antigen
Naïve T-cell
IL12
Th1
IL23
IFNγ
TNFα
TH17
IL17, IL21,
IL22, TNFα
Psoriasis &
Psoriatic
Arthritis


Endothelial cell
Monocyte
Dysfunctional angiogenesis
Pericyte
T cell and B cell
Macrophage
Dendritic cell
Immune cell infiltration
Synovium
B cell
Antigens
IL-12, IFNγ
Th1
IL-4
Th2
IL-23, IL-21, IL-6, TGFβ
Th17
TNF, IL-6
Th22
IL-4, TGFβ
Th9
IL-12, TGFβ-1
Treg
T NAIVE
Dendritic cell
IL-23
IL-17
IL-22
Macrophages
IL-1, TNFα, IL-6
ILC
IL-17A, IL-22
NK
TNFα, IFNγ
MAIT
IL-17A, IFNγ
Mast cell
IL-17A, IL-17F
Synovial fibroblast activation
IL-6, IL-8, RANKL, MMPs
Cartilage damage
MMPs, ADAMTS
Bone
Osteoclast
Enthesis
IL-23, IL-17A, IL-22, TNF


Dysfunctional blood vessels
Endothelial cells
Leucocyte invasion
Th1
Th2
Treg
Th9
Th22
Th17
ILC
NK
MAIT
Dendritic cell
Macrophage
Mast cell
Neutrophil
TNFα, IFNγ, IL-2, RANTES
IL-4, IL-5, IL-10, IL-13
IL-10, IL-35, TGFβ
IL-9, IL-17, IL-21
IL-22, TNFα
IL-17A, IL-17F, IL-22, TNFα
IL-17A, IL-22
IFNγ, TNFα
IL-17A, IFNγ
IL-23, IL-6, IL-12, IL-18, IL-21, IL-23, IL-33, TNFα, IFNγ, TGFβ
TNFα, IL-18, IL-6, IL-12, IL-15, IL-19, IL-20, IL-23, IL-24, IL-26, IL-32, IL-33, IL-38, OSM, GM-CSF, ROS, NO
IL-17A, IL-17F
IL-1B, OSM, IL-6, IL-17, IL-18, TNFα, GM-CSF, MMPs, MIF
Inflammation
IL-1B, IL-6, IL-8, IL-15, IL-18, IL-19, IL-20, IL-26, IL-34,IL-38, MIF, MMPs, GM-CSF, growth factors, RANKL
MMPs, NO, ADAMTS
RANKL
Cathepsin K, MMPs
Fibroblast
Chondrocyte
Osteoblast
Osteoclast
Synovitis, cartilage damage, and bone erosion
Disability


Enthesis
TNFα, IL-1, IL-6
FLS
CD59
C3 and C4
C5a, MAC
Immune cell recruitment
MΦ
MΦ
MΦ
Immune cell recruitment
TNFα
INFγ
CD4
VEGF
SelfDNA
DC
DC
MCP-1,
IL-8,
MMPs
Th17
Th17
Th17
Blood Vessels
Blood Vessel
Blood Vessels
CD80/86-CD28
INFα
CD4
IL-12/IL-23
RANK/RANKL
OC
Bone erosion

	Site of expression	Source	Key functions
Tumour necrosis factor	Increased in synovial tissue and synovial fluid	Macrophages, T cells, fibroblast-like synoviocytes, B cells	Activation of circulating and resident cells to induce production of cytokines, adhesion molecules, chemokines, and matrix metalloproteinases; activation of osteoclasts to enhance cartilage and bone resorption
Interleukin 23a	Increased in synovial tissue, synovial fluid, and enthesis	Macrophages, dendritic cells	Promotion of T-helper-17 cell differentiation and granulocyte-macrophage colony-stimulating factor production
Interleukin 17A/F	Increased in synovial tissue, synovial fluid, and enthesis	T cells, mast cells, natural killer cells	Activation of fibroblast-like synoviocytes, chondrocytes, and osteoclasts; stimulation of proinflammatory cytokine and matrix metalloproteinase production, and neutrophil recruitment
Interleukin 22	Increased in synovial tissue, synovial fluid, and enthesis	T cells, innate lymphoid cells	Activation of fibroblast-like synoviocytes; induction of osteoclastogenesis and bone resorption via RANKL
Interleukin 9	Increased in synovial tissue	T cells	Activation of peripheral blood mononuclear cells; stimulation of proliferation of pathogenic T cells
Interleukin 6	Increased in synovial tissue and serum	Macrophages, activated fibroblast-like synoviocytes, B cells	Activation of STAT3 signalling to enhance proinflammatory cytokine production
Interleukin 15	Increased in synovial tissue	Macrophages	Promotion and maintenance of T-cell and natural killer cell activation
Interleukin 12	Increased in synovial tissue and synovial fluid	Macrophages, dendritic cells	Promotion of T-helper-1 cell differentiation through STAT4
Interleukin 1	Increased in synovial tissue	Macrophages, neutrophils, B cells	Proinflammatory signalling
Granulocyte-macrophage colony-stimulating factor	Increased in synovial tissue	T cells, macrophages, fibroblast-like synoviocytes	Recruitment and activation of immune cells
Interferon γ	Increased in synovial tissue	T cells	Promotion of macrophage phagocytosis, T-cell activation, and RANKL secretion
Interleukin 10	Decreased in synovial tissue	T cells, macrophages, fibroblast-like synoviocytes	Anti-inflammatory signalling

RANKL=TNF superfamily member 11. STAT=signal transducer and activator of transcription.

Table 2: **Key cytokines and their expression, source, and function in psoriatic arthritis**

İmmünopatogenezden sorumlu hücreler

Doğal immün yanıt

- Dentritik h.
- Makrofajlar
- Innate lenfoid h.
- MAIT ve NK
- Mast h.

Kazanılmış immün yanıt

- T lenf.
- B lenf.

Sinovial fibroblastlar

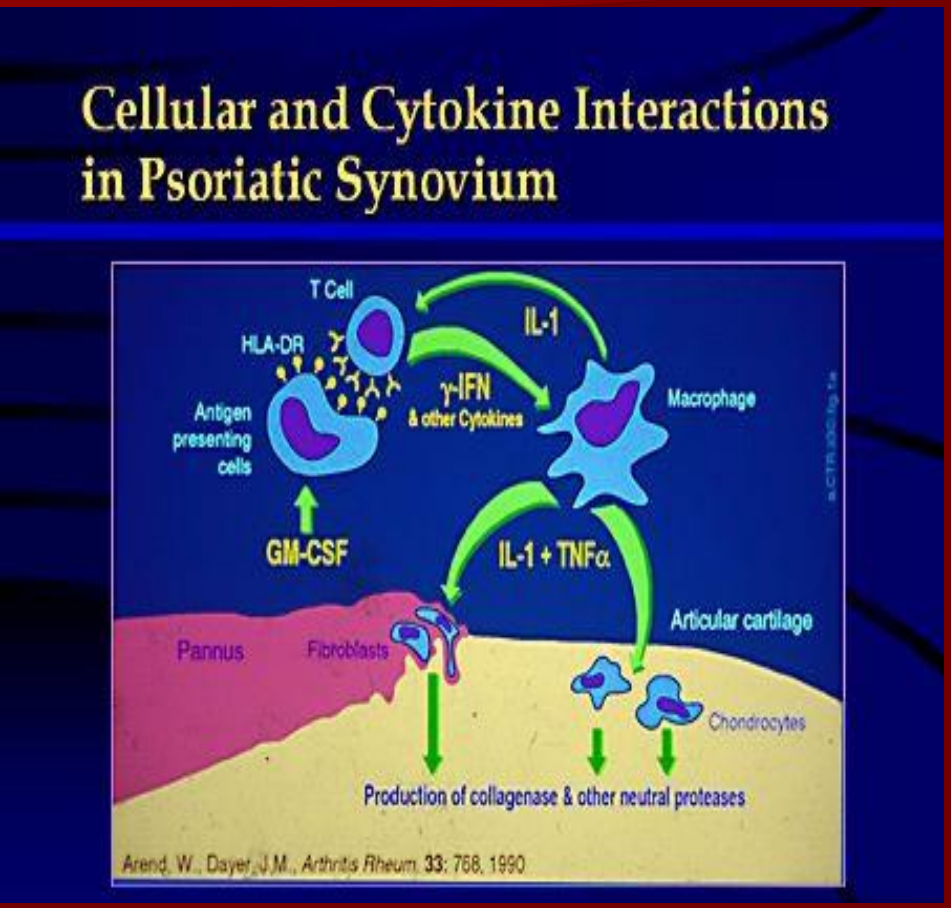
Psöriatik artritte güncel tedavi yolakları

PsA'de güncel tedavi yolakları

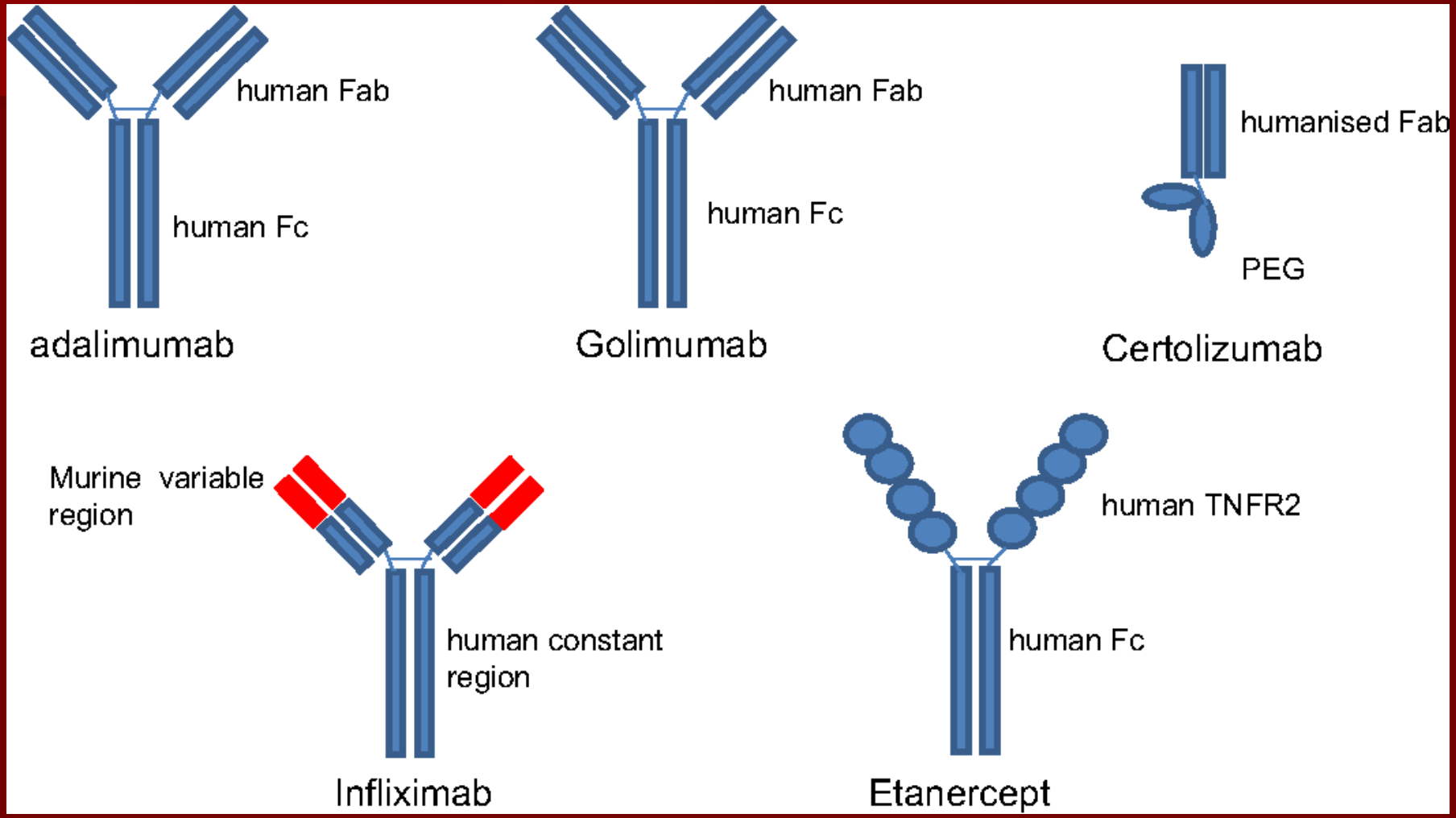
PsA tedavisinde kullanılan/kullanılabilecek DMARD'ların Sınıflaması

csDMARD	bDMARD	tsDMARD
MTX	**Anti-TNF**	Fosfodiesteraz inh.
SSZ	Etanersept	(PDE-4 inh)
LEF	Adalimumab	JAK inhibitörleri
CyA	İnfliksimab	Tofasitinib
	Golimumab	
	Certolizumab pegol	
	IL12/23 yolağını kullanan	
	Ustekinumab	
	IL-17 yolağını kullanan	
	Secukinumab	
	Brodalumab	
	Ixekizumab	
	T hücre kostimülasyon blokajı	
	Abatasept	

TNF- α ve inhibisyonu



- Sinovial sıvıda ve sinovial dokuda
- K: Makrofajlar, T, Fibroblast benzeri sinovisitler, B
- F:Sitokinlerin, adezyon moleküllerinin, kemokinlerin, MMP üretiminin indüklenmesi; osteoklast aktivasyonu ve kemik kıkırdak rezorbsiyonu


human Fab
human Fc
adalimumab
human Fab
human Fc
Golimumab
humanised Fab
PEG
Certolizumab
Murine variable region
human constant region
Infliximab
human TNFR2
human Fc
Etanercept

- Sinovial sıvı CD8 lenfosit sayısı yüksek
- CD141 dentritik hücreler CLEC9A ekspresyonu-Anti-TNF CLEC9A belirgin azalma
- CD141 dentritik hücreler-CD8 T lenfosit co-lokalizasyon ortak antijen sunumu
- Anti-TNF- aynı zamanda CD8 T lenfosit sayısında azalma

PsA immünopatogenezinde CD 8 T lenfositler

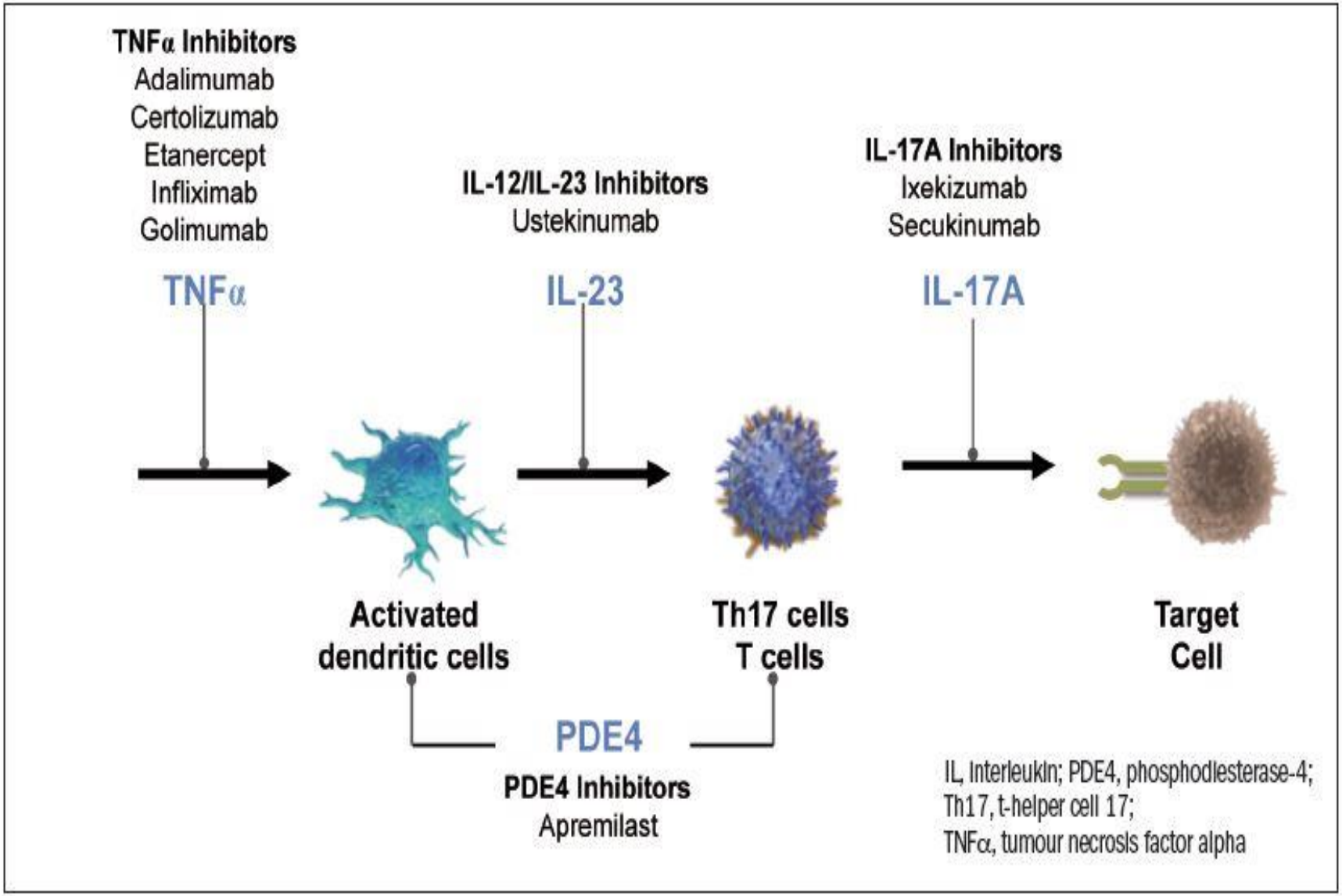
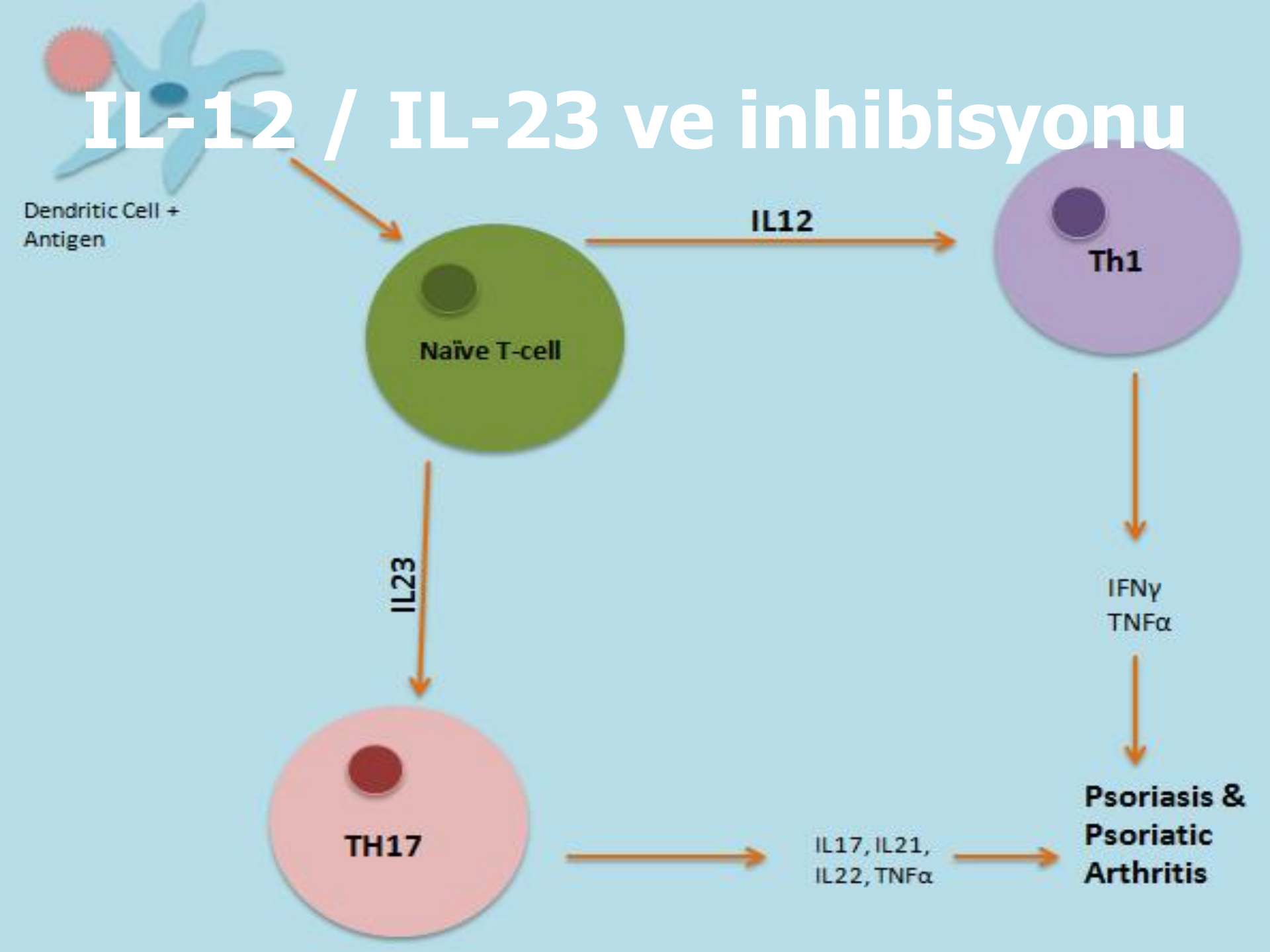


Figure 1. Pathogenesis-based approach to treatment of psoriasis and psoriatic arthritis. Adapted from Lynde et al. 2014[5]

IL-12 / IL-23 ve inhibisyonu



IL-12 / IL-23 ve İNHİBİSYONU

- Psöriatik deride IL-12 ekspresyonu Th1 sitokin profilini desteklemiştir (IFN-γ, TNF α)
- Yapısal olarak IL-12 ile ilişkili olan yeni sitokin IL-23'ün keşfi, Th17 ailesine ve IL-17'ye dikkat çekmiştir

IL-12;

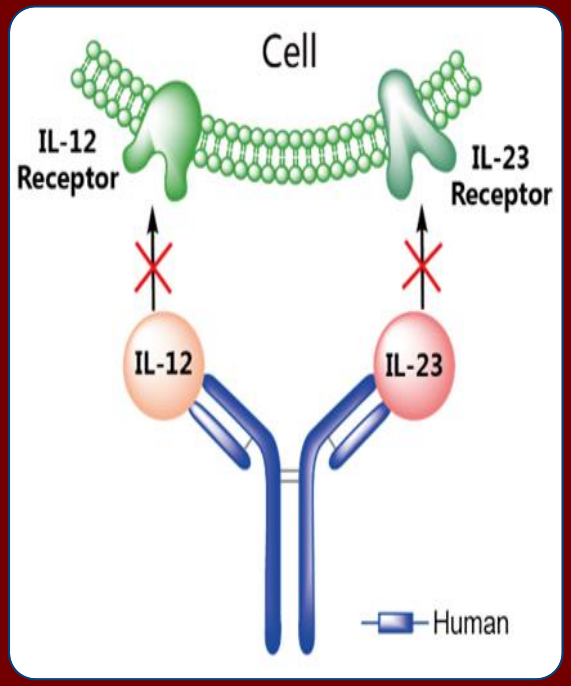
- Sinovial sıvı ve sinovial doku
- K:Makrofajlar, dentritik h
- F: STAT 4-Th1 dif.

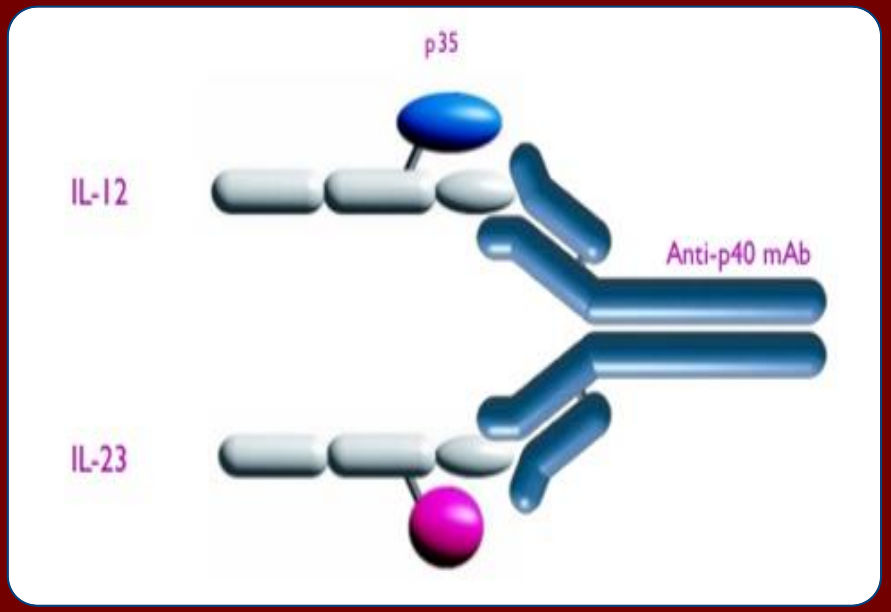
IL-23;

- Sinovial sıvı ve sinovial doku, entesis
- K:Makrofajlar, dentritik h
- F: Th17 dif., GM-CSF üretimi

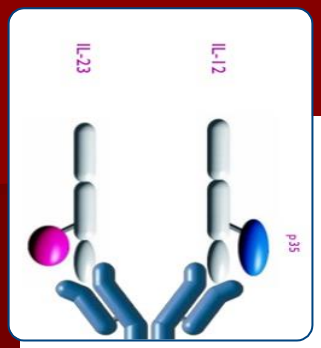
IL-12 ve IL-23 yolağı inhibisyonu

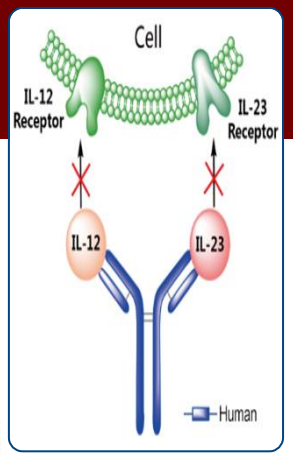
- **Ustekinumab**, gerek psoriasis gerekse psoriatik artritte klinik etkisini,
- **IL-12 ve IL-23'ün ortak p40 alt-ünitesine bağlanıp**, bu hastalıkların patolojisinde merkezi bir yer oluşturan Th1 ve Th17 sitokin yolaklarını kesintiye uğratarak etki göstermektedir.

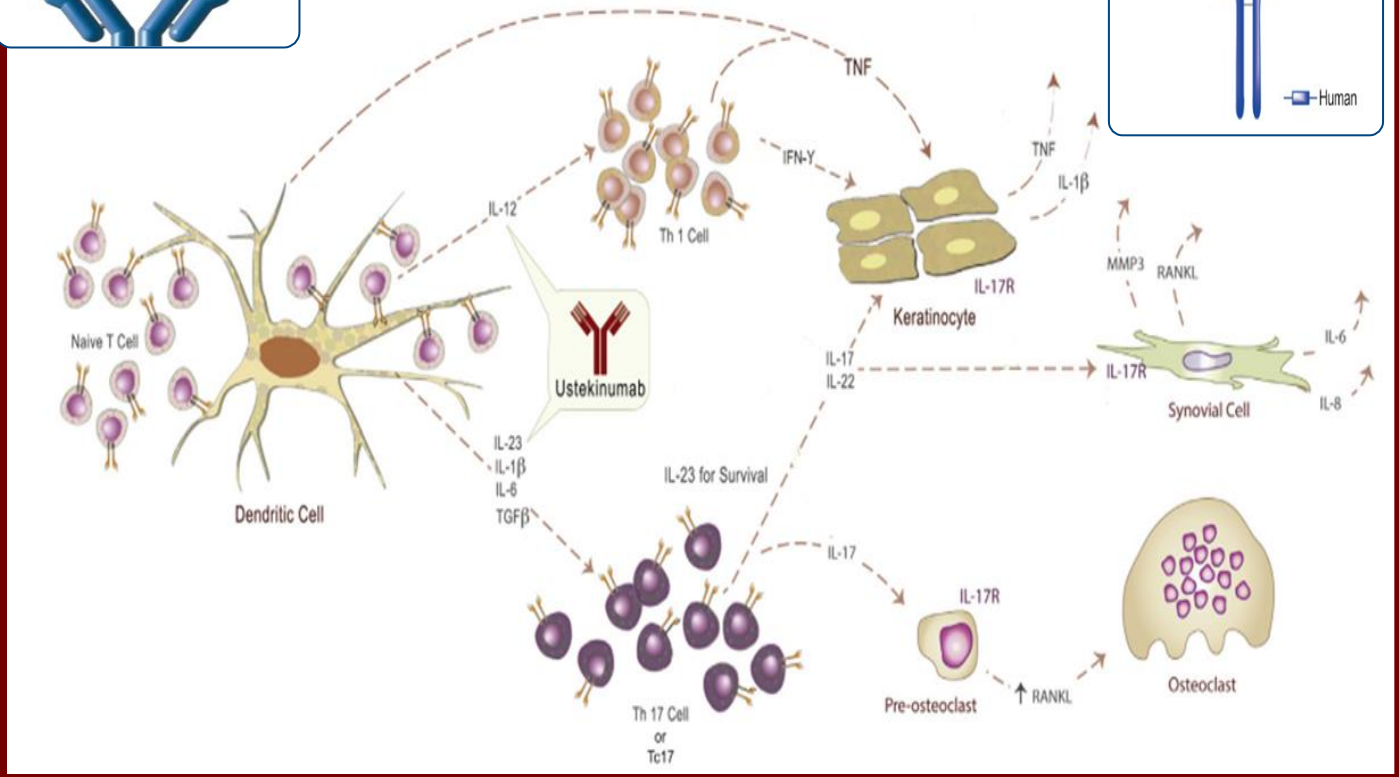




İnsan anti p40 monoklonal antikor (IL-12/IL-23)



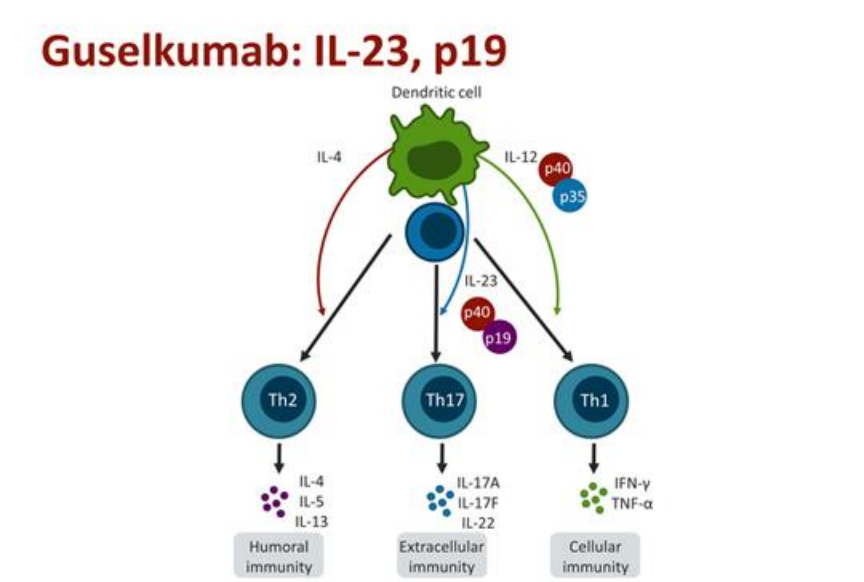




Anti-IL-12 ve Anti-IL-23

- **IL-12 ve IL-23 ortak blokaj**;
  Ustekinumab;
  P40-İnsan MAb
- **Sadece IL-23 blokajı;**
  Guselkumab,
  Tildrakizumab
  Risankizumab
  P-19 MAb

(Faz 1,2 çalışma)



Boyd T, et al. *Expert Opin Biol Ther*. 2016;16:173-186.

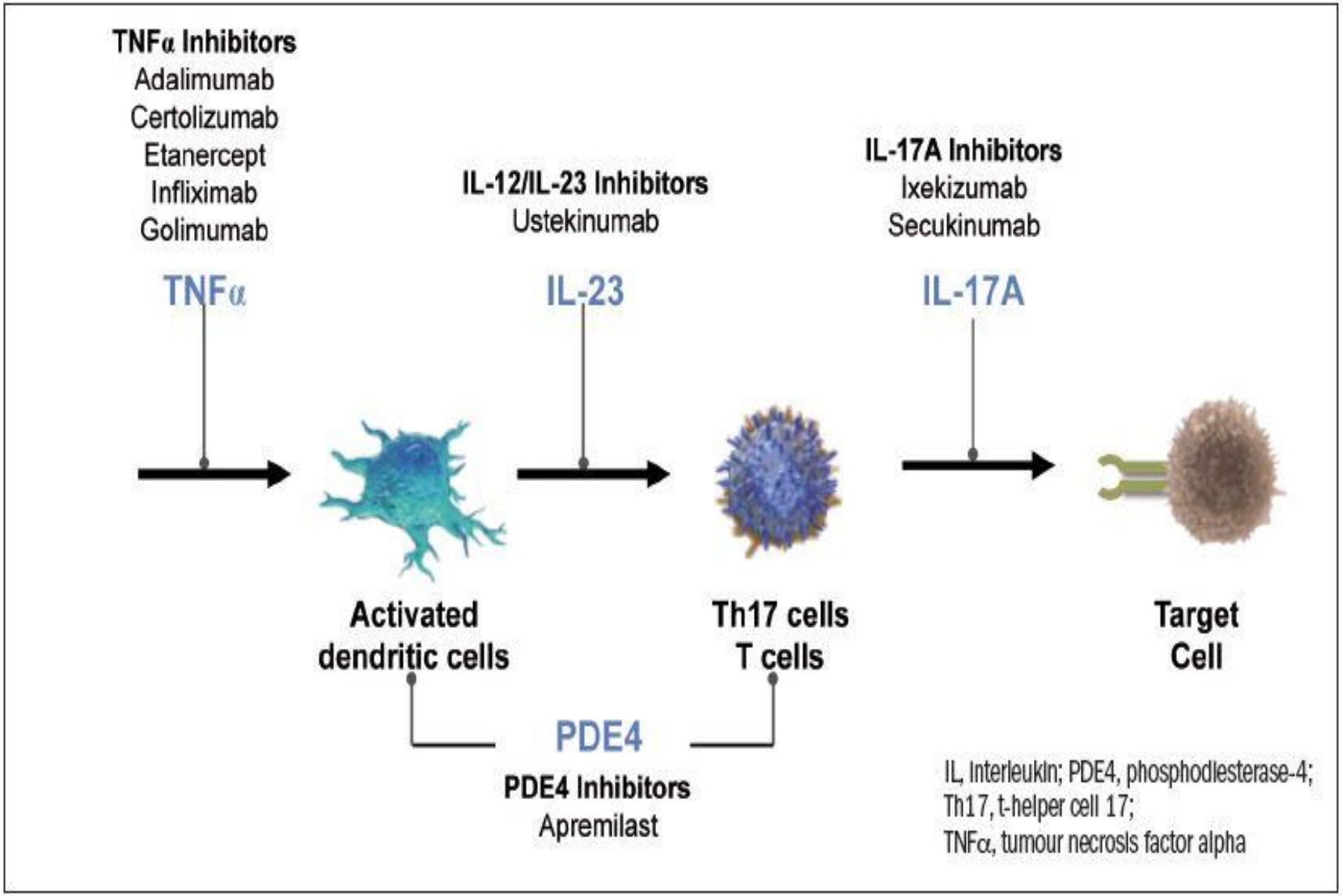


Figure 1. Pathogenesis-based approach to treatment of psoriasis and psoriatic arthritis. Adapted from Lynde et al. 2014[5]

IL-7 A ve inhibisyonu

- Sinovial doku, sinovial sıvı, entesis
- K: T, mast h., NK, vb.
- F: Fibroblast benzeri sinovisit, kondrosit ve osteoklast akt-proinf. sitokin salınımı ve MMP üretimi, nötrofillerin akt.

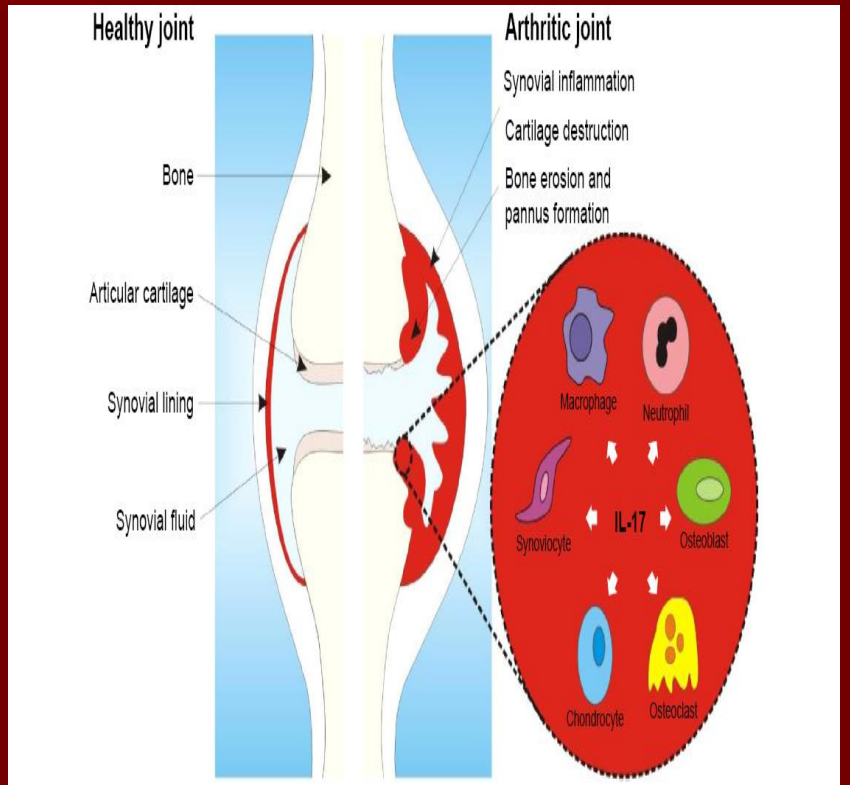
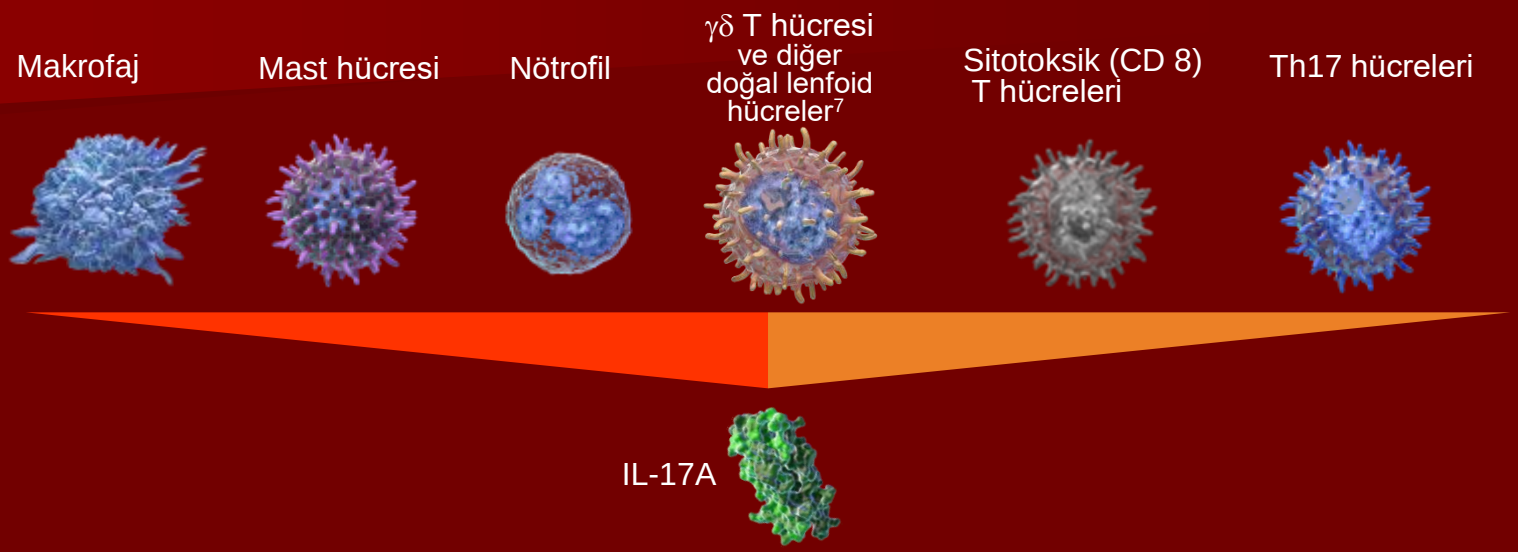


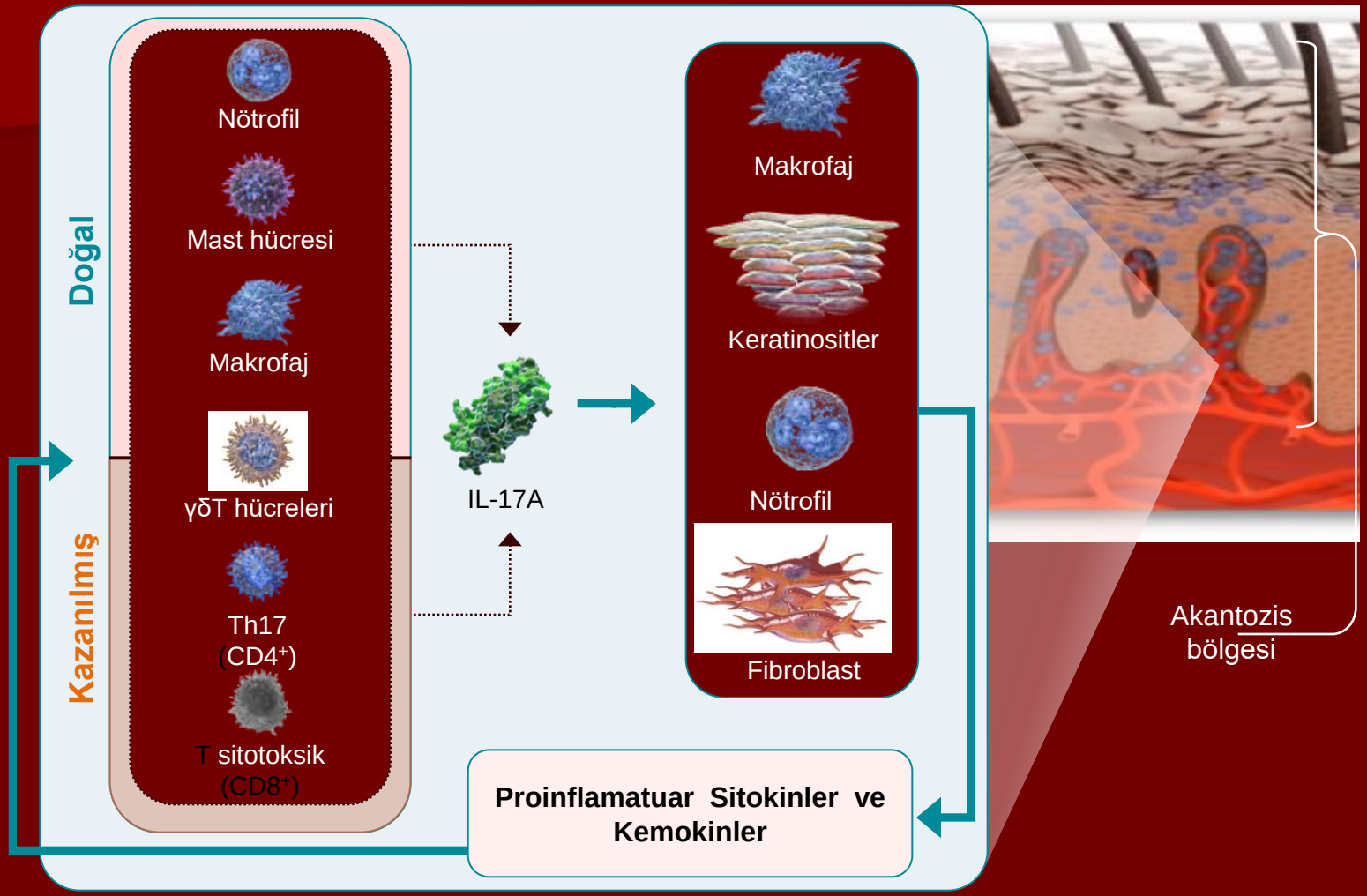
Figure 2 Simplified scheme of IL-17 and its effector cells in the inflamed arthritic joint.
Notes: In the inflamed arthritic joint, IL-17 activates resident cells like synovial fibroblasts and chondrocytes, and recruits proinflammatory immune cells thereby contributing to joint inflammation, cartilage destruction, and bone erosion.
Abbreviation: IL-17, interleukin 17.

IL-7 A ve inhibisyonu

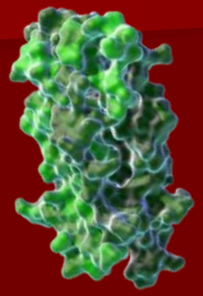


IL-17A eksprese eden diğer hücreler

IL-17A, Keratinosit Aktivasyonu ve Geri Besleme Döngüsü



IL-17A Sitokin Ailesi
IL-17A Proinflamatuar Sitokin

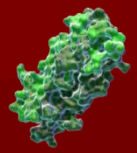


IL-17A

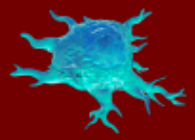
- IL-17 olarak bilinir
- Homodimerik bir glikoproteindir (35 kDa)
- IL17F'ye göre 10-30 kat daha güçlü gen eksprese eder
- Doğal ve kazanılmış immün sistem arası köprüdür
- Hücre dışı patojenlere karşı önemli rol oynar

IL-17A'nın Etkilediği Diğer Hücreler

Hedef hücreler

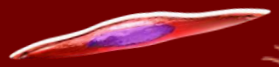


IL-17A



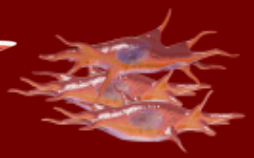
Makrofaj, dendritik hücre

- IL-1
- TNF
- IL-6
- CRP
- MMP9



Endotelyal hücre

- IL-6
- MMP'ler

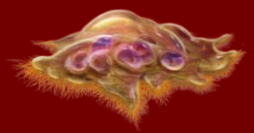


Fibroblast

- IL-6
- Kemokinler
- Büyüme faktörleri
- MMP1,3,13

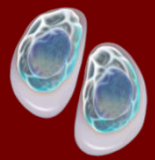
Osteoblast*

- RANKL
- MMP
- Osteoklastogenezis



Osteoklast*

- RANKL
- MMP1,2, 3 ve 9

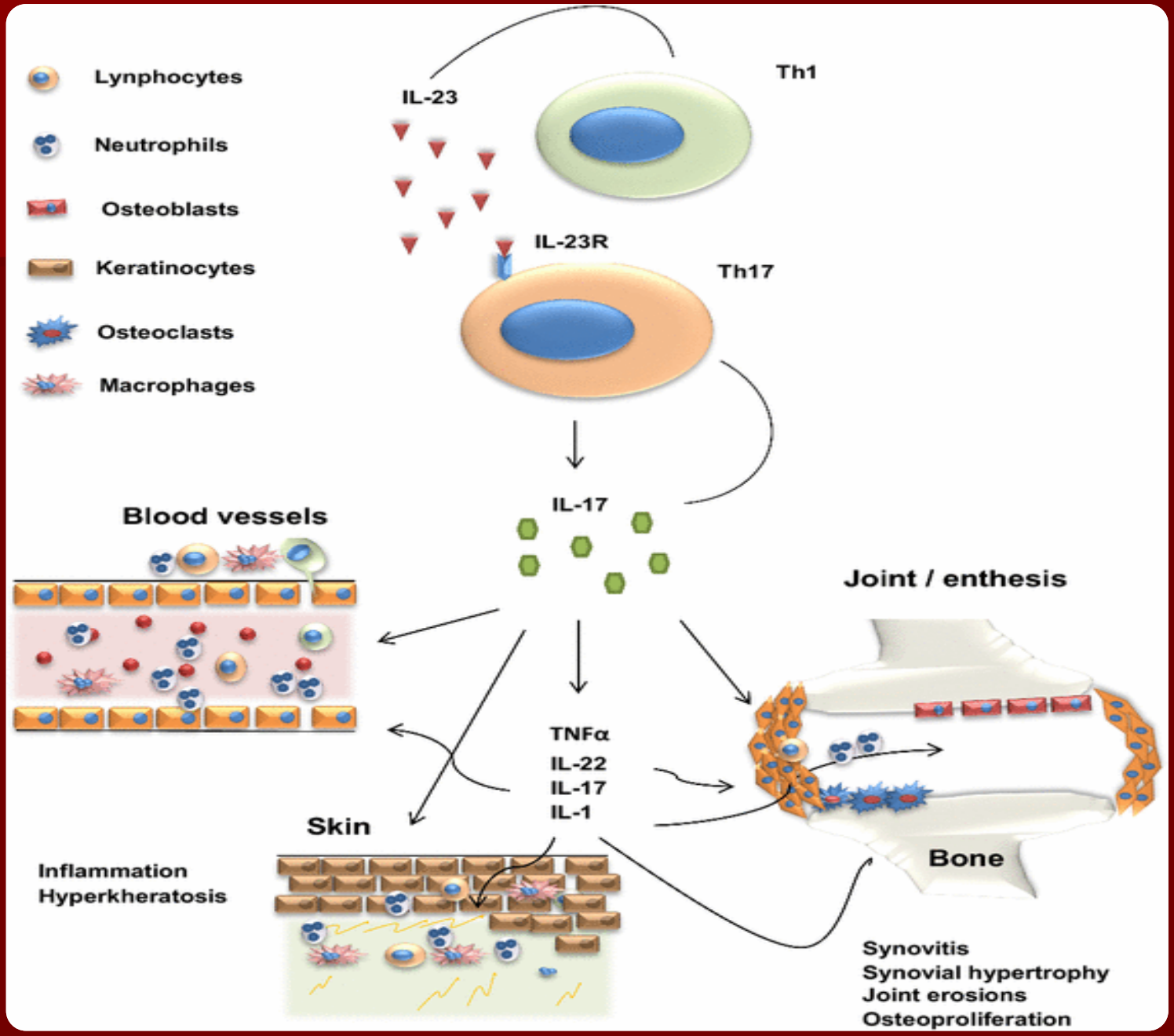


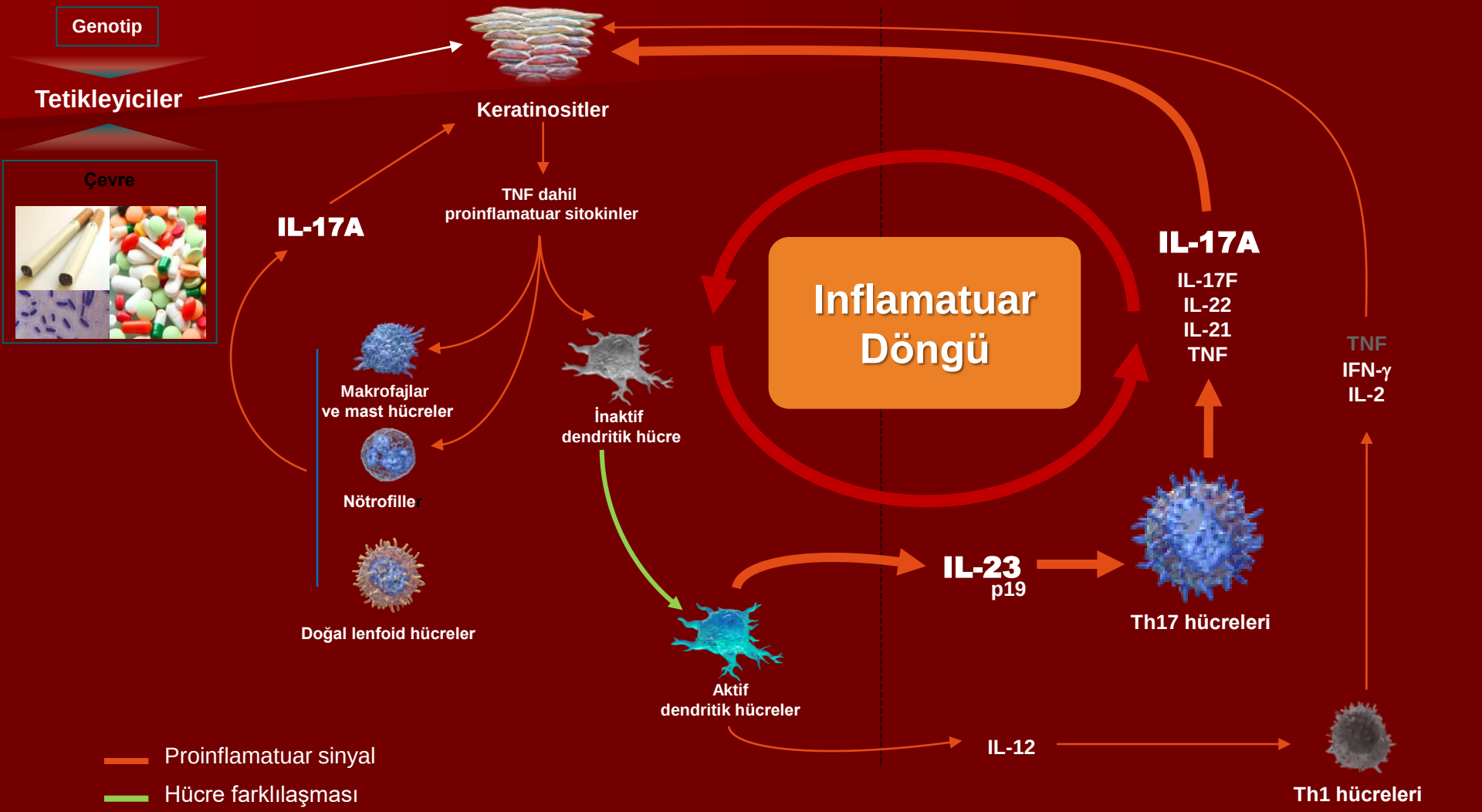
Kondrosit

- IL-1
- IL-6
- iNOS
- Kemokinler
- MMP

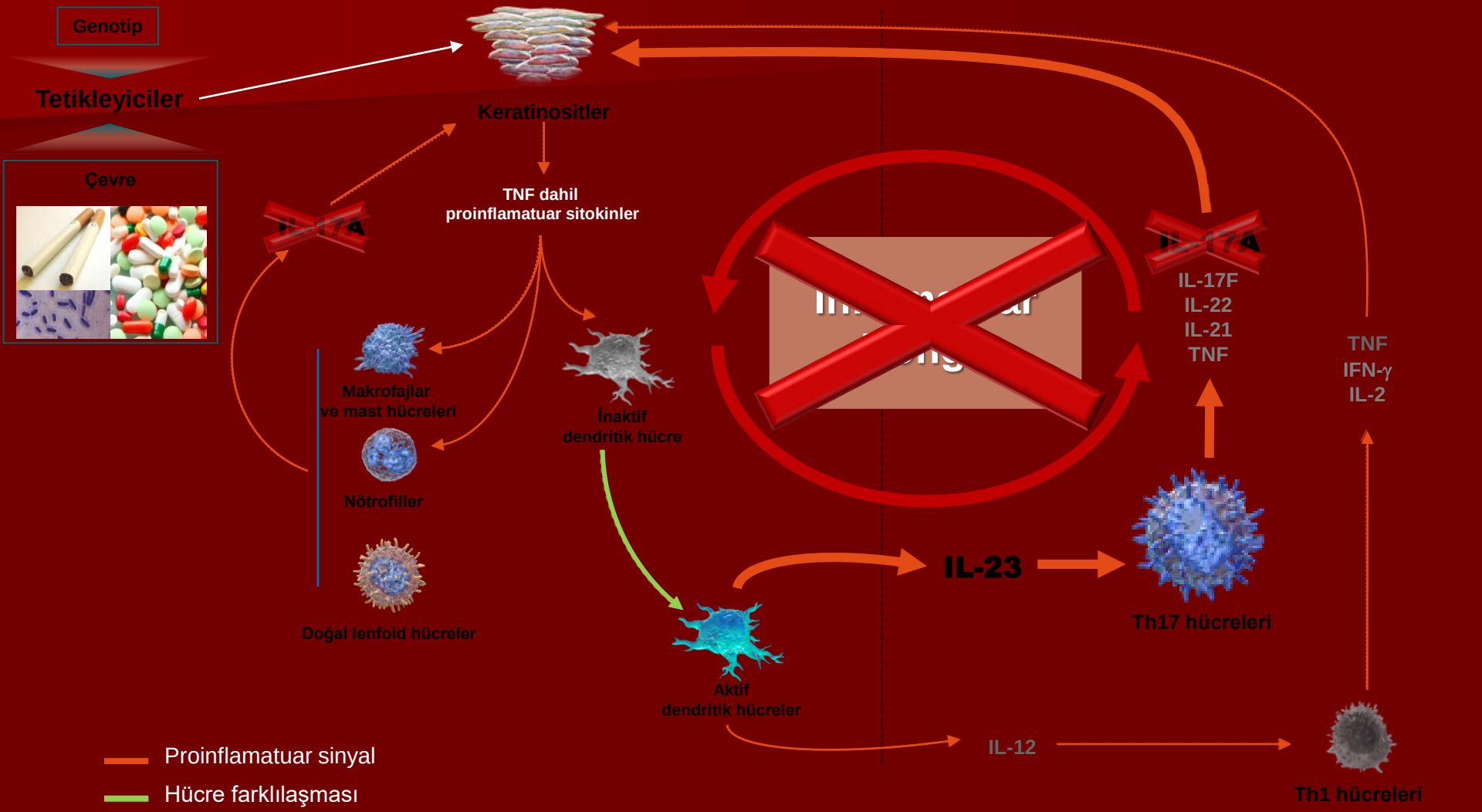
Keratinosit

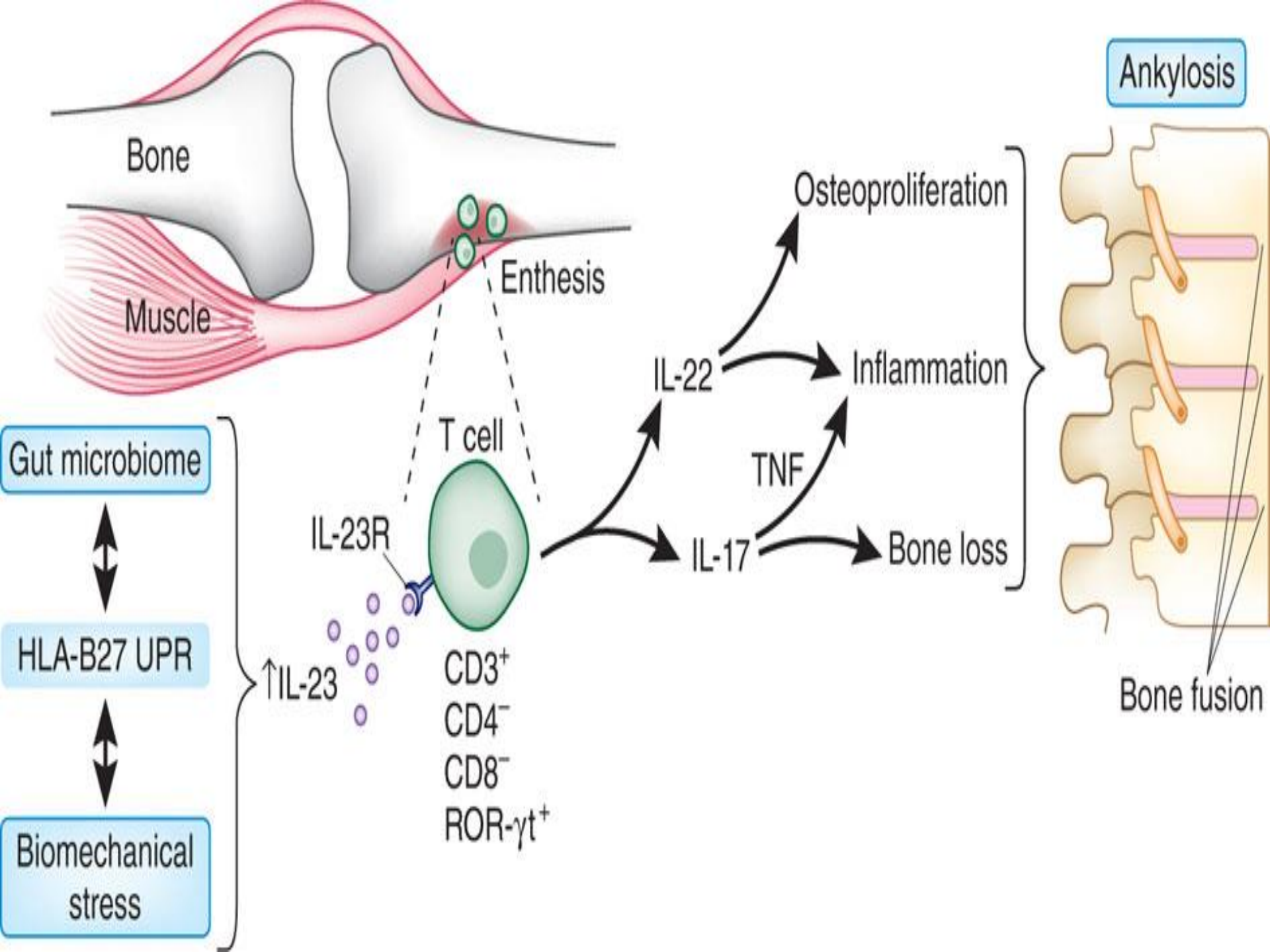
- IL-6
- Kemokin
- Antimikrobiyal peptidler
- Ki67 (proliferasyon)


Lynphocytes
Neutrophils
Osteoblasts
Keratinocytes
Osteoclasts
Macrophages
IL-23
Th1
IL-23R
Th17
IL-17
Blood vessels
Joint / enthesis
TNFα
IL-22
IL-17
IL-1
Skin
Bone
Inflammation
Hyperkheratosis
Synovitis
Synovial hypertrophy
Joint erosions
Osteoproliferation


Genotip
Tetikleyiciler
Çevre
Keratinositler
TNF dahil
proinflamatuar sitokinler
IL-17A
Inflamatuar
Döngü
IL-17A
IL-17F
IL-22
IL-21
TNF
TNF
IFN-γ
IL-2
Makrofajlar
ve mast hücreler
Nötrofiller
Doğal lenfoid hücreler
İnaktif
dendritik hücre
IL-23
p19
Th17 hücreleri
Aktif
dendritik hücreler
IL-12
Th1 hücreleri
Proinflamatuar sinyal
Hücre farklılaşması

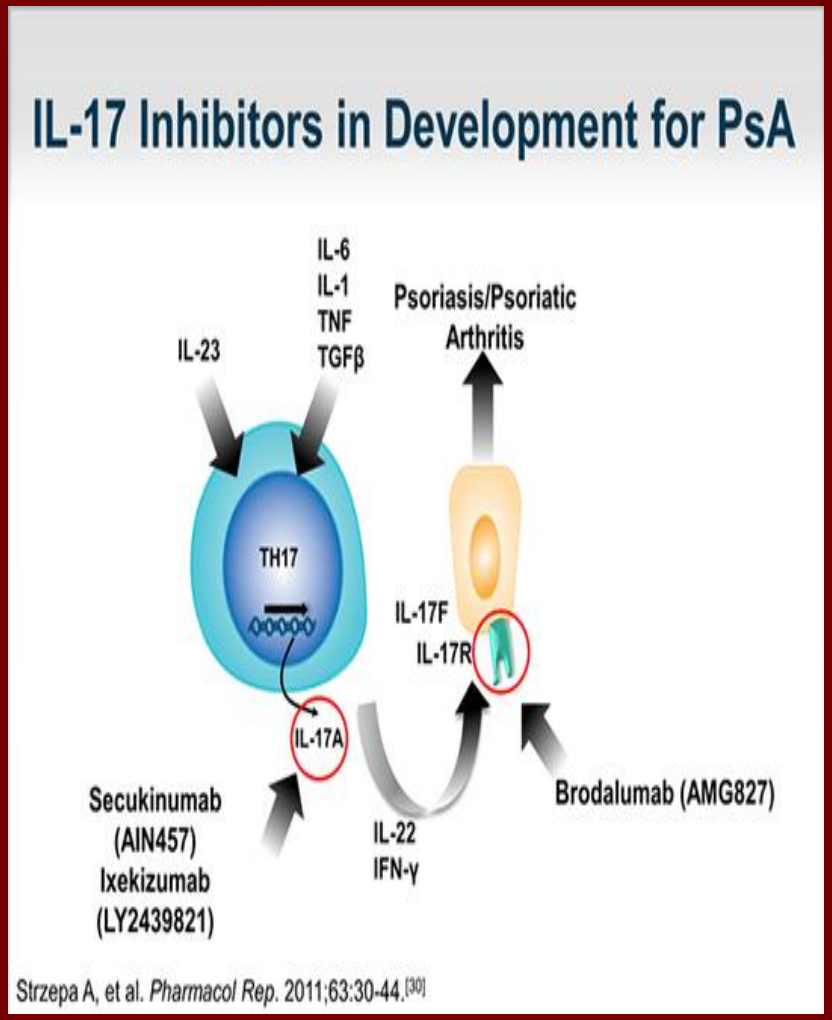
IL-17A Engellenirse Ne Olur?

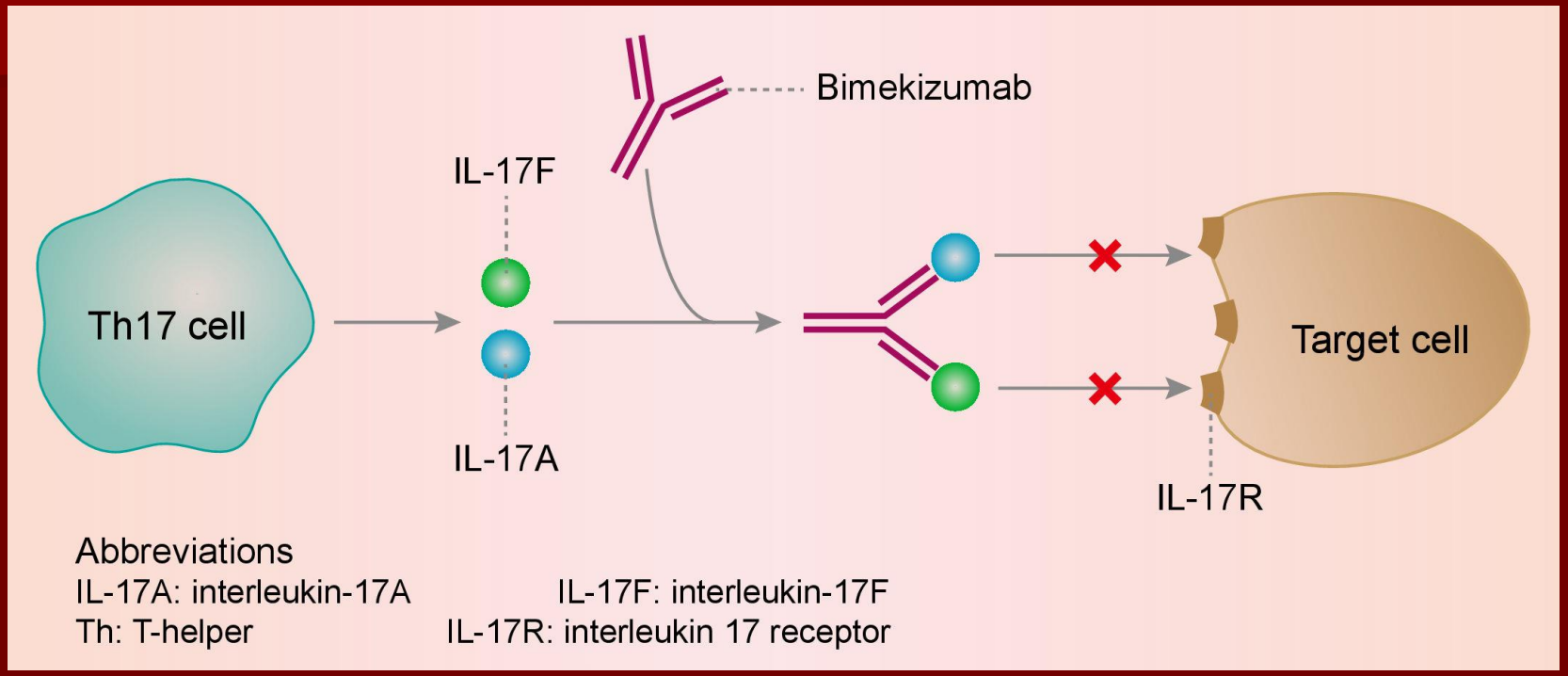



Bone
Muscle
Enthesis
Ankylosis
Osteoproliferation
IL-22
Inflammation
T cell
TNF
IL-23R
IL-17
Bone loss
Gut microbiome
HLA-B27 UPR
Biomechanical stress
↑IL-23
CD3+
CD4−
CD8−
ROR-γt+
Bone fusion

Anti-IL-17

Secukinumab;
İnsan IL-17A MAb
Ixekizumab;
Humanize IL-17A MAb
Brodalumab;
İnsan IL-17 reseptör MAb (IL-17RA)





Abbreviations
IL-17A: interleukin-17A
IL-17F: interleukin-17F
Th: T-helper
IL-17R: interleukin 17 receptor

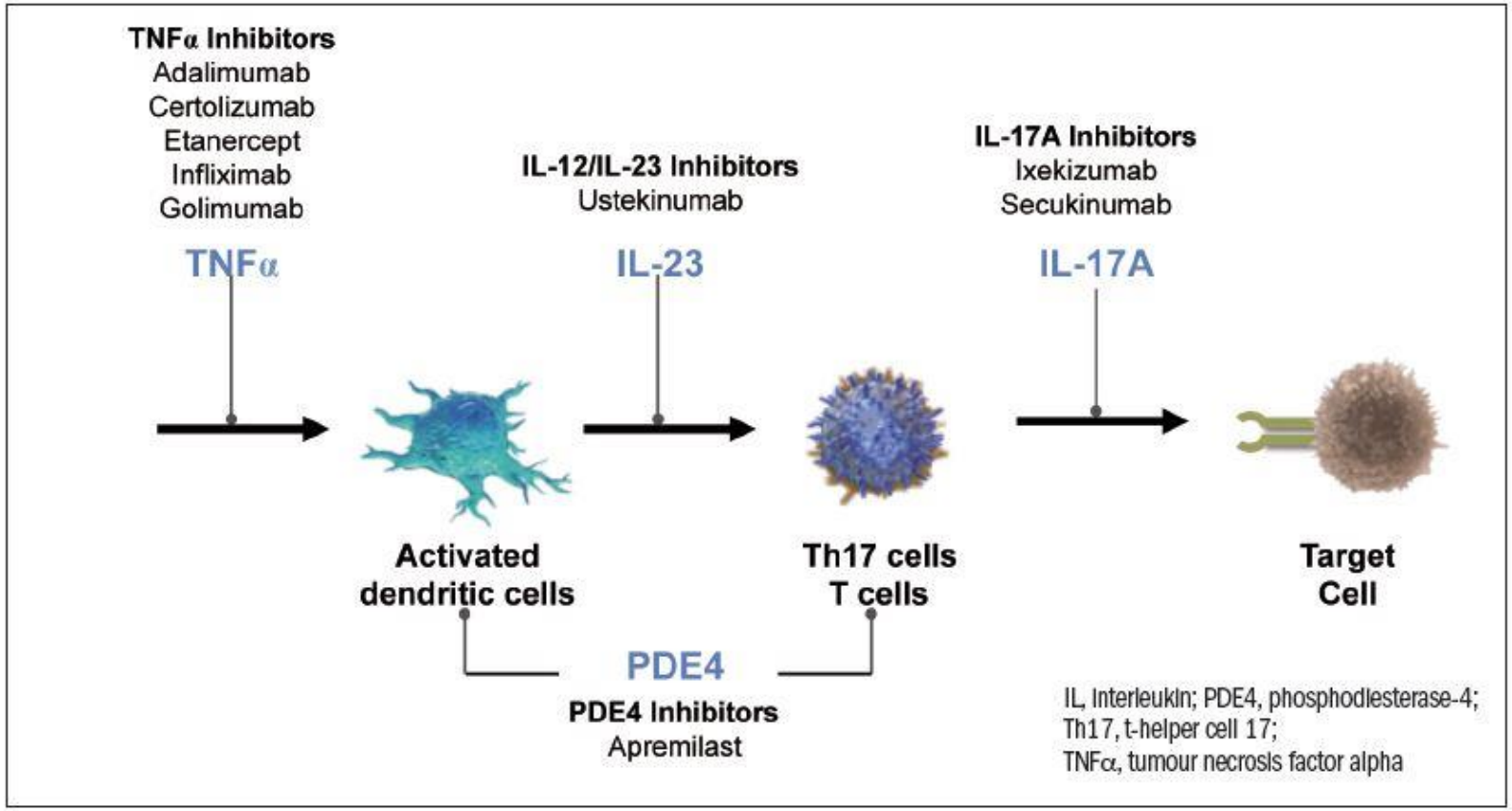
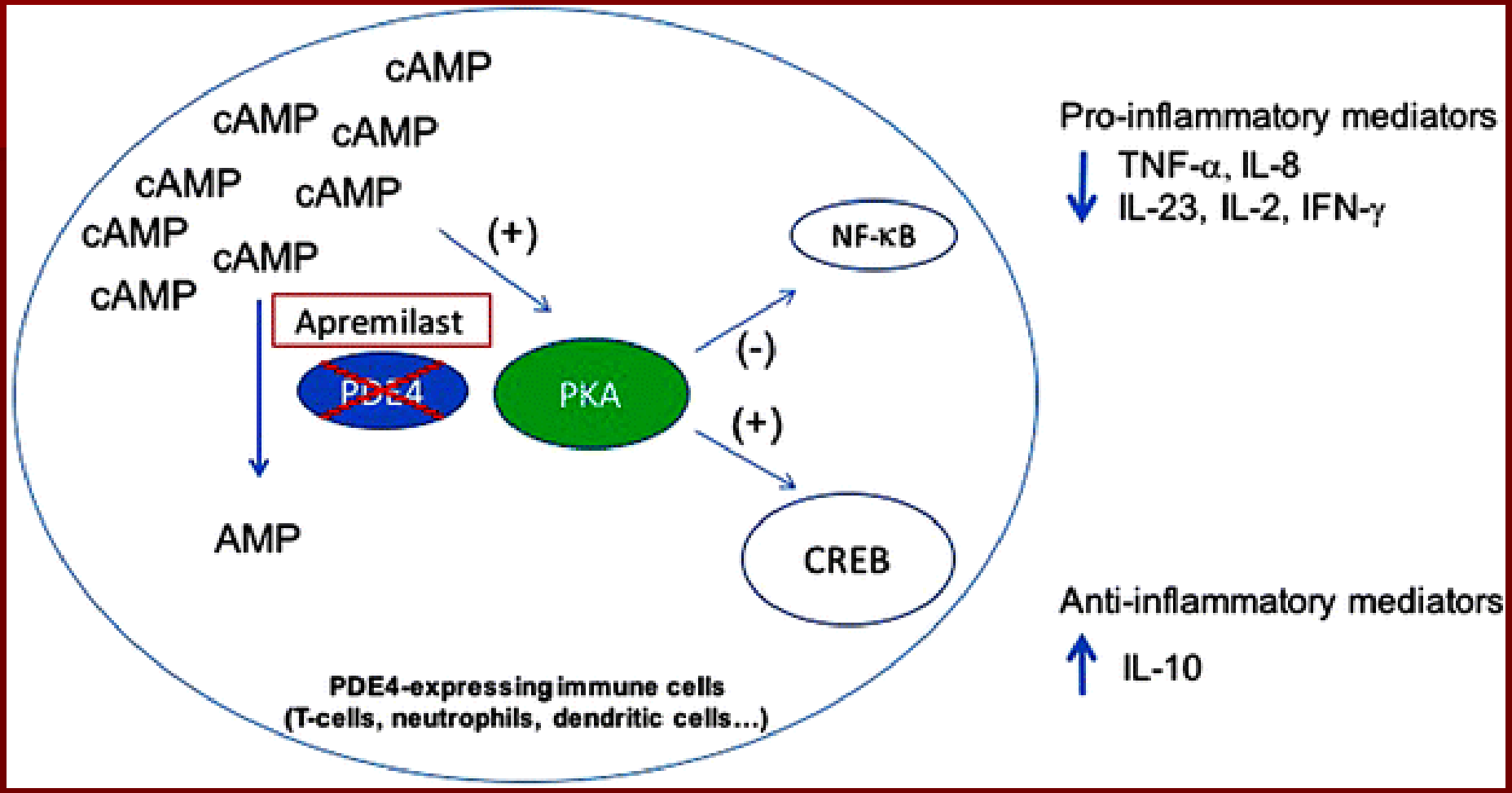


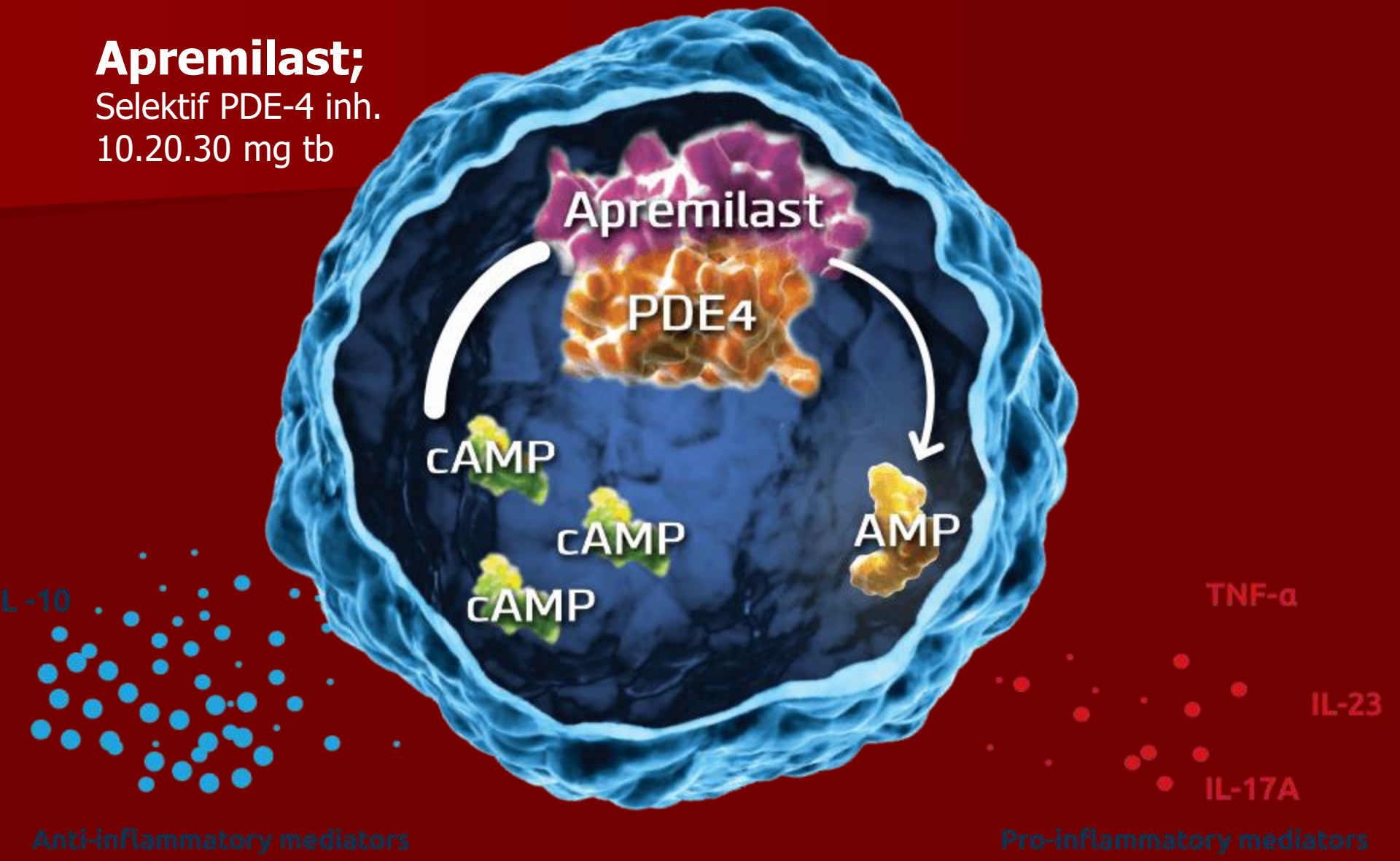
Figure 1. Pathogenesis-based approach to treatment of psoriasis and psoriatic arthritis. Adapted from Lynde et al. 2014[5]

Fosfodiesteraz-4 (PDE-4) ve inhibisyonu

- PDE-4; monosit, nötrofil, T lenfositler gibi immün sistem hücrelerinde bulunan PDE formu
- cAMP'nin enzimatik degradasyonunu sağlar-AMP
- H. içi sinyal yolunda ikinci habercil


cAMP
cAMP
cAMP
cAMP
cAMP
cAMP
cAMP
cAMP
Apremilast
PDE4
PKA
(+)
(-)
(+)
NF-κB
CREB
AMP
PDE4-expressing immune cells
(T-cells, neutrophils, dendritic cells…)
Pro-inflammatory mediators
TNF-α, IL-8
IL-23, IL-2, IFN-γ
Anti-inflammatory mediators
IL-10

Apremilast;
Selektif PDE-4 inh.
10.20.30 mg tb



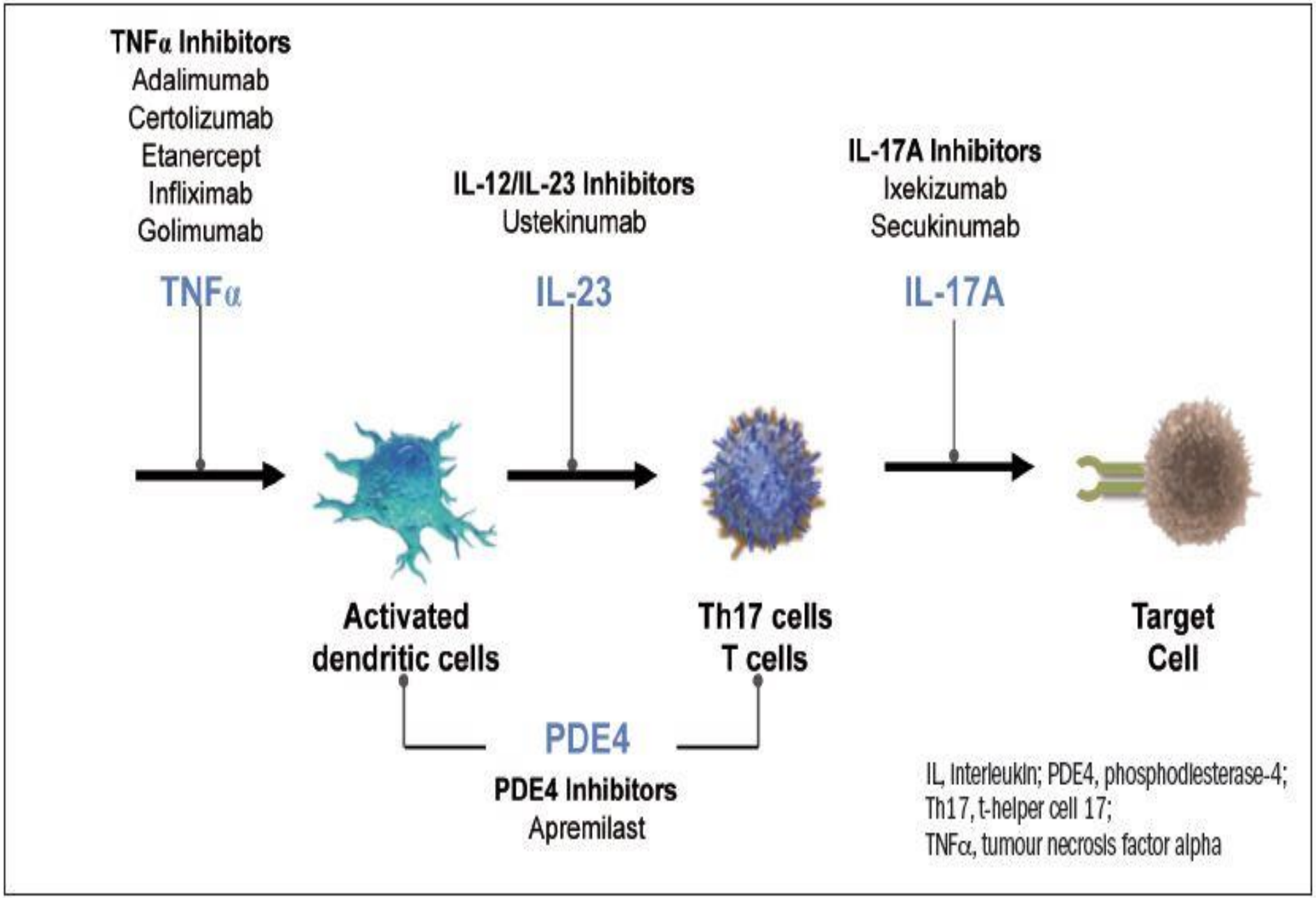
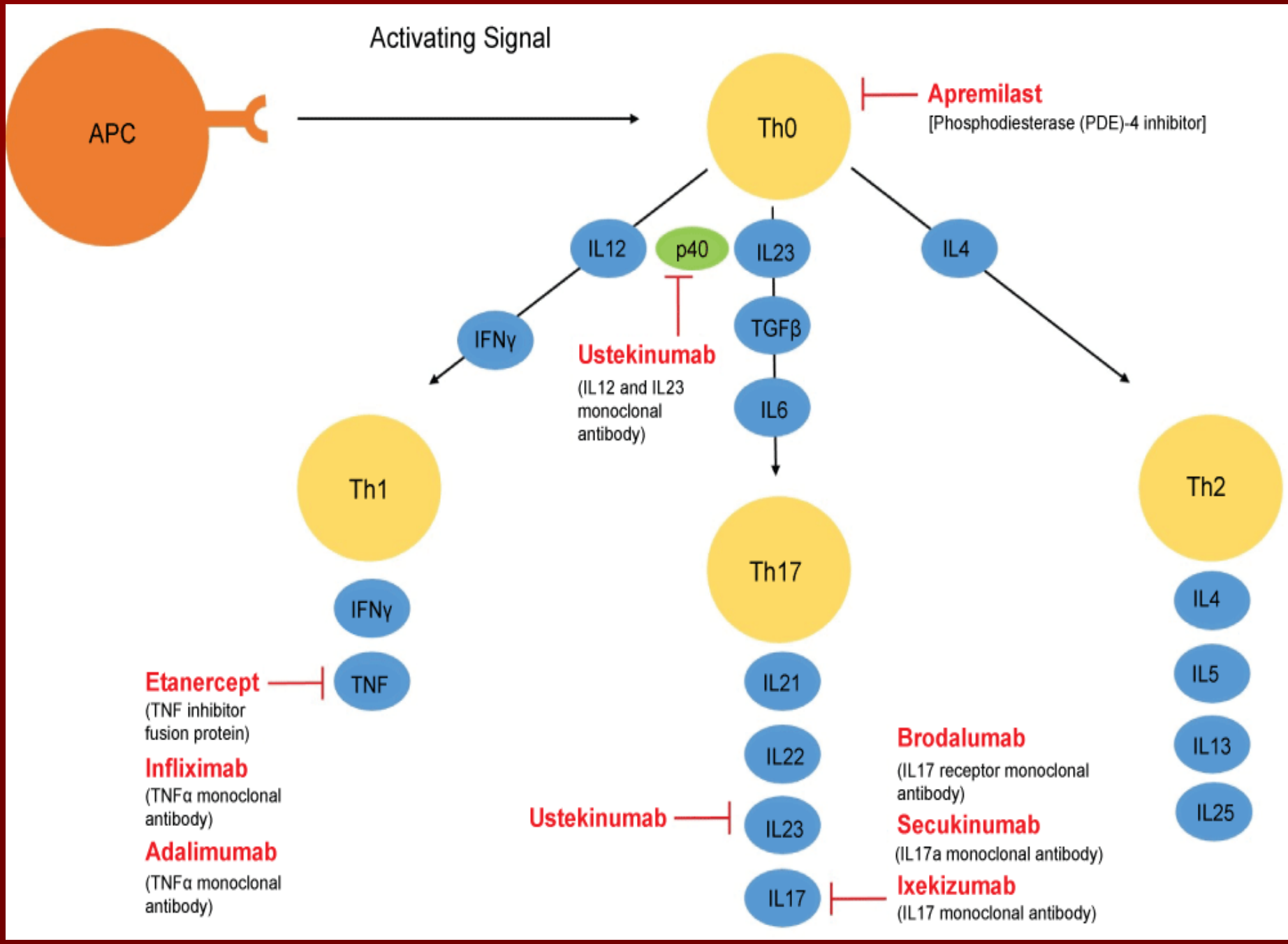


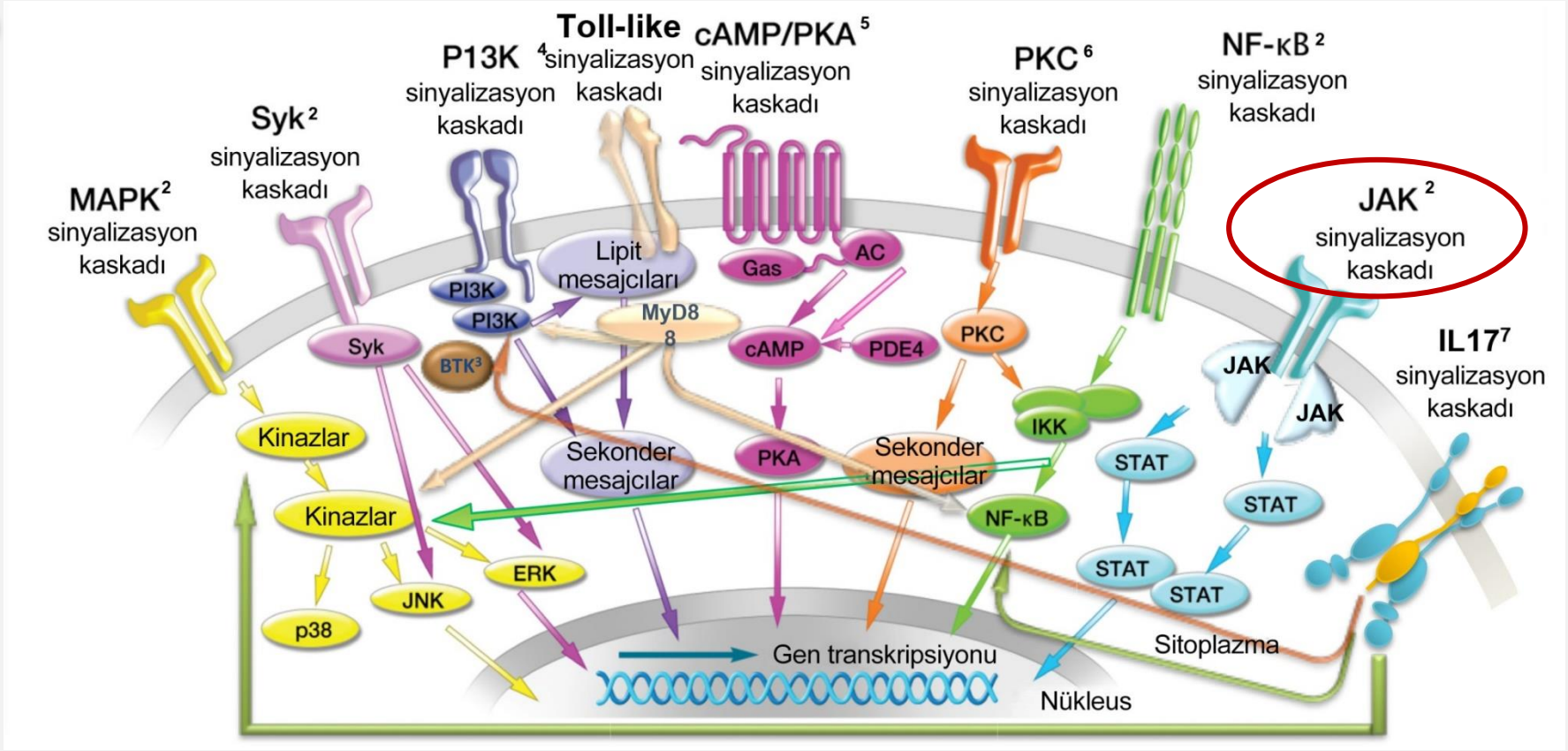
Figure 1. Pathogenesis-based approach to treatment of psoriasis and psoriatic arthritis. Adapted from Lynde et al. 2014[5]


Activating Signal
APC
Th0
Apremilast
[Phosphodiesterase (PDE)-4 inhibitor]
IL12
p40
IL23
IL4
IFNγ
Ustekinumab
(IL12 and IL23 monoclonal antibody)
TGFβ
IL6
Th1
Th17
Th2
IFNγ
IL4
Etanercept
(TNF inhibitor fusion protein)
TNF
IL21
IL5
Infliximab
(TNFα monoclonal antibody)
IL22
Brodalumab
(IL17 receptor monoclonal antibody)
IL13
Ustekinumab
IL23
Secukinumab
(IL17a monoclonal antibody)
IL25
Adalimumab
(TNFα monoclonal antibody)
IL17
Ixekizumab
(IL17 monoclonal antibody)

JANUS KİNAZ ve İnhibisyonu

- JAK hücre yüzeyi sitokin aracılı sinyalleri JAK-STAT sinyal iletim yolu ile hücrenin iç kısmına ileten hücre içi, reseptör olmayan tirozin kinazların bir ailesidir.
- Çeşitli pro-inflamatuar sitokin reseptörleri, T hücresi aktivasyonu ve fonksiyonu için gerekli olan JAK-STAT sinyal transdüksiyon yolağını kullanır.

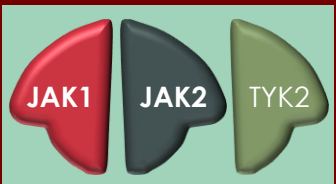
Sitokin Sinyalizasyonunda Rol Oynayan Kinaz Yolakları

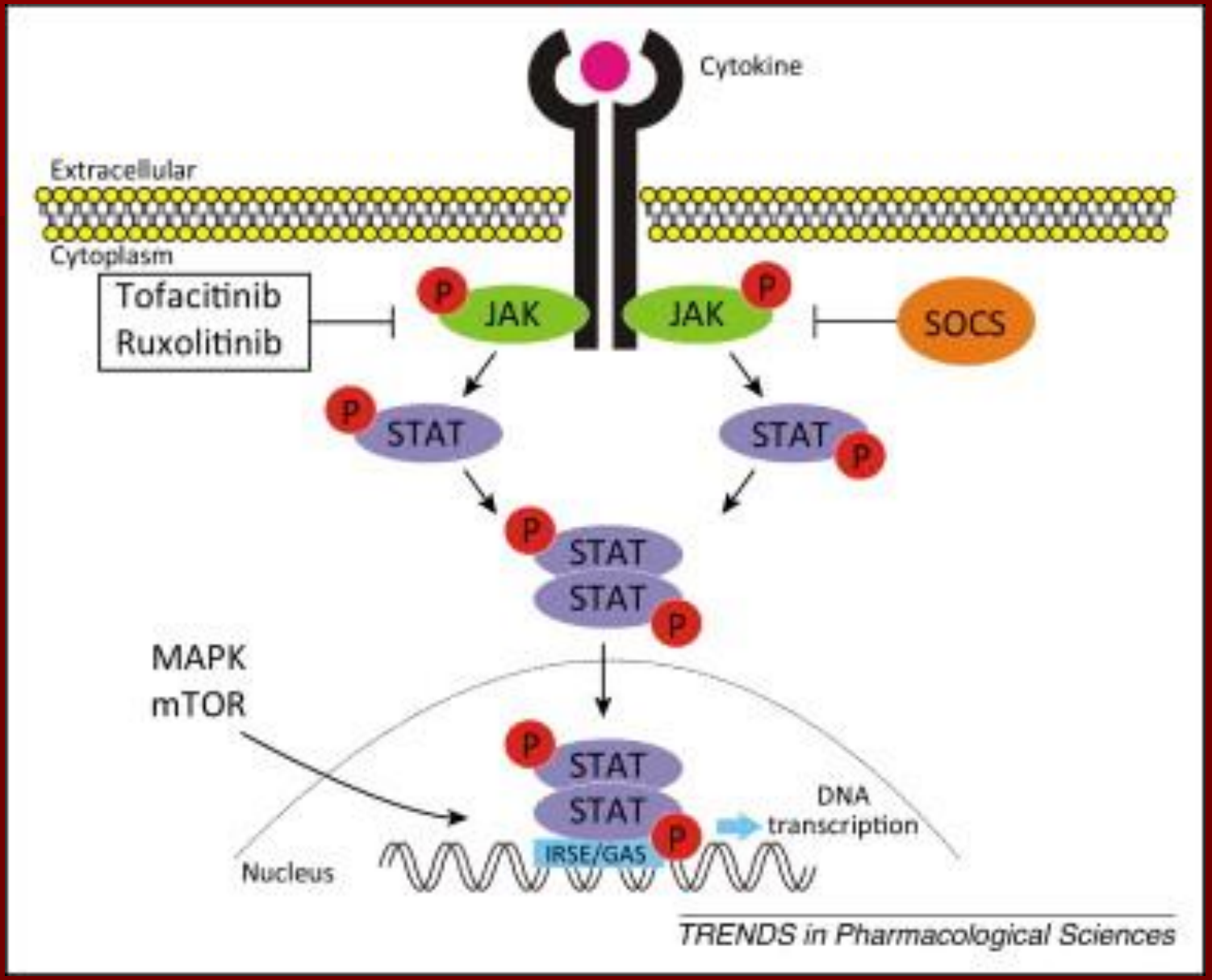


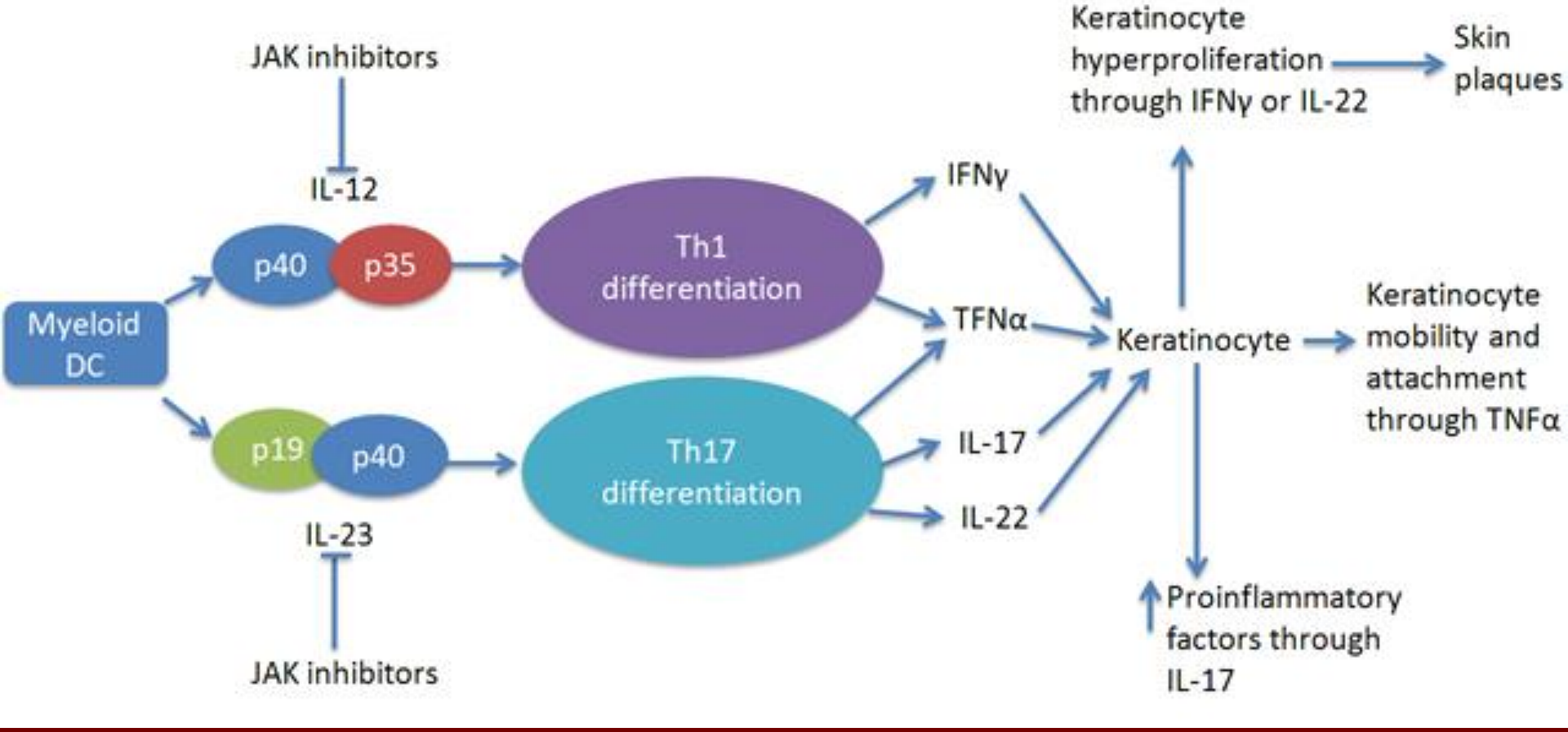
JAK Kombinasyonları ve Sitokinler

- JAK'lar değişik kombinasyonlar halinde çalışırlar

JAK / STAT kombinasyonları yoluyla sinyalizasyon yapan sitokin örnekleri

γ-zincirli sitokinler*	IFN-γ	IL-10, IL-20 IL-22 Tip I IFNlar (IFNα/IFNβ)	IL-12 IL-23	IL-6†, IL-11, IL-27, CTF-1, CNTF, G-CSF, LIF, OSM	EPO, TPO GM-CSF, BH, IL-3, IL-5
					
STAT 1, 3, 5, 6	STAT 1, 3, 5	STAT 1, 3, 5	STAT 3, 4	STAT 1, 3, 5	STAT 5


Cytokine
Extracellular
Cytoplasm
Tofacitinib
Ruxolitinib
JAK
JAK
SOCS
STAT
STAT
STAT
STAT
MAPK
mTOR
STAT
STAT
DNA
transcription
IRSE/GAS
Nucleus
TRENDS in Pharmacological Sciences


JAK inhibitors
IL-12
p40
p35
Myeloid DC
p19
p40
IL-23
JAK inhibitors
Th1 differentiation
Th17 differentiation
IFNγ
TFNα
IL-17
IL-22
Keratinocyte
Keratinocyte hyperproliferation through IFNγ or IL-22
Skin plaques
Keratinocyte mobility and attachment through TNFα
Proinflammatory factors through IL-17

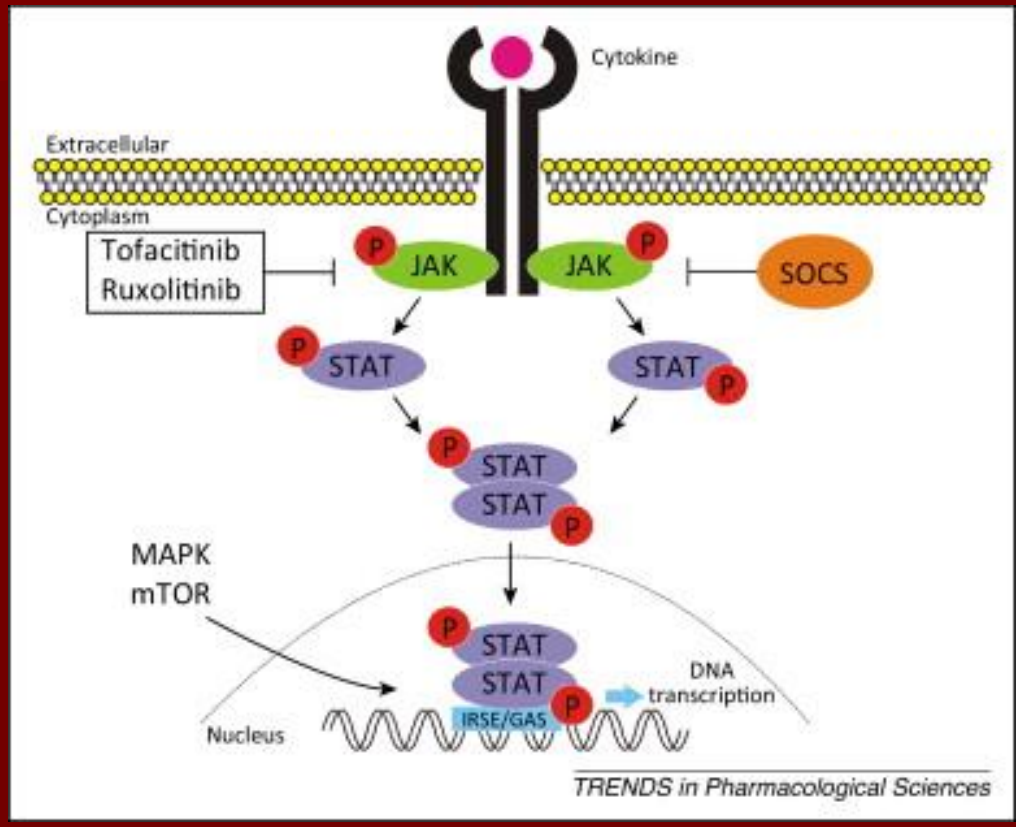
- **JAK inhibitörleri;**

Tofacitinib;

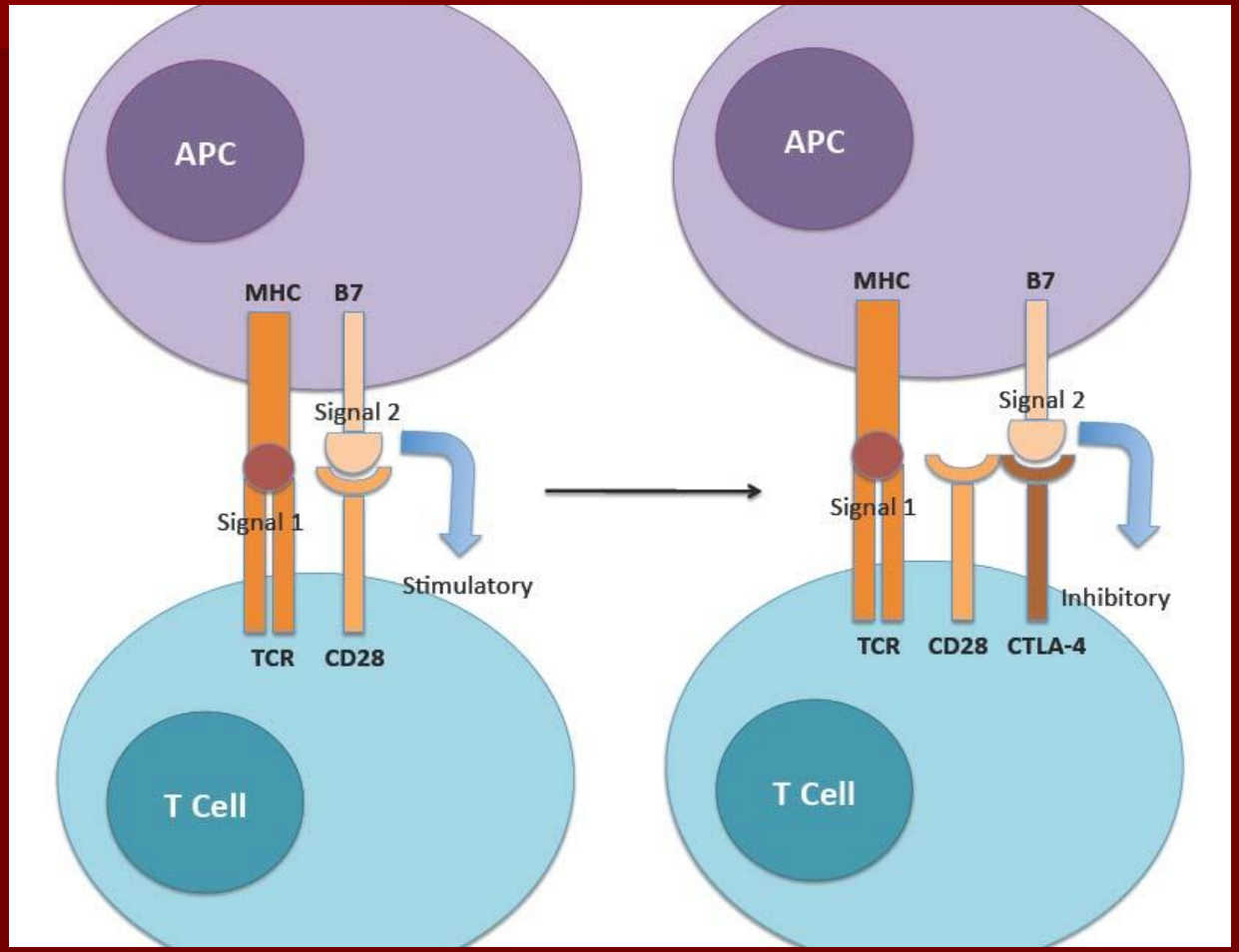
Oral JAK1 ve JAK 3 inh.

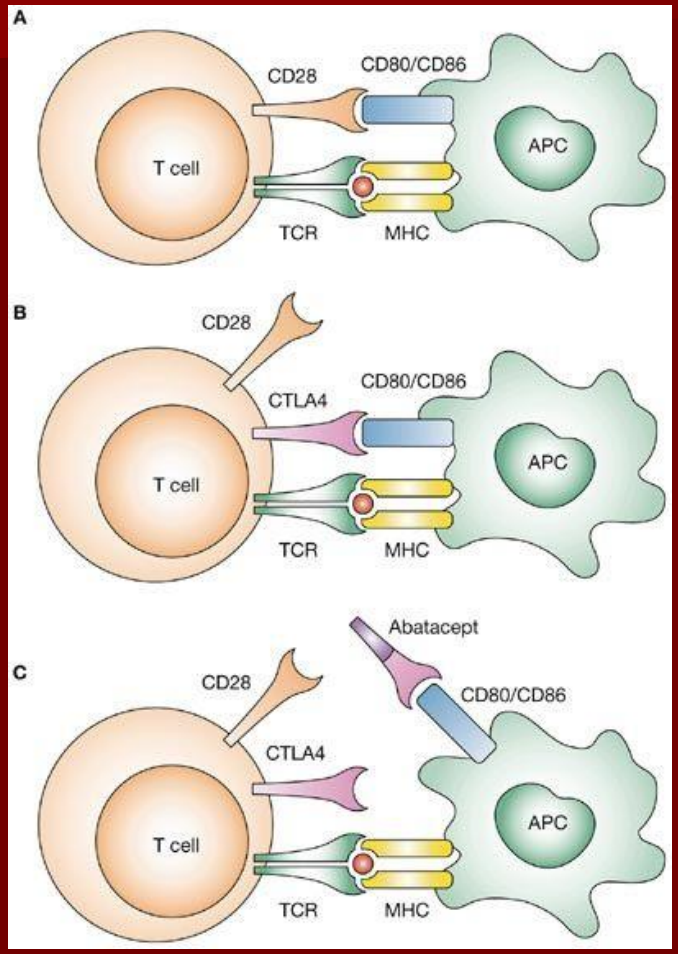
Ruxolitinib;

Topikal JAK 1 ve JAK 2 inh.



CTLA-4 Co-stimülasyon ve blokajı



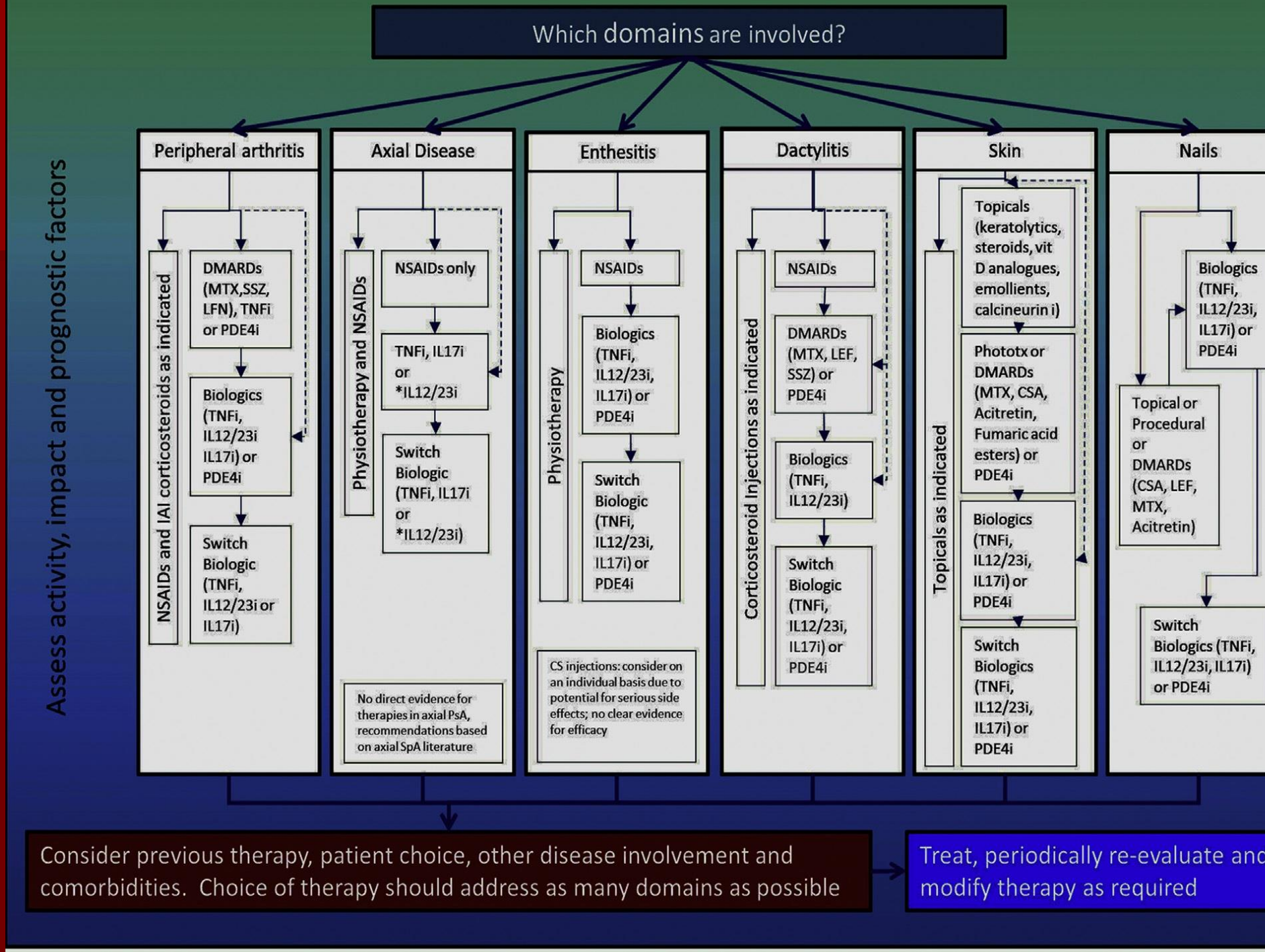


- **Abatacept;**

  Solubl füzyon proteini

CTLA-4'in exraselüler parçası ve IgG'in modifiye edilmiş Fc parçasını içerir

bDMARD	PsA	Psöriazis
Etanercept	EMA, FDA	EMA, FDA
İnfliximab	EMA, FDA	EMA, FDA
Adalimumab	EMA, FDA	EMA, FDA
Golimumab	EMA, FDA	-
Certolizumab p	EMA, FDA	Faz 3
Ustekinumab	EMA, FDA	EMA, FDA
Secukinimab	EMA, FDA	EMA, FDA
Ixekizumab	EMA, FDA	EMA, FDA
Brodalumab	Faz 2	EMA, FDA
Guselkumab	Faz 2	EMA, FDA
Abatacept	EMA, FDA	Faz 2
tsDMARD		
Apremilast	EMA, FDA	EMA, FDA
Tofacitinib	FDA	Faz 3


Which domains are involved?
Assess activity, impact and prognostic factors
Peripheral arthritis
NSAIDs and IAI corticosteroids as indicated
DMARDs (MTX,SSZ, LFN), TNFi or PDE4i
Biologics (TNFi, IL12/23i IL17i) or PDE4i
Switch Biologic (TNFi, IL12/23i or IL17i)
Axial Disease
Physiotherapy and NSAIDs
NSAIDs only
TNFi, IL17i or *IL12/23i
Switch Biologic (TNFi, IL17i or *IL12/23i)
No direct evidence for therapies in axial PsA, recommendations based on axial SpA literature
Enthesitis
Physiotherapy
NSAIDs
Biologics (TNFi, IL12/23i, IL17i) or PDE4i
Switch Biologic (TNFi, IL12/23i, IL17i) or PDE4i
CS injections: consider on an individual basis due to potential for serious side effects; no clear evidence for efficacy
Dactylitis
Corticosteroid Injections as indicated
NSAIDs
DMARDs (MTX, LEF, SSZ) or PDE4i
Biologics (TNFi, IL12/23i)
Switch Biologic (TNFi, IL12/23i, IL17i) or PDE4i
Skin
Topicals as indicated
Topicals (keratolytics, steroids, vit D analogues, emollients, calcineurin i)
Phototx or DMARDs (MTX, CSA, Acitretin, Fumaric acid esters) or PDE4i
Biologics (TNFi, IL12/23i, IL17i) or PDE4i
Switch Biologics (TNFi, IL12/23i, IL17i) or PDE4i
Nails
Biologics (TNFi, IL12/23i, IL17i) or PDE4i
Topical or Procedural or DMARDs (CSA, LEF, MTX, Acitretin)
Switch Biologics (TNFi, IL12/23i, IL17i) or PDE4i
Consider previous therapy, patient choice, other disease involvement and comorbidities. Choice of therapy should address as many domains as possible
Treat, periodically re-evaluate and modify therapy as required

TEŞEKKÜRLER