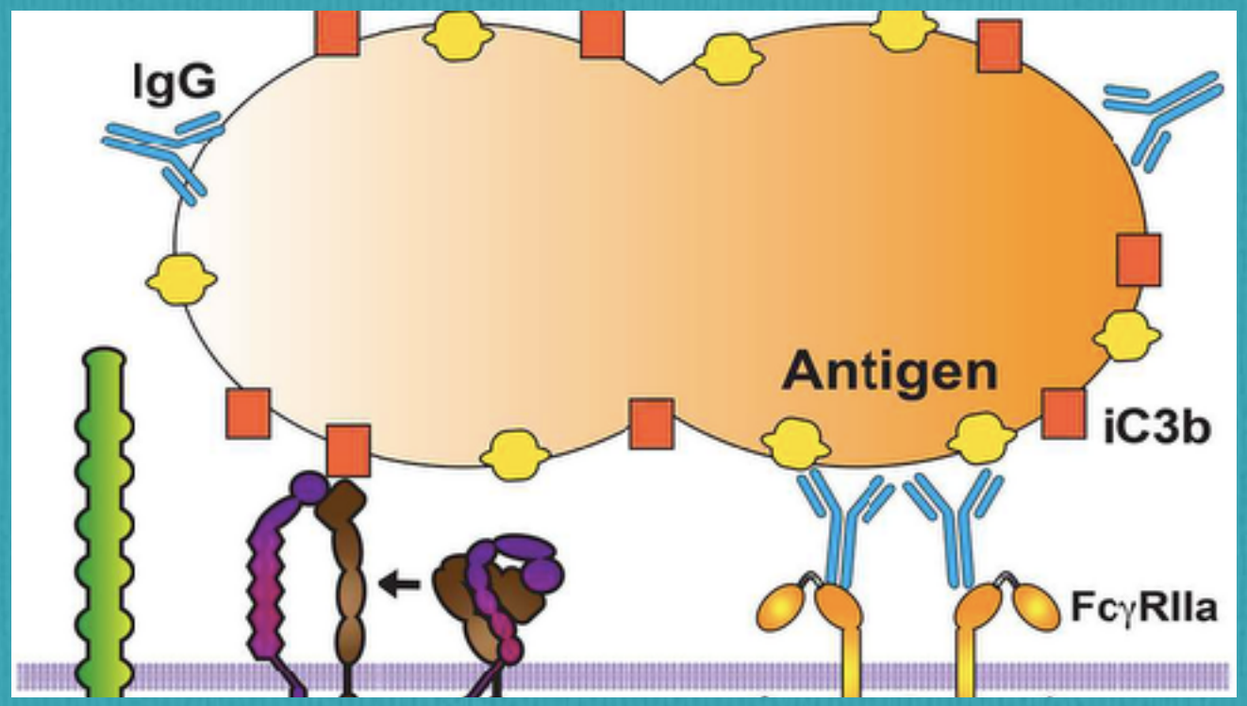
Programa de Pôs-graduação em Imunologia ICB/USP

Disciplina BMI 5904
Reconhecimento no Sistema Imune

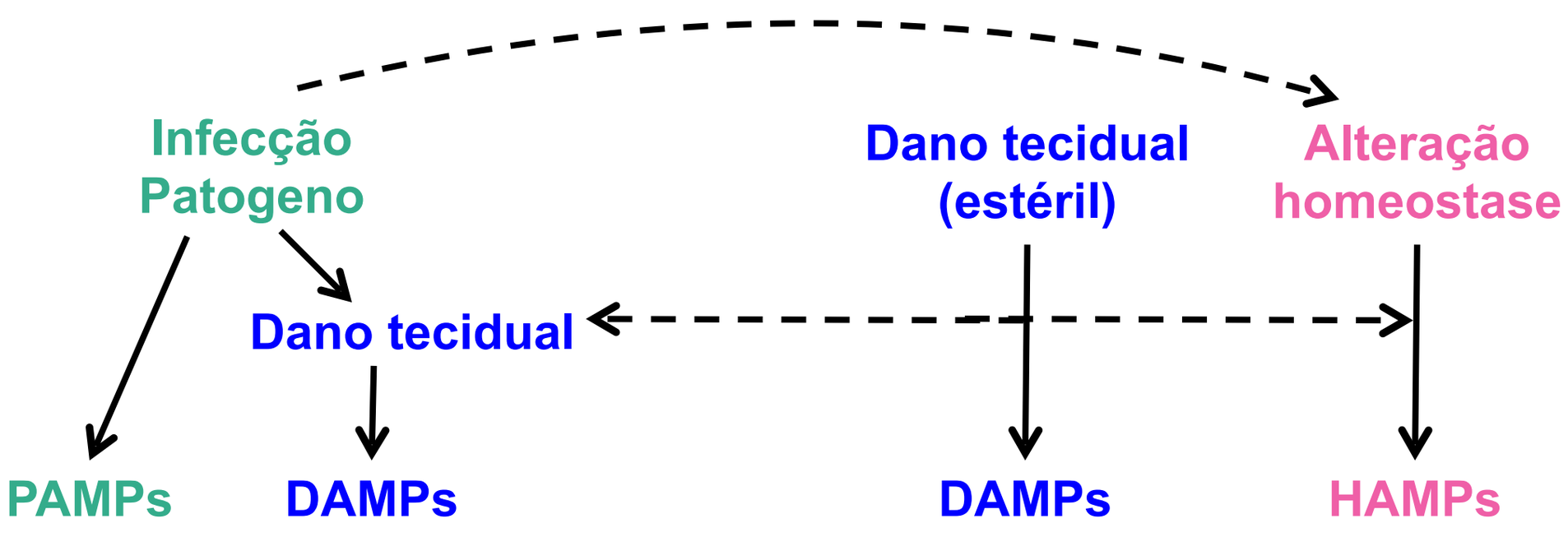


Aula 2

Alessandra Pontillo

Lab. Imunogenetica/Dep.Imunologia/ICB/USP

Reconhecimento de padrões

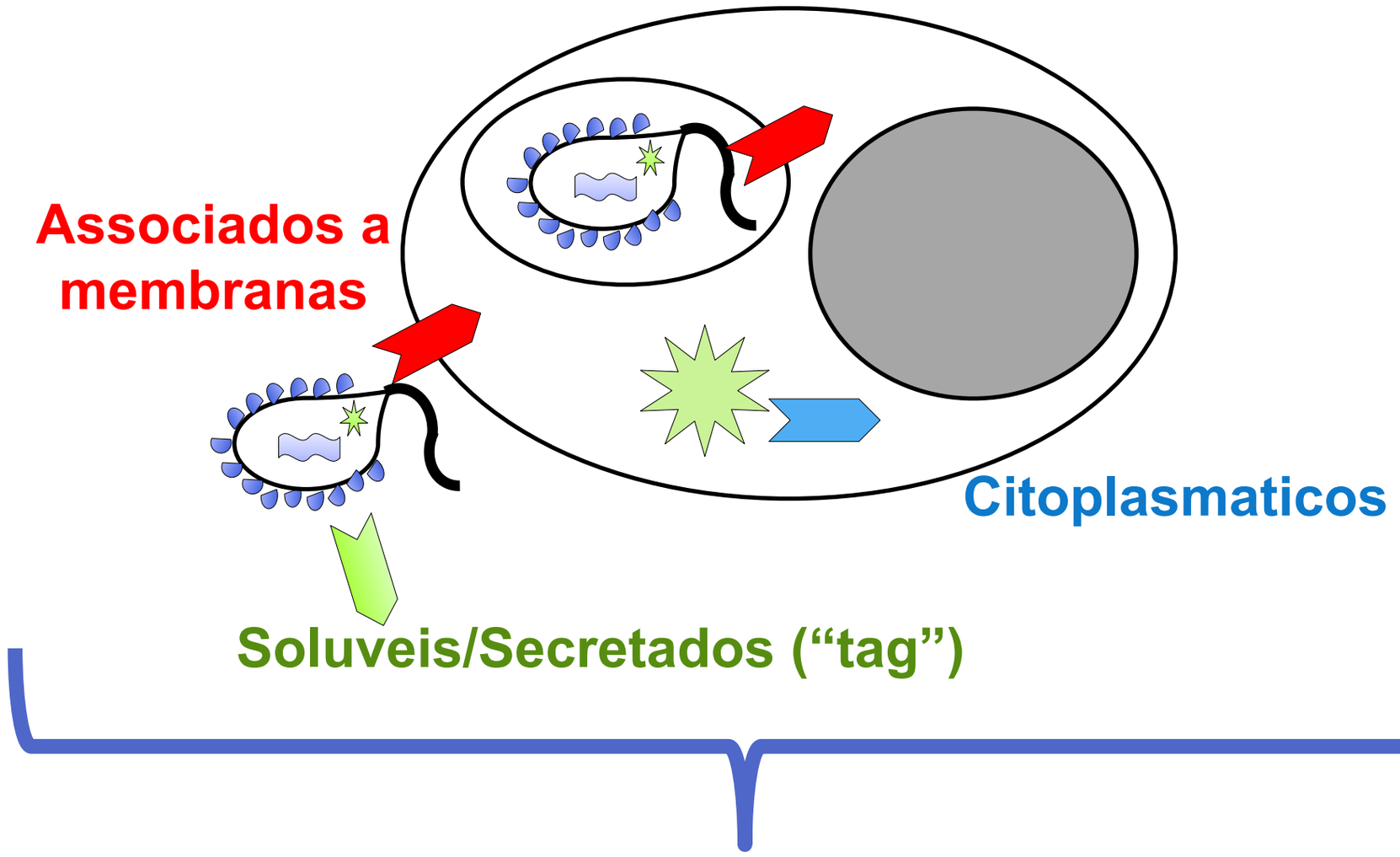


Sistema imune inato = "orgao de percepçao"

Reconhecimento feito por quase todas as celulas somaticas

Receptores de reconhecimento de padrões: PRRs

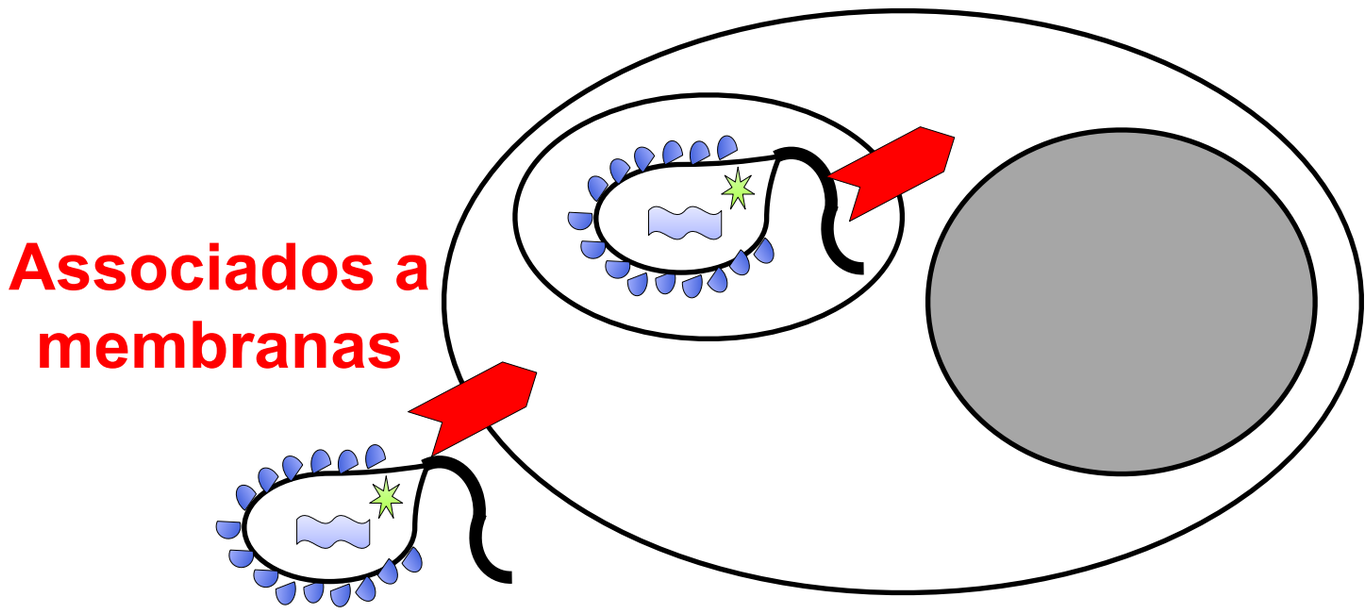
PRRs



Ativação do sistema imune inato

- Fagocitose
- Mediadores inflamatorios
- IFN tipo 1
- Ativação complemento
- Opsonização
- Neutralização, aglutinação
- Morte da célula infectada/danificada

PRRs



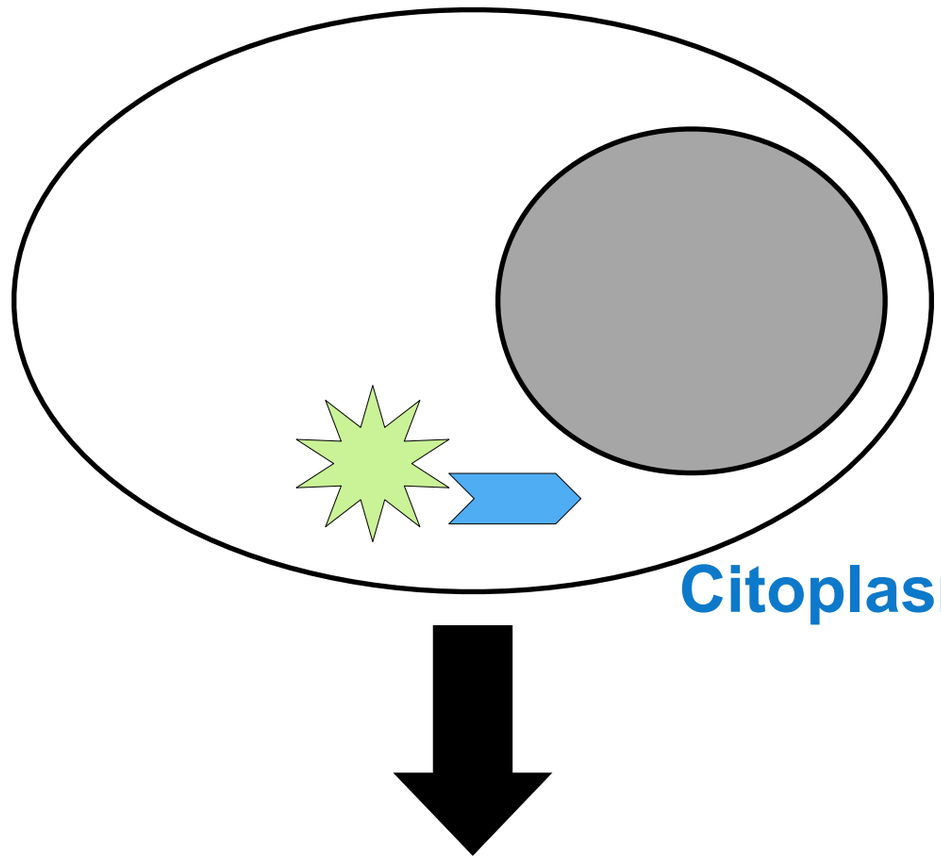
RECEPTORES DE FAGOCITOSE

Receptores de carboidratos (CLRs)
Receptores Scavenger

RECEPTORES DE SINALIZACAO

TLRs

PRRs



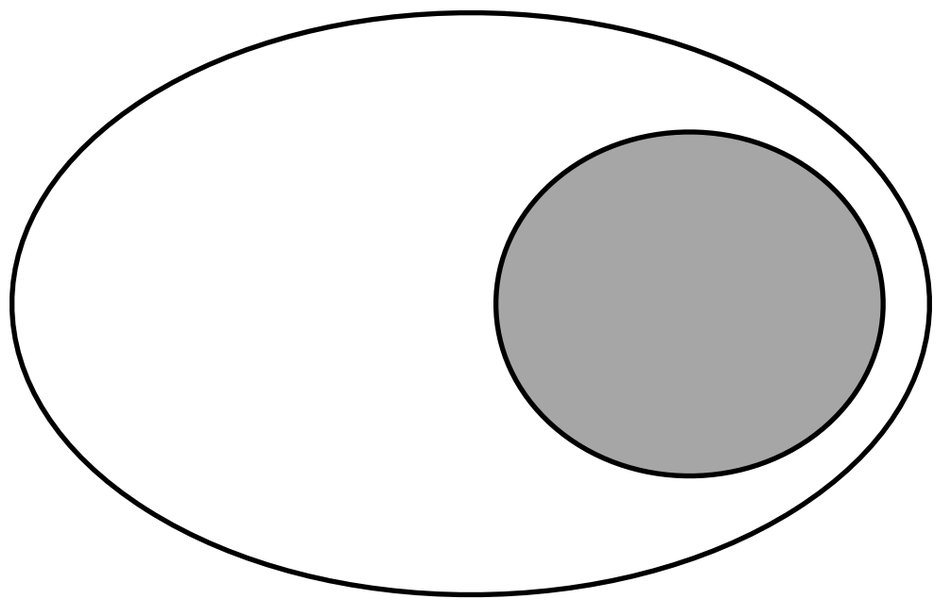
Citoplasmaticos

RECEPTORES DE SINALIZACAO

NACHT and LRRs containing receptors (NLRs)
PYD and HIN containing receptors (PYHIN)
RIG-like receptors (RLRs)

morte (da célula infectada)

PRRs



Soluveis/Secretados (“tag”)

PRMs

ATIVACAO S. COMPLEMENTO

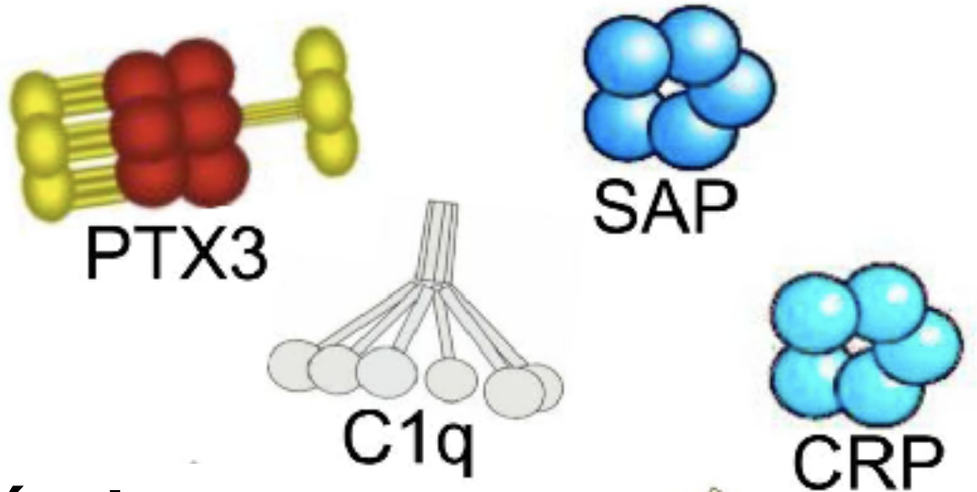
MBL, ficolin
C1q, C3

OUTRAS FUNÇÕES

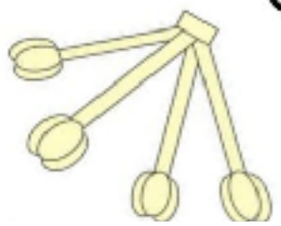
- neutralização
- agglutinação
- opsonização

PRMs & Imunidade inata humoral

PENTRAXINAS



Moléculas de reconhecimento de padrões (PRMs)



FICOLINAS

COLECTINAS

MBL, SP-A, SP-D

Reconhecimento de patogeno/ celula danificada (circulante/tecidual)

- **Sistema complemento**
- **Opsonização (fagocitose)**
- **Aglutinação**
- **Neutralização**
- **Prevenção expansão viral**

PRMs

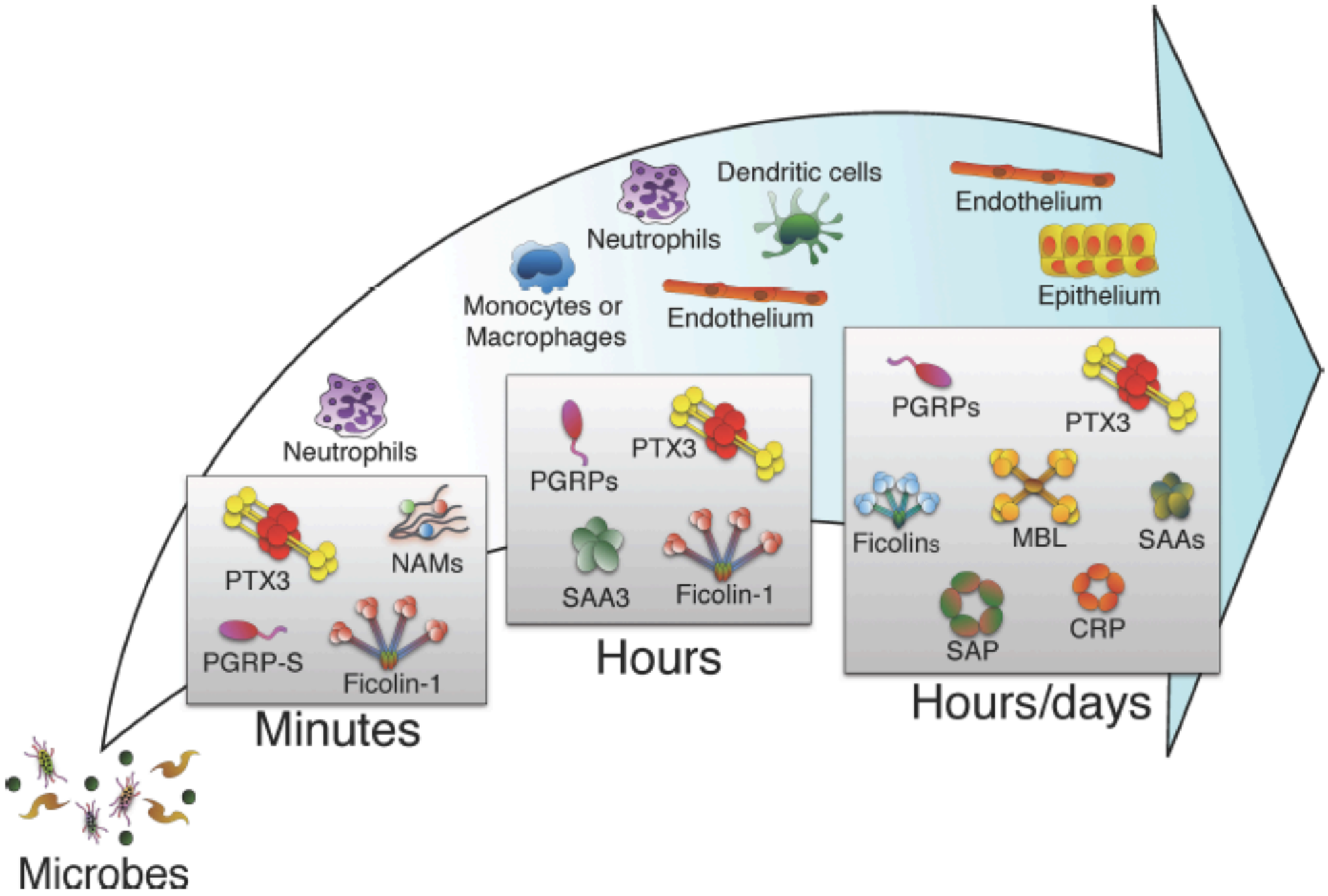
PRMs	Locus	PAMP/DAMP	Origem
Pentraxinas Short: SAP, CRP Long: PTX3	Plasma	Carboidratos, Fibras amiloide Material nuclear Proteinas da ME	Bacteria/Parasitas Celulas mortas/ danificadas
Colectinas (MBL, SP-A/D)	Plasma (MBL) Alveolo (SPs)	Carboidratos (Man) Material nuclear	Bacteria/virus/fungo Celulas mortas
Ficolinas (Ficolina)	Plasma	Carboidratos (GlcNAc, SA)	Microbios Celulas mortas
Complemento (**C1q**, C3)	Plasma	Superficie microbiana	

PRMs

PRMs	Produçao	Orgao/celula
Pentraxinas **Short:** SAP, CRP **Long:** PTX3	**Infecçao/inflamaçao** IL-6 IL-1ß, TNF, TLR-agonists	Figado/hepatocitos PMN, Mø, DC
Colectinas (MBL, SP-A/D)	**Consitutiva** **Infecçao/inflamaçao** Citocinas proinflamatorias	Figado/hepatocitos Mø (?)
Ficolinas (Ficolina)	**Consitutiva** **Infecçao/inflamaçao** Citocinas proinflamatorias	
Complemento (**C1q**, C3)	**Consitutiva** **Infecçao/inflamaçao** Citocinas proinflamatorias	Figado/hepatocitos PMN, Mø, DC

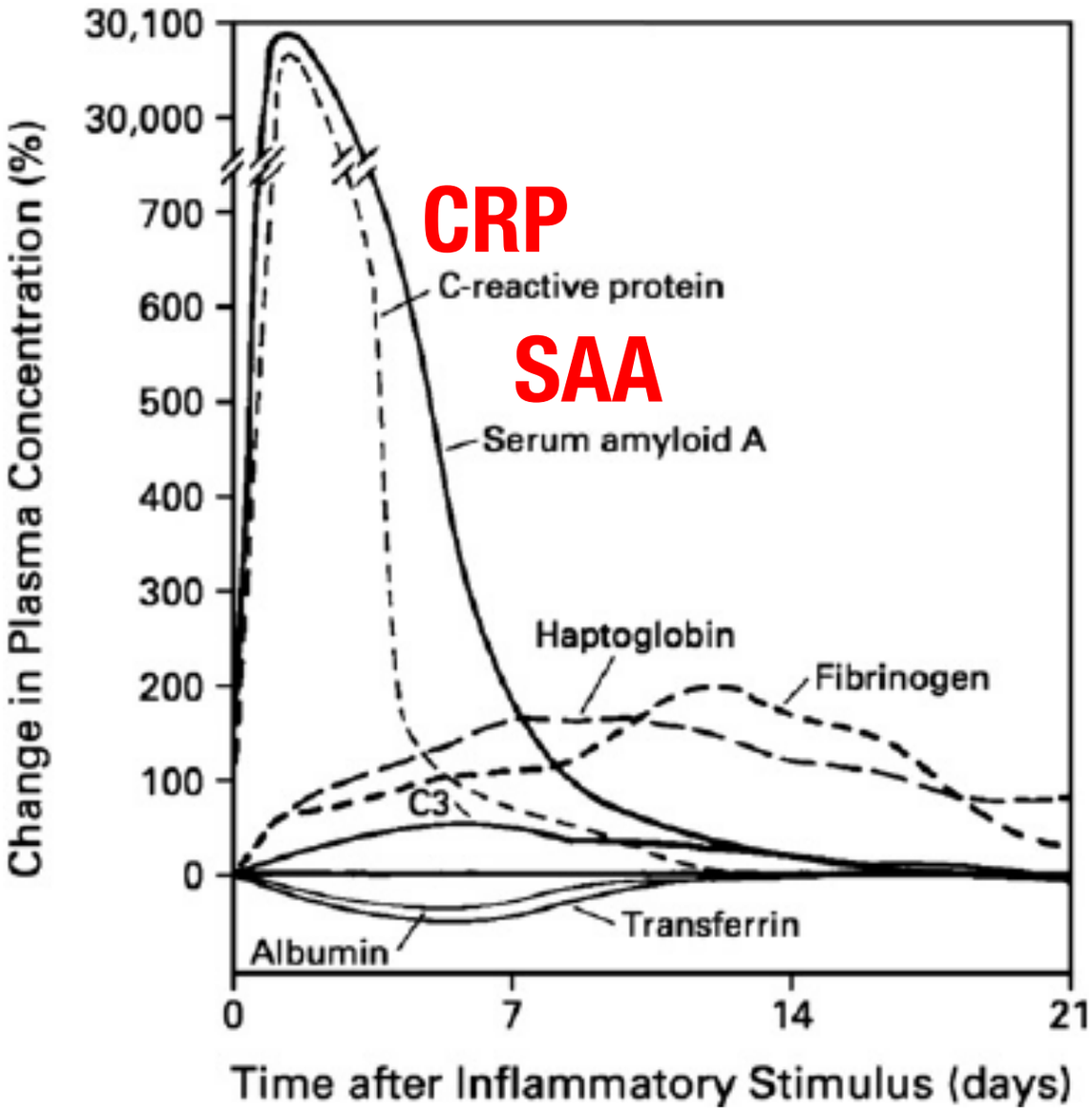
PRMs

expressos e secretados por varias células, incluindo as c. mieloides, permitindo a produção alongo do tempo



Jaillon, …., Mantovani 2017

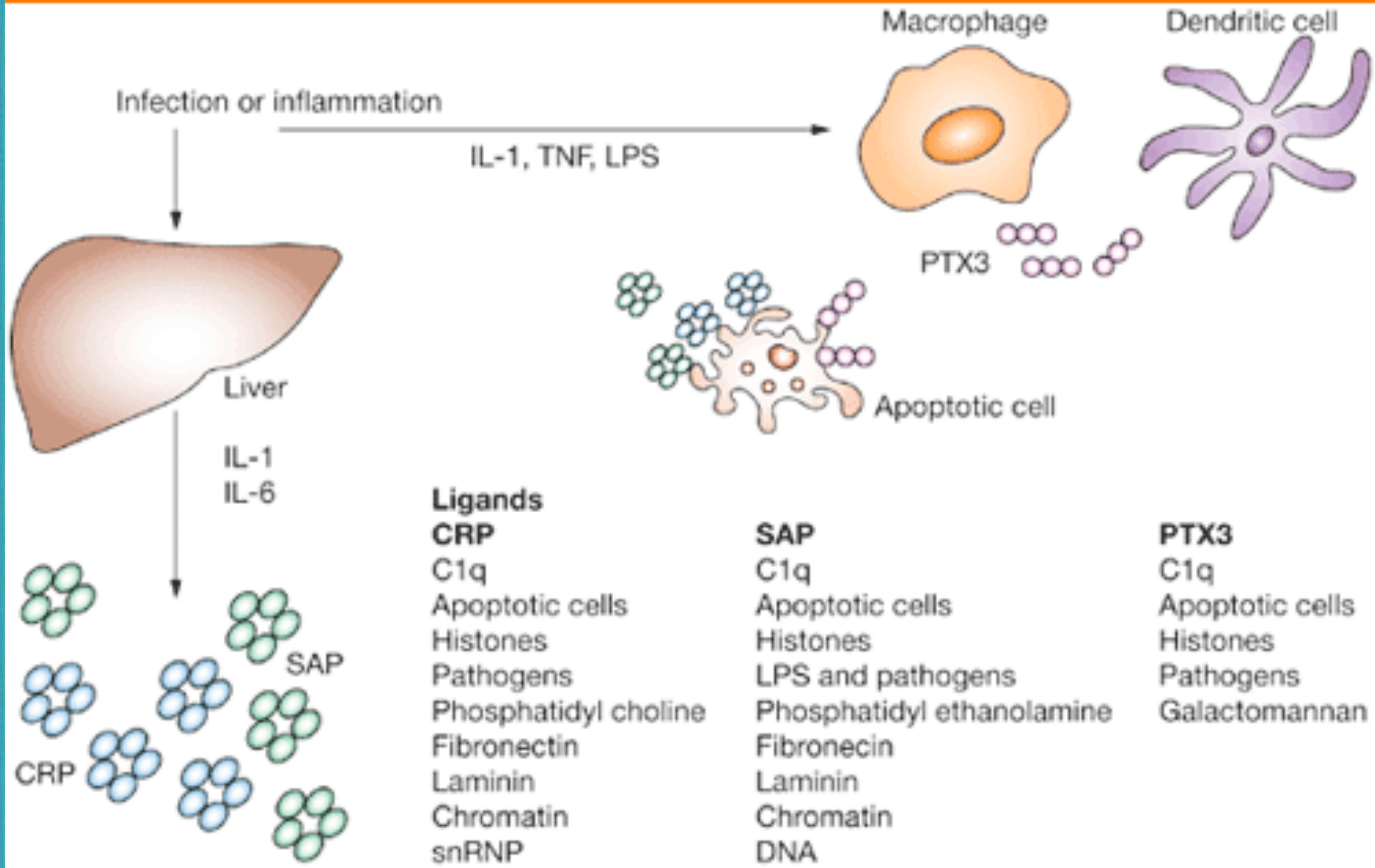
Moléculas da “fase aguda”



PRMs

PRMs	Expression sites	Ligands	Activities
Collectins (MBL, SP-A, SP-D)	Liver (hepatocytes) Lung (type II alveolar cells)	Microorganisms (bacteria, fungi, viruses) and microbial moieties (LPS, LTA, LOS, PDG) Carbohydrates and lipids exposed on pathogens (gp55, viral glycoprotein envelopes)	Activation and regulation of the complement system Opsonic activity
Ficolins	Liver (hepatocytes) Lung (type II alveolar cells) Myeloid cells (neutrophils, monocytes, macrophages)	Microorganisms (bacteria, fungi, viruses) and microbial moieties [LPS, LTA, β-(1, 3)-D-glucan] Carbohydrates	Activation and regulation of the complement system Opsonic activity Inhibition of viral infectivity
Short pentraxins (CRP, SAP)	Liver (hepatocytes)	Microorganisms (bacteria, fungi, viruses) and microbial moieties (phosphorylcholine [CRP], LPS [SAP]) Complement components Apoptotic cells Phosphorylcholine, carbohydrates Extracellular matrix protein (fibronectin, collagen IV, laminin, proteoglycan) Amyloid fibrils	Activation and regulation of the complement system Opsonic activity (controversial data) Elimination of apoptotic cells
Long pentraxin PTX3	Myeloid cells (neutrophils, monocytes, macrophages, dendritic cells) Epithelial cells Endothelial cells Fibroblasts Adipocytes	Microorganisms (bacteria, fungi, viruses) and microbial moieties (OmpA) Complement components Extracellular matrix protein (Iαl, TSG-6, fibrin) Plasminogen	Activation and regulation of the complement system Opsonic activity Inhibition of viral infectivity Elimination of apoptotic cells Matrix remodeling Fibrinolysis Regulation of P-selectin-dependent leukocyte recruitment
SAA	Liver (hepatocytes) Myeloid cells (monocytes, macrophages) Synovial cells Adipocytes	Microorganisms (bacteria, viruses) and microbial moieties (Omp)	Opsonic activity Inhibition of viral infectivity
PGLYRPs	Epithelial cells Liver Neutrophils	Bacteria PDG	Bactericidal activity

Jaillon, …., Mantovani 2017



Ligands

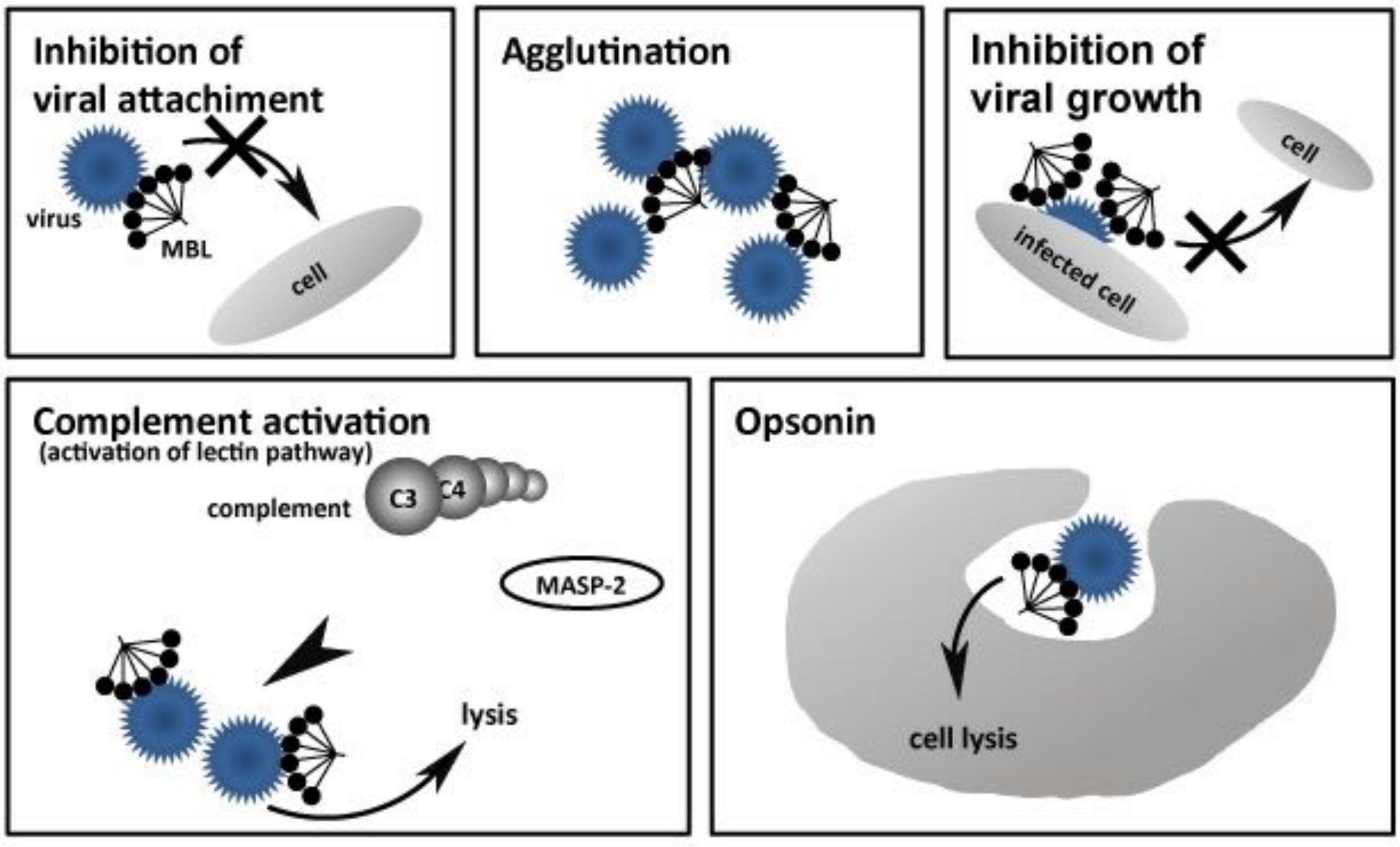
CRP	SAP	PTX3
C1q	C1q	C1q
Apoptotic cells	Apoptotic cells	Apoptotic cells
Histones	Histones	Histones
Pathogens	LPS and pathogens	Pathogens
Phosphatidyl choline	Phosphatidyl ethanolamine	Galactomannan
Fibronectin	Fibronecin	
Laminin	Laminin	
Chromatin	Chromatin	
snRNP	DNA	

Source: Nat Clin Pract Oncol © 2006 Nature Publishing Group]

Ações das PRMs

- Neutralização
- Prevenção expansão viral
- Aglutinação

- Ativação S. complemento
- Opsonização (fagocitose)

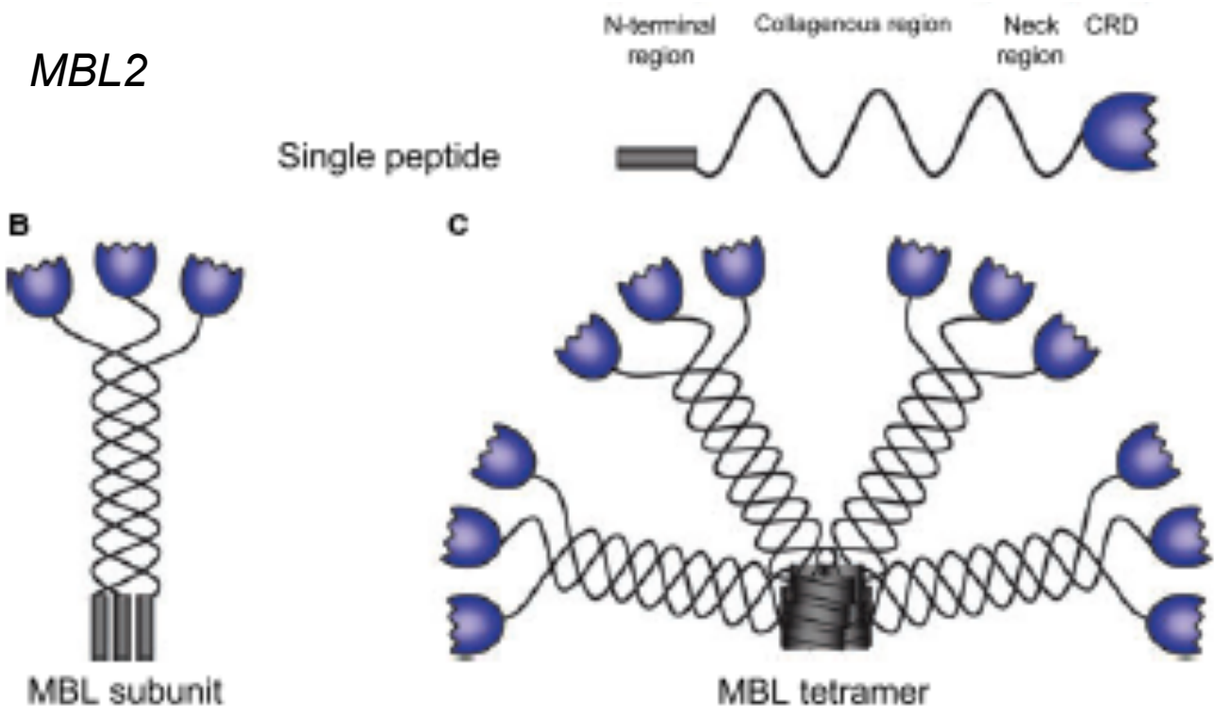


Mannose-binding lectin (MBL)

Lectina ligadora de manose

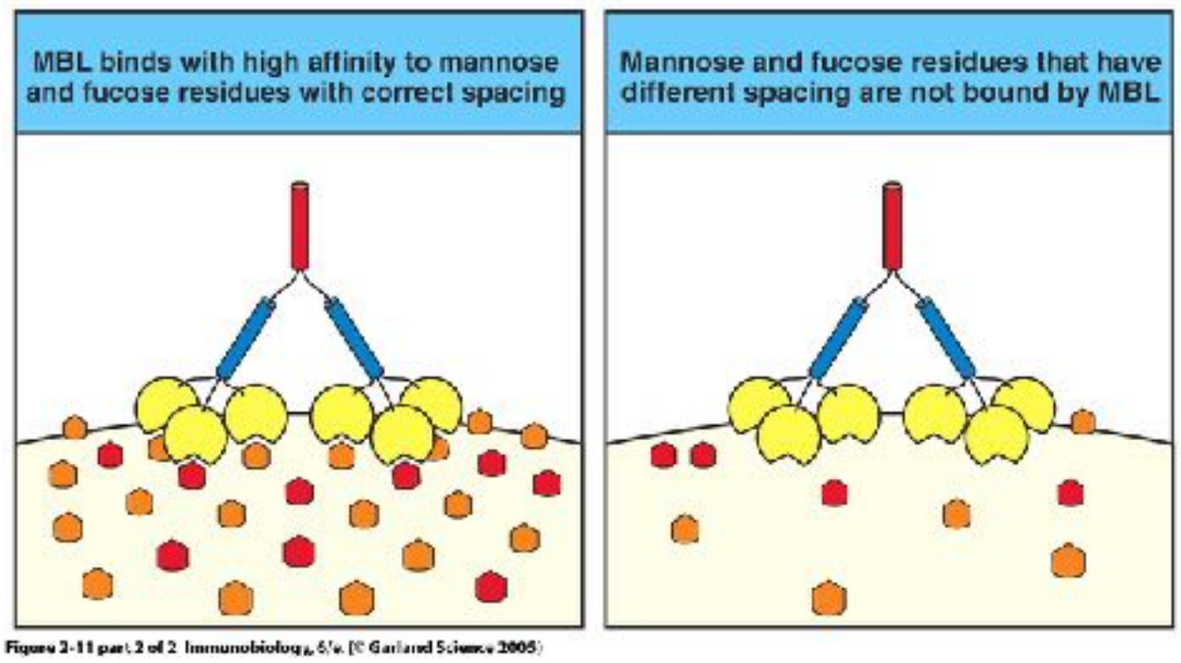
- Proteína do soro (opsonina)
- 3 cadeias polipeptídicas formam a subunidade
- Presente como multímero de trimeros (400-700 kDa)
- Sintetizada no fígado
- “proteína de fase aguda”
- Pode aumentar ate 3x em 1-2 semanas

MBL2



Immunological Reviews 230/2009

Reconhece padrões de mannose, fucose e N-AGA em especifica orientação espacial típica dos micróbios

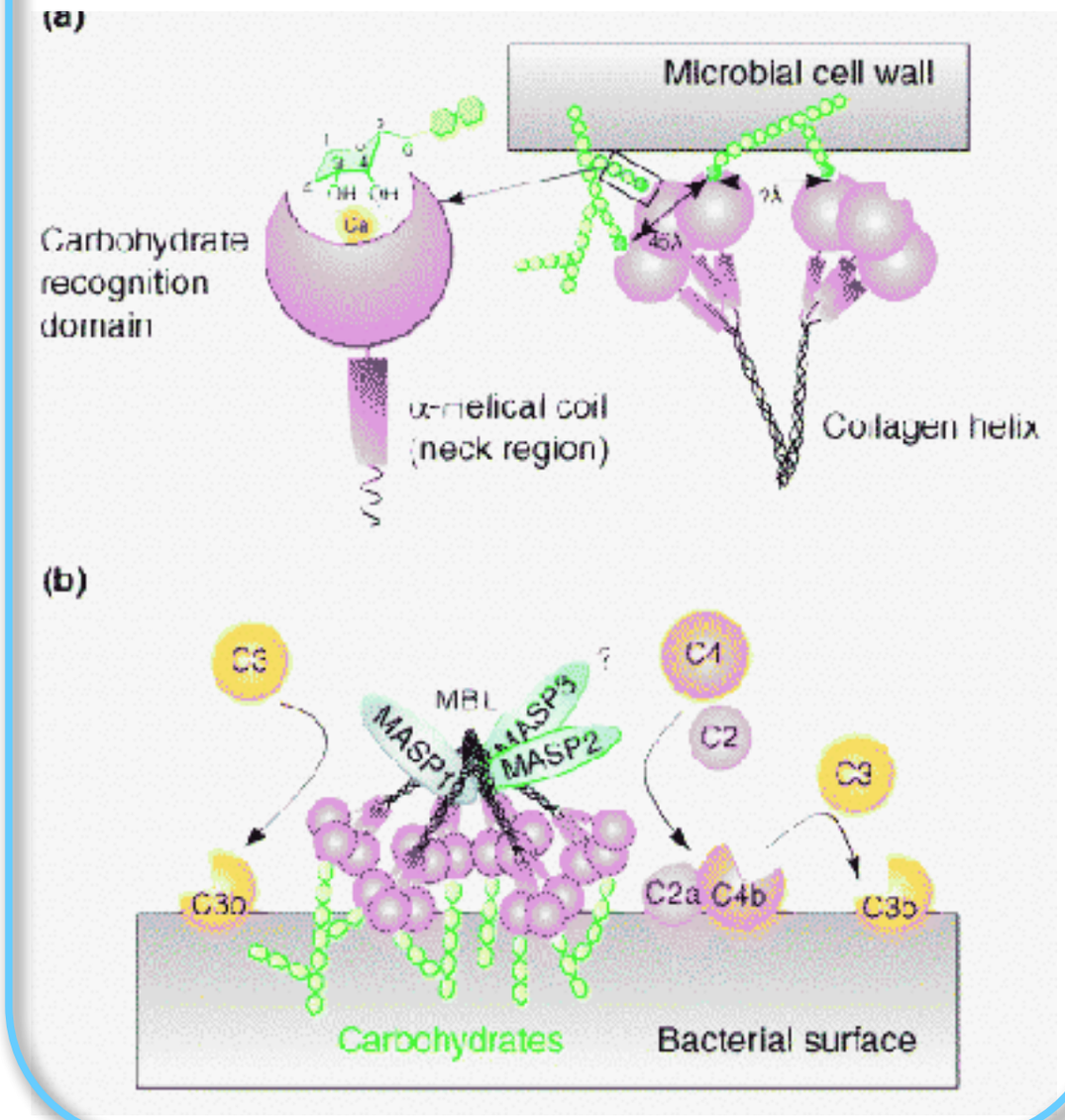


Janaway 8th ed

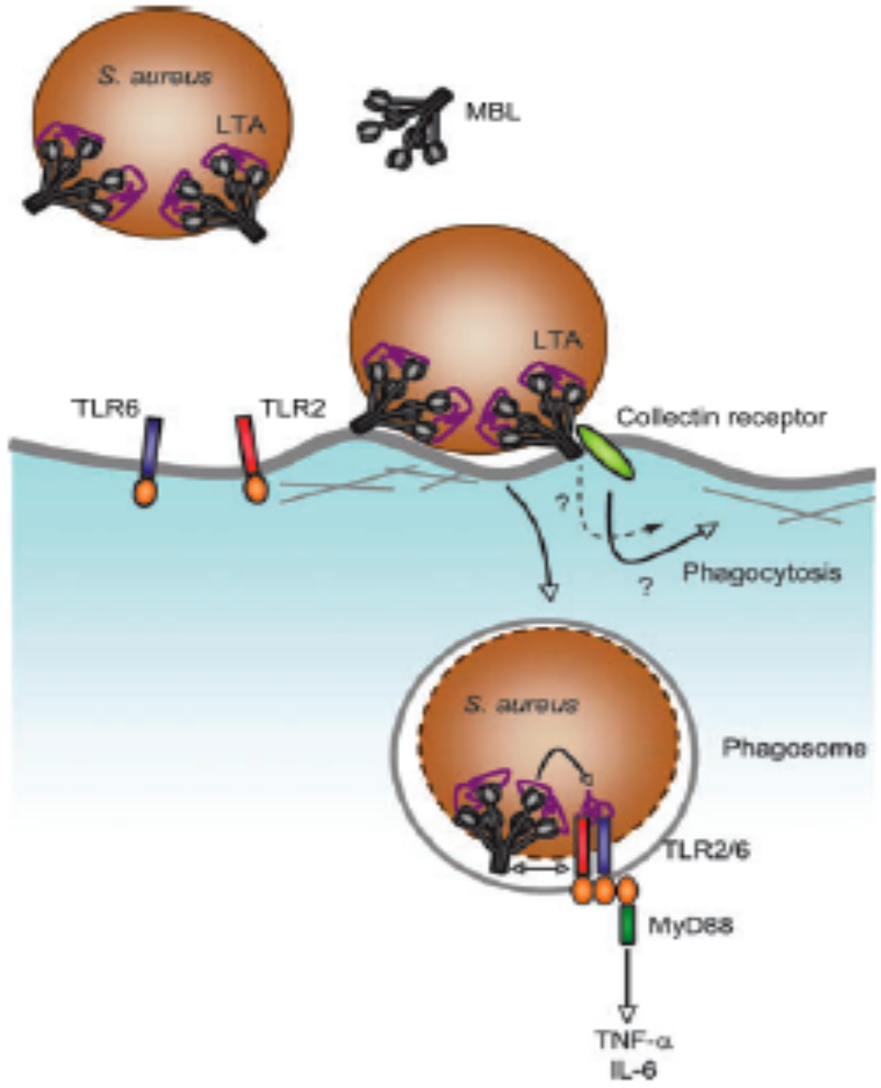
Mannose-binding lectin (MBL)

liga carboidratos (manose) na superficie do patógeno

-inicia a via lectinica do sistema do complemento



- liga o receptor C1qRp na superficie dos fagocitos e age como opsonina



Immunological Reviews 2009

Mannose-binding lectin (MBL)

Table 1 Some clinically relevant microorganisms recognized by MBL

Bacteria	Viruses	Fungi	Protozoa
Staphylococcus aureus	HIV-1 and 2	*Aspergillus fumigatus*	*Plasmodium falciparum*
Streptococcus pneumoniae	Herpes simplex 2	*Candida albicans*	*Cryptosporidium parvum*
Streptococcus pyogenes	Influenza A	*Cryptococcus neoformans*	*Trypanosoma cruzi*
Enterococcus spp.	Hepatitis B virus	*Saccharomyces cerevisiae*	
Listeria monocytogenes	Hepatits C virus		
Haemophilus influenzae			
Neisseria meningitidis			
Neisseria gonorrhoeae			
Escherichia coli			
Klebsidla spp.			
Pseudomonas aeruginosa			
Salmonella montevideo			
Salmonella typhimurium			
H pylori			
Chlamydia trachomatis			
Chlamydia pneumonia			
Proprionibacterium acnes			
Mycobacterium avium			
Mycobacterium tuberculosis			
Mycobacterium leprae			
Leishmania chagasi			

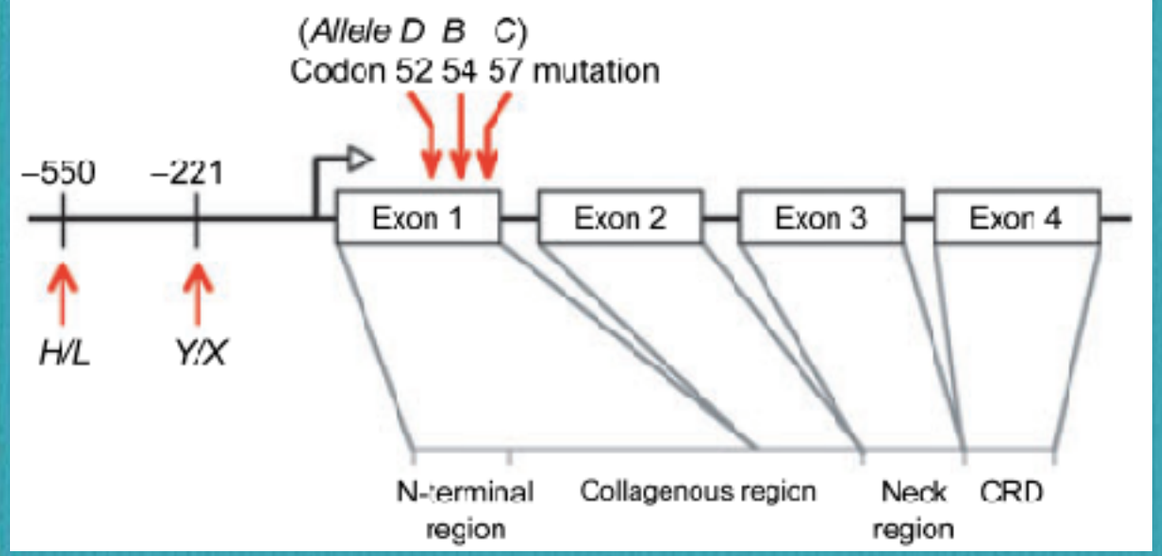
Table 1

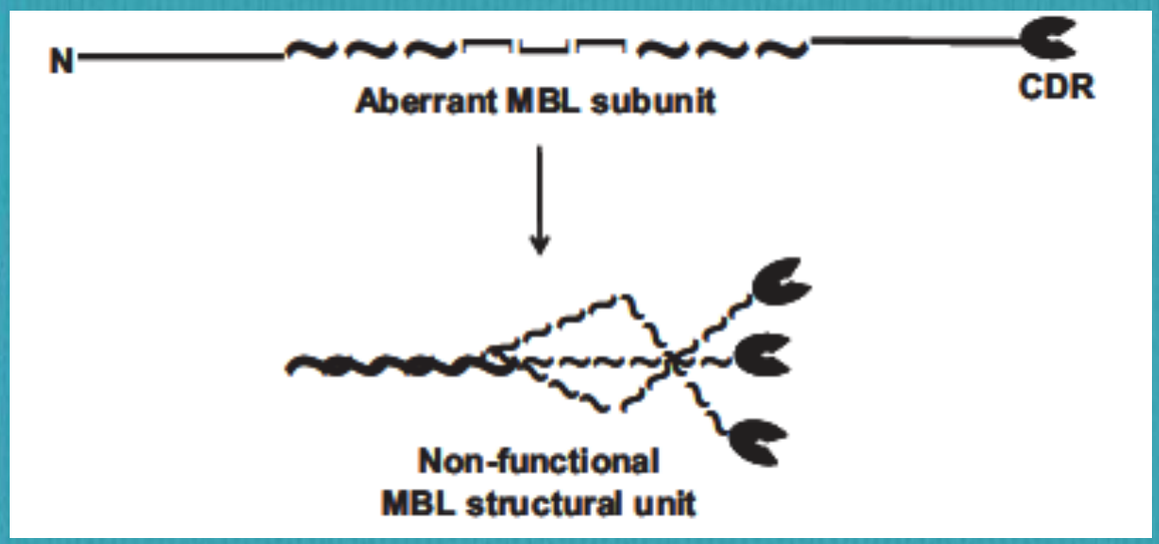
The endogenous ligands of MBL.

Endogenous ligands of MBL
Dying cells
Apoptosis
Necrosis
Ischemic tissues
Myocardial reperfusion injury
Renal reperfusion injury
Gastrointestinal reperfusion injury
Anoxic endothelia cells
Endothelial oxidative stress
Transformed cells
Colon adenocarcinoma
Colorectal carcinoma
Immunogloublins
Agalactosyl IgG
Dimeric/polymeric IgA
IgM
Nucleic acids
DNA
RNA
Phospholipids
Phosphatidylserine
Phosphatidylinositol
Phosphatidylcholine
Zinc metalloproteases
Meprin α and β

MBL: protege mesmo?

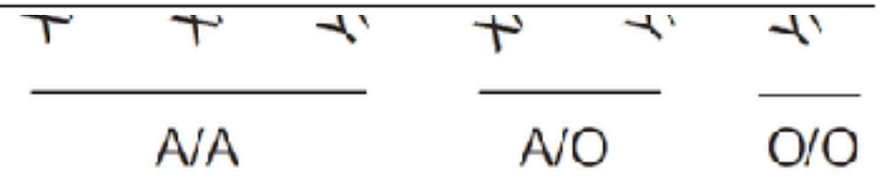
Variantes perda-de-função no gene MBL2





Haplotype	Common reference	Phenotype (MBL production)
HYA	A	High
LYA	A	High/intermediate
LXA	A	Low
HYD	D	Deficient
LYB	B	Deficient
LYC	C	Deficient

Genotype	Common reference	Phenotype (MBL production)
HYA/HYA HYA/LYA HYA/LXA LYA/LXA	HP	High
LXA/LXA HYA/O LYA/O	LP	Low
LXA/O O/O	DF	Deficient

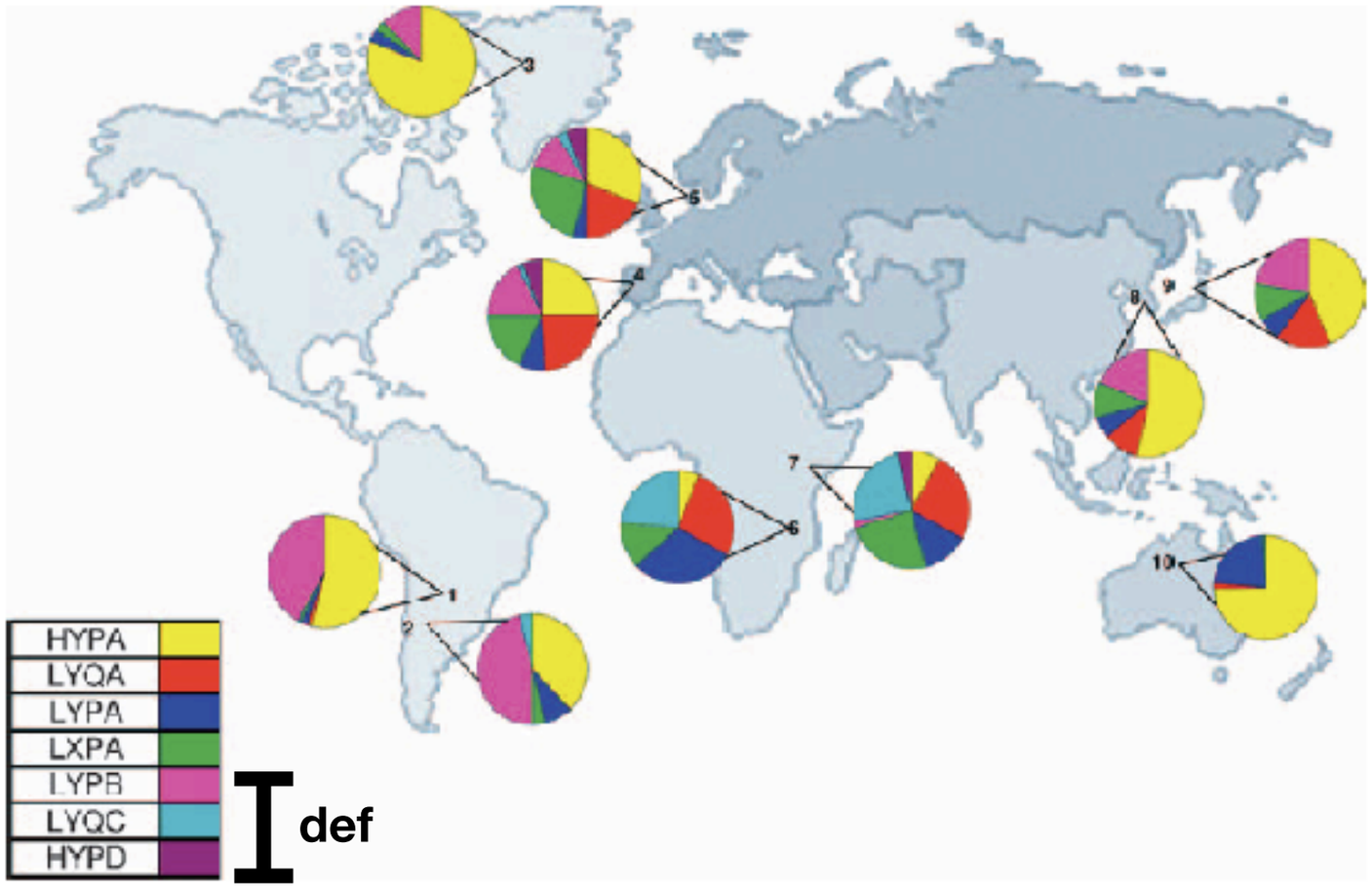


Bouwman, Human Immunology, 2006

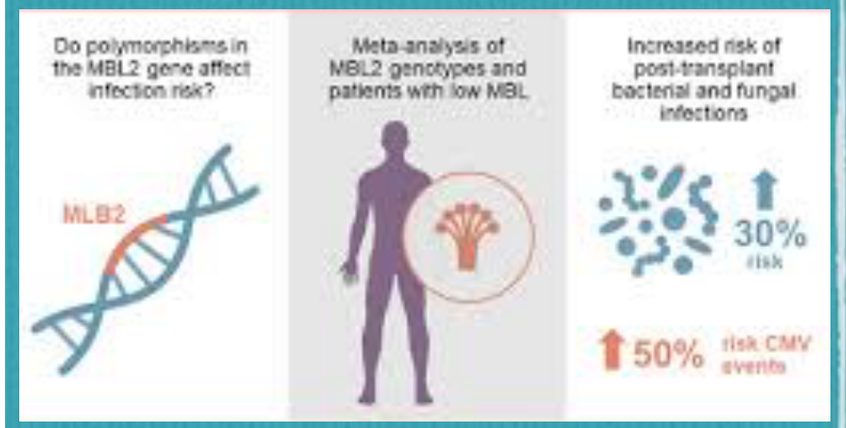
Immunological Reviews 2009

MBL: protege mesmo?

Distribuiçao mundial dos SNVs



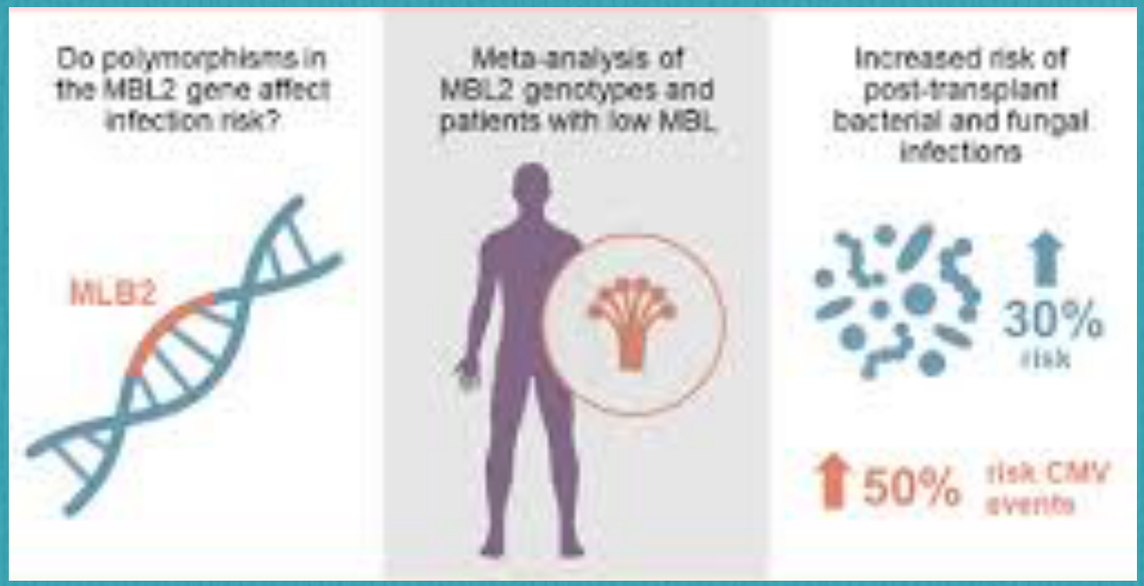
Deficiencia de MBL:
25% população mundial



Deficiencia de MBL: como afeta a resposta imune?

MBL: protege mesmo?

Deficiencia de MBL:
25% população mundial

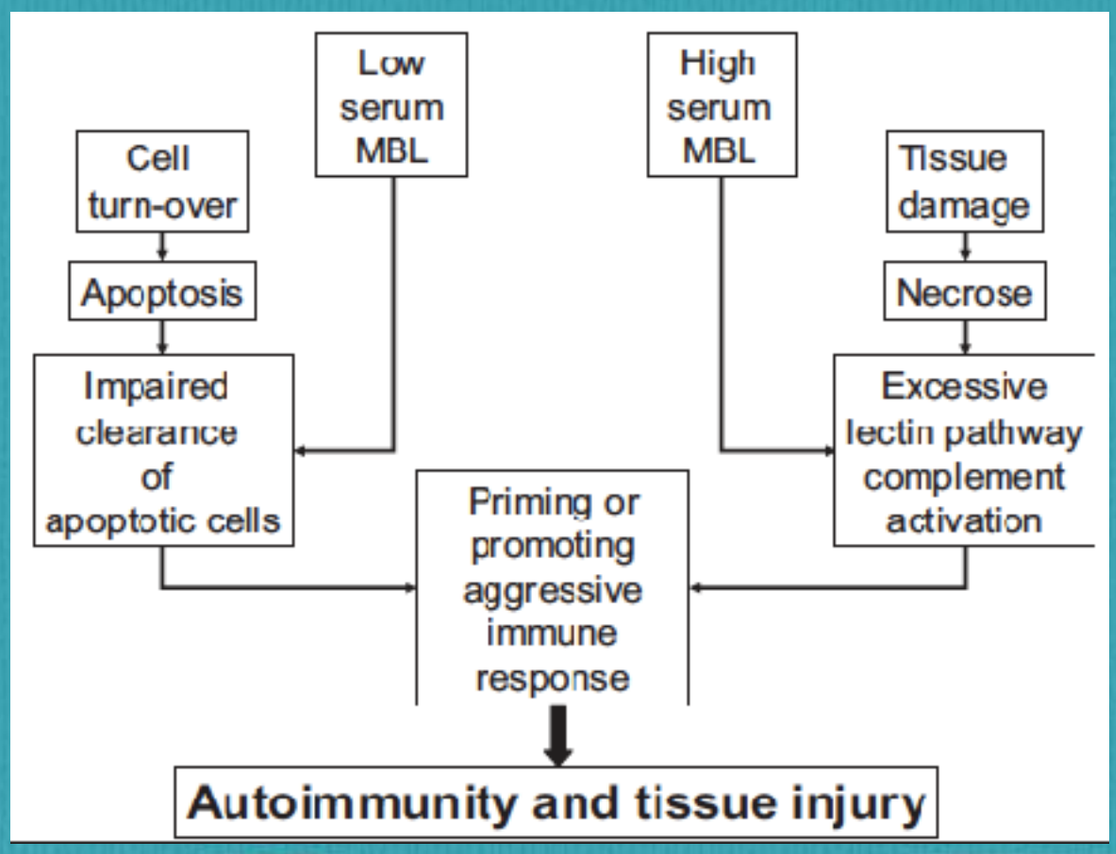


↑ infecçoes respiratorias (pneumococco)

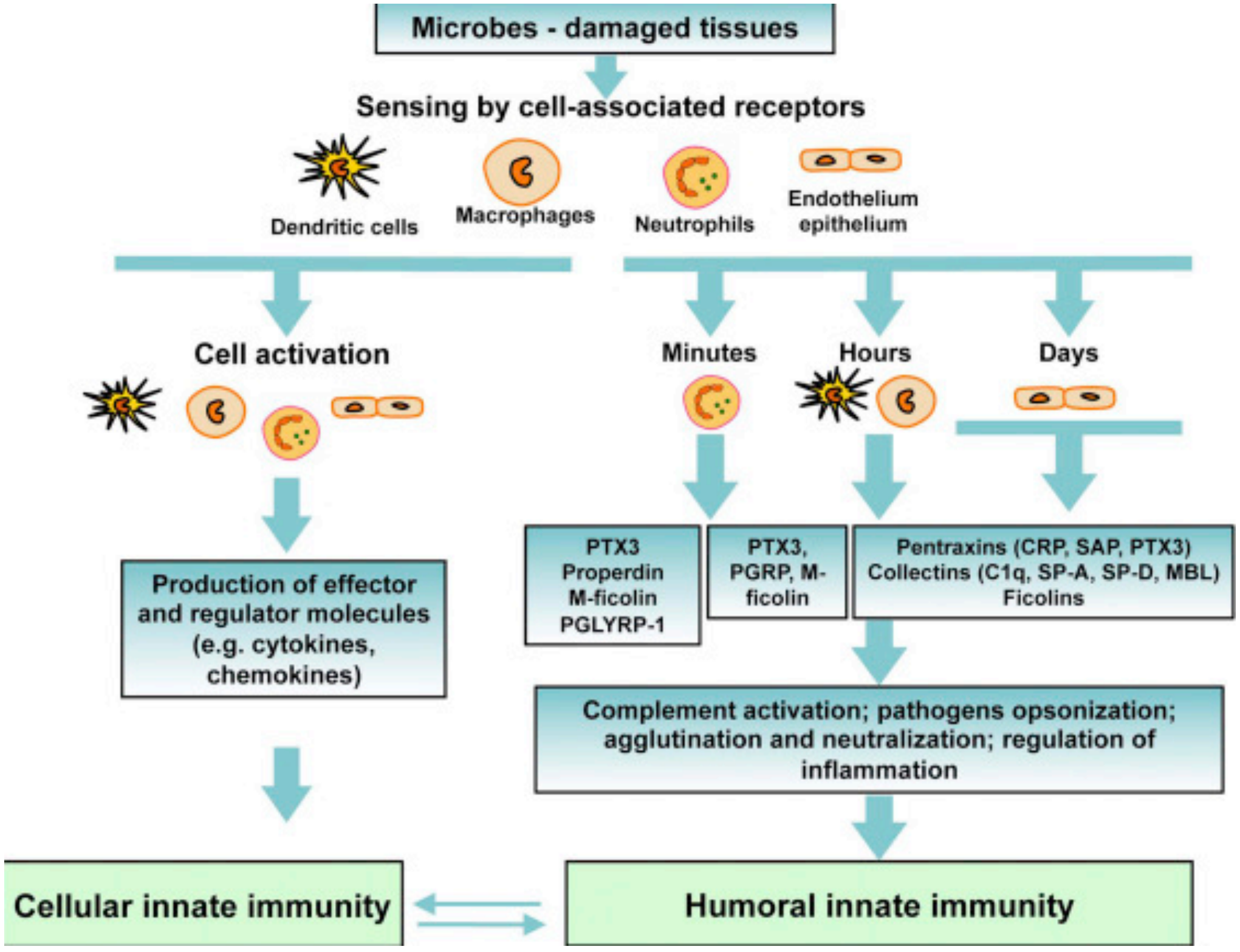
The Lancet, Vol. 359, No. 9317, p1569–1573
Published: May 04, 2002

↓ TB

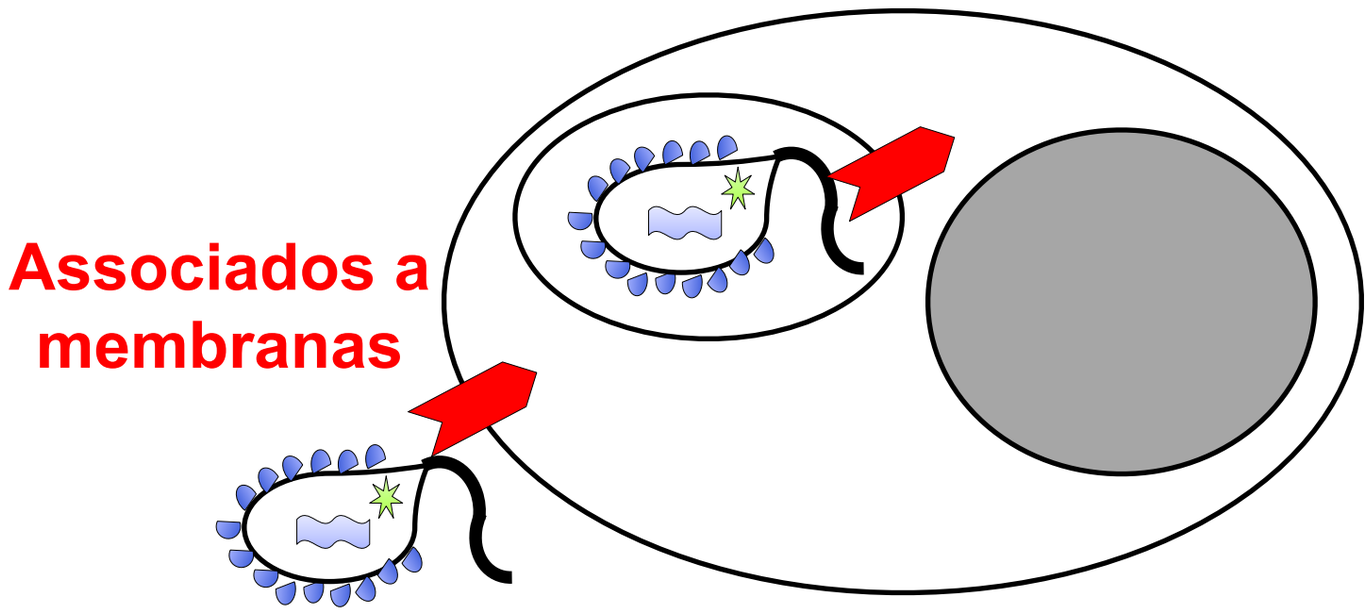
Impairment of dead cells removal



Acoes das PRMs



PRRs



Receptores de carboidratos (CLRs)
Receptores Scavenger

TLRs

Fagocitose, endocitose (Cytotoxicity in NK)

Sinalização intracelular

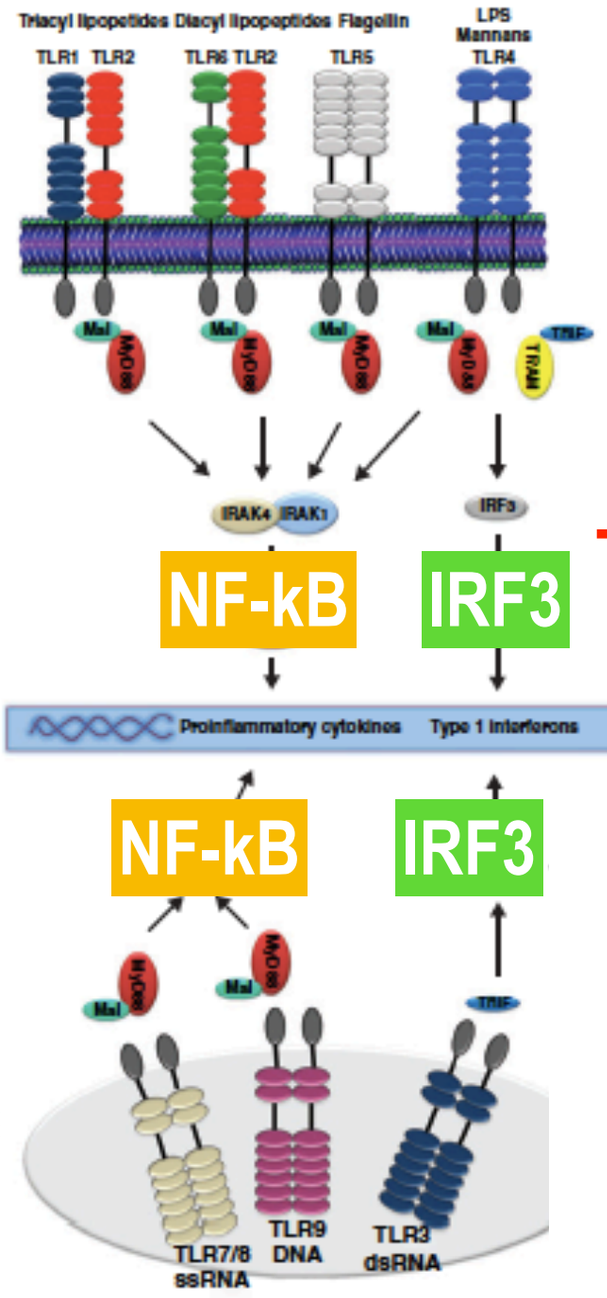
Inflamação

Ação anti-viral

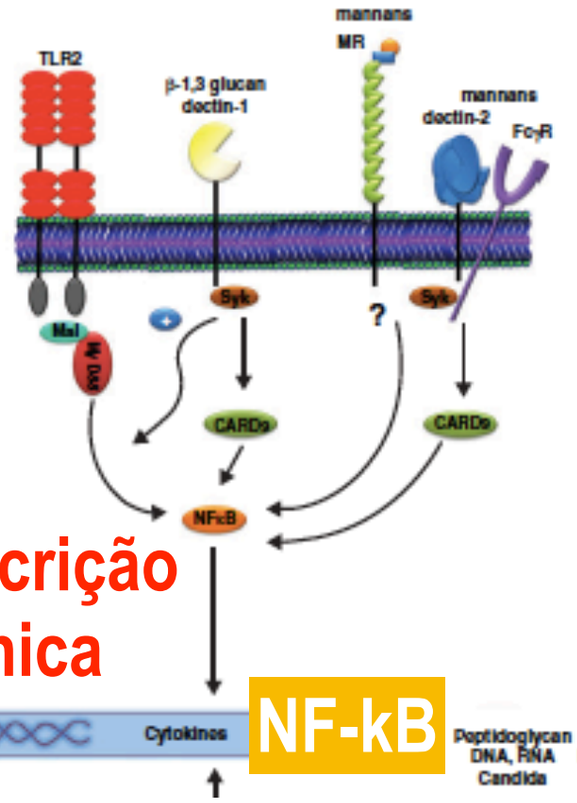
Ativação Im adaptativa

Receptores & Sinalização

TLRs



CLRs



Scavenger Rec

non PRRs (opsonin Rec)

Citosolic Rec

TLRs

Netea. Curr.Op.Pharmacol 2011

Receptores & Sinalização

Respostas rápidas

NF-kB

IRF3

Proinflammatory cytokines Type 1 interferons

IFN-I

IFNRs

Fatores de restrição viral

Resposta antiviral

Resposta inflamatoria

IL-6R **TNFR** **IL1R**

AP-1

NF-kB

SOCS

Inflamassoma

Moleculas antimicrobianas
Enzimas
Citocinas, Quimiocinas
Sist.Complem., APPs

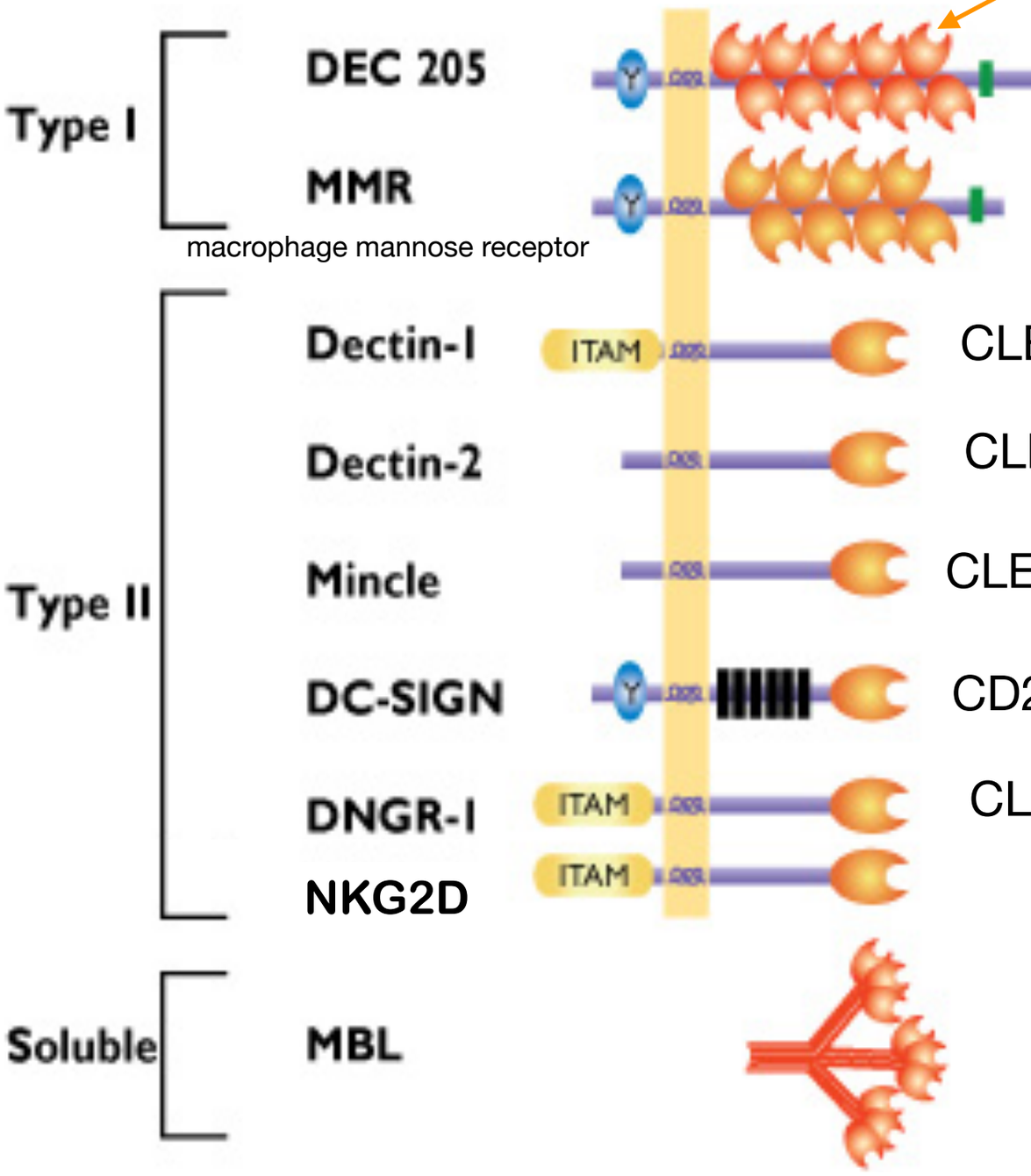
IL-1ß
IL-18
TNF
IL-6

Receptores semelhantes a lectina tipo C (CLRs)

Glu-Pro-Asn (EPN) **Manose**

C-type lectin domain (CTLD)

Gln-Pro-Asp (QPD) **Galactose**



CD205

MRC1, CD206; MRC1L1; CLEC13D; CLEC13DL

CLEC7A, CLECSF12, BGR, CANDF4

CLEC4N, CLEC6A, CLECSF10, Nkcl

CLEC4E, CLECSF9

CD209, CDSIGN, CLEC4L

CLEC9A

MAS… CLRs não ligam apenas Man e Gal containing molecules, mas outros carboidratos e tbm proteínas, lipídios e moléculas inorgânicas

modified from Invivogen

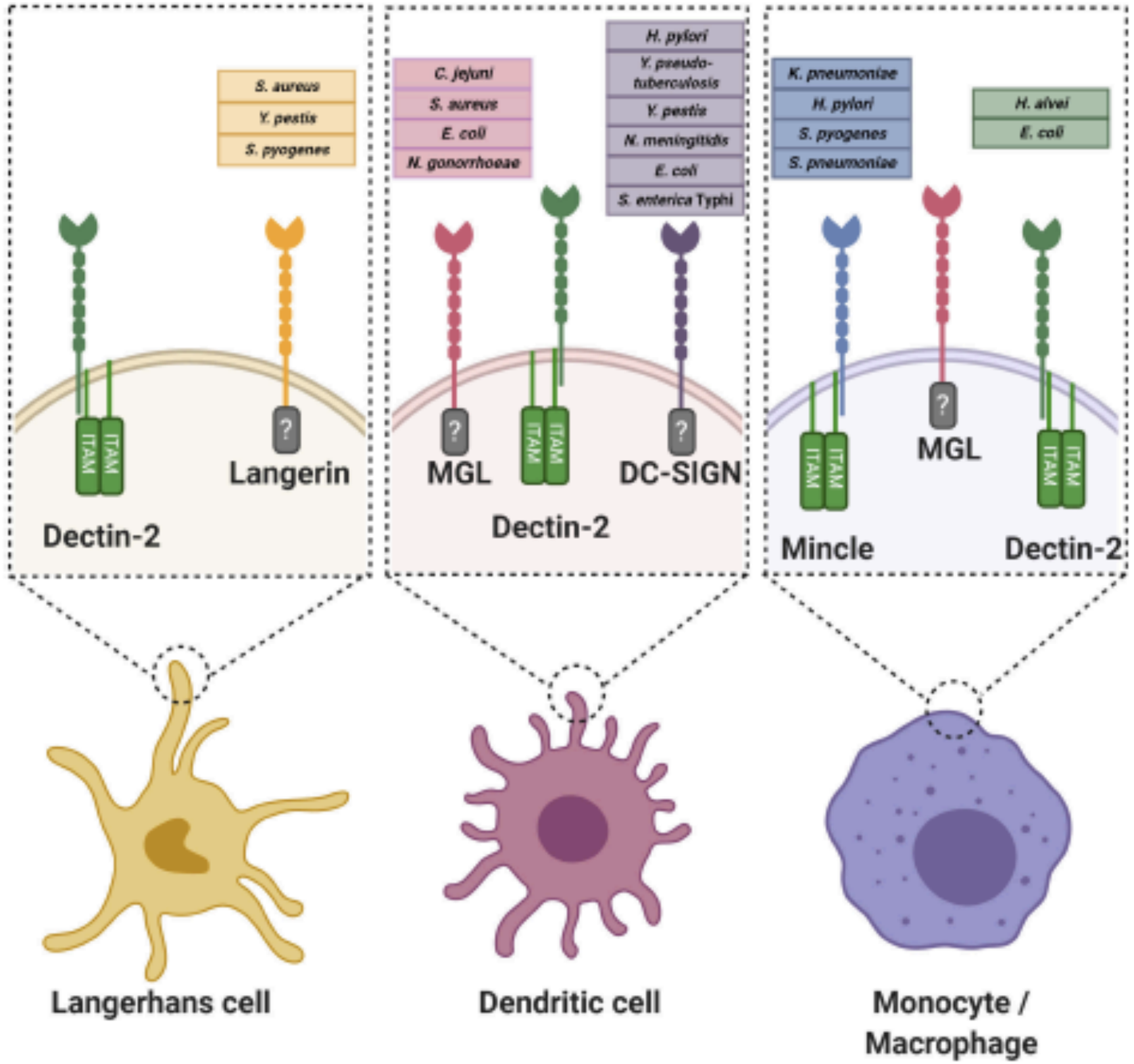
CLRs

Perfil de expressão célula-especifico

Tecido-especifico

Defesa

Tolerancia
(ex: microbiota)



Mnich et al. Front Cell Infect Micr 2020

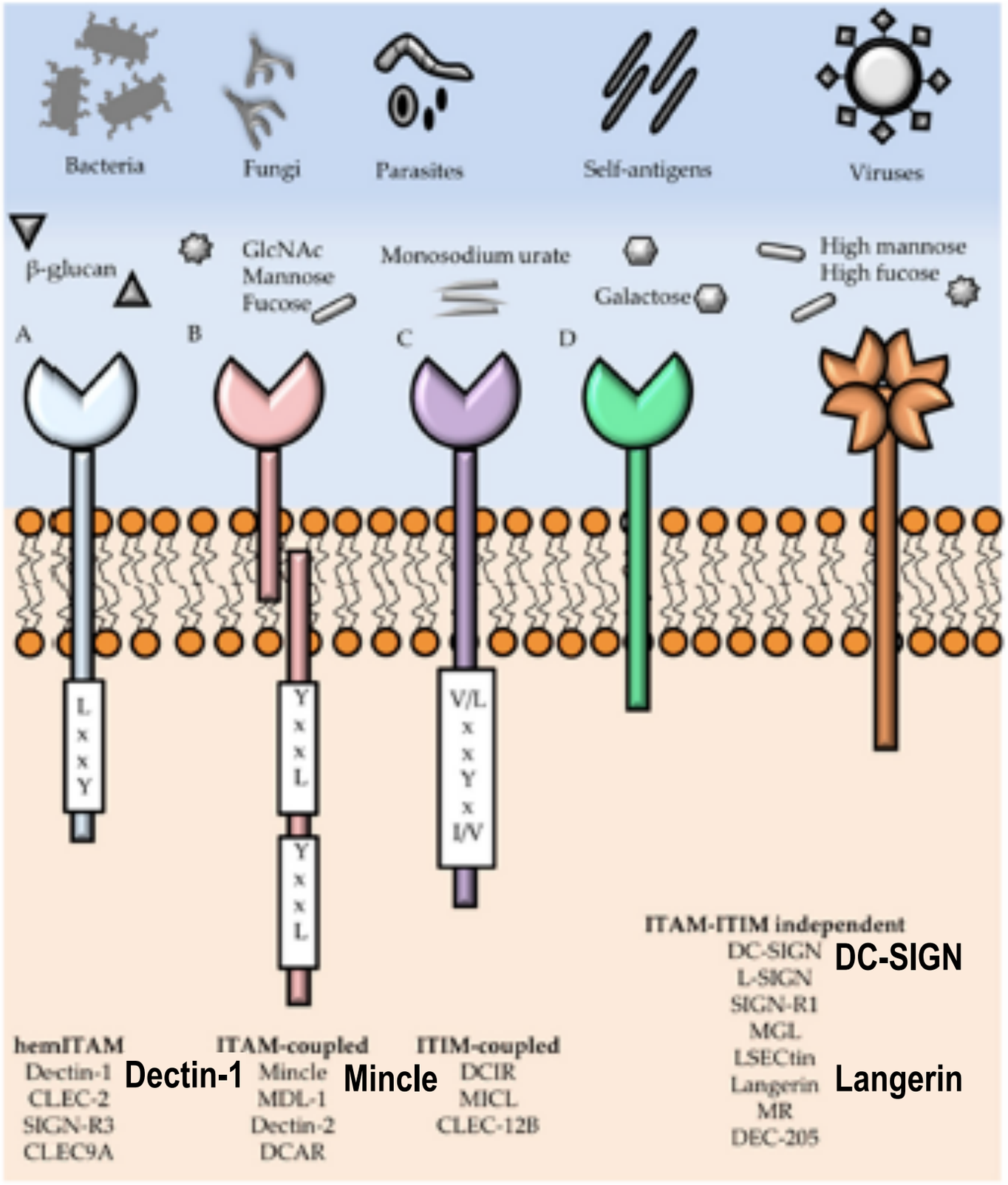
CLRs

PAMPs e DAMPs podem ser reconhecidos

PAMPs from bacteria, viruses, fungi and parasites;
DAMPs from damaged host cells.

A vast type of glycan structures (fucose, mannose, glucan, galactose, GlcNAc)

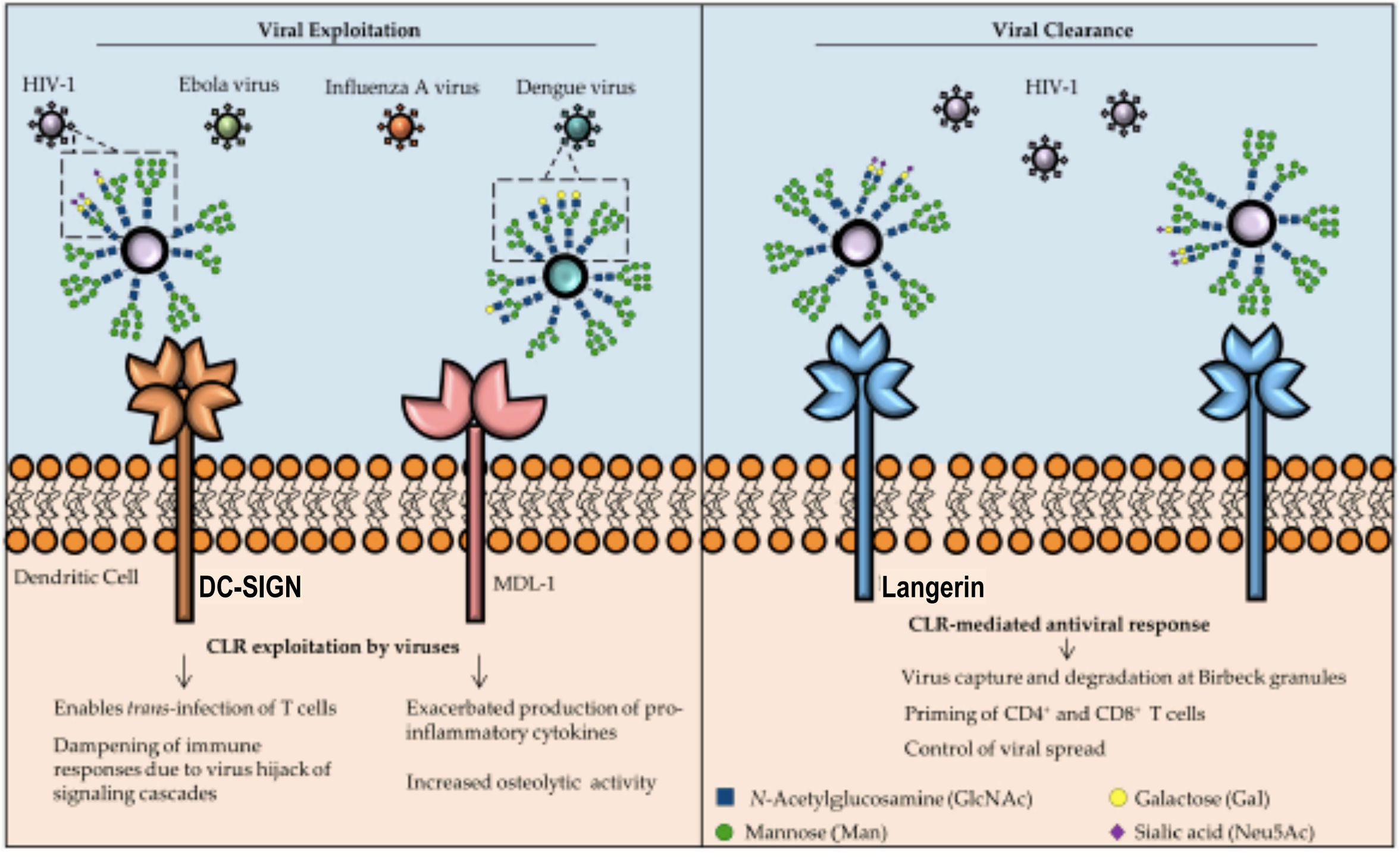
but also non-glycan ligands such as monosodium urate (MSU)



Monteiro & Lepenies Viruses 2017

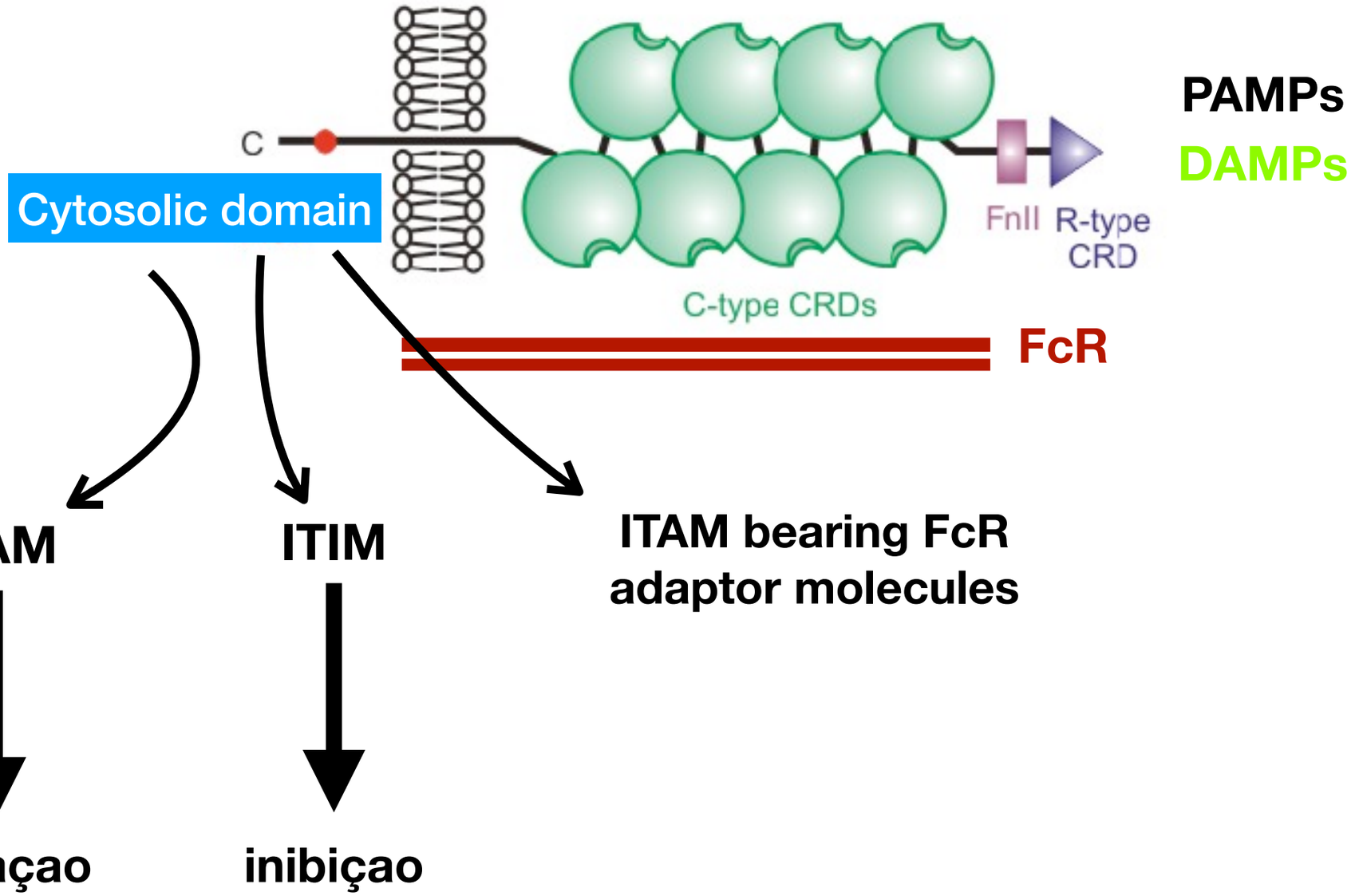
CLRs

pro-virus **activating response - virus control**



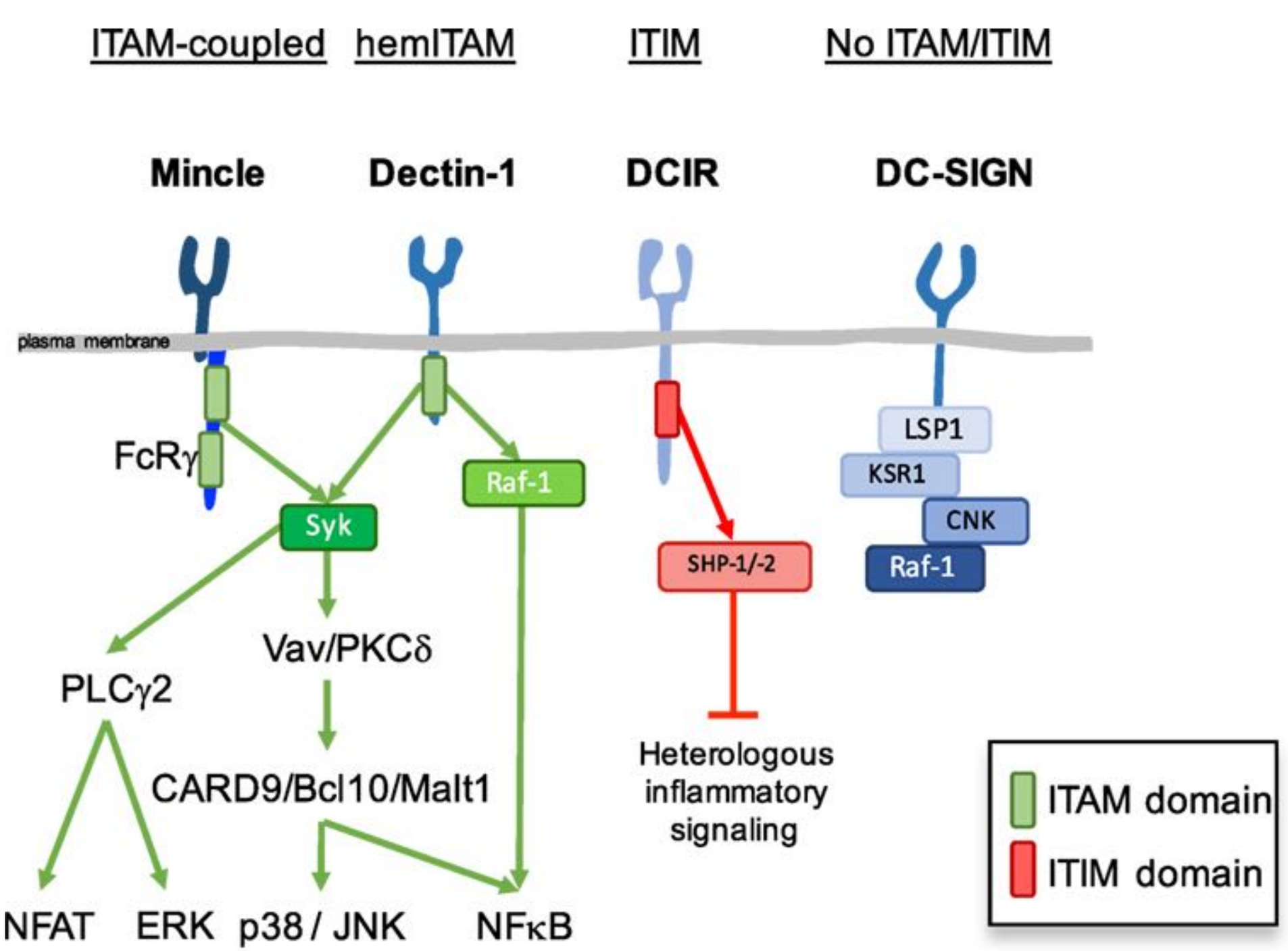
Monteiro & Lepenies Viruses 2017

CLRs

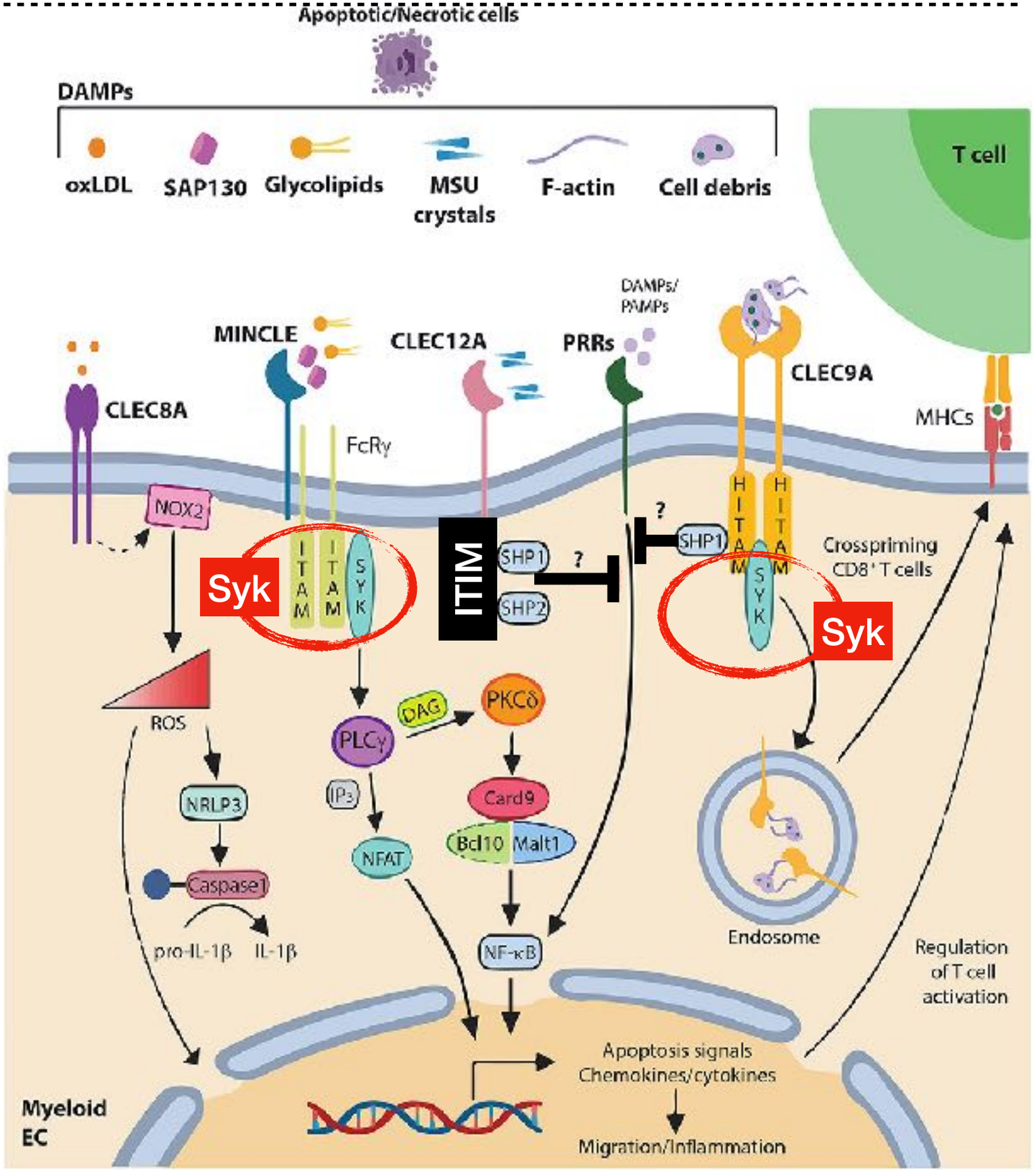


expressos em celulas mieloides (Mø, DC) mas tbm em linfócitos e NK

CLRs

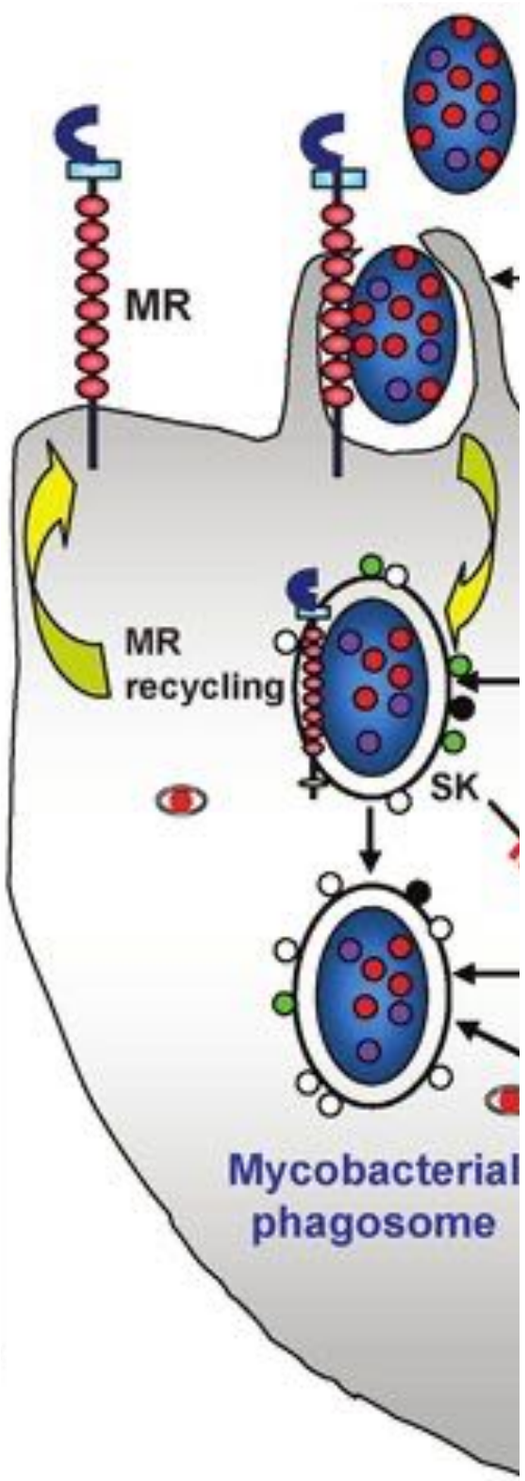

ITAM-coupled
hemITAM
ITIM
No ITAM/ITIM
Mincle
Dectin-1
DCIR
DC-SIGN
plasma membrane
FcRγ
Syk
Raf-1
PLCγ2
Vav/PKCδ
CARD9/Bcl10/Malt1
NFAT
ERK
p38 / JNK
NFκB
SHP-1/-2
Heterologous inflammatory signaling
LSP1
KSR1
CNK
Raf-1
ITAM domain
ITIM domain

CLRs

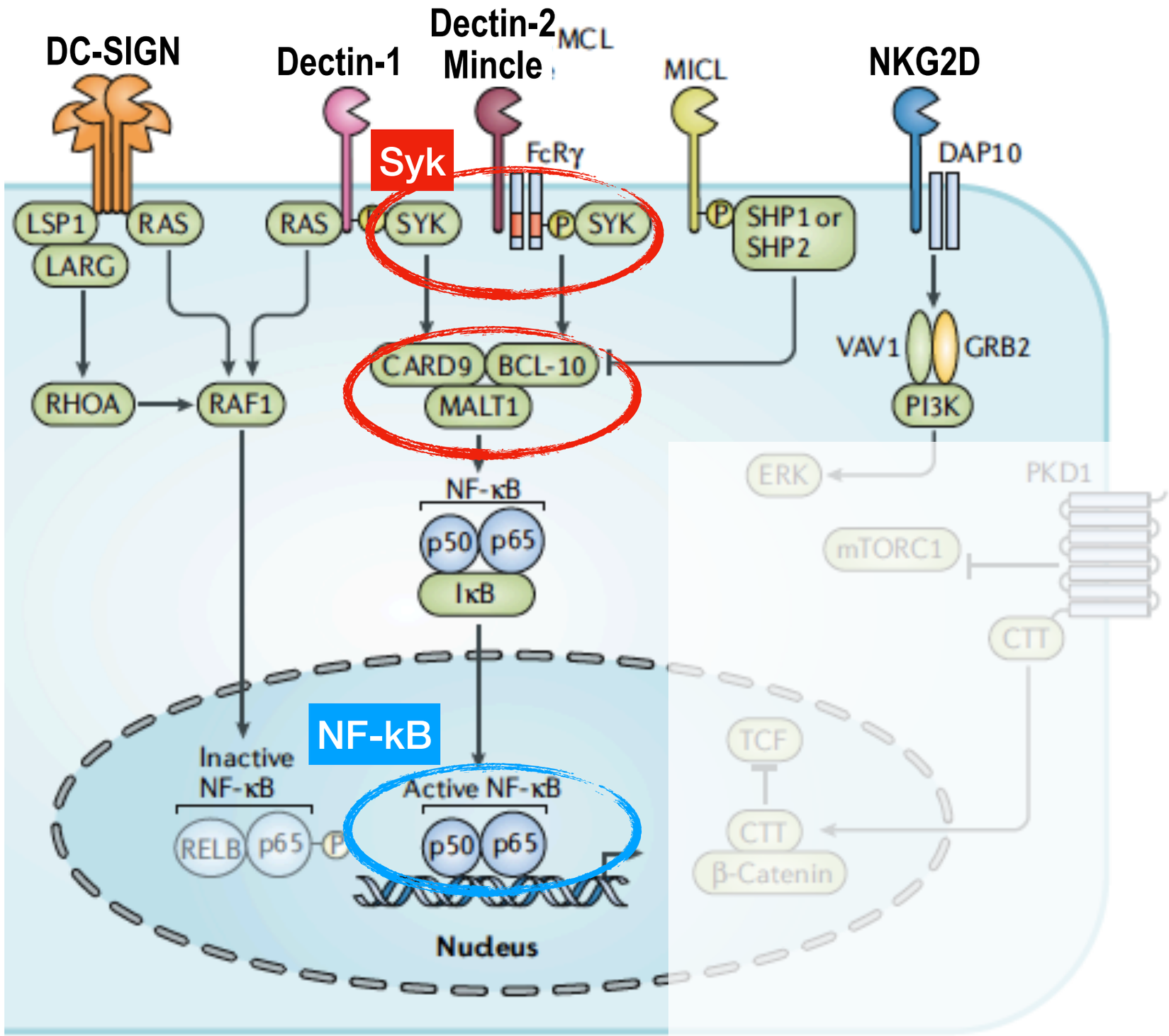


Drouin et al. Front. Immunol.2020

CLRs



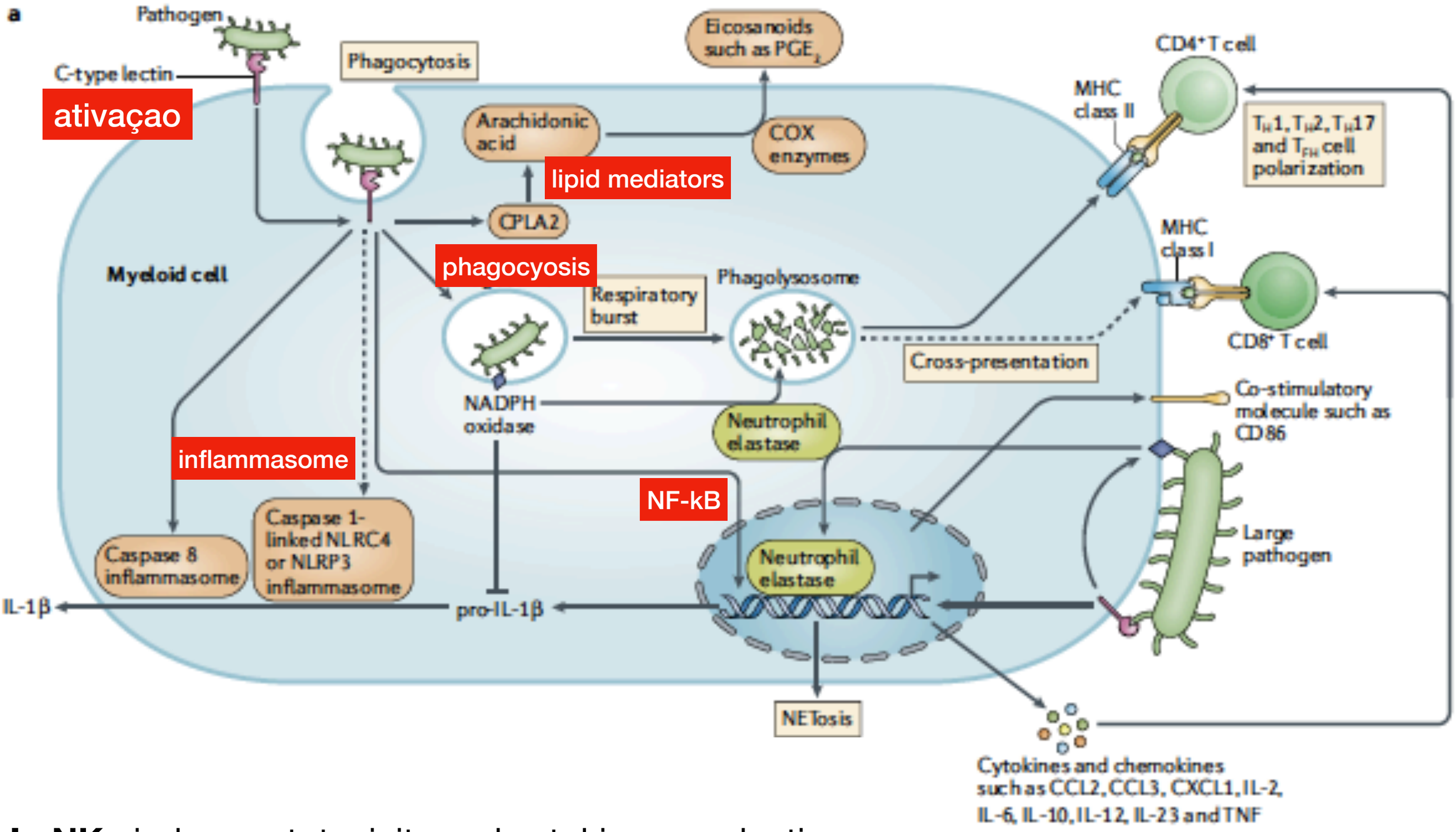
Schlesinger et al 2008 Imm Cell Biol



Brown 2018 Nature Reviews

CLRs in antimicrobial immunity

Phagocytes, DC



In NK : induce cytotoxicity and cytokines production

In B lymphcytes: induce cytokine production, inflammasome

Brown et al.Nature Reviews | Immunology 2018

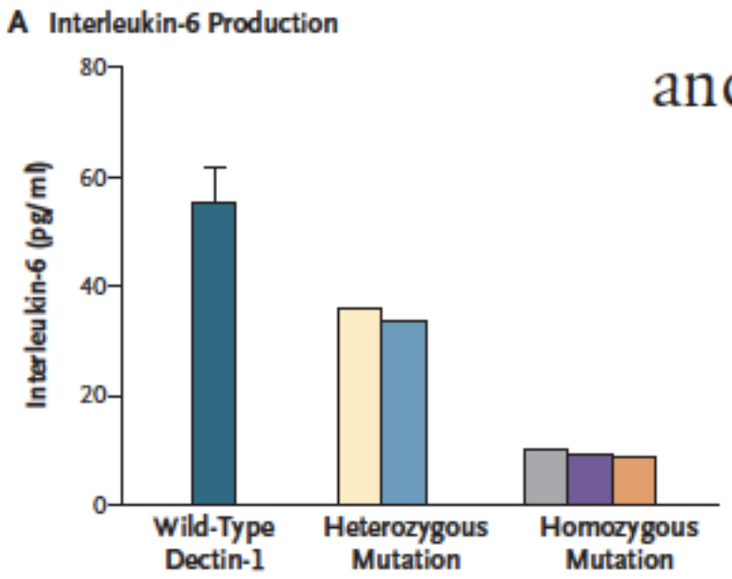
CLRs in antimicrobial immunity

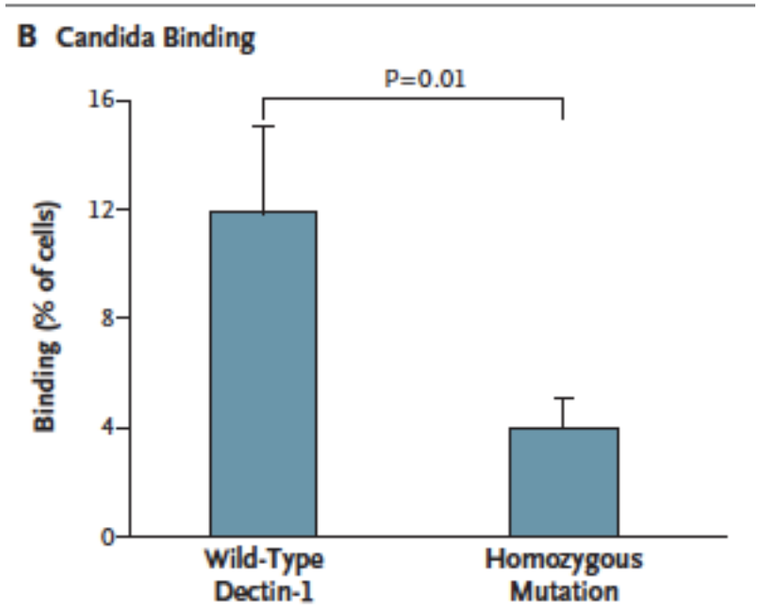
PRR Defect	Presumed Pathogenesis	Infections or Conditions for Which Susceptibility Is Conferred	Inheritance	Frequency
Dectin-1 deficiency	Beta-glucan–recognition defect	Candida, trichophyton	Autosomal recessive	Common
CARD9 deficiency	Beta-glucan–recognition defect	Candida	Autosomal recessive	Very rare
Mannose-binding lectin deficiency	Complement-activation defect	Bacteria and fungi	Autosomal recessive	Common

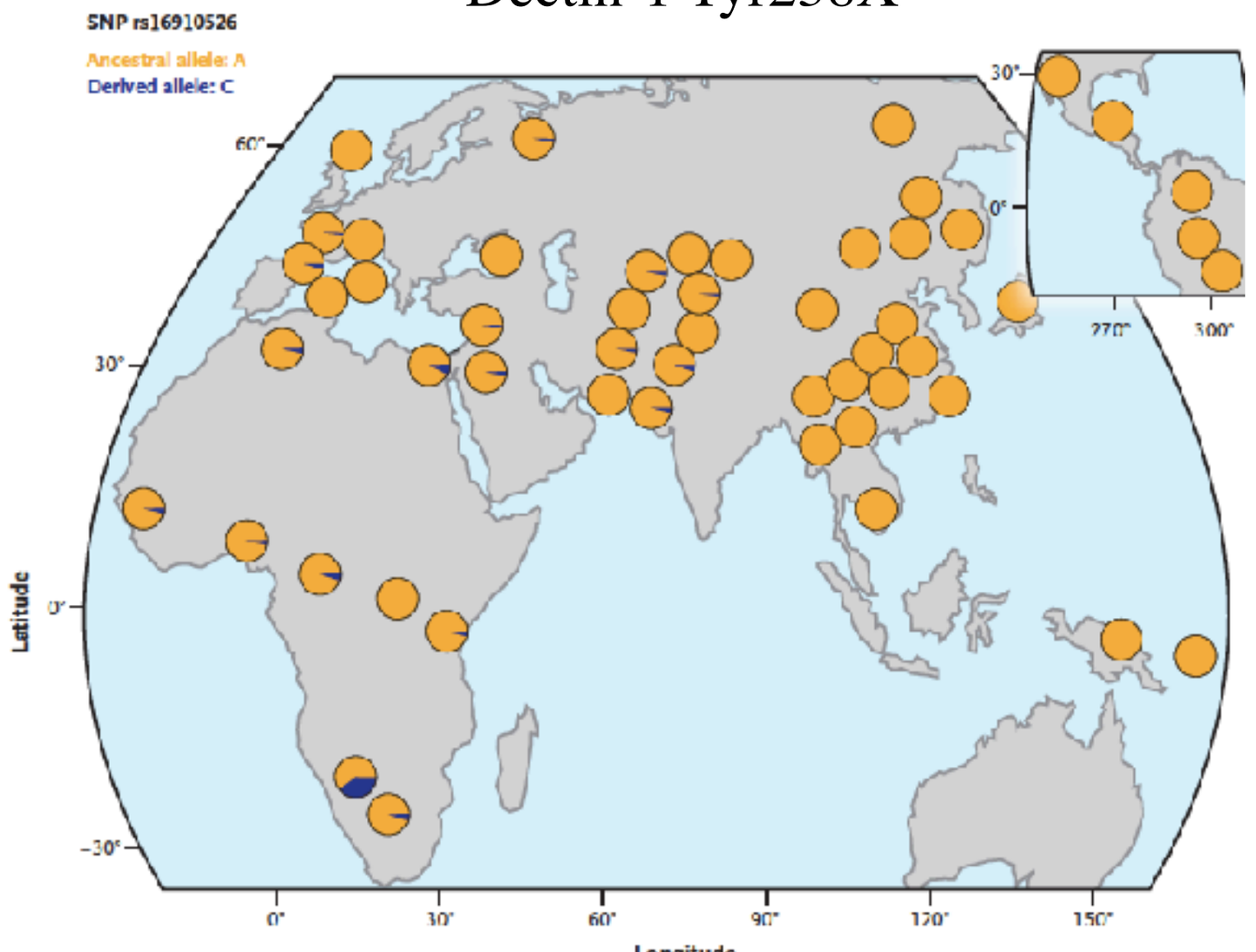
N ENGL J MED 361;18 NEJM.ORG OCTOBER 29, 2009

Human Dectin-1 Deficiency and Mucocutaneous Fungal Infections

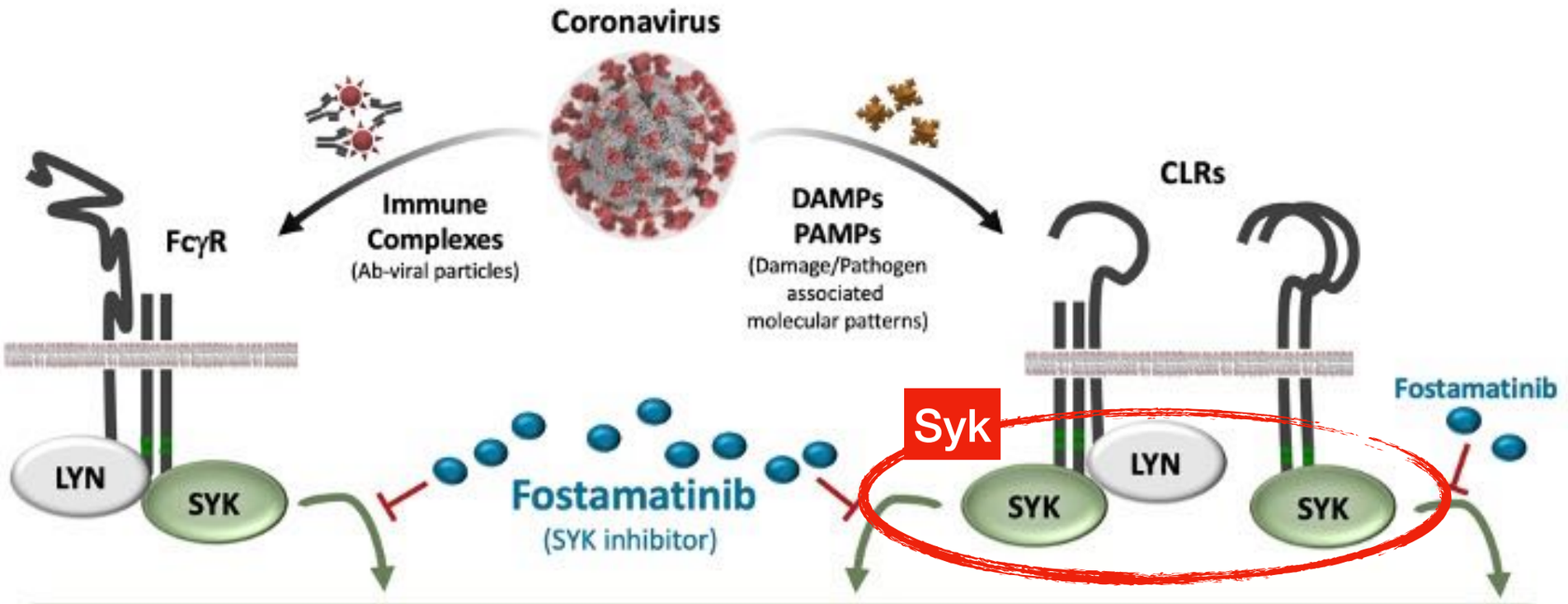
Dectin-1 Tyr238X







SYK known to mediate aspects of COVID-19 pathogenesis[2,3]



Cytokine release
monocytes, macrophages, dendritic cells, endothelial cells

Edema
endothelial cells

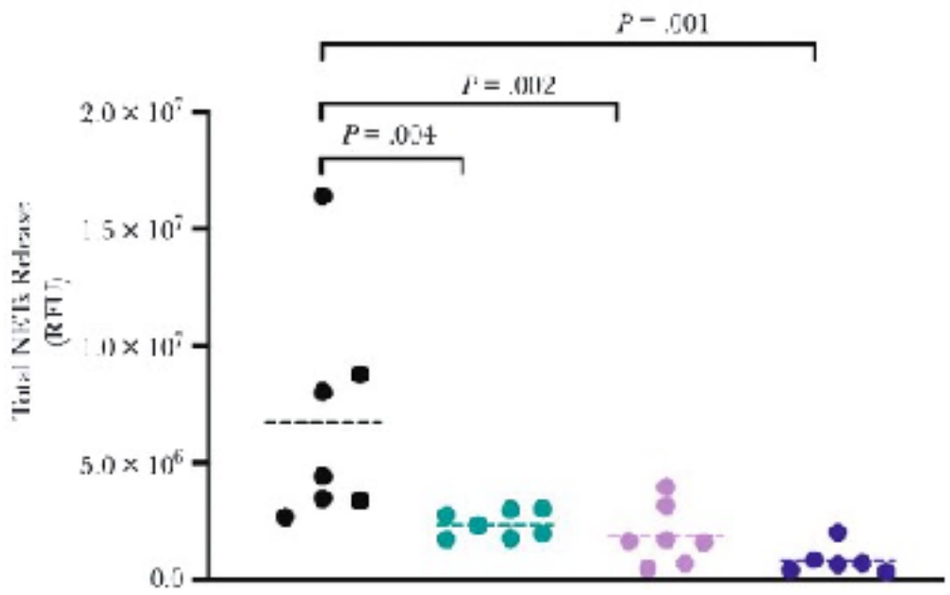
NETosis
Cytotoxicity
neutrophils

Coagulopathy
endothelial cells, neutrophils, platelets

Cytokine storm / ALI / ARDS / Thrombosis

Syk & NETs

- COVID-19 (+)
- COVID-19 (+) + R406 [1 μM]
- COVID-19 (+) + R406 [4 μM]
- Healthy Control



www.rigel.com/pipeline/proprietary-programs/covid-19

PLA
Y.pestis

High mannose
Omega-1
ManLam

F-actin
Dead cell

ß-glucan
L infantum,
Mtb

a-mannan,
glicoproteins
Mtb, C
albicans, S
massoni

a-mannose,
glicolipids
Mtb, C
albicans

Fungi

TDM
Mtb
Bacteria

??
Virus

??
HIV
Malaria

High mannose
SlpA
HIV, Measles
Mtb

Leishmania

MICA/B
ULBP1-6

DC-205 MR DNGR-1 Dectin-1 Dectin-2 Mincle CLECSF8 CLEC5A DCIR DC-SIGN

NKG2D

CR FNII CR FNII

PKC

Syk Syk Syk Syk Syk Syk Syk

Raf-1

FcRγ FcRγ FcRγ Dap12

PKC

CARD9
MALT1
Bcl10

ITAM

SHP1 SHP2
or

ITIM

Raf-1

Dap10

PI3K
AKT

? ?

ativaçao

inibiçao

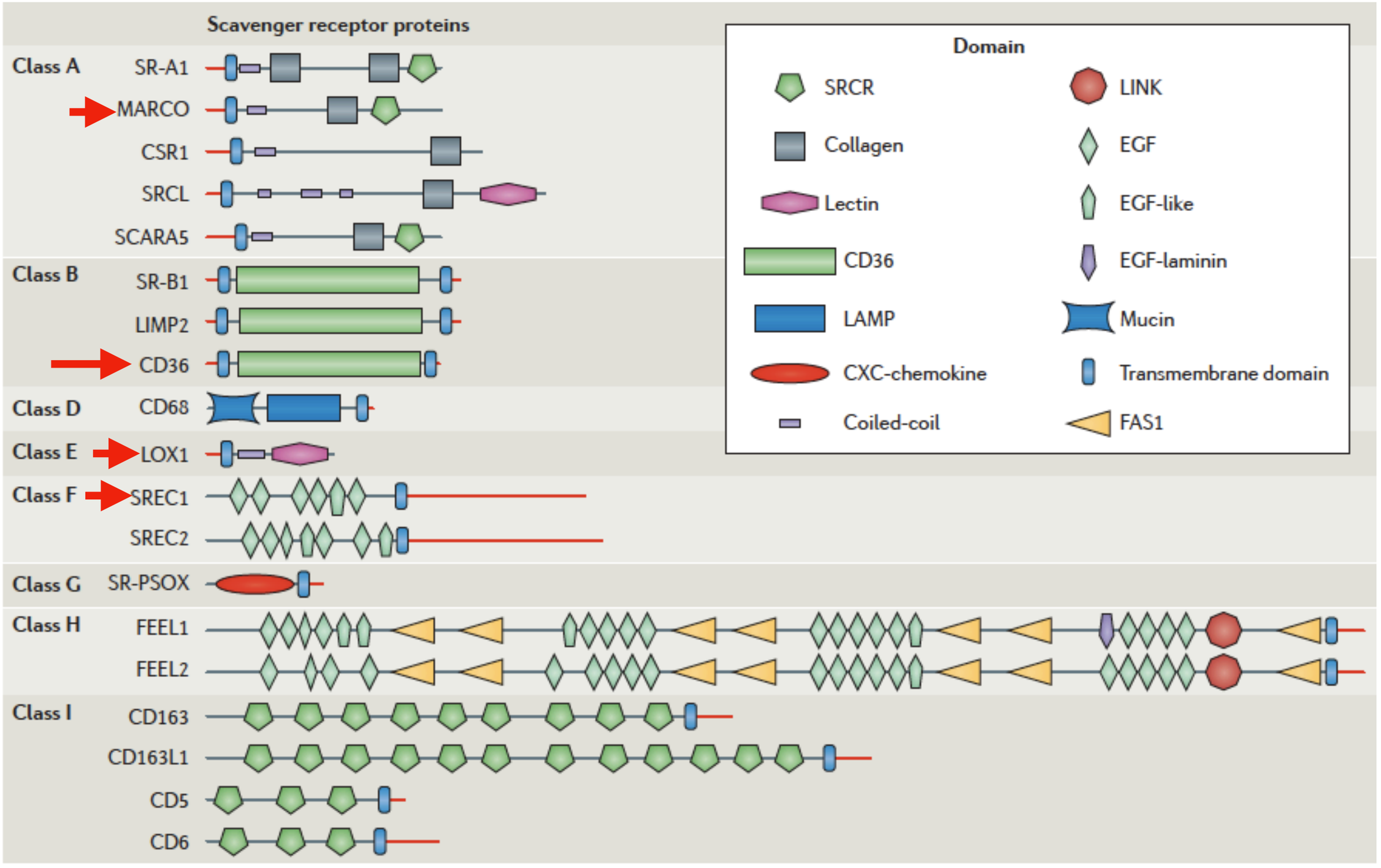
ativaçao

Phagocytosis
Cross presentation
Inflammasome activation

Inflammatory mediator production
Innate and adaptive immunity
Antimicrobial responses

Modified from Hoving, Wilson,& Brown 2018

Receptores "*Scavanger*"

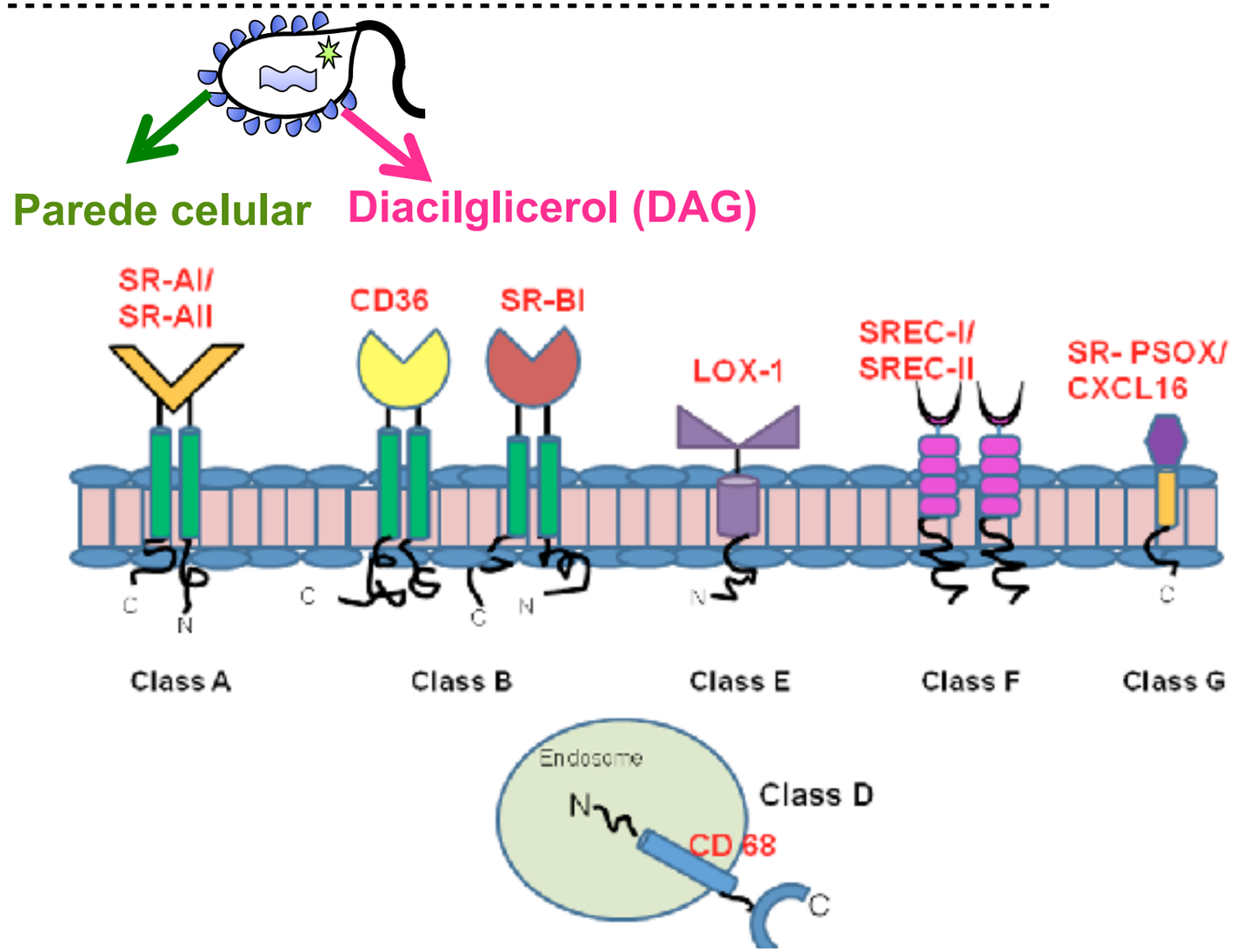


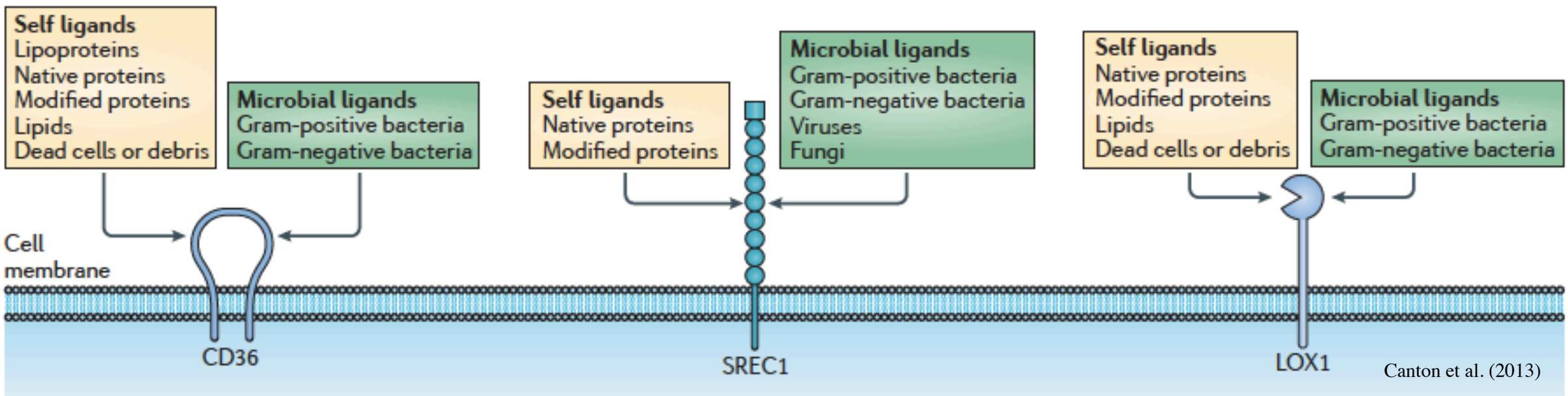
Canton et al. (2013)

Receptores "*Scavanger*"

PAMPs: LPS, acido lipoteicoico, acidos nucleicos, ß-glucanas e proteinas.

DAMPs: LDL, HDL

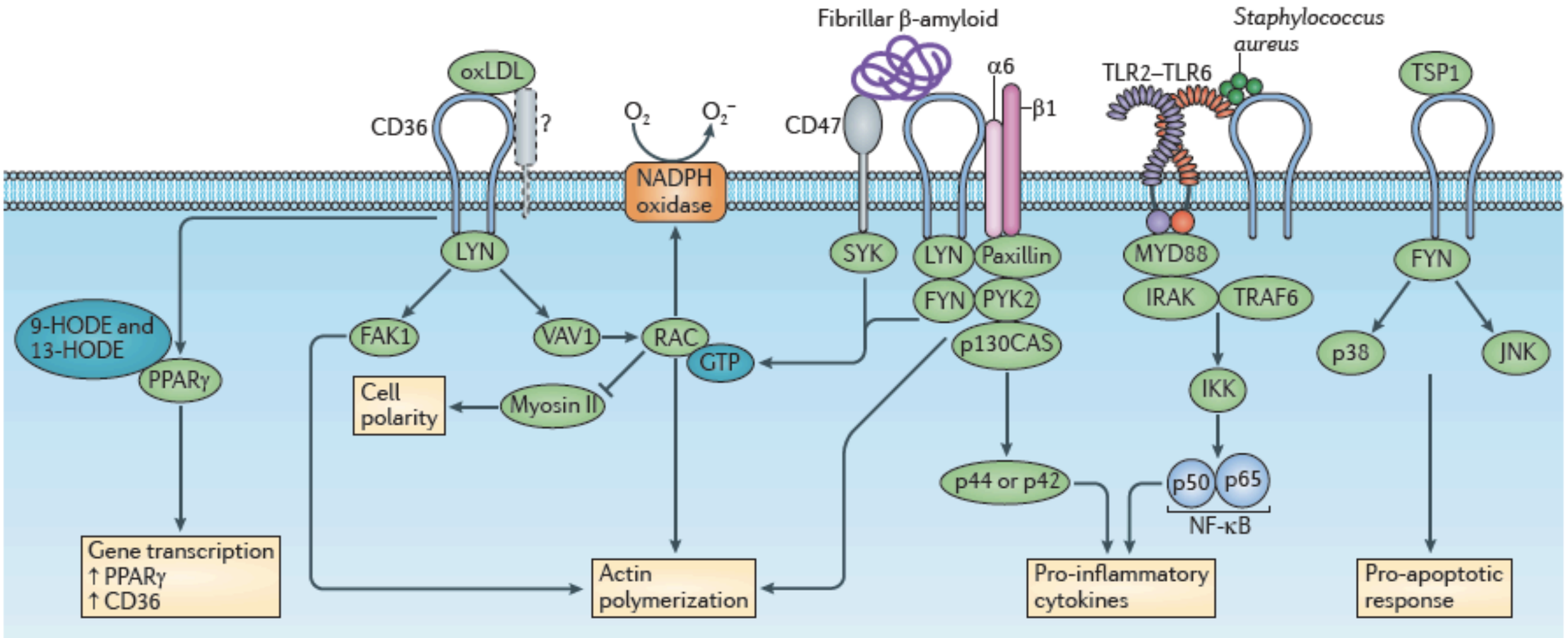




Canton et al. (2013)

Receptores "*Scavanger*"

Os Rec Scavanger interagem com diferentes ligantes dependendo da célula e do contexto e esta interação determina a via de sinalização intracelular

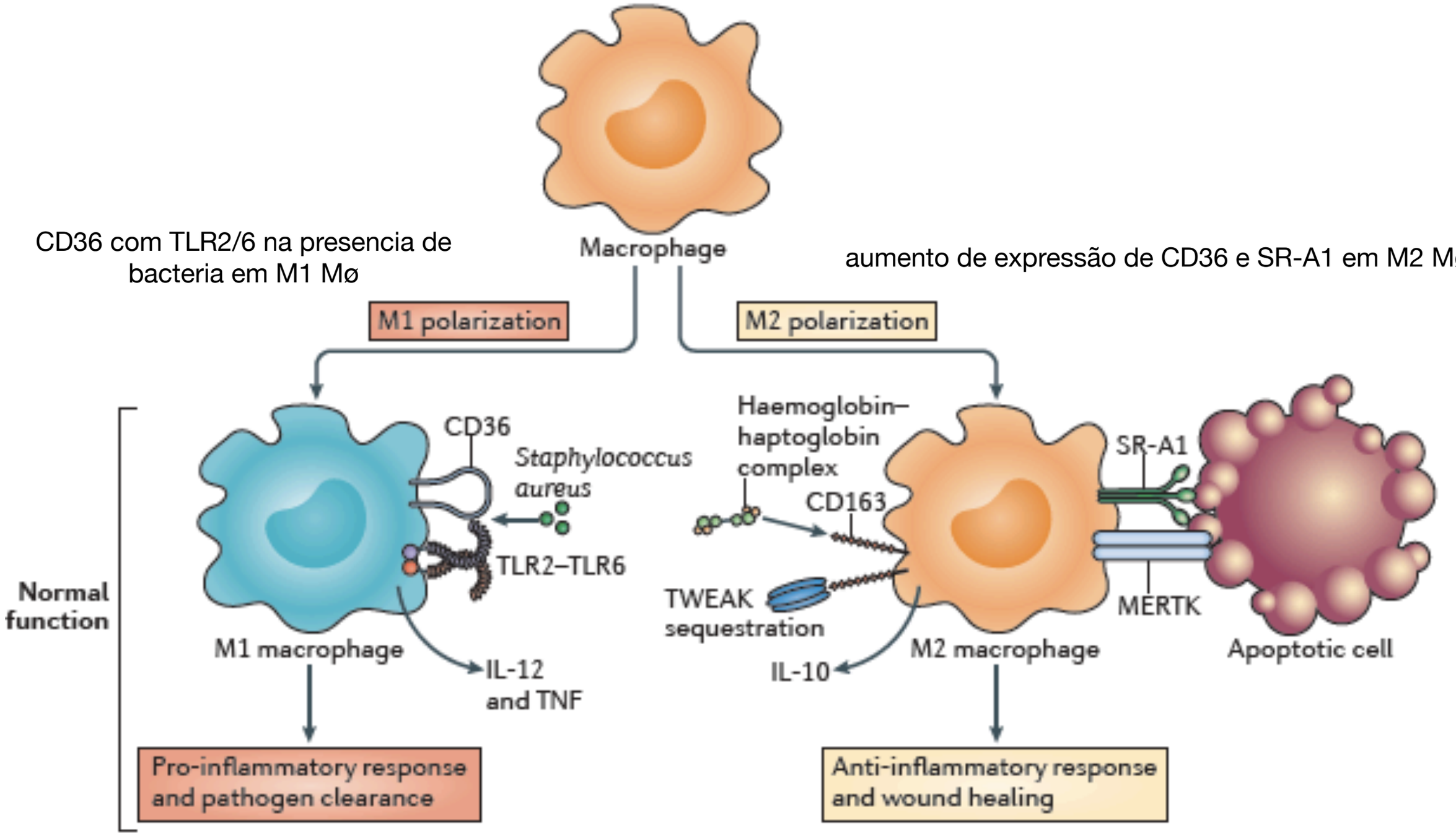


Canton et al. (2013)

Receptores "*Scavanger*"

CD36 com TLR2/6 na presencia de bacteria em M1 Mø

aumento de expressão de CD36 e SR-A1 em M2 Mø

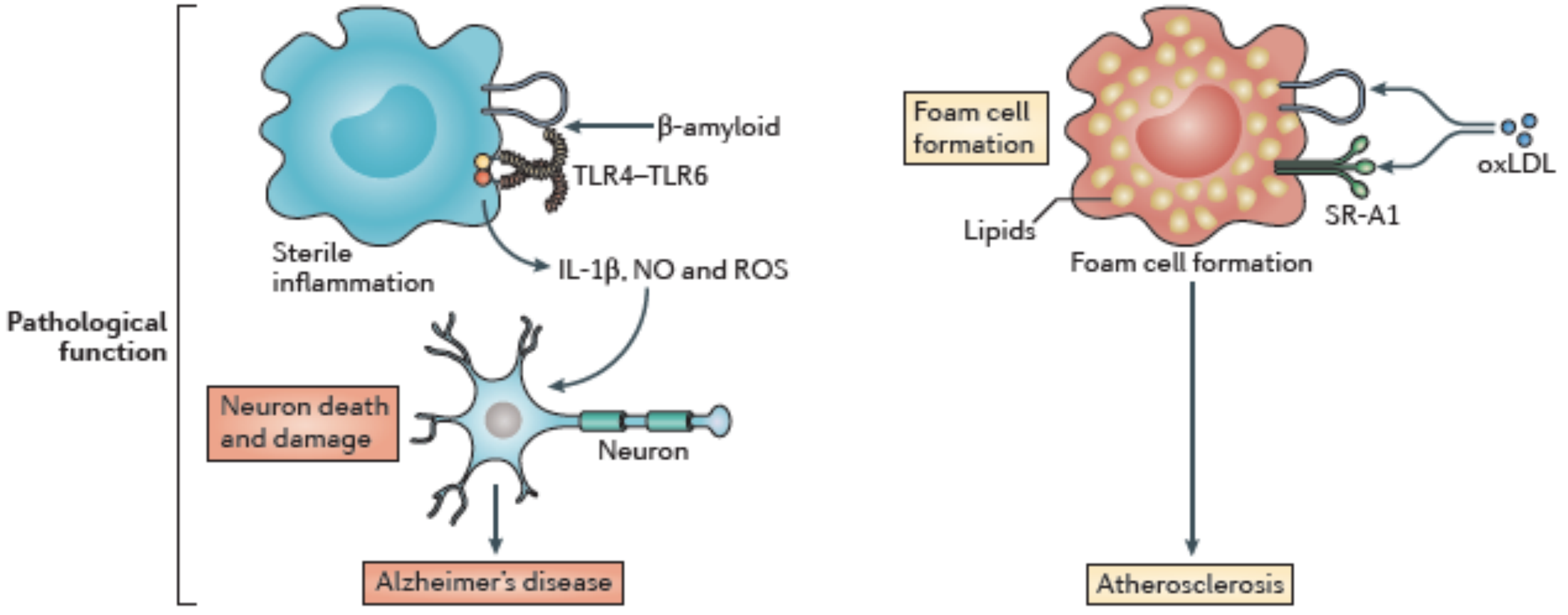


Canton et al. (2013)

Receptores “*Scavanger*”

CD36 com TLR4/6 na presencia de ß-A em M1 Mø

aumento de expressão de CD36 e SR-A1 em M2 Mø



Canton et al. (2013)

Receptores "*Scavanger*"

Malaria susceptibility and *CD36* mutation

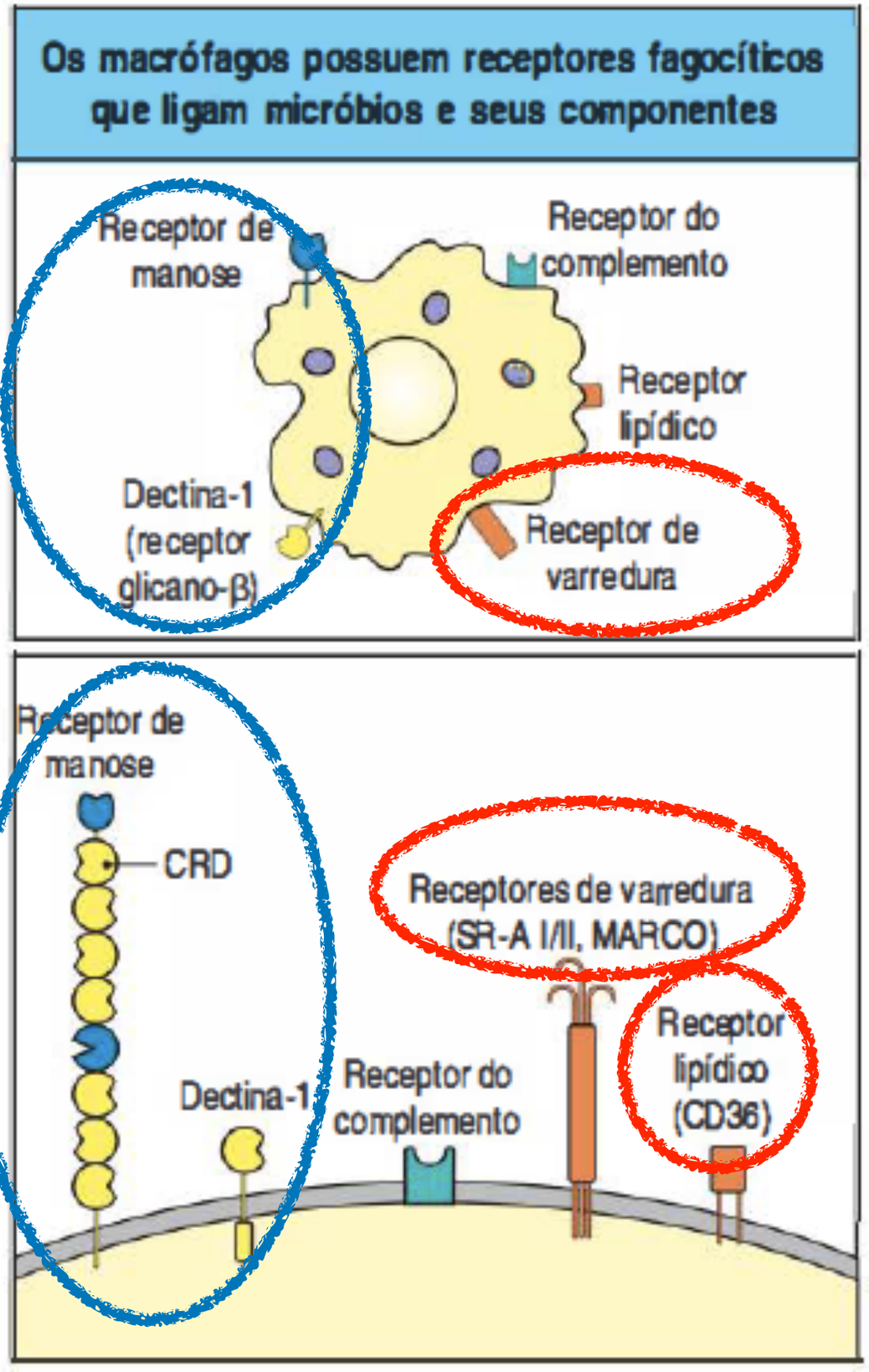
NATURE | VOL 405 | 29 JUNE 2000 | www.nature.com

Timothy J. Aitman*, Lisa D. Cooper*, Penny J. Norsworthy*, Faisal N. Wahid*, Jennefer K. Gray*, Brian R. Curtis†, Paul M. McKeigue‡, Dominic Kwiatkowski§, Brian M. Greenwood§, Robert W. Snow||, Adrian V. Hill¶, James Scott*

Genotype		All malaria	Cerebral	Anaemia	Controls
Gambians		(*n*=415)	(*n*=291)	(*n*=157)	(*n*=430)
Exon 10	WT	95.0	94.5	96.8	97.2
	T1264G/WT	5.0	5.5	3.2	2.6
	T1264G/T1264G	0	0	0	0.2
Exon 12	WT	95.9	96.0	94.9	96.3
	G1439C+1444delA/WT	4.1	4.0	5.1	3.7
Total mutant allele frequency		4.5*	4.6†	4.1	3.3
Kenyans		(*n*=183)	(*n*=97)	(*n*=86)	(*n*=331)
Exon 10	WT	79.2	76.3	82.6	82.8
	T1264G/WT	19.1	20.6	17.4	16.9
	T1264G/T1264G	1.6	3.1‡	0	0.3
Total mutant allele frequency		11.2*	13.4†	8.7	8.8

p = 0.01

Receptores de fagocitose



Janaway 8th ed

Reconhecimento direto

Receptores de carboidrados (CLRs)

Receptores de varredura (*Scavanger*)

Fagocitose

quimiotatico

BACTERIA

Formil-peptideos

PAMPs

opsoninas

reconhecimento

A bacteria é reconhecida e “presa” pelos pseudopodia

1

A bacteria é ingerida (FAGOSOMA)

2

O fagosoma se fonde com os lissosomos (em PMN, tbm com granulos)

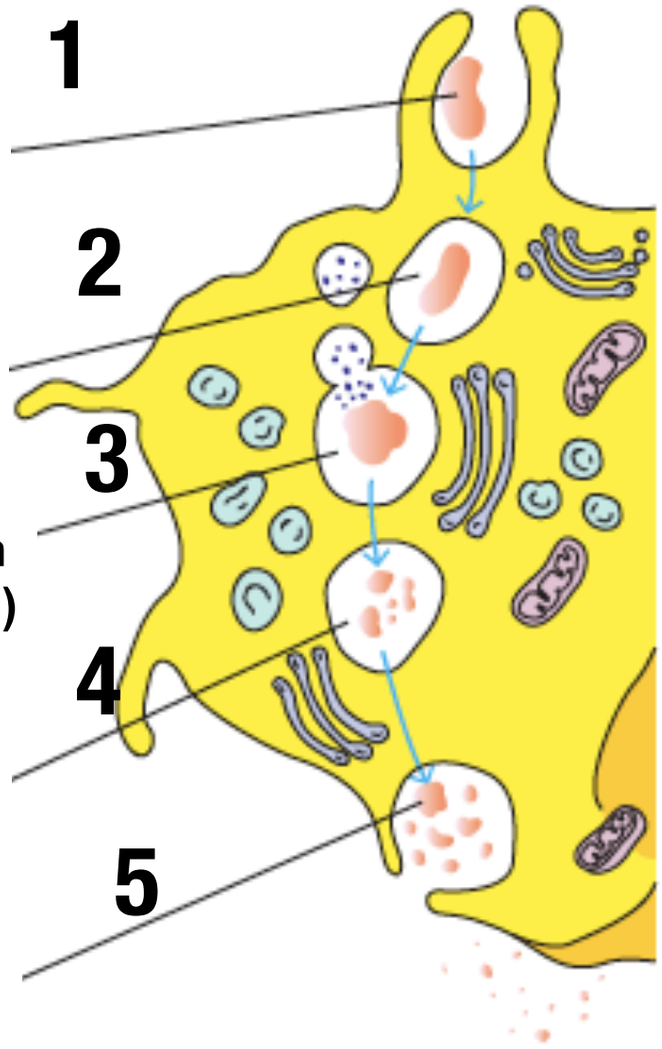
3

DIGESTÃO/KILLING no FAGOLISSOSOMA

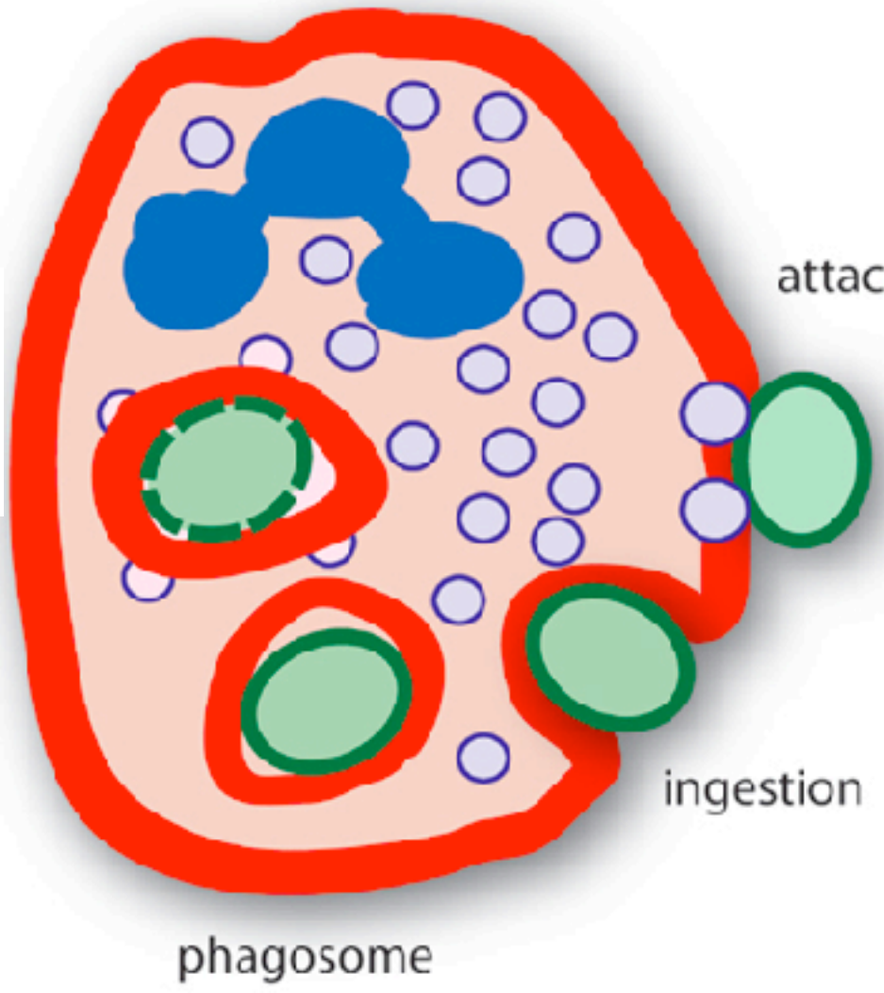
4

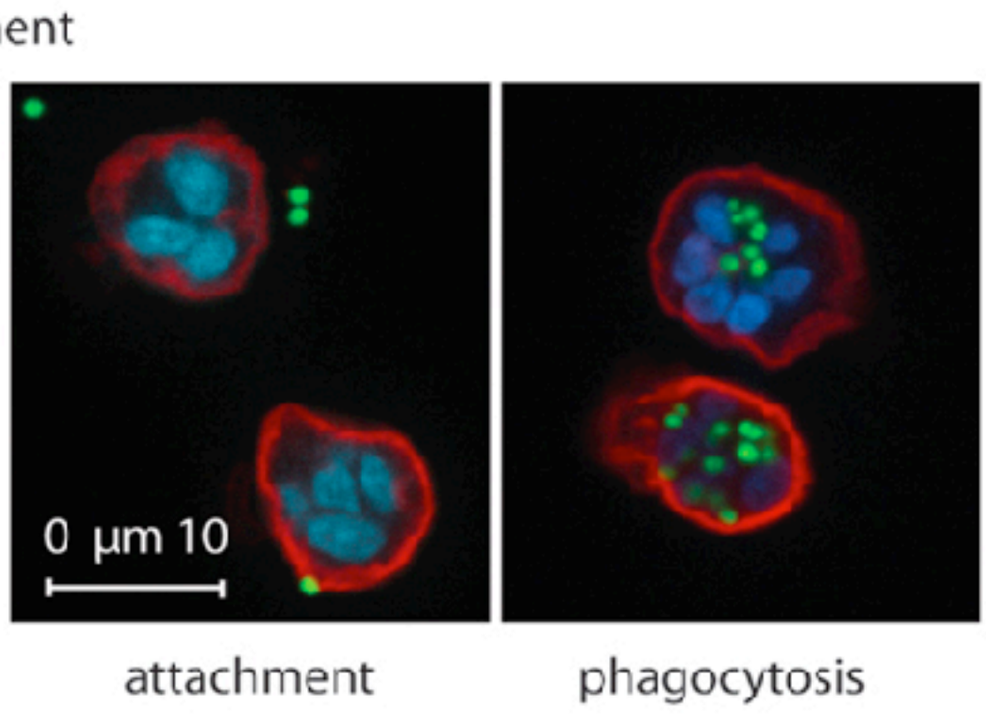
Produtos da digestão são liberados por exocitose ou “apresentados”

5



Fagocitose & Killing





Fagolisossoma: killing/digestao

Agentes anti-microbianos

- **Proteinas e peptideos antimicrobianos**
- **pH acido**
- **Enzimas idroliticos ativados a pH acido (lisozima, protease)**
- **ROS produzidos via NADPH-oxidase**
- **ROS+NO (produzido via iNOS)→RNS**

Fagocitose

Receptor type on phagocytes	Examples	LIgands
Reconhecimento direto do patogeno		
C-type lectin receptors (CLRs)	Mannose receptor	Mannans (bacteria, fungi, parasites)
	Dectin 1	β-glucans (fungi, some bacteria)
	DC-SIGN	Mannans (bacteria, fungi, parasites)
Scavenger receptors	SR-A	Lipopolysaccharide (LPS), lipoteichoic acid (LTA) (bacteria)
	SR-B	LTA, lipopeptides, diacylglycerides (bacteria), β-glucans (fungi)
Reconhecimento indireto (das OPSONINAS)		
Collagen-domain receptor	CD91/calreticulin	**PRMs** Collectins SP-A, SP-D, MBL; L-ficolin; C1q
Complement receptors	CR1, CR3, CR4, CRIg, C1qRp	Complement components and fragments*
Immunoglobulin Fc receptors	FcαR	**ACs** Specific IgA antibodies bound to antigen#
	FcγRs	Specific IgG antibodies bound to antigen;# C-reactive protein

→ ***Produção de mediadores***

- ***Recrutar e ativar leucocitos***
- ***Inflamaçao***

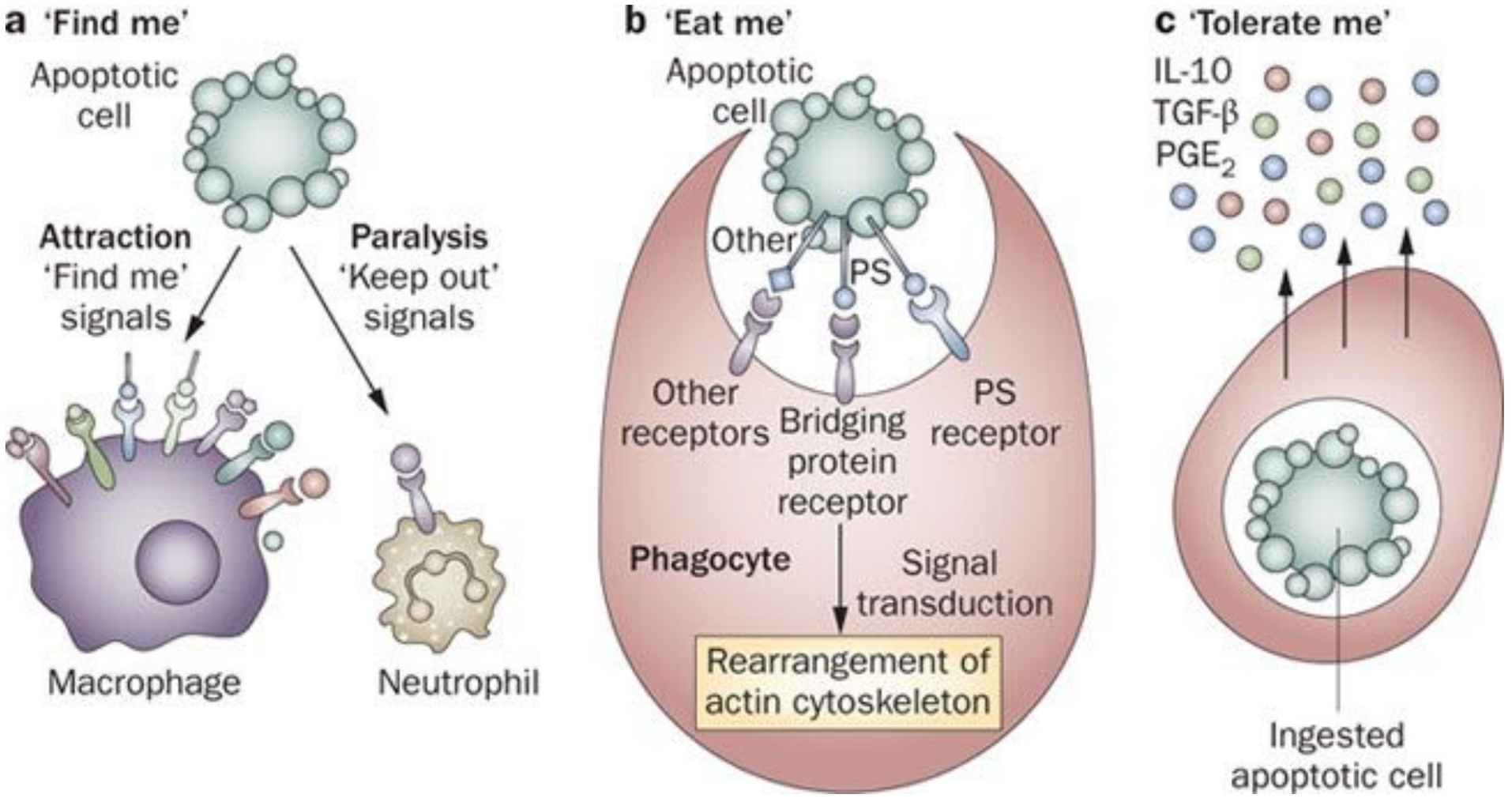
Help!!!!

Fagocitose “fisiologica”

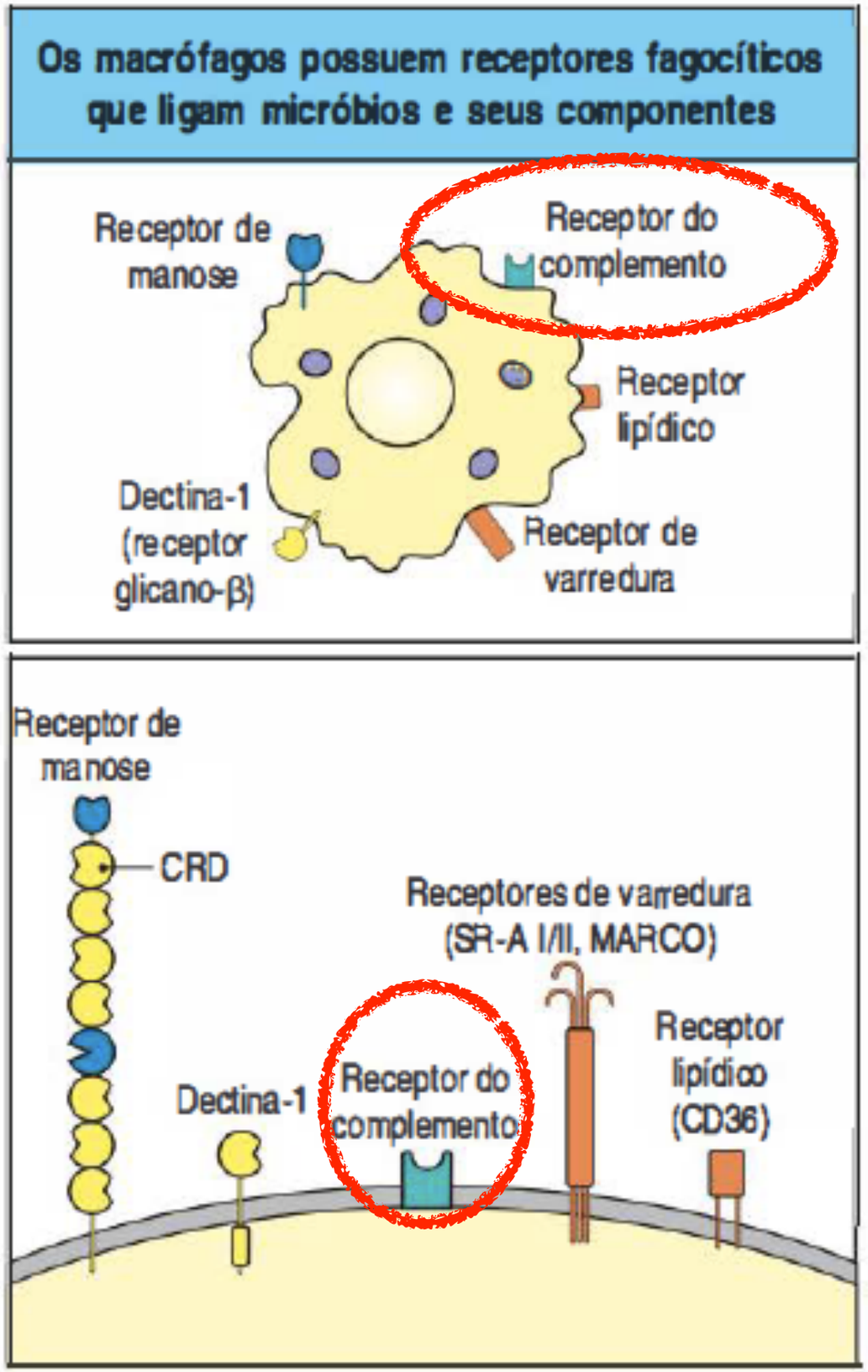
- Celulas mortas (necrose, apoptose)
- Debris celulares
- Emacias velhas (figado/Kupffer c.; baço/Mø)
- Complexos Ag/AC

Silence please

CD36, SRA1, MERTK, TIM-1,4



Receptores de fagocitose non PRRs



Janaway 8th ed

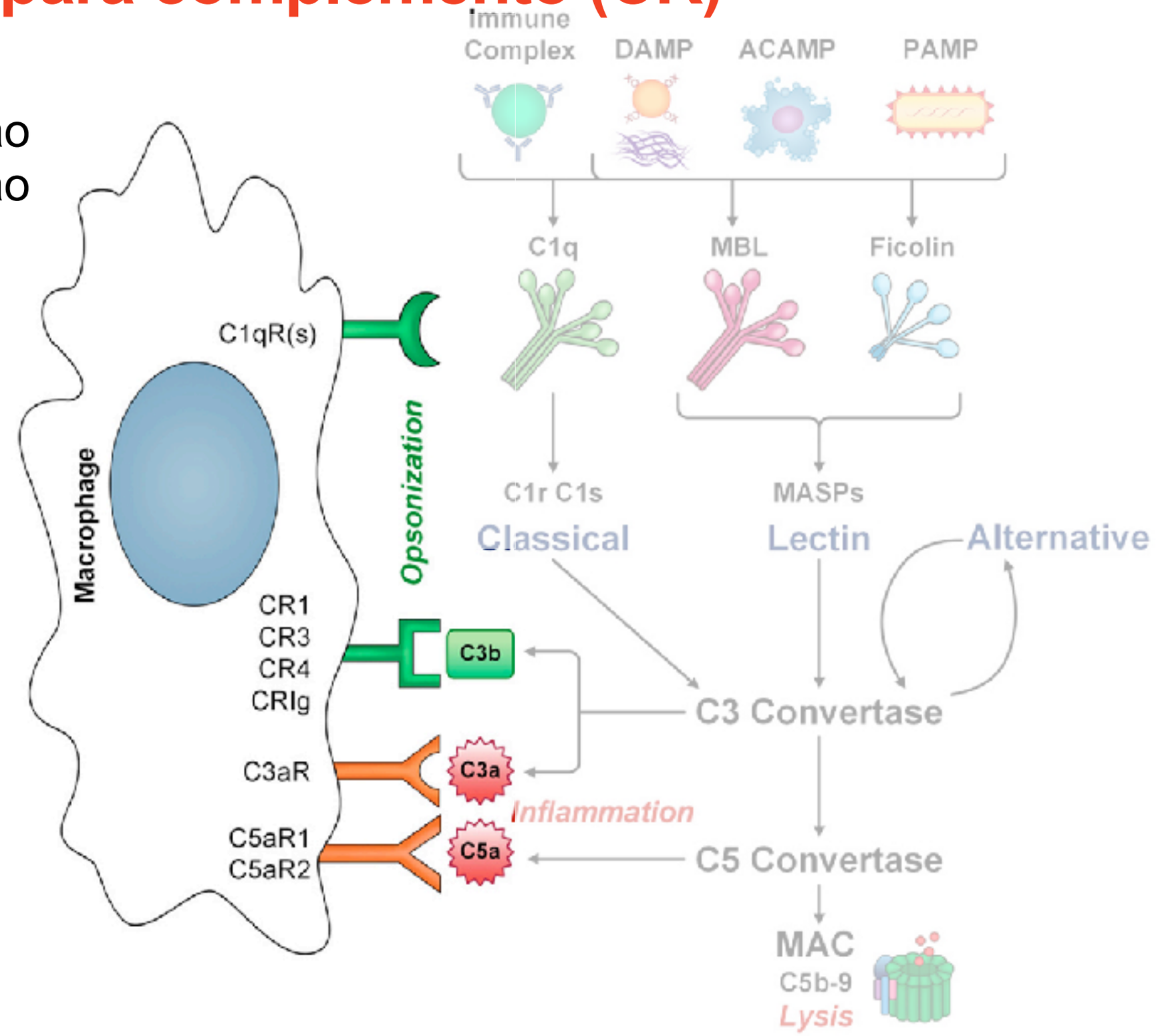
Reconhecimento direto
Receptores de carboidrados (CLRs)
Receptores de varredura (*Scavanger*)

Reconhecimento indireto (opsoninas)
Receptores do complemento (CR)
Receptor dos anticorpos (FcR)

Reconhecimento indireto

Receptores para complemento (CR)

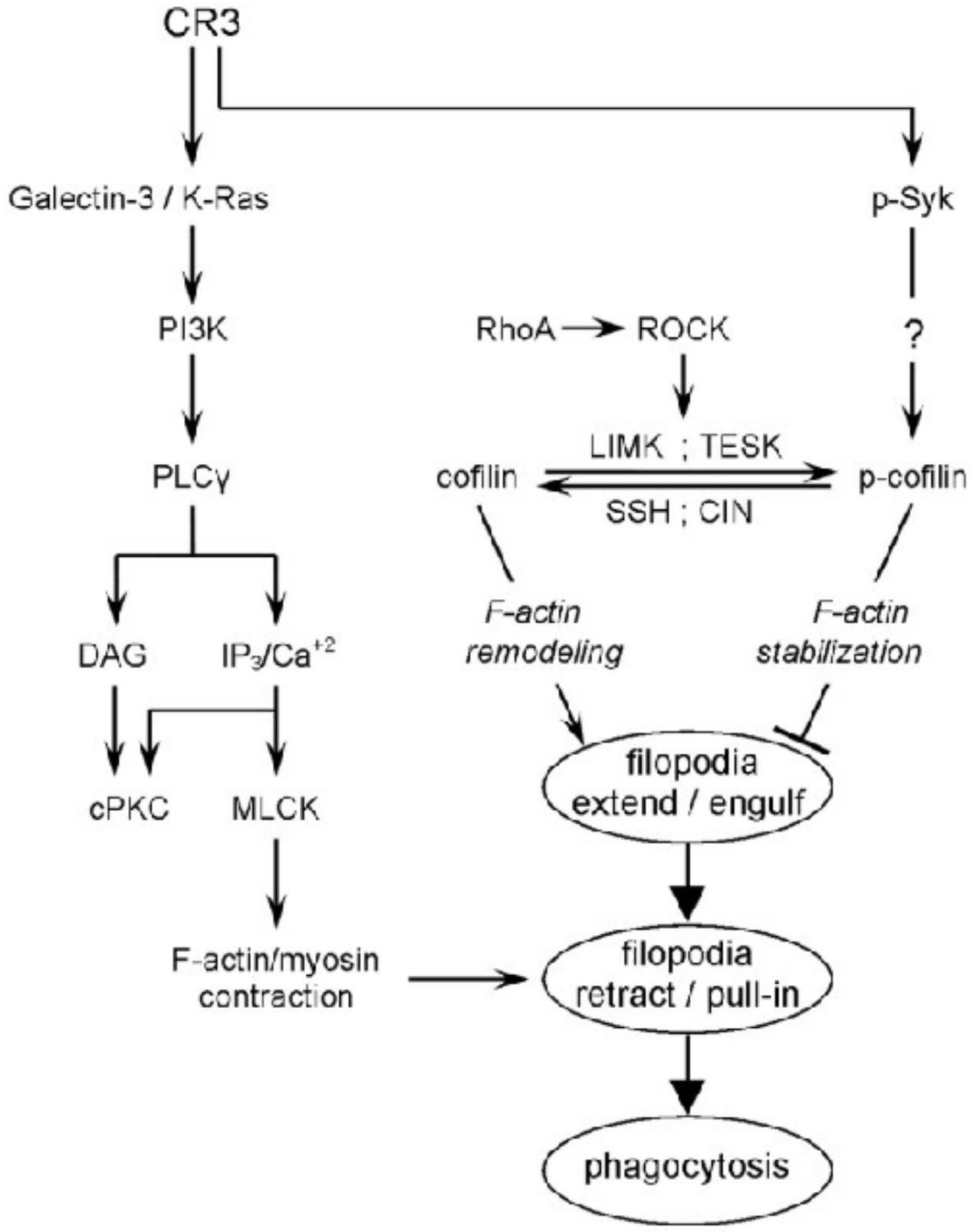
- Fagocitose
- Desgranulaçao
- Pro-inflamaçao



CRs

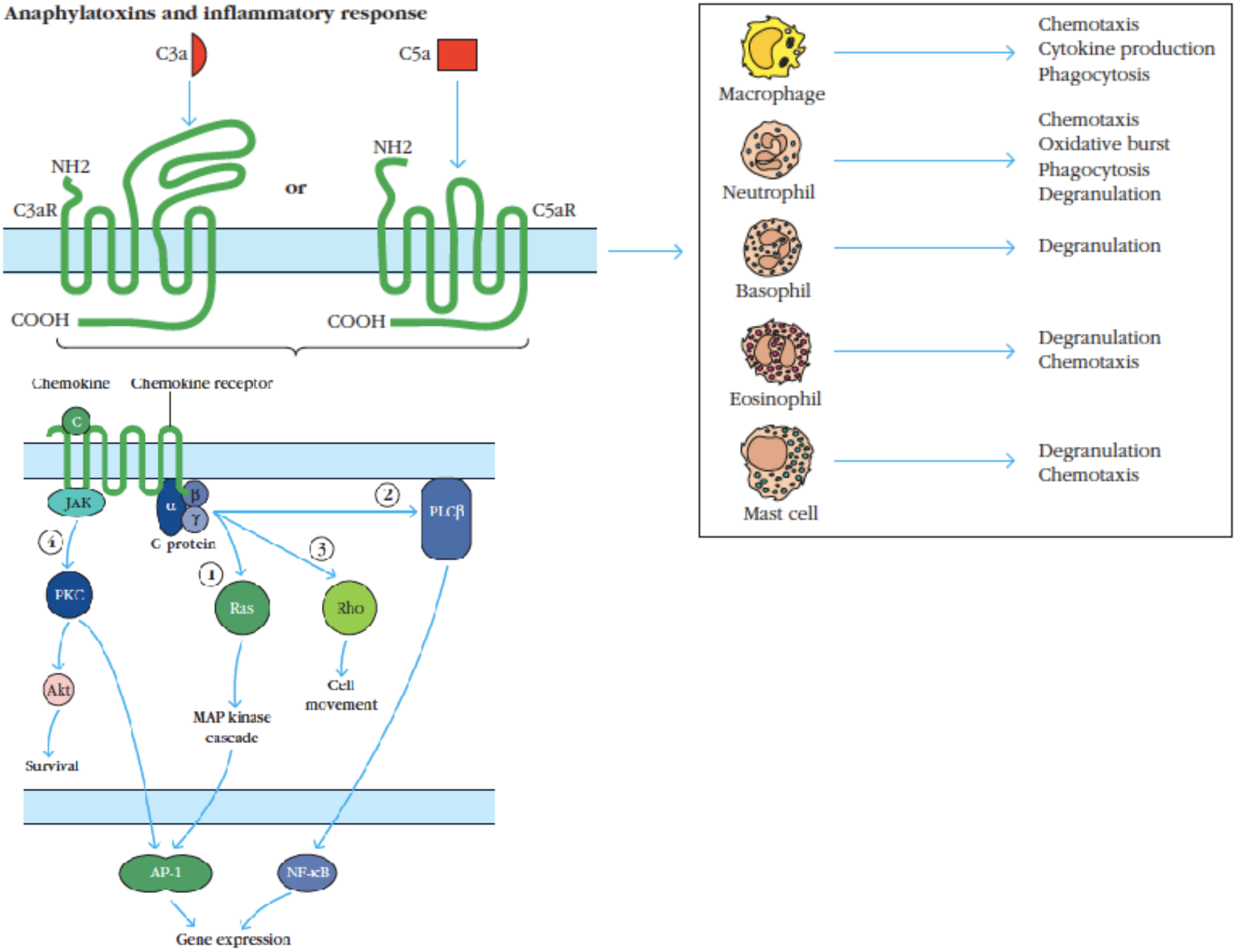
Receptor	Alternative name(s)	Ligand	Cell surface binding or expression	Function
CR1	CD35	C3b, C4b, C1q, iC3b	Erythrocytes, neutrophils, monocytes, macrophages, eosinophils, FDCs, B cells, and some T cells	Clearance of immune complexes, enhancement of phagocytosis, regulation of C3 breakdown
CR2	CD21, Epstein-Barr virus receptor	C3d, C3dg (human), C3d (mouse) iC3b	B cells and FDCs	Enhancement of B-cell activation, B-cell coreceptor, and retention of C3d-tagged immune complexes
CR3	CD11b/CD18, Mac-1	iC3b and factor H	Monocytes, macrophages, neutrophils, NK cells, eosinophils, FDCs, T cells	Binding to adhesion molecules on leukocytes, facilitates extravasation; iC3b binding enhances opsonization of immune complexes
CR4	CD11c/CD18	iC3b	Monocytes, macrophages, neutrophils, dendritic cells, NK cells, T cells	iC3b-mediated phagocytosis
CRIg	VSIG4	C3b, iC3b, and C3c	Fixed-tissue macrophages	iC3b-mediated phagocytosis and inhibition of alternative pathway
$C1qR_p$	CD93	C1q, MBL	Monocytes, neutrophils, endothelial cell, platelets, T cells	Induces T-cell activation; enhances phagocytosis
SIGN-R1	CD209	C1q	Marginal zone and lymph node macrophages	Enhances opsonization of bacteria by MZ macrophages
C3aR	None	C3a	Mast cells, basophils, granulocytes	Induces degranulation
C5aR	CD88	C5a	Mast cells, basophils, granulocytes, monocytes, macrophages, platelets, endothelial cells, T cells	Induces degranulation; chemoattraction; acts with IL-1β and/or TNF-α to induce acute phase response; induces respiratory burst in neutrophils
C5L2	None	C5a	Mast cells, basophils, immature dendritic cells	Uncertain, but most probably down-regulates proinflammatory effects of C5a

CR3 & Phagocytosis



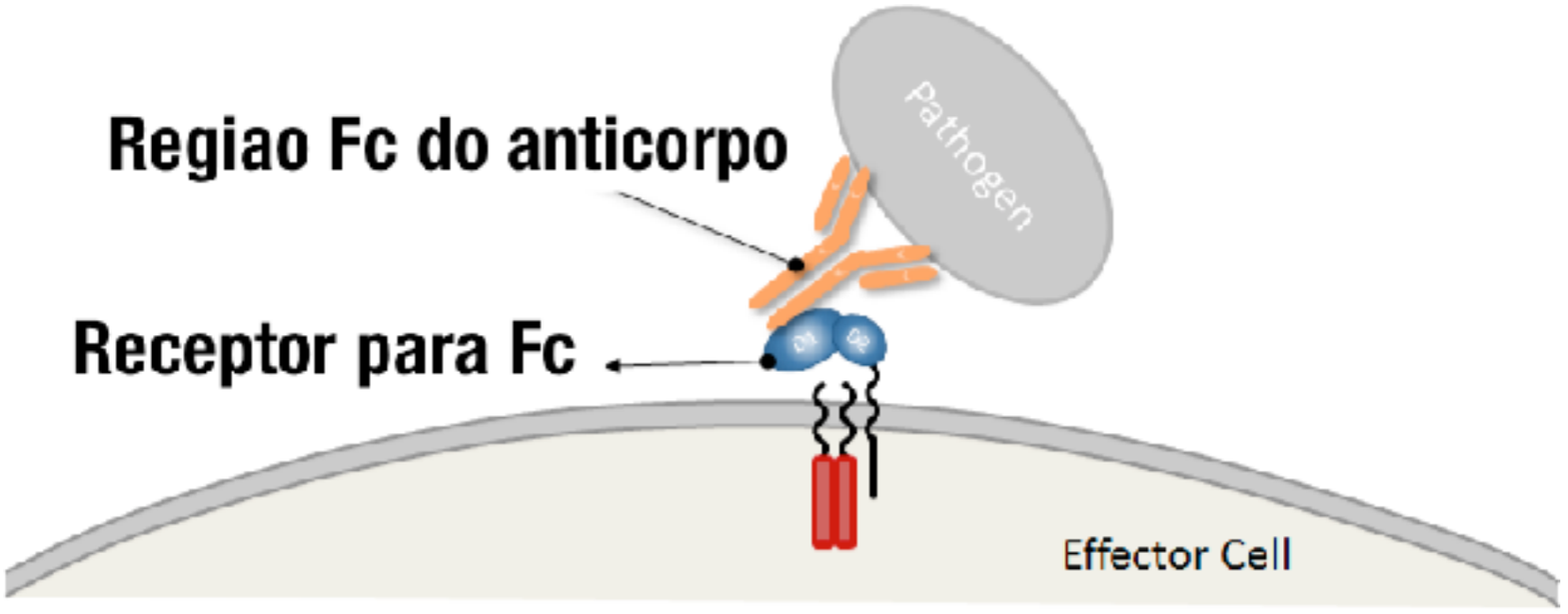
Smadar Hadas et al, 2012

Anaphylatoxins & inflammation

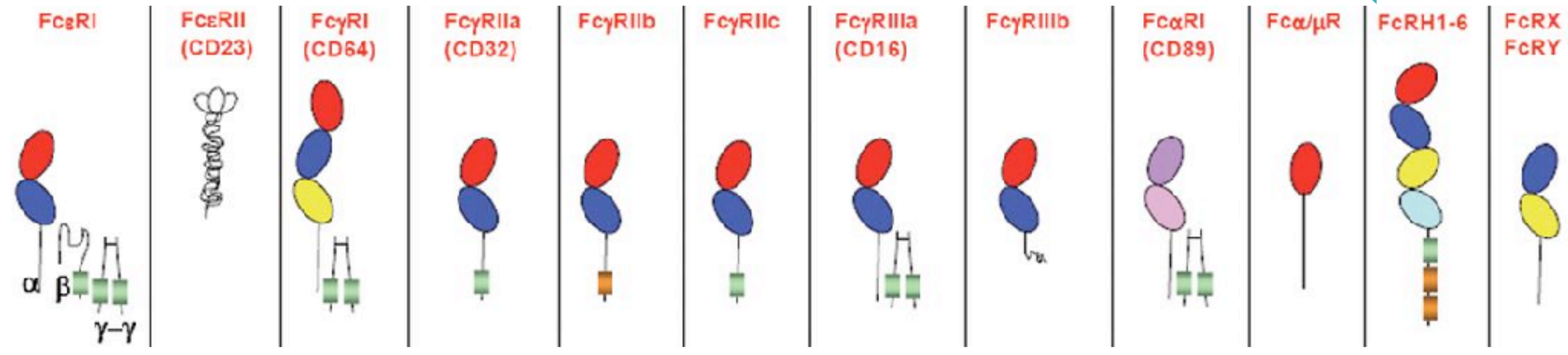


Reconhecimento indireto

Receptores para Fc dos AC (FcR)

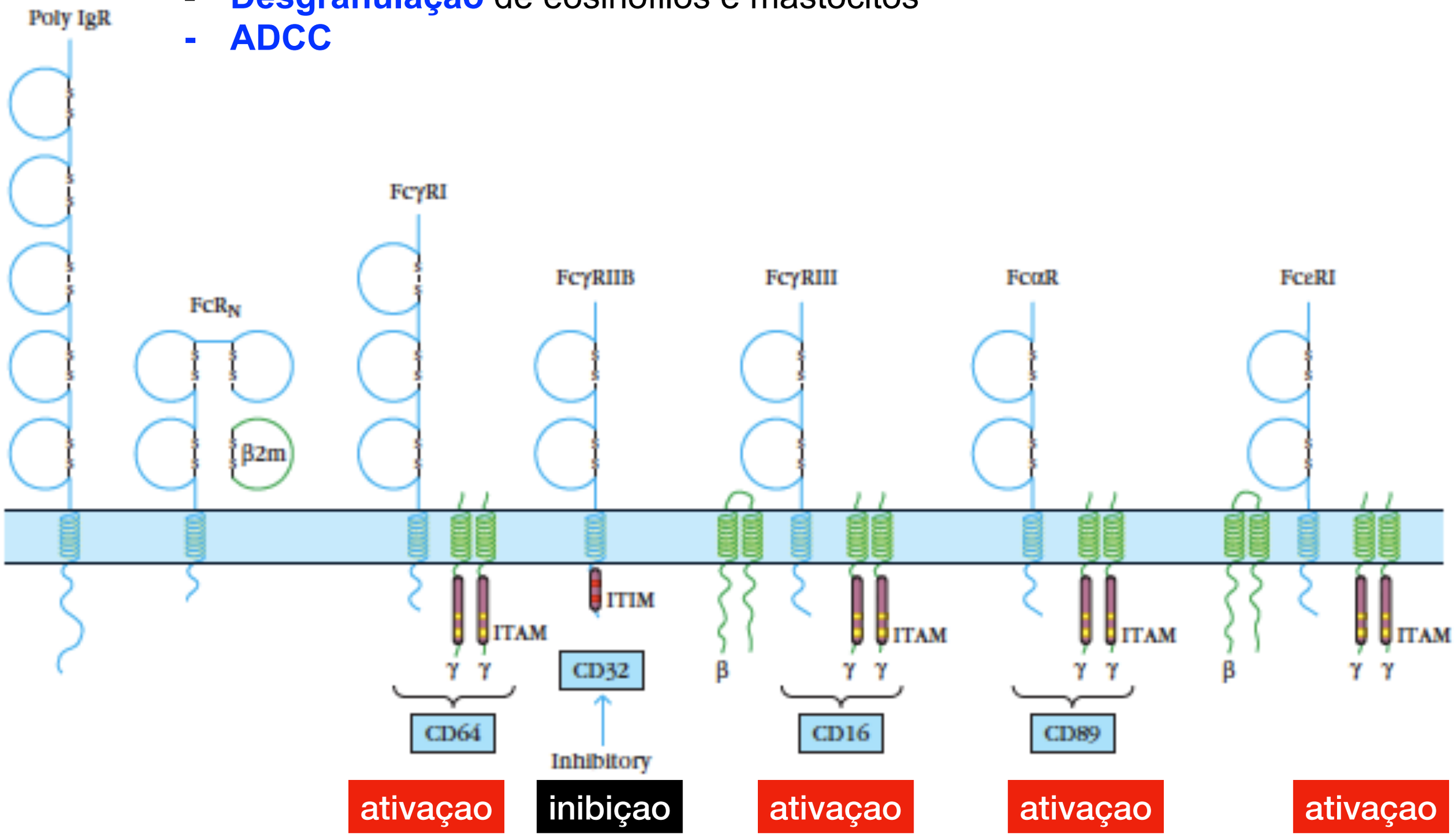


IgM, IgG, IgA, IgE

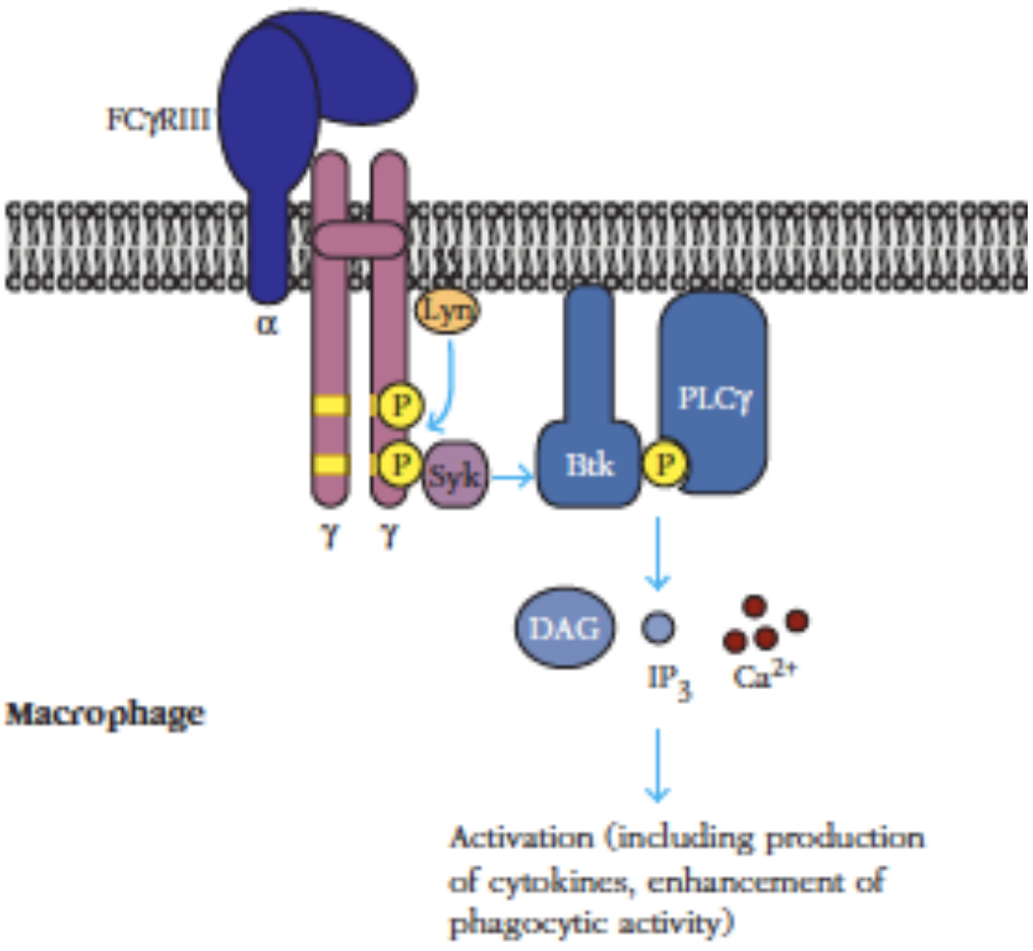


FcRs

- ✓ na superficie de muitos leucocitos
- ✓ induzem
- - **Fagocitose** da célula opsonizada pelos AC e potenciamento do *Killing*
- - **Desgranulaçao** de eosinofilos e mastocitos
- - **ADCC**

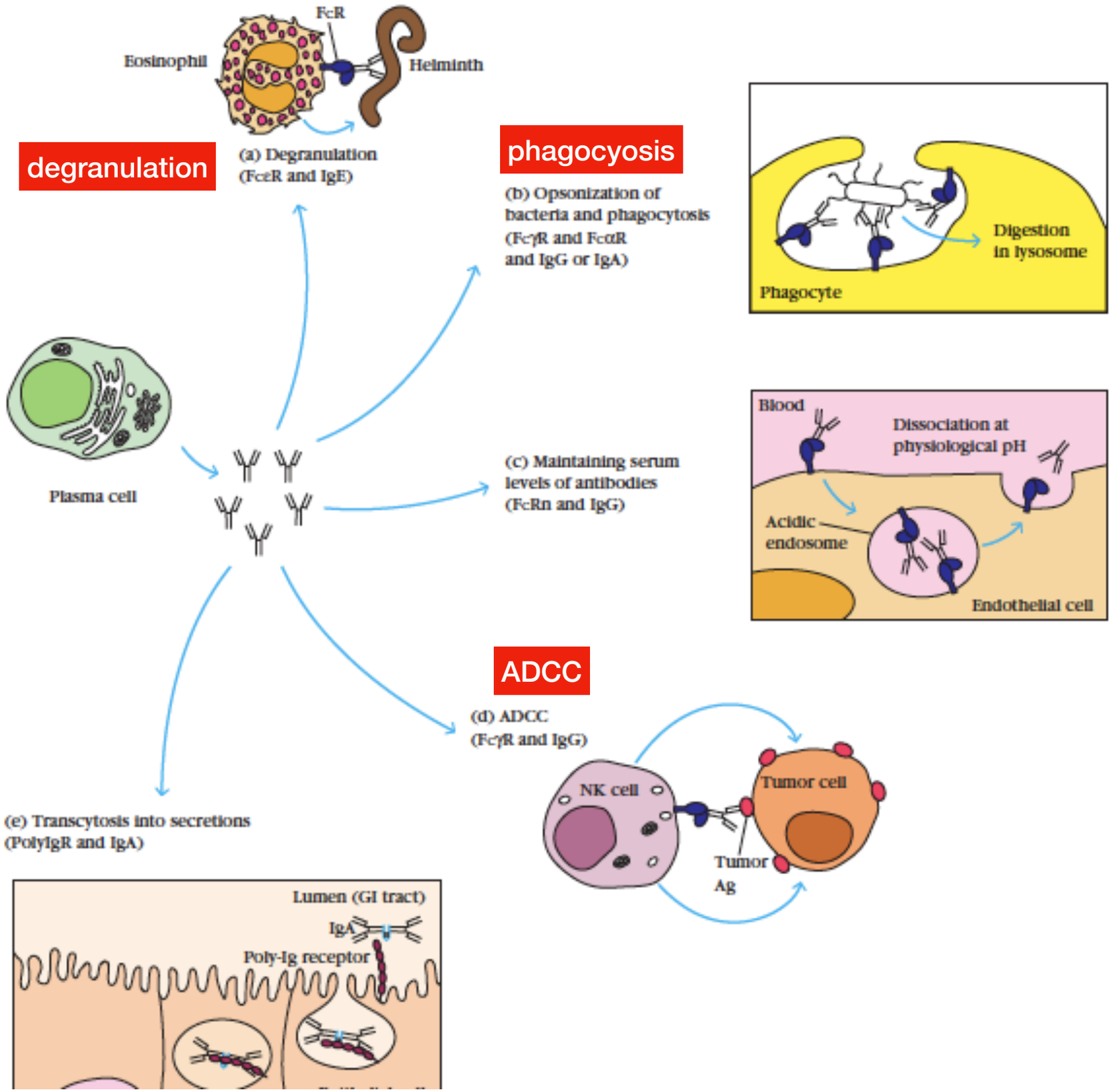


FcRs

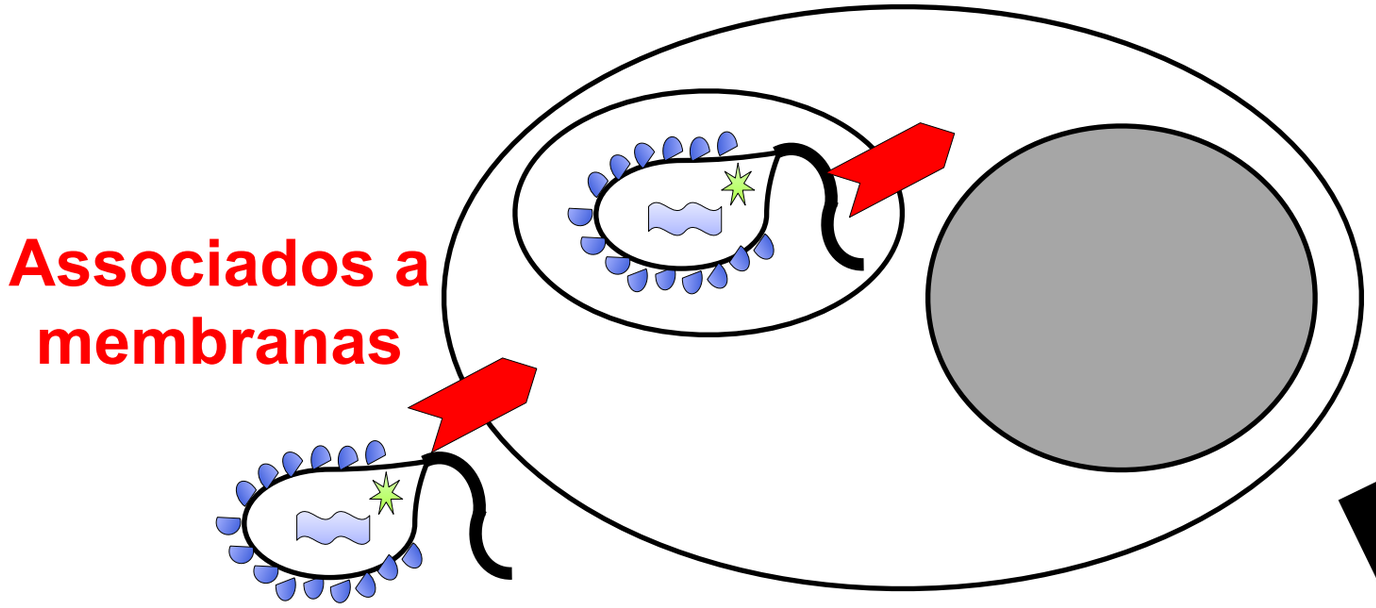


FcR	Isotypes they bind	Cells that express them	Function
FcγRI (CD64)	IgG2a in mice, IgG1 and IgG3 in humans High-affinity receptor	Dendritic cells, monocytes, macrophages, granulocytes, B lymphocytes	Phagocytosis Cell activation
FcγRII (CD32)	IgG	Dendritic cells, monocytes, macrophages, granulocytes, B lymphocytes, some immature lymphocytes	Inhibitory receptor Traps antigen-antibody complexes in germinal center Abrogates B-cell activation
FcγRIII (CD16) Humans generate two versions: FcγRIIIA (CD16a) and FcγRIIIB (CD16b)	IgG1, IgG2a, and IgG2b in mouse; IgG1 in human Low -affinity receptor Only FcR that binds mouse IgG1	Dendritic cells, monocytes, macrophages, granulocytes, B lymphocytes Only FcR expressed by NK cells	ADCC Cell activation
FcγRIV (in mouse, with some similarity to human FcγRIIIA and/or human FcεRI)	IgG2a and IgG2b in mice; IgG1 in humans Intermediate affinity receptor, although exhibits higher affinity for human IgG1 than FcgRIIA.	Monocytes, macrophages, granulocytes Not on lymphocytes	ADCC Cell activation
FcεRI	IgE	Eosinophils, basophils, mast cells	Degranulation of granulocytes, including eosinophils, basophils, mast cells
FcεRII (CD23)	IgE (low affinity)	B lymphocytes	Regulation of B-cell production of IgE Transport of IgE-antigen complexes to B-cell follicles
FcαRI (CD89)	IgA	Dendritic cells, monocytes, macrophages, granulocytes, some liver cells	Phagocytosis Cell activation ADCC
pIgR	IgA and IgM	Multiple epithelial cells	Transport of antibody from blood to the lumens of GI, respiratory, and reproductive tracts (transcytosis)
FcRn (neonatal FcR)	IgG	Epithelial cells (including intestinal epithelium) Endothelial cells of mature animals	Transport of antibodies from milk to blood (transcytosis) Transport of antibody-pathogen complexes from gut to mucosal immune tissue Phagocytosis Maintenance of levels of serum IgG and albumin

FcRs & Functions



Membrane-associated PRRs & non-PRRs



non-PRRs

CRs, FcRs, opsonin R

Fagocitose, Endocitose, Desgranulação ADCC

PRRs

Receptores de carboidratos (CLRs)
Receptores Scavenger

Fagocitose, endocitose (Cytotoxicity in NK)

Sinalização intracelular