

In Scope

R&D Systems, the world leader in cytokine research reagents, offers an extensive selection of reagents for arthritis research applications.

The In Scope series of product newsletters highlight products that are applicable for a particular research topic. Due to space constraints, only a select list of products are provided in the table on p. 4-5. For more information about additional products, refer to our web site, RnDSystems.com. Please inquire about availability with a customer service representative at 1-800-343-7475 or e-mail us at info@RnDSystems.com. New products are released daily, thus the available products listed within this issue are only current for the date provided.

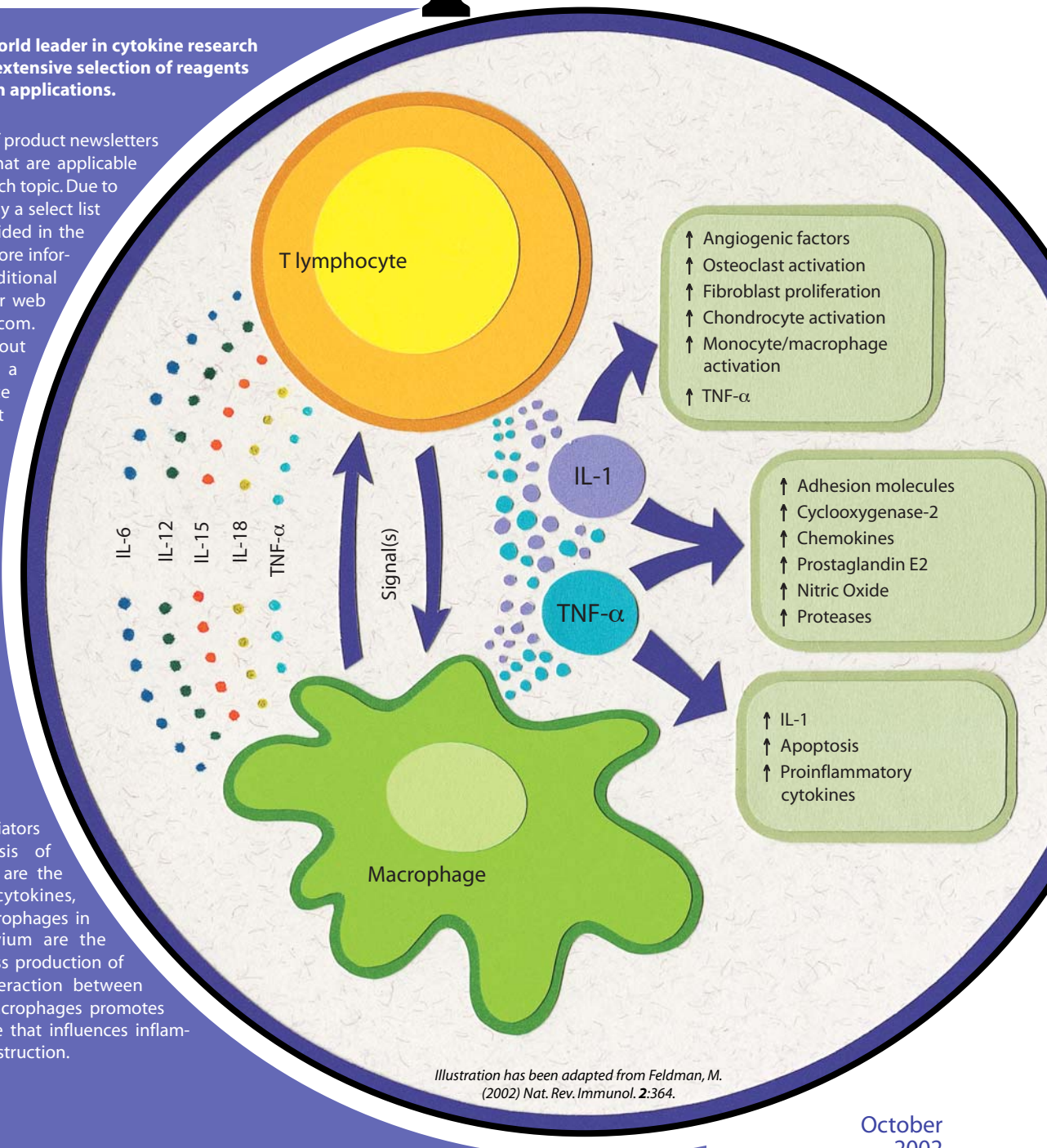


Figure Legend

The two central mediators of the pathogenesis of rheumatoid arthritis are the proinflammatory cytokines, IL-1 and TNF- α . Macrophages in the inflamed synovium are the main source of excess production of IL-1 and TNF- α . Interaction between CD4⁺ T cells and macrophages promotes the cytokine cascade that influences inflammation and tissue destruction.

Illustration has been adapted from Feldman, M. (2002) Nat. Rev. Immunol. 2:364.

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*Making the discoveries of today,
 your research tools tomorrow.*

October
 2002



Novel Interleukin Involvement in Rheumatoid Arthritis

It is well established that IL-1, TNF- α and matrix metalloproteinases are important mediators of tissue damage associated with rheumatoid arthritis (RA). A more recent study,¹ however, implicates additional proinflammatory interleukins in the development and progression of RA. Three interleukins, IL-15, IL-17 and IL-18, may play pivotal roles in RA. IL-15 is a chemoattractant and may promote bone degradation. IL-17 stimulates metalloproteinase production, and IL-18 is angiogenic, chemotactic, and promotes destruction of cartilage. Targeting these additional interleukins may also prove therapeutically beneficial for RA patients.

R&D Systems has the following IL-15, IL-17 IL-18, and IL-18BP products available

- Recombinant proteins
- Polyclonal antibodies
- Monoclonal antibodies
- Labeled antibodies
- ELISA kits
- ELISA development kits
- Primer Pairs

Please consult our on-line catalog, RnDSystems.com, for product specification sheets.

Reference

1. Bessis, N. & M.C. Boissier (2001) Joint Bone Spine **68**:477.

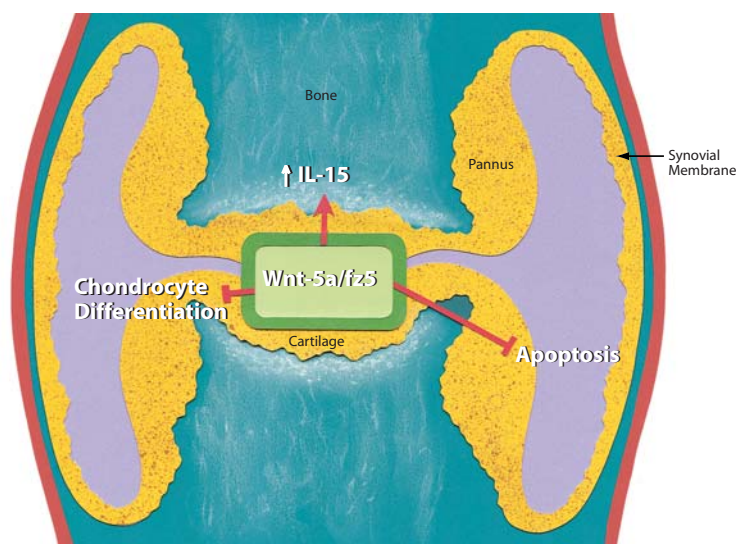
Wnt Signaling in Rheumatoid Arthritis

Synovial fibroblasts of the rheumatic joint remain in a persistently activated state despite removal from the inflammatory environment.¹ The Wnt-5a/fz5 signaling pathway may influence the activated state of synovial fibroblasts in rheumatoid arthritis (RA) patients.^{1,2} Sen *et al.*^{1,2} postulate that immature cells migrate from the bone marrow to sites of joint inflammation. These mesenchymal-derived fibroblasts express Wnt-1, Wnt-5a, Wnt-11, Wnt-13 and Wnt-10b, as well as the receptors, fz2, fz5, fz7.² Interfering with the Wnt-5a/fz5 signaling pathway in RA synovial fibroblasts inhibits expression of proinflammatory cytokines and RANKL.^{1,2}

Understanding the role that Wnt and fz molecules play in the development of the normal joint may explain the aberrant effects of Wnt signaling on the rheumatic joint. Wnt-5a is required for all outgrowth along the posterior-distal (P-D) body axis. Loss of function studies show shortening of elements and truncation of more distal structures.³ Wnt-5a expression maintains cells in an undifferentiated proliferative state. As Wnt-5a signaling is lost, cells adopt a determined cell fate. In the limb, outgrowth along the P-D axis is driven by the expansion of cells in the Progress Zone (PZ) where Wnt-5a expression is high. Cells leave the

PZ and begin to form the structures of the limb. Wnt-5a negatively regulates chondrogenesis, the first step in skeleton formation.⁴ Wnt-5a is also down-regulated in the interdigital cells destined for apoptosis.⁴ In the rheumatoid arthritic joint, Wnt-5a signaling may contribute to the hyperplasia of synovial tissue by negatively regulating apoptosis and interfering with joint repair by inhibiting differentiation of chondrocytes.

Wnt signaling may also impact RA by contributing to late stage bone erosions. Both IL-15 and RANKL are important signaling molecules in the recruitment and maturation of osteoclasts, the predominant cell type mediating bone erosions seen in late stage RA.⁵ Wnt-5a expression in synovial fibroblasts elevates expression of IL-15.¹ This effect is abrogated by transfection of either a Wnt-5a antisense or a truncated dominant negative Wnt-5a-encoding vector, as well as treatment with an antibody to the extracellular domain of fz5. Treatment with fz5 antibody also decreases expression of RANKL.¹ Collectively, these results indicate that the Wnt-5a/fz5 signaling pathway may be an alternate target for RA drug development, especially for patients that do not respond to anti-inflammatory therapy.



The Wnt-5a/fz5 signaling pathway may be an alternate target for RA drug development since disruption of this network decreases the expression of inflammation-, bone erosion-, and apoptosis-promoting factors.

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Aggrecan Degradation By Metalloproteases

Aggrecan and type II collagen make up to 90% of the dry weight of healthy cartilage. Aggrecan hydrates the collagen network and thus provides cartilage with its properties of compressibility and elasticity. Maintenance of aggrecan content in articular cartilage is therefore critical to the function of the tissue and aggrecan degradation is an important factor in the erosion of articular cartilage in arthritic diseases.^{1,2}

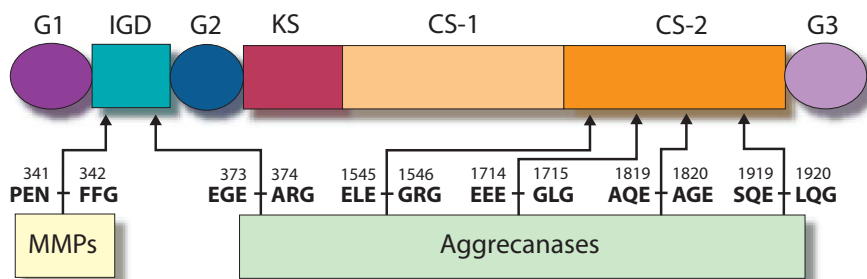
As the key component of the cartilage extracellular matrix, aggrecan monomers consist of a 250 kDa core protein with a multidomain structure.³ With attachment of chondroitin sulfate and keratan sulfate glycosaminoglycan side chains, aggrecan monomers exist as 1000-2000 kDa molecules. In addition, aggrecan monomers interact with hyaluronan through their G1 domain, resulting in larger aggregates containing 10-100 aggrecan monomers on a hyaluronan backbone.¹

Aggrecan degradation via proteolytic cleavage has been attributed to metalloprotease activity. Members of the matrix metalloproteinase (MMP) family present in cartilage, MMP-1, -2, -3, -7, -8, -9, -13 and -14, are capable of cleaving aggrecan at the Asn341-Phe342 bond in the IGD domain. Members of the ADAMTS family, ADAMTS4 and ADAMTS-5/11, referred to as aggrecanase-1 and aggrecanase-2,

respectively, cleave aggrecan at the Glu373-Ala374 bond in the IGD domain.^{1,4} In addition, recombinant ADAMTS4 also cleaves the relevant aggrecanase sites (Glu-Xaa bonds) in the CS-2 domain.⁵ While MMPs and aggrecanases have unique peptide bond specificity in the IGD domain, this may not be absolute. For example, ADAMTS4 is capable of cleaving the Asn341-Phe342 site and MMP cleavage at the Asn341-Phe342 interferes with aggrecanase activity.^{6,7}

Activities of MMPs and aggrecanases are regulated at various levels, such as activation of proenzymes by additional proteases. For example, MMP-14, ADAMTS4 and ADAMTS5 all contain a furin processing site located between the C-terminus of the proregion and the N-terminus of the mature and active enzyme. Processing by furin or furin-like enzymes removes the inhibitory proregion from these proteins. In addition, ADAMTS4 activity requires removal of a portion of its C-terminal spacer domain, a processing event mediated by MMP-like enzymes.⁸ Inactivation of active enzymes can be achieved by other proteases or by endogenous inhibitors. Tissue inhibitors of metalloproteinases (TIMP-1, -2, -3 and -4), inhibit MMP activity and TIMP-3 is capable of inhibiting ADAMTS4 and ADAMTS5 activity.^{9,10}

Metalloprotease cleavage sites in the human aggrecan core protein



Cleavage sites by MMPs and aggrecanases are represented by arrows below the domain structure of the human aggrecan core protein. Amino acids flanking the cleavage sites are shown and the numbering corresponds to the position of these sites within the aggrecan core protein. G1, G2 and G3: globular domains 1, 2, 3; IGD: interglobular domain; KS: keratan sulfate attachment domain; CS-1 and CS-2: chondroitin sulfate attachment domains 1 and 2.

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MMP-3, SDF-1 and CXCR4 Products

MMPs degrade collagen, proteoglycans, and other matrix macromolecules within bone and articular cartilage. This degradation process leads to the pathological joint destruction associated with rheumatoid arthritis and osteoarthritis. Various chemokines and cytokines have been implicated in activating the cells responsible for MMP production. For example, synovial fluid SDF-1 interacts with CXCR4 expressed on chondrocytes, resulting in production and secretion of the cartilage matrix-degrading enzyme MMP-3.¹

RECOMBINANT PROTEINS

Product	Catalog #
Human MMP-3513-MP
Mouse MMP-3548-MM

ANTIBODIES

Anti-human MMP-3AF513, BAF513, MAB905
Anti-mouse MMP-3AF548, BAF548, MAB548

OTHER

Human MMP-3 ELISA KitDMP300
Human MMP-3 Primer PairRDP-85

RECOMBINANT PROTEINS

Product	Catalog #
Human SDF-1 α350-NS
Human SDF-1 β351-FS
Mouse SDF-1 α460-SD

ANTIBODIES

Anti-human SDF-1AF-310-NA, BAF310, MAB310
Anti-human SDF-1 βAF-351-NA, BAF351
Anti-human/mouse SDF-1MAB350

KITS

Human SDF-1 α ELISA KitDSA00
Human SDF-1 mRNA KitKRN310
Human SDF-1 α Biotin Receptor Detection KitNNS00

ANTIBODIES

Product	Catalog #
Anti-human CXCR4MAB170, MAB171, MAB172, MAB173, FABSP2, FAB170B, FAB171B, FAB172B, FAB173B, FABSP2B, FAB170F, FAB170P, FAB173P

mRNA KIT

Human CXCR4KRN170
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Please consult our on-line catalog, RnDSystems.com, for a list of additional MMP, chemokine and chemokine receptor products that are available.

Reference

- Kanbe, K. *et al.* (2002) *Arthritis Rheum.* **46**:130.

Name	Protein	Antibody	ELISA/Assays	mRNA Quantitation Kit	ELISA/Assay Development Kit	Primer Pair	Other
Activin A	•	• ♦ •	• ♦				
Activin RIA/ALK-2	•	•					
Activin RIB/ALK-4	•	•					
Activin RIIA	•	•					
Activin RIIA/B		•					
Activin RII B	•	•					
β ₂ M			•				
Caspase-1 (ICE)			• ○				○ FMK Inhibitor
Caspase-3	•	• ♦	• ○				
Caspase-7	•	• ♦	•				
Caspase-8	•	•	○				○ FMK Inhibitor
Cathepsin B	• ♦	•					
Cathepsin L	•	•					
CCR1		•				• ♦ •	
CCR2		•				• ♦	
CCR3		• ♦				• ♦ •	
CCR5		•				• ♦ •	
CD40/TNFRSF5		• ♦					
CD40 Ligand/TNFSF5	• ♦	•	•				
Common γ Chain	• ♦	• ♦					
COX-2				•			
CXCR3		•					
CXCR4		•		•			
ENA-78/CXCL5	•	•	•		•		
Fas (CD95)/TNFRSF6	• ♦	• ♦	• ♦	•		• ♦	
Fas Ligand/TNFSF6	• ♦	• ♦	♦	•	♦	• ♦	
FGF acidic/FGF-1	• •	• •					
FGF basic/FGF-2	• •	• •	•		•	•	• FMAP
FGF R1α	•						
FGF R1β	•						
FGF R2α	•						
FGF R2β	• ♦						
FGF R2		• ♦					
FGF R3	• ♦	• ♦					
FGF R4	•						
FLIP		• ♦					
Fractalkine/CX3CL1	• ♦ •	• ♦ •			• ♦ •		
Frizzled 7		♦					
GM-CSF	• ♦ • ■ ▲	• ♦ • ■ ▲	• ♦ •	•	• ♦ •	•	• ELISpot, • FMAP, • RD
GM-CSF Rα		•					
gp130	• ♦	• ♦	•				
GROα/CXCL1	•	•	•		•		
ICAM-1 (CD54)	• ♦ •	• ♦ •	•	•	•	• ♦ •	
IFN-γ	• ♦ • • ♦ ▲ ■ ●	• ♦ • • ♦ ▲ ■ ●	• ♦ •	• ♦	• ♦ •	• ♦ •	• ♦ • ELISpot, • FMAP
IFN-γ R1	• ♦	• ♦					
IFN-γ R2		• ♦					
IGF-I	• ♦	• ♦	•		•		
IGF-I R	•	•			•		
IGFBP-3	• ♦	• ♦	•		• ♦		
IGFBP-4	•	•			•		
IGFBP-5	• ♦	• ♦					
IL-1α/IL-1F1	• ♦ • • ■	• ♦ • • ■	• ♦		• ♦ •	• ♦ •	• RD
IL-1β/IL-1F2	• ♦ • • ■	• ♦ • • ■	• ♦ • ■	• ♦ •	• ♦ •	• ♦ •	• ELISpot, • FMAP, • RD
IL-1 RI	• ♦	• ♦			•		
IL-1 RII	• ♦	• ♦	•				
IL-1 R3/IL-1 R AcP	•	•					
IL-1 R6/IL-1 R rp2	• •	• •					
IL-2	• ♦ • • ■	• ♦ • • ■	• ♦ •	• ♦	• ♦ •	• ♦ •	• ♦ • ELISpot, • RD
IL-2 Rα	•	•	•		•		
IL-2 Rβ	•	• ♦					
IL-6	• ♦ • • ■	• ♦ • • ■	• ♦ • ■	•	• ♦ • ■	• ♦ •	• ♦ ELISpot, • FMAP, • RD
IL-6 R	•	•	•		•		
IL-8/CXCL8	• ■	• ■	• ■	•	•	•	• ELISpot, • FMAP, • RD
IL-10	• ♦ • • ■ ♦ ▲ ●	• ♦ • • ■ ♦ ▲ ●	• ♦ •	•	• ♦ •	• ♦ •	♦ ELISpot, • FMAP, • RD
IL-10 Rα	• ♦	• ♦					
IL-10 Rβ	•	•					
IL-11	• ♦	• ♦	•			♦ •	
IL-11 Rα	♦	♦					



- Human •
- Mouse ♦
- Rat •
- Cotton Rat •
- Bovine •
- Porcine ■
- Canine ♦
- Feline ▲
- Rhesus macaque •
- Viral •
- Multi-species ○

- ELISpot - ELISpot Kit
- FMAP - Multi-Analyte Profiling Kit
- RD - Receptor Detection Kit

Name	Protein	Antibody	ELISA/Assays	mRNA Quantitation Kit	ELISA/Assay Development Kit	Primer Pair	Other
IL-12	• ♦ ■	• ♦ ■	• ♦		• ♦	• ♦ •	
IL-12 Rβ1	•	•					
IL-15	• ♦	•	•		•	• ♦ •	
IL-15 Rα	• ♦	• ♦					
IL-17	• ♦	• ♦	• ♦		• ♦	• ♦	
IL-17 R	•	• ♦					
IL-18/IL-1F4	• ♦ ■ ■	• ♦ ■ ■	• ♦				
IL-18 Rα/IL-1 R5	•	• ♦					
IL-18 Rβ/IL-1 R7	•	•					
IP-10/CXCL10	• •	• •	•		•		
LFA-1		♦					
LFA-1α		• •					
LFA-1β		•					
LIF		• ♦	• ♦				• RD
MCP-1/CCL2	•	•	•	•	•	•	• RD
MIF	•	•			•		
MIG/CXCL9	• ♦	• ♦	•		•		
MIP-1α/CCL3	• ♦ •	• ♦	• ♦	•	• ♦		• ♦ RD
MIP-1β/CCL4	• ♦ •	• ♦ •	• ♦		• ♦		• RD
MIP-3α/CCL20	• ♦ •	• ♦ •	•		• •		
MMP-1	•	•	•			•	
MMP-2	•	•				• ♦	
MMP-3	• ♦	• ♦	•			•	
MMP-7	•	•	•			•	
MMP-8	•	•	•				
MMP-9	• ♦	• ♦	• ♦			•	
MMP-13	•	•	•				
MMP-14		•					
NO			•				
eNOS		•	•			• ♦	
iNOS		•	•	• ♦		• ♦	
Notch-1	•						
Osteopontin (OPN)	♦ •	♦					
Osteoprotegerin/TNFRSF11B	• ♦	• ♦	♦		•	• ♦	
p53		•		•		• •	
PDGF	• ■	• •					
PDGF-A						• ♦	
PDGF-AA	• •	•	•				
PDGF-AB	•		•				
PDGF-B						•	
PDGF-BB	• •	•	•				
PDGF Rα	• ♦	•				•	
PDGF Rβ	• ♦	• ♦				• ♦ •	
PGE ₂			•				
RANK/TNFRSF11A	• ♦	• ♦				• ♦	
RANTES/CCL5	• ♦ •	• ♦	• ♦	•	• ♦	•	• RD
SDF-1 (PBSF)/CXCL12		• ♦		•			
SDF-1α (PBSF)/CXCL12	• ♦		•				• RD
SDF-1β (PBSF)/CXCL12	•	•					
Substance P			•				
TACE	•	•					
TGF-β1	• ■	• •	•	•	•	• ♦	• ELISpot, • RD
TGF-β RI/ALK-5	♦	♦				• ♦ •	
TGF-β RII	• ♦	• ♦					
TGF-β RIIB	•						
TGF-β RIII	•	•					
TIMP-1	• ♦ •	• ♦ •	• ♦		• ♦	• ♦ •	
TIMP-2	•	•	•		•	• ♦ •	
TNF-α/TNFSF2	• ♦ • • ■ •	• ♦ • • ■	• ♦ • ■	• ♦ •	• ♦ •	• ♦	• ♦ ELISpot, • FMAP, • RD
TNF RI/TNFRSF1A	• ♦	• ♦	• ♦		• ♦	• ♦	
TNF RII/TNFRSF1B	• ♦	• ♦	• ♦		•	• ♦	
TRANSC/RANK L/TNFSF11	• ♦	• ♦	♦			• ♦	
uPAR	• ♦	• ♦	•				
uPAR-1		♦					
VCAM-1 (CD106)	• ♦	• ♦	• ♦	•		• ♦	
VEGF	• ♦ •	• ♦ •	• ♦	• ♦	• ♦	• ♦	• FMAP, • RD
VEGF R1 (Flt-1)	• ♦	• ♦	• ♦			• ♦	
VLA-4		•					
Wnt-5a		♦					

Key

Human •	Cotton Rat •	Canine ♦	Viral •
Mouse ♦	Bovine •	Feline ▲	Multi-species •
Rat •	Porcine ■	Rhesus macaque •	

ELISpot - ELISpot Kit
FMAP - Multi-Analyte Profiling Kit
RD - Receptor Detection Kit

iNOS, eNOS, and Nitric Oxide Assays

Nitric Oxide (NO), synthesized by the nitric oxide synthase (NOS) enzymes, inducible NOS (iNOS), endothelial NOS (eNOS) and neuronal NOS (nNOS), is involved in a variety of physiological and pathological processes. Overproduction of NO has been associated with a number of clinical disorders including stroke, chronic neurodegenerative diseases (e.g. Alzheimer's Disease, Parkinson's Disease, AIDS dementia, etc.), convulsions, septic shock, tissue damage following inflammation, and rheumatoid arthritis, among others. R&D Systems offers an extensive array of assays for measuring total NO, NO₂⁻/NO₃⁻, iNOS and eNOS in various biological fluids as well as cell lysates and supernates. The Quantikine human iNOS and human eNOS ELISAs are the first commercial ELISA kits available for iNOS and eNOS. An nNOS ELISA is currently in development.

Available Kits

Quantikine Human iNOS ELISA

Catalog #	DNS00
Sensitivity	0.15 U/mL
Range	1.2 - 40 U/mL
Sample Volume	100 µL
Sample Type	Cell lysates

Quantikine Human eNOS ELISA

Catalog #	DEN00
Sensitivity	0.15 pg/mL
Range	62.5 - 4000 pg/mL
Sample Volume	100 µL
Sample Type	Cell lysates

Total NO Assay

Catalog #	DE1600
Sensitivity	1.35 pmol/L
Range	3.12 - 100 µmol/L
Sample Volume	100 µL
Sample Type	Serum, plasma, urine, culture supernatants and other biological fluids

NO₂⁻/NO₃⁻ Assay

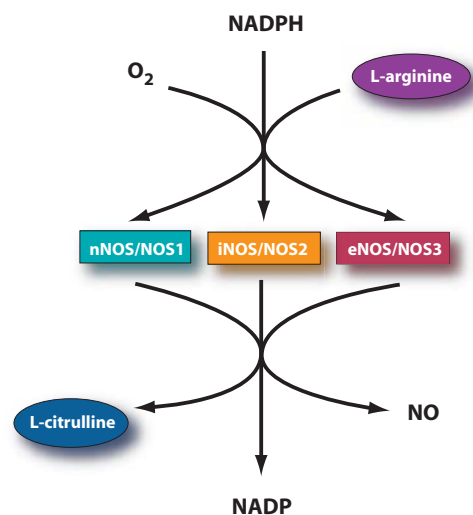
Catalog #	DE1500
Sensitivity	0.15 µmol/L
Range	0.05 - 4.46 µmol/L
Sample Volume	100 µL
Sample Type	Serum, plasma, urine, saliva, culture supernatants and other biological fluids

NO and iNOS in Rheumatoid Arthritis

Nitric oxide (NO) is a pleiotropic signaling molecule implicated in regulating diverse physiological processes, host defense, immune response, and inflammation.¹ NO is synthesized from L-arginine and O₂ by three nitric oxide synthase (NOS) enzymes, two of which are constitutive [endothelial NOS (eNOS) and neuronal NOS (nNOS)] and one that is inducible [inducible NOS (iNOS)]. iNOS expression can be induced by inflammatory stimuli such as cytokines, microbial components, immune complexes and mechanical stress and is associated with both normal and pathological immune response.¹ Overproduction of NO by iNOS plays an important role in the pathogenesis of rheumatoid arthritis (RA). Elevated levels of NO and proinflammatory cytokines such as IL-1β, IFN-γ, and TNF-α have been observed in the synovial fluid, serum, and urine of patients with RA.^{2,3} The presence of proinflammatory cytokines indicates that iNOS is most likely the isoform responsible for generating these high levels of NO. Indeed, histochemical and *in situ* hybridization studies have confirmed that iNOS is strongly expressed in the cells and tissues of the rheumatoid synovium.⁴⁻⁸

Although the mechanism by which NO mediates joint tissue destruction in RA is unknown, there are many potential contributing activities. These include apoptosis, increasing permeability of the local vasculature, inhibition of chondrocyte-mediated matrix generation, activation of matrix degrading metalloproteinases, modulation of cell-mediated immune response, production of toxic free radicals, and ischemia-reperfusion injury.^{4,8-12} Administration of NOS inhibitors in experimentally-induced arthritis models and in RA patients have resulted in

reduction of synovial inflammation, apoptosis and matrix destruction. For example, treatment of RA patients with an anti-TNF-α monoclonal antibody (cA2) significantly reduced iNOS protein expression and enzyme activity, correlating with clinical improvement of symptoms within a majority of the patients receiving treatment.¹³ In animal models of inflammatory arthritis, the severity of disease can be reduced by the administration of L-N^G-monomethylarginine (L-NMMA), a NOS inhibitor, thus demonstrating the significant role that NO plays in this disease.^{14,15}



Nitric oxide synthases catalyze the production of NO and L-citrulline from L-arginine, O₂, and NADPH-derived electrons.

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Cytokine mRNA Expression in *Rheumatoid Arthritis*

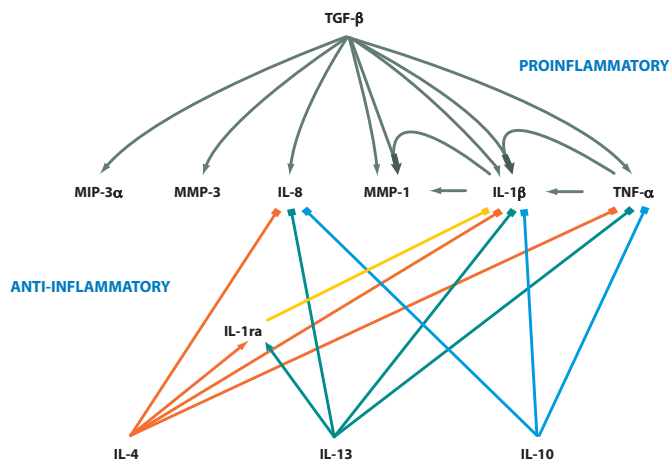
Although the exact cause of rheumatoid arthritis (RA) is still unknown, recent progress has been made in elucidating the roles of cytokines participating in the progression of this putative autoimmune disorder. As this type of arthritis is of an inflammatory nature, much of the current research has focused on the role and balance of both proinflammatory and anti-inflammatory cytokines. Moreover, because some of these cytokines can either direct expression at the mRNA level, or are themselves transcriptionally regulated, the mRNA expression patterns for several cytokines that play a central role in RA have been examined.

Cheon *et al.*¹ recently observed the effects of TGF- β 1, which is abundantly expressed in the rheumatoid synovium, on the mRNA levels of TNF- α , IL-1 β , IL-8, and MIP-1 α , as well as MMP-1 and MMP-3 in cultured fibroblast-like synoviocytes. Although TGF- β 1 has traditionally been thought of as an anti-inflammatory cytokine, this study demonstrates that within the RA synovial membrane, TGF- β 1 acts both alone and in concert with other cytokines to increase the transcription of several genes. By itself, TGF- β 1 was able to induce mRNA expression for all the genes investigated in this study. When TGF- β 1 was used in conjunction with TNF- α , however, IL-1 β expression was enhanced above the levels seen with either TGF- β 1 or TNF- α alone. In turn, IL-1 β was also shown to act synergistically with

TGF- β 1 to increase the expression of MMP-1 to levels not observed with TGF- β 1 or IL-1 β alone. Thus, TGF- β 1 is able to induce mRNA expression for several arthritis-related inflammatory cytokines and chemokines, as well as act in concert with several of these same proteins to further increase expression of additional key genes, such as IL-1 β and MMP-1.

Since many proinflammatory cytokines are expressed in RA tissue (in particular, IL-1 β and TNF- α), an attempt to cancel out the inflammatory challenge is accomplished by the production of cytokines that have the ability to ameliorate or block the effects of the proinflammatory cytokine network. There are a few notable players in this arena, including IL-4, IL-10, IL-13, and IL-1ra (IL-1 receptor antagonist).² IL-4, IL-10 and IL-13 all have the ability to block the production of TNF- α , IL-1 β and IL-8,³ thereby exerting certain anti-inflammatory effects. IL-4 and IL-13 further potentiate their anti-inflammatory effects by inducing IL-1ra,^{3,4} a natural antagonist of IL-1. Interestingly, IL-4 transduces its anti-inflammatory effects by increasing IL-1ra mRNA levels while down-regulating transcription of IL-1 β .⁴

Collectively, the molecules that play a role in RA participate in a fragile balance between inflammation and normal homeostasis. This equilibrium is maintained partially through regulation of mRNA expression.



Cytokines and chemokines interact in a complex fashion in RA tissue and synovium at least partially at the level of transcription.

References

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IFN-γ	EL285
IL-1β	EL201
IL-2	EL202
IL-4	EL204
IL-5	EL205
IL-6	EL206
IL-8	EL208
IL-13	EL213
Latent TGF-β1	EL246
TNF-α	EL210

MOUSE

Analyte	Catalog #
IFN-γ	EL485
IL-2	EL402
IL-4	EL404
IL-6	EL406
IL-10	EL417
TNF-α	EL410

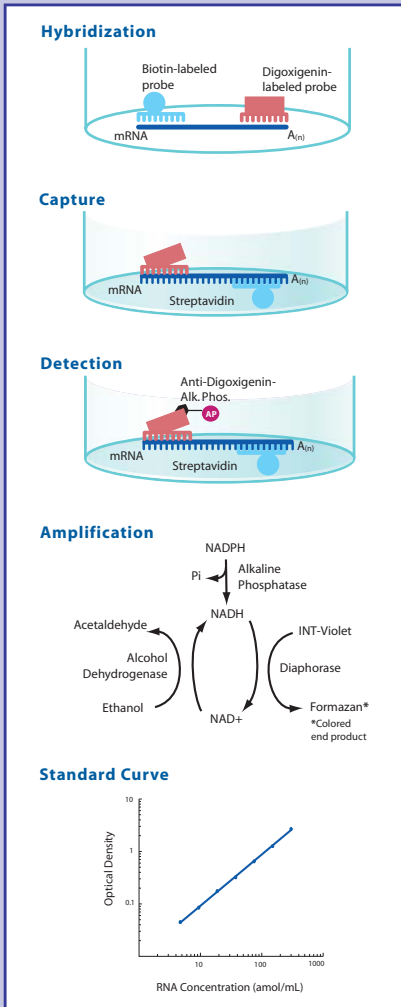
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Probes and Calibrator Kit Contents

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HUMAN

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- COX-2
- CXCR4
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- Fas Ligand/TNFSF6
- GAPDH
- GM-CSF
- ICAM-1 (CD54)
- IFN-γ
- IL-1β
- IL-2
- IL-6
- IL-8/CXCL8
- IL-10
- MCP-1/CCL2
- MIP-1α/CCL3
- iNOS
- p21
- p53
- RANTES/CCL5

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- IL-2
- KC
- iNOS
- TNF-α
- VEGF

RAT

- IL-1β
- GAPDH
- KC
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