Complement Receptors

Robert Graham Quinton Leslie, *Odense University, Odense, Denmark*

Complement receptors are membrane proteins expressed on the surface of immune cells. They interact specifically with complement factors leading to the removal of antigen from the circulation.

Secondary article

Article Contents

Introduction

I

, -

. , -

;

- - -

;

;

(IC) ;

B- .

C1, C3 C5

.

: (1)

, C3 , C5 C5 - , (2)

C3 , C3 ,

, C3 C3 , (3)

C1 .

Table 1. A

, ;

.

The Anaphylatoxin Receptors

The C5a receptor (C5aR, CD88)

C5 R 42 D

C5 C5

C5 - .

Structure

C5 R G -

,

. O

C3 ,

M L P (MLP), 8 (IL-8) -

(PAF) ,

. C5 R

13.3 13.4 19,

MLPR 34% .

C5 R ,

(68% , , ,

) G

- (85 98%);

.

.

Table 1 The complement receptors

Receptor	Ligand	CD number	Protein superfamily	Function
C5aR	C5a; C5a-desarg	CD88	G protein-coupled receptors	Leucocyte chemoattraction, degranulation
C3aR	C3a	–	G protein-coupled receptors	NO synthesis
CR1	C3b	CD35	Regulators of complement activation	Promotion of phagocytosis, immune complex (IC) clearance, processing of IC-bound C3b
CR23b1/rsIi3b			activation	CB-cellproclifeCaion, dalternaive pathwCay ctiva

ROM, reactive oxygen metabolites; NO, nitric oxide; MBL, mannan-binding lectin; SPA, lung surfactant protein A

Cellular distribution

C5 R , , , , , K , , , , (**Tables 2** **3**). C5 R (50 55 D 42 D)

C5 R . E C5 R

γ (IFNγ) (PMA).

Function

42- D C5 R C5 (K ∼1 L^{-1}) C5 - 10- . O , 200 000 , , ; (15 000) K 31 L^{-1} (375 000) K 100 L^{-1}. C C5 ; N- - C5 , N- , , G 199 A 206 C5 R L 58 C5 . A C5 R , L- / - (CR1, CR3 CR4), , (ROM). C5 R P- , E- 1 (ICAM-1), , C5 R - .

Signalling

C5 R, A 206 (R et al., 1996), - , - (αβγ) G P- , α , $G_{\alpha 2}$ $G_{\alpha 3}$, (P)- , / P - $G_{\alpha 16}$. G P- βγ α , , (PI)- C-β2 A_2 D. , , , - , C (PKC) 3- (PI3) , , - (MAPK) , . I , C5 , G - , - , . I , C5 R 10 (N et al., 1997). C5 R .

Table 2 Distribution of complement receptors on blood cells in humans

Cell type	C5aR	C3aR	CR1	CR2	CR3/4	cC1qR	C1qRp	gC1qR
Monocytes (macrophages)	+	+	+	–	+	+	+	–
Neutrophils	+	+	+	–	+	+	+	+
Eosinophils	+	+	+	–	+	–	–	+
Basophils (mast cells)	+	+	+	–	+	+	+	+
Natural killer cells	–	–	+	–	+	–	–	–

fT 1 9F B cellsT) . s t e l e (2 0 0 . . 4 e r (2 . –6 e r P 0 – [a] c T 1 0 2 8 c (+) T D T j D T 9 1 4 2 f 0 4 4 0 . 1 6 3 6 0 T E D 5 7 c (– 3 T – j / F f 5 T 1 T f 3 5 7 3 9 6 / 0 T D T 4 . R C

[a] C3aR has been detected on tonsillar B cells.
[b] Present on a minor T-cell subpopulation.
[c] On human and primate cells only.
[d] C3aR is expressed on guinea-pig platelets.
[e] CR1 is expressed on murine and rabbit platelets.

Table 3 Distribution of complement receptors in human tissues

Tissue and cell type	C5aR	C3aR	CR1	CR2	CR3/4	cC1qR	C1qRp	gC1qR
Lymphoid organs								
Follicular dendritic cells (FDCs)	–	–	+	+	+[a]	–	–	–
Liver								
Kupffer cells	+	–	+	–	+	–	–	–
Stellate cells	+	–	–	–	–	–	–	–
Brain								
Microglia	+	–	–	–	+	–	–[b]	–
Astrocytes	+	–	–	+	–	–	–	–
Other tissues								
Vascular endothelial cells	+	–	–	–	–	+	+	–[e]
Epithelial cells	+[c]	–	+[d]	–	–	+	–	–
Gingival fibroblasts	–	–	–	–	–	+	–	–

[a] CR3 only.
[b] Present on rat microglial cells.
[c] On bronchial and alveolar cells.
[d] On glomerular podocytes.
[e] Found in association with mitochondria.

The C3a receptor (C3aR)

Structure

H C3 R C5 R 482 37% C5 R (A et al., 1996). H , C3 R 175 , (A et al., 1996; C et al., 1996). M C3 R 65% 165 . L C5 R, C3 R ; 54 61 D 86 107 D HMC-1, - (83 114 D).

Cellular distribution

C3 R / , - , , (**Table 2**). A , B . , , , , - .

Function

C3 R , C3 . - (K = 2 5 L^{-1}) (200, 63 000 30 000 60 000 - HMC-1 ,) - (K = 30 150 L^{-1}) (500, 120 000 5 23×10^5 , ,). O , - 40 000 . E C3 R IFNγ. C3 R , . I / , ROM , - . I , IL-3 - – - (GM-C F). C3 R B- .

Signalling

L C3 R C^{2+} P , G . I HMC-1 , C^{2+} , C^{2+} . C5 R, - - , . I ,

PI3 C3 R , (IP_3) . C3 R- , PMA , PKC .

The Complement Receptors for C3b and its Derivatives

Complement receptor type 1 (CR1)

C 1 (CR1, CD35) 210 290 D C3 , C4 , , C3 .

Structure

CR1 , H, C4- (C4), - (DAF), (MCP), CR2, C1 , IL-2 , β_2- 1, α III , .

(RCA) . CR1 30 (, CR) 60 65 , 10 15 ; - – , – - CR (**Figure 1a**). D CR1 CR (LHR) CR 70 95% LHR. CR1 25 C- 39 . LHR CR LHR, CR1 LHR. , CR1 C (F = 80% 20%,) LHR , LHR , . I , CR1 1, 32, CR2, DAF, H C4 . M CR1 CR N- CR1 15 CR CR2 ( ).

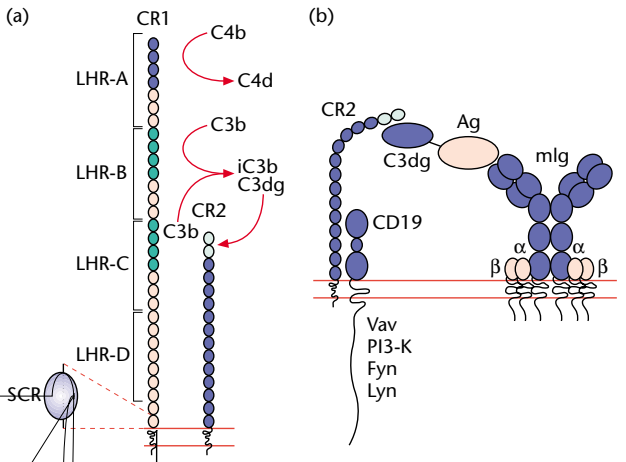

Figure 1 Structure and function of CR1 and CR2. (a) The most prevalent allele of CR1 is comprised of 30 short consensus repeats (SCRs) arranged in four long homologous regions (LHRs), where the ligand-binding sites are contained in the four N-terminal SCRs of each of the first three LHRs, while the ligand-binding site of the 15 (or 16) SCR CR2 is located in SCR1/2. On B cells, CR1 and CR2 are found in noncovalent association with each other. As a cofactor for factor I, CR1 promotes degradation of its ligand C3b, to iC3b and then C3dg, thus providing CR2 with its ligand. (b) The association of CR2 with CD19 ensures recruitment of the latter to the B cell receptor (BCR) complex upon BCR/CR2 crosslinking by opsonized antigen. By binding and activating the protein tyrosine kinases Lyn and Fyn, and PI3 kinase, CD19 supplements the signalling transduced through BCR upon antigen engagement. (Figure 1b is adapted from O'Rourke L, Tooze R and Fearon DT (1997) Co-receptors of B lymphocytes. *Current Opinion in Immunology* **9**: 324 329.)

CR1/2 CR2 1.

Cellular distribution

CR1 / , - , , , (NK) , B , (FDC), , K , , (**Tables 2 3**). A CR1 (250) 25- 50- , 85 90% - CR1 . CR1 , 5- 10- MLP C5 - , GM-C F , 60 70% PMA. CR1, , , - . A CR1 (CR1), (30 L^{-1})

,
CR1 .

Function

CR1 , C3 ,
(K), , 2
5×10^7 L $^{-1}$, C4 , C3
100- . E CR1
C3 -
CR LHR , - C4 -
LHR. I
, CR1
I- C3
C3 , , C3 C3 , C4 C4
C4 . CR1 C1 K
2.6×10^8 L $^{-1}$.
CR1

(. . , MLP, , C1 ,
-
PA). H ,
IL-1 , -
-κB (NF-κB)
CR1
. CR1
B - -
. H ,
CR1 B -
C3 C3 ,
CR2 (**Figure 1a**).
I , - CR1
(IC) . B C3 -
K ,
IC
,
, .
F ,
IC , -
IC . I
, CR1
(1) CR1 C3 -
IC (2) IC- C3 C3 ,
, C3 ;
IC ,
CR3, B -
CR2 (N et al., 1997).
- - ,
(LE),
IC
. I
,
C3 - .

Signalling

CR1, ,
, .
P CR1
(B), PKC
- PMA,
,
. H ,
CR1 .

Complement receptor type 2 (CR2)

C 2 (CR2, CD21) 145- D
C3 C3 . I E –
B (EB),
.

Structure

L CR1, CR2 RCA . CR2
15 16 CR ; CR
CR10 CR11
CR2. C- CR 24
34
. E CR2
.
A ( )
.

Cellular distribution

CR2 B (8000),
, FDC , ,
( ) (**Tables 2 3**).
-B B
B -
.

Function

CR2 C3 , C3 ( ), C3 ,
C3 (C3) ( ), 350/
220 EB , , CR
. H , CR3 CR4
C3 C3 . CR2
(AP)
C3 B P
(. . AP) - .
In vitro, , B ,
C3
5-
CR2, in vivo
10- .
A CR2
-

CR2
,
CR2, CR2 . I ,
. C , -
C3
10 000- ,
(D
et al., 1996). ,
CR2 B FDC,
CR2 B
FDC CR2

CR2
, CR1, CD19 CD23
(- E'),
B .
A B- CR1
CR2,
CR1 - C3 (
), ,
CD19, B
(BCR) (**Figure 1b**).
CR2 CD23;
E ,
B CD23-
FDC .

Signalling

CR2
. H ,
CD19/CD81(APA-1)/L 13, CR2
B-
CD19 BCR.
C CD19 BCR
BCR .
CD19
BCR
(P K), L F , PI3 R
,
MAPK (**Figure 1b**). -
BCR CD19
: (1) ,
CD19- L , BCR
(2) C $^{2+}$ PI3 -
(B et al., 1997),
Cγ-
BCR.

Complement receptors types 3 and 4 (CR3 and CR4)

C 3 (CR3, M -1, CD11 /CD18)
4 (CR4, 150/95, CD11 /
CD18) β
(CD18). B C3
.

Structure

CR3 CR4
. β2 ,
- 1
(LFA-1, CD11 /CD18), β ;
95- D
,
22 21 -
10 . β2 678
57 C ,
24
, 23 46
.
- (MIDA)
A 134, 136, A 232
G 235, -
. α CR3 155- D
, 1092
, 26 19
. CR3 α
63% CR4, 150- D
, , -
1081, 26
29 , . B
11
13.1 16.
(87%)
- ,
60 ,
200 , N-
- .
I'
B C2.
I
α/β R , MIDA -
M $^{2+}$ - .

Cellular distribution

CR3 CR4 , -
, , / , NK ,
K , , CR3
FDC (**Tables 2 3**). L CR1, CR3
, GM-C F, MLP, C5 , PMA,
A23187 IL-4,
CR3
CR1.

Function

CR3 CR4 C3 , M $^{2+}$ -
2×10^6 L $^{-1}$, CR3. CR3
, ICAM-1 (CD54),

(LP)
(NIF) Ancylostoma caninum;
I
α . CR3 (Z) β- -
I (
et al., 1996).
CR3
CR4 , ROM ,
, . CR3
I E -
ROM,
/ . B CR3
CR4, LFA-1,
.

Signalling

CR3 CR4
. C
PKC- β_2
CR3
(GPI) ,
(CD87)
F γRIII (CD16). CR3, ,
, A2 D
NADPH . C
, C^{2+}
, ,
C^{2+} (P H , 1998). B C^{2+} ,
CR3 ,
,
CR3 .
CR3
CR3.

The C1q Receptors

- C1
: C1 R, 56- D -
- C1 ;
C1 R , - 126 D
, C1 R, 33- D
,
C1 .

Structure

C1 R
42% 12.6% ,
I 5.5 6.0. C1 R
C^{2+}-
(CR); 475 52- D
- ,
( )- . CR
C-
KDEL , C1 R
.
C1 R 641
, 21 ,
156 C- -
- , EGF- , 25
(47
) C-
C1 R (I = 4.5) 33 D
88 90 D
. C1 R 282
13
60
. O
209 C1 R, 73
, : 2:1,
.

Cellular distribution

C1 R , , B ,
, ,
(**Tables 2 3**), ,
-B B- .
, 8000 B- R
1.6106 937 3106
. E C1 R -
PMA.
C1 R , ,
30 60% IL-1
(GF),
, A23187,
937 .
C1 R , -
, (N , 1998)
,
(**Tables 2 3**).
MLP PMA
,
IFN .
C1 R , ,
B , ,
, (**Table 2**). A
C1 R ,
,
(D ., 1998).

C, K L D MP (1997) C RA (1995) ,
HI . Immunological Reviews **159**: 49 67. . Current Opinion in Immunology
AJ (1993) F C1 . Behring **7**: 48 53.
Institute Mitteilungen D (93): 241 253.