Bağışıklık

- **İlk savunma hattı**
  - Patojenlerin vücuda girişinin engellenmesi
- **İkinci savunma hattı**
  - **Vücuda girerse, iç savunma olarak**
    - **Fagositoz**
    - **Komplement**
    - **yangı**
- **Üçüncü savunma hattı**
  - Spesifik immün yanıt
    - Antikorlar
    - T hücreleri

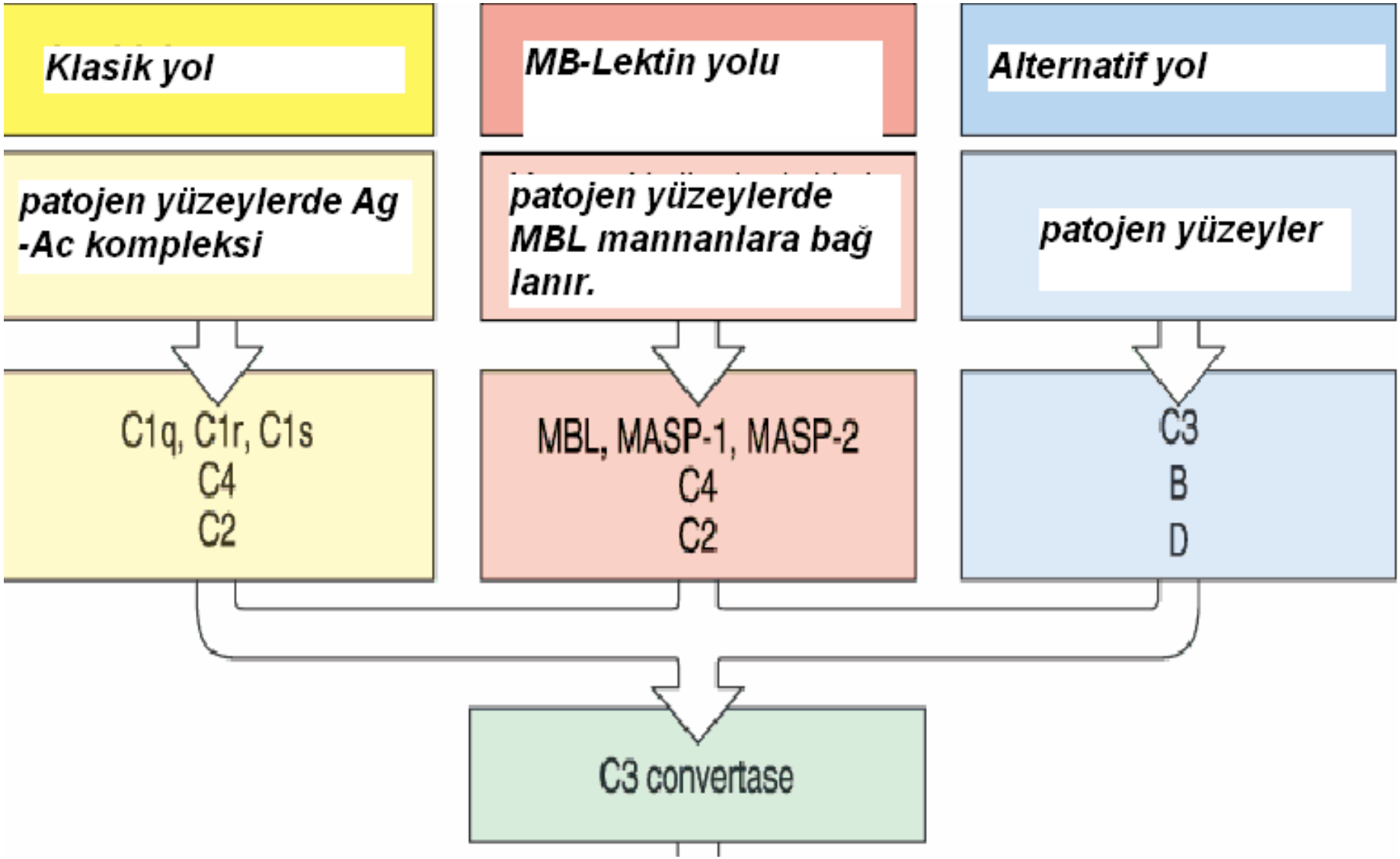
Komplement

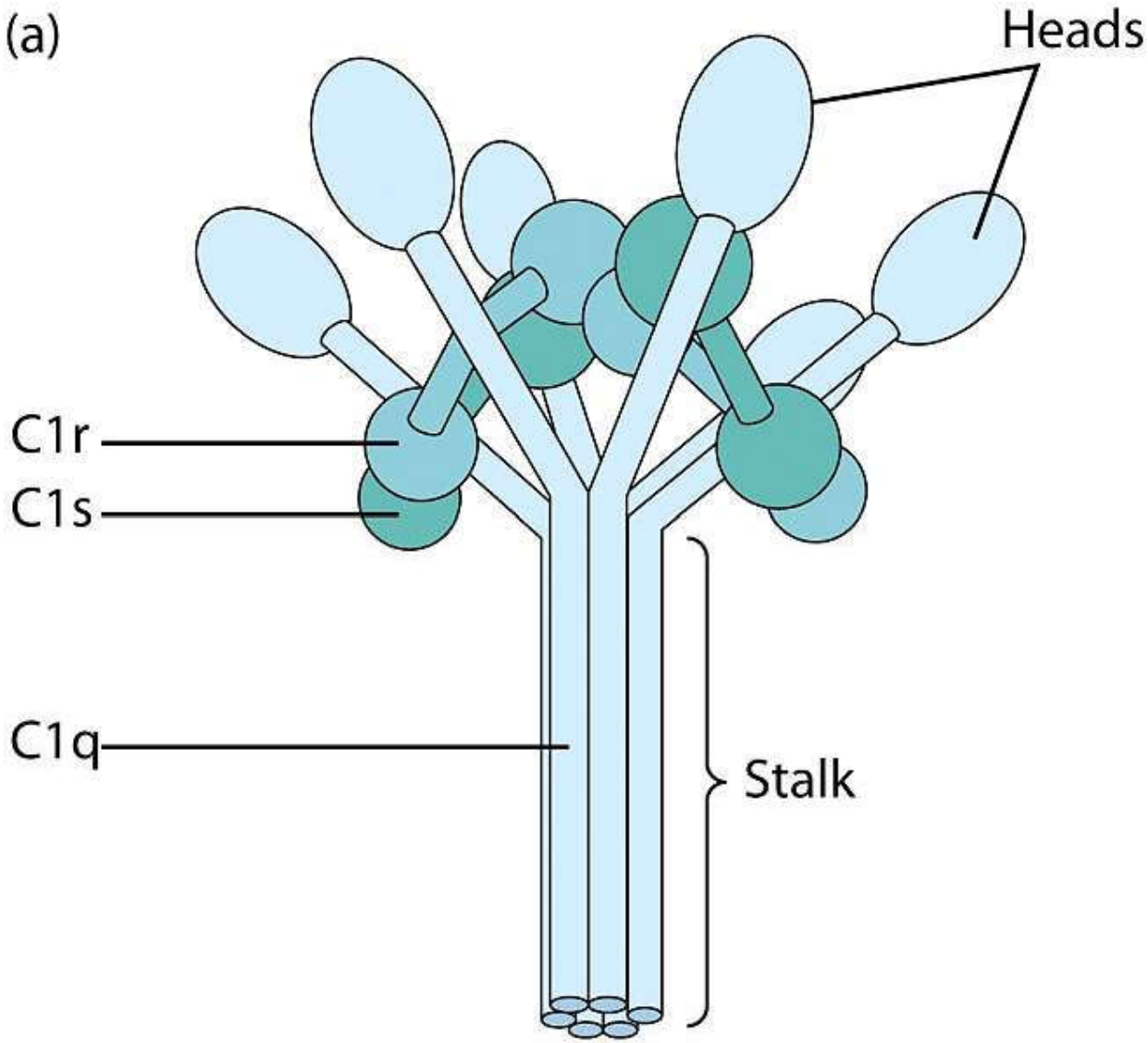
- Tanım
- Karaciğer, makrofajlar ve barsak epitel hücreleri tarafından salgılanır.
- C3,C6,C8 ve B karaciğerde
- C2,C3,C4,C5,B,D,P,I makrofajlarca
- 30 dan fazla protein ve protein ürünlerinden oluşmuştur.
- **Aktif fonksiyon**
- **İnaktif**

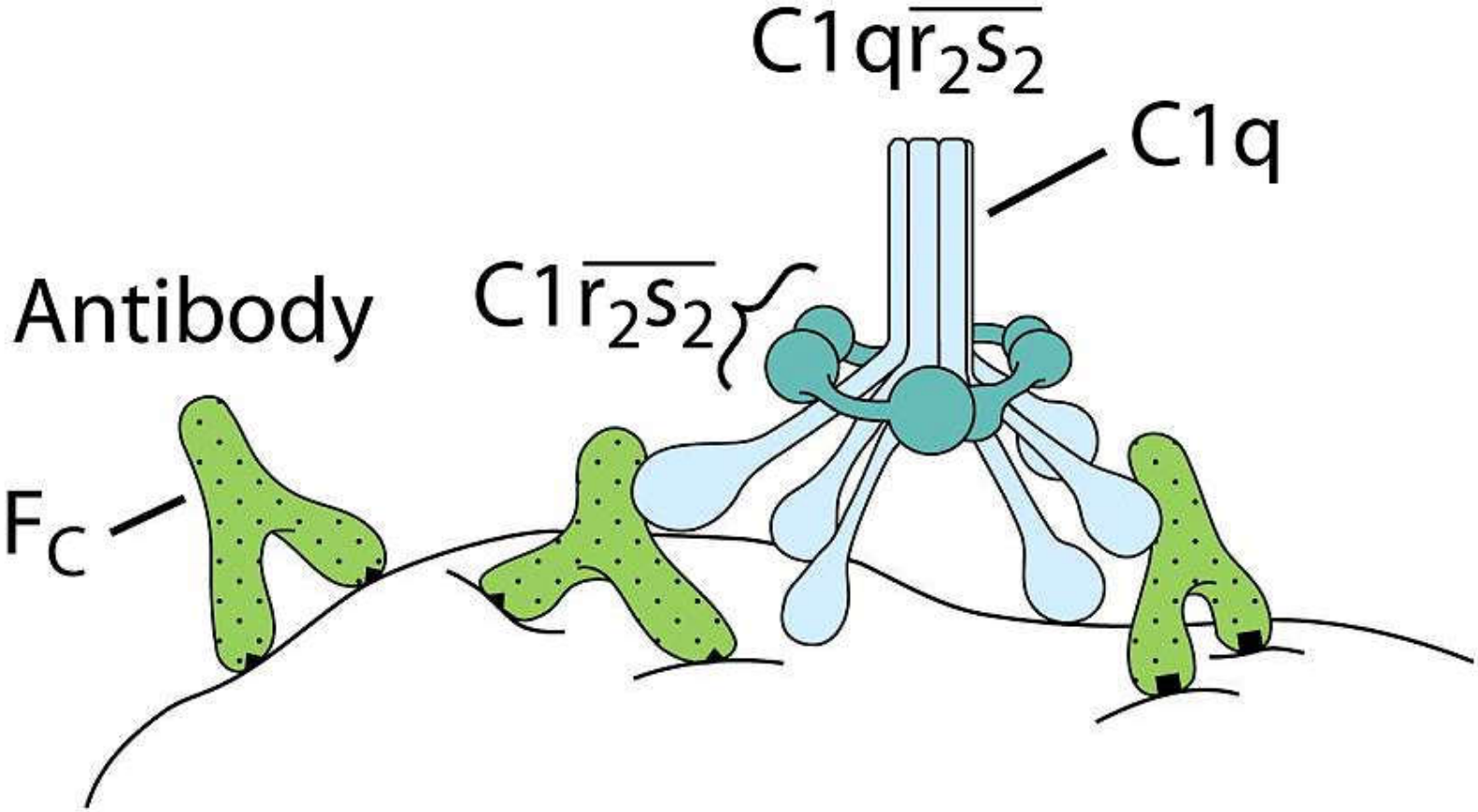
Fonksiyonları

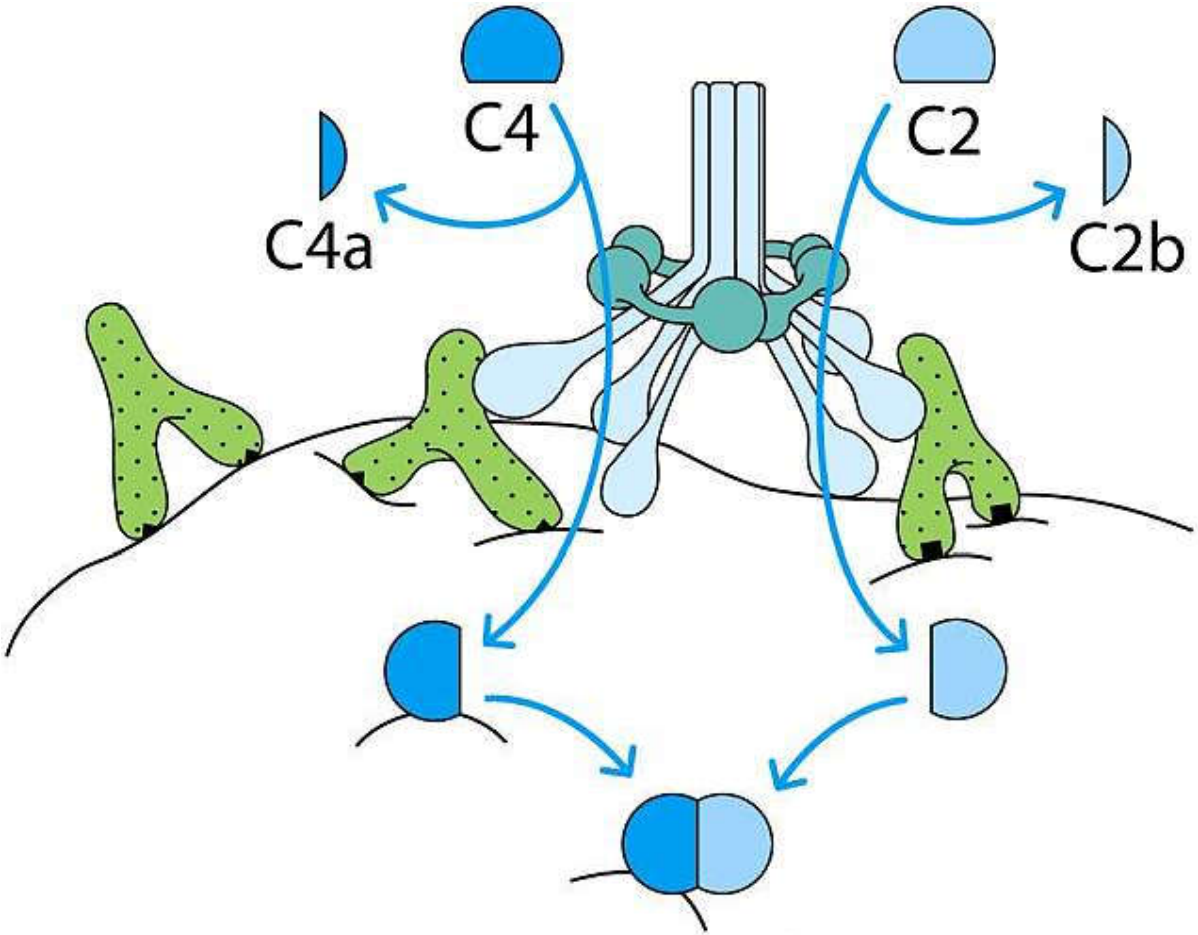
- 1- Opsonizasyon
- 2- Kemotaksis
- 3- Hücre ölümü (MAK)
- 4- Yangı uyarımı
- 5-İmmunkomplekslerin uzaklaştırılması
- (eritrositler ve fagositik hücrelerle)

Komplement aktivasyon yolları

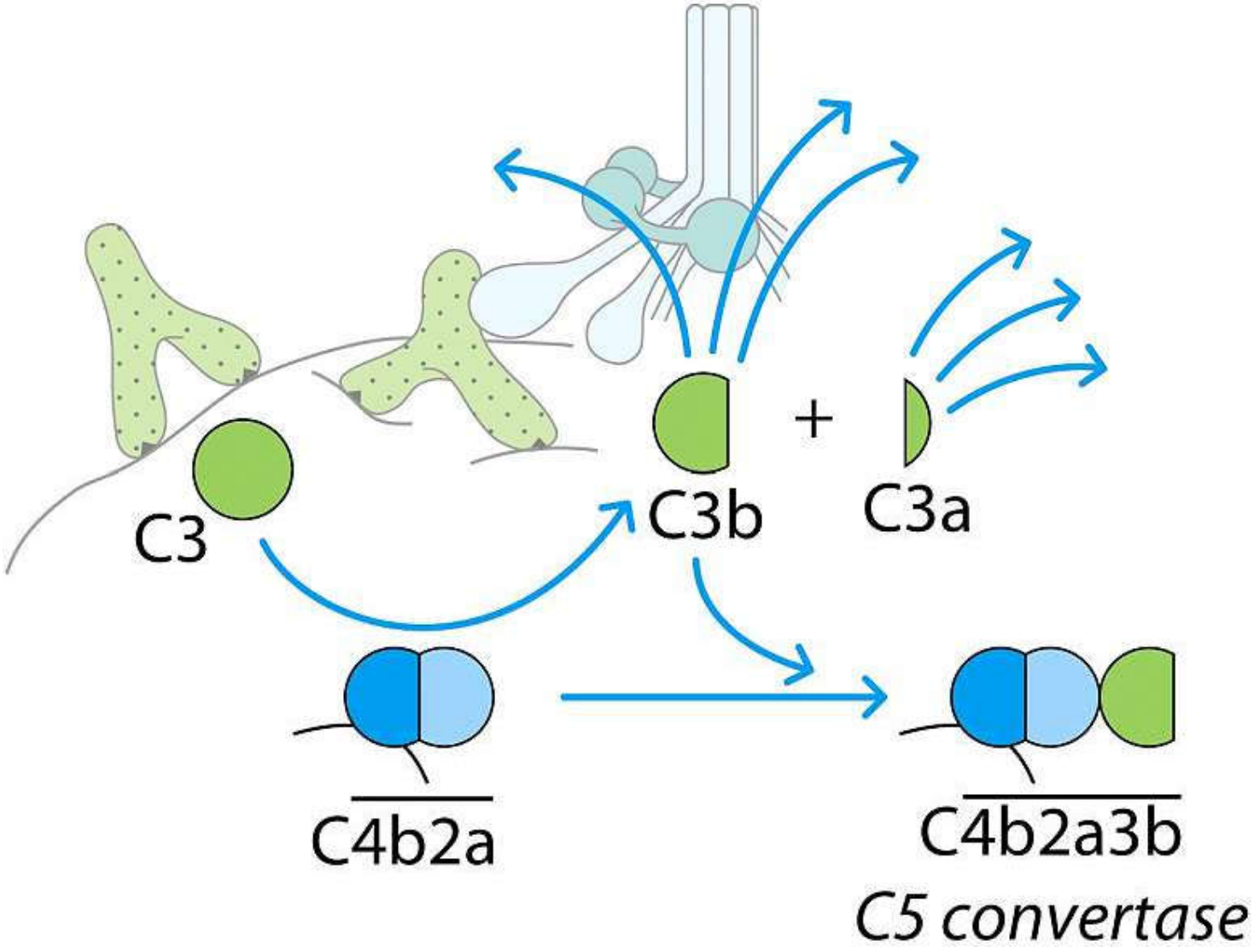


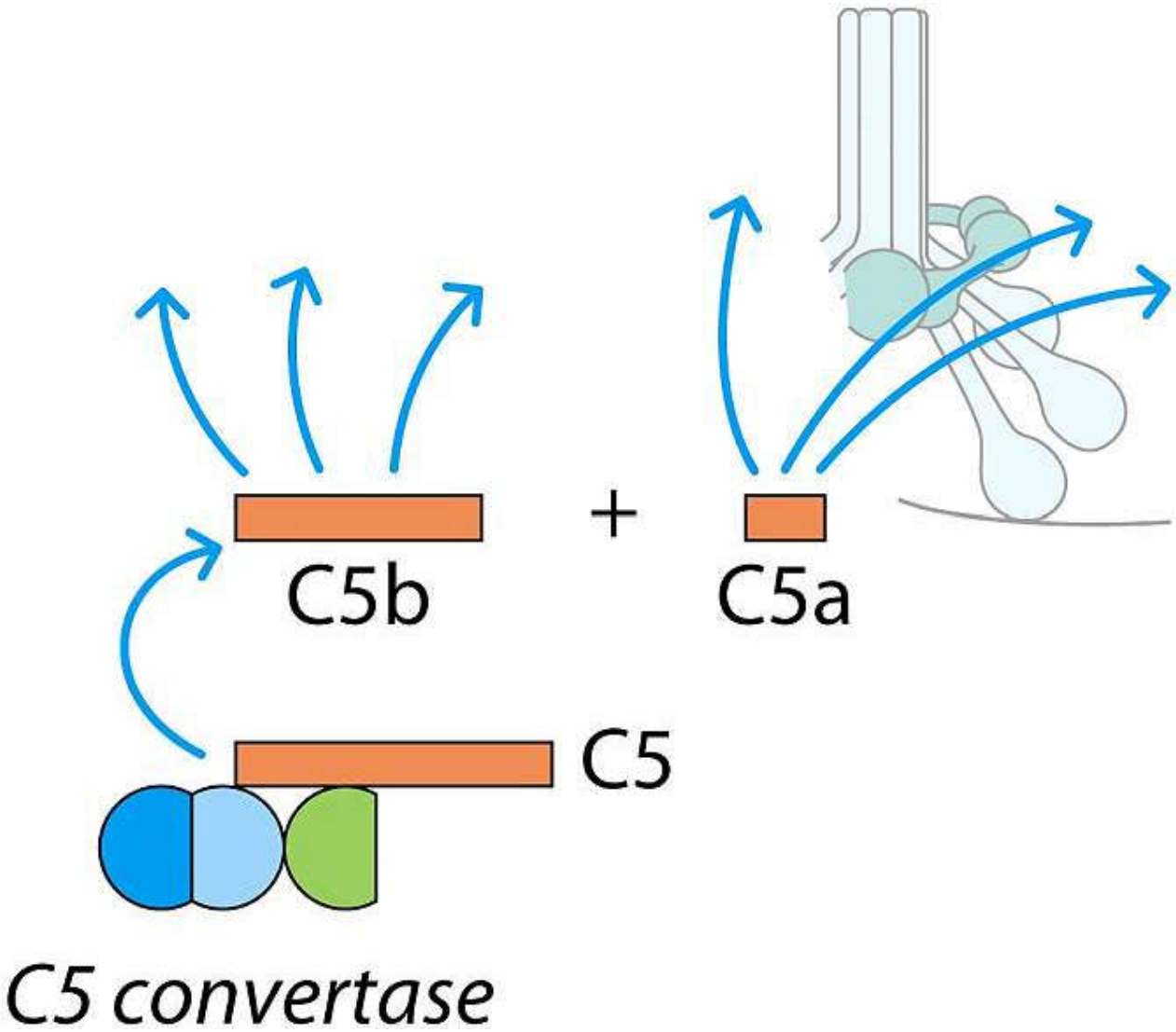

(a)
Heads
C1r
C1s
C1q
Stalk


C1q$\overline{r_2s_2}$
C1q
Antibody
C1$\overline{r_2s_2}$
F_C



C3 convertase


C3
C3b
+
C3a
C4b2a
C4b2a3b
C5 convertase


C5b
+
C5a
C5
C5 convertase

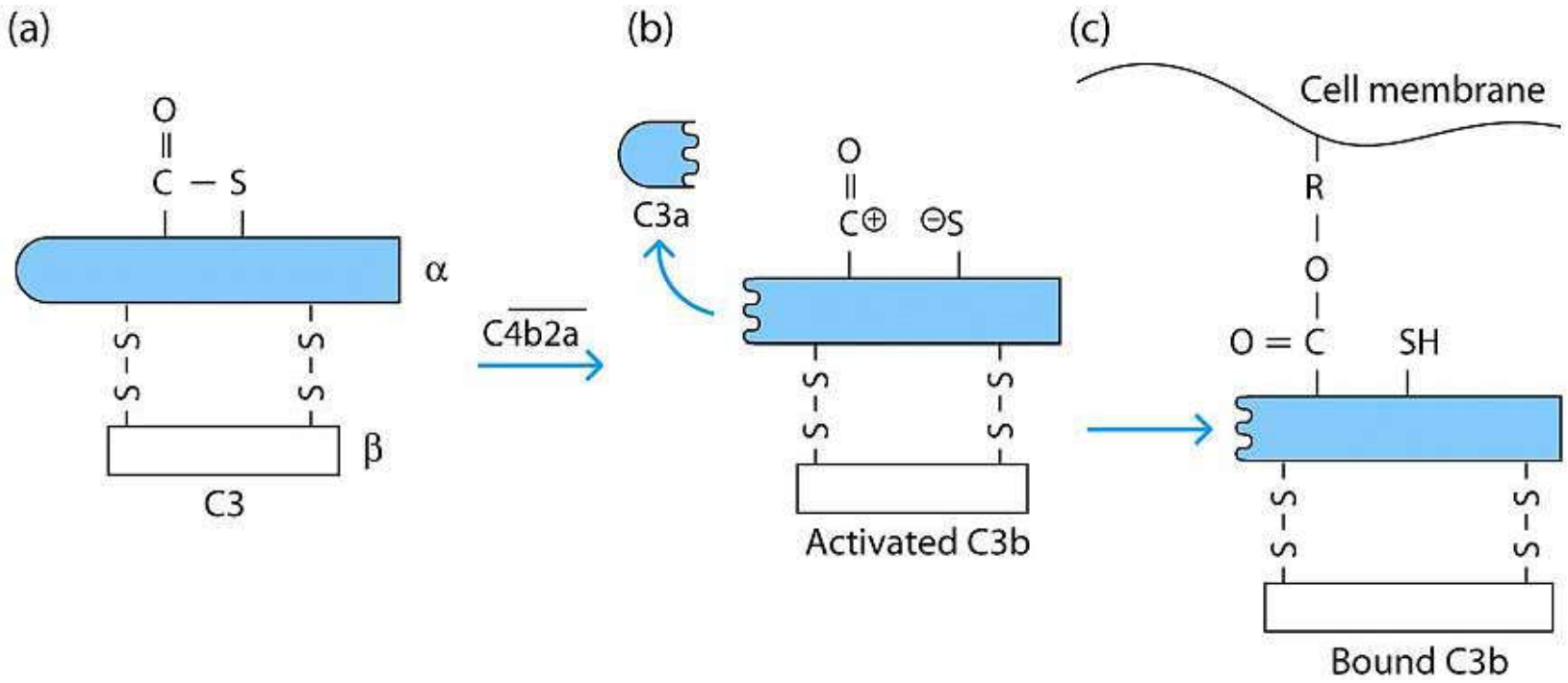

(a)
O
C — S
α
S–S
S–S
β
C3
C4b2a
(b)
C3a
O
C⊕ ⊖S
S–S
S–S
Activated C3b
(c)
Cell membrane
R
O
O = C
SH
S–S
S–S
Bound C3b

TABLE	ALTERNATİF KOMPLEMENT YOLU UYARIMI

Gram negatif çoğu bakteri suşu

Lipopolisakkarid

Gram pozitif bakteri suşlarının çoğu

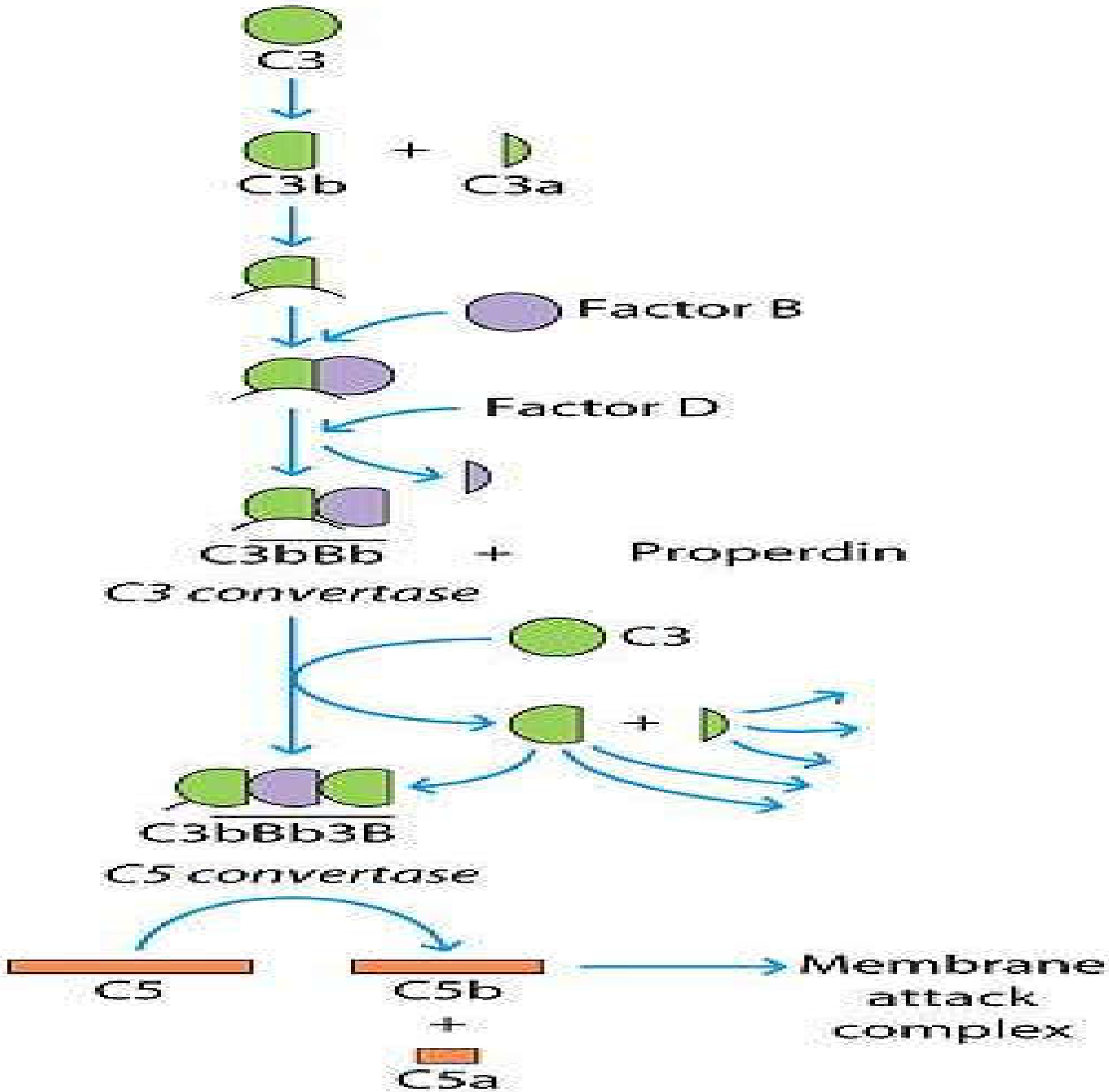
Teikoik asit

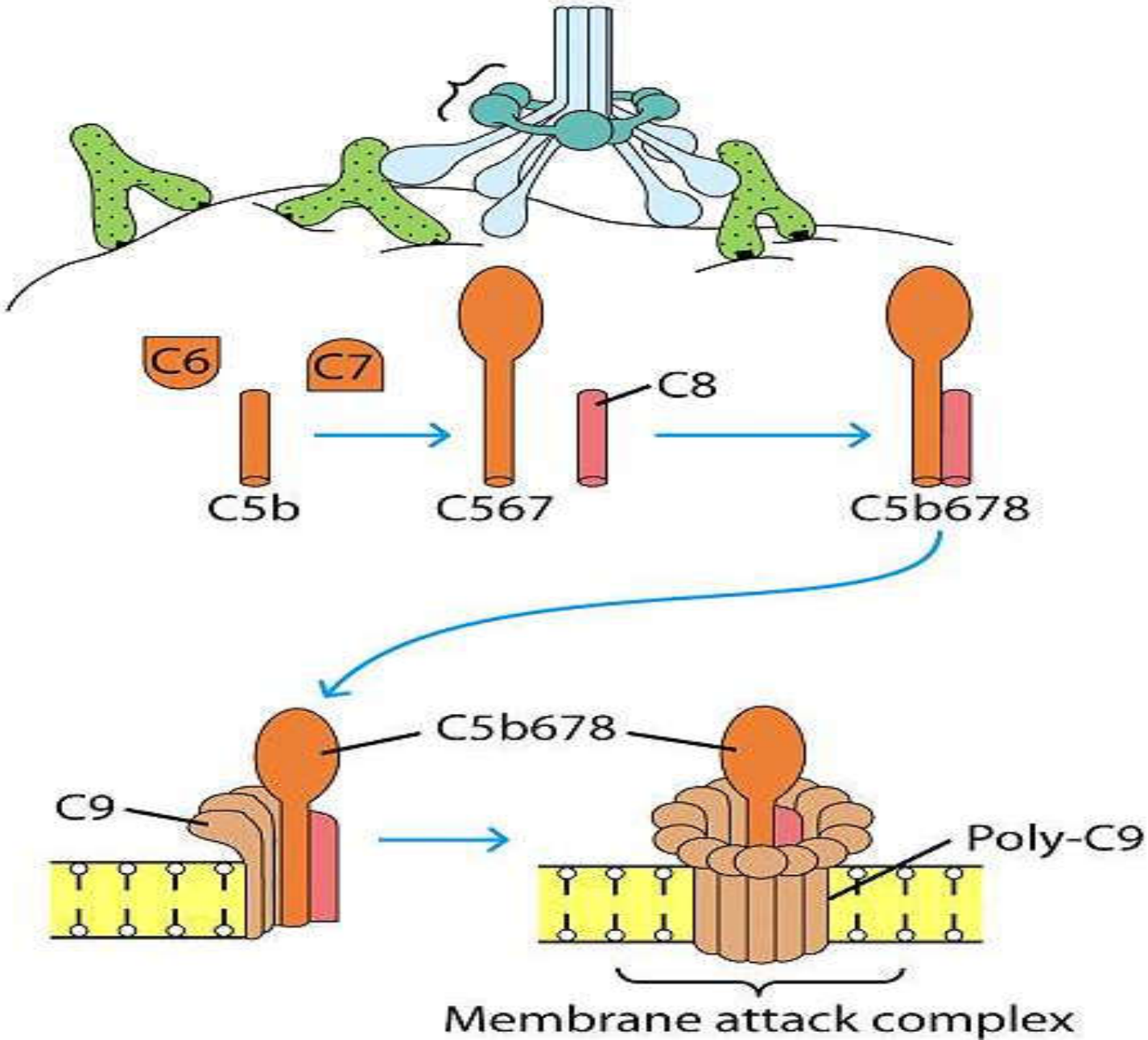
Mantar ve maya hücre duvarı (zymosan)

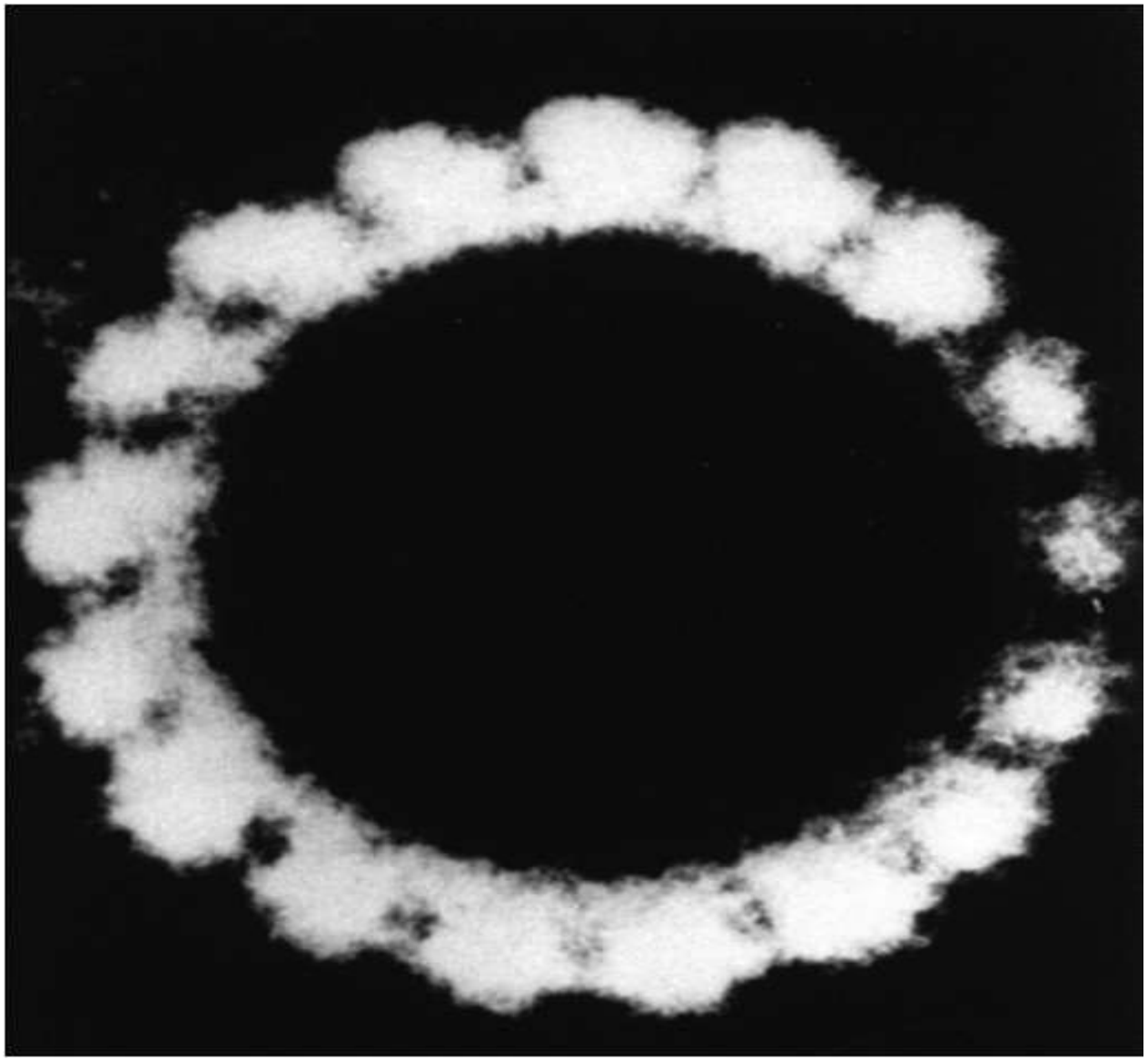
Bazı viruslar ve virus ile infekte hücreler

Bazı tümör hücreleri (Raji)

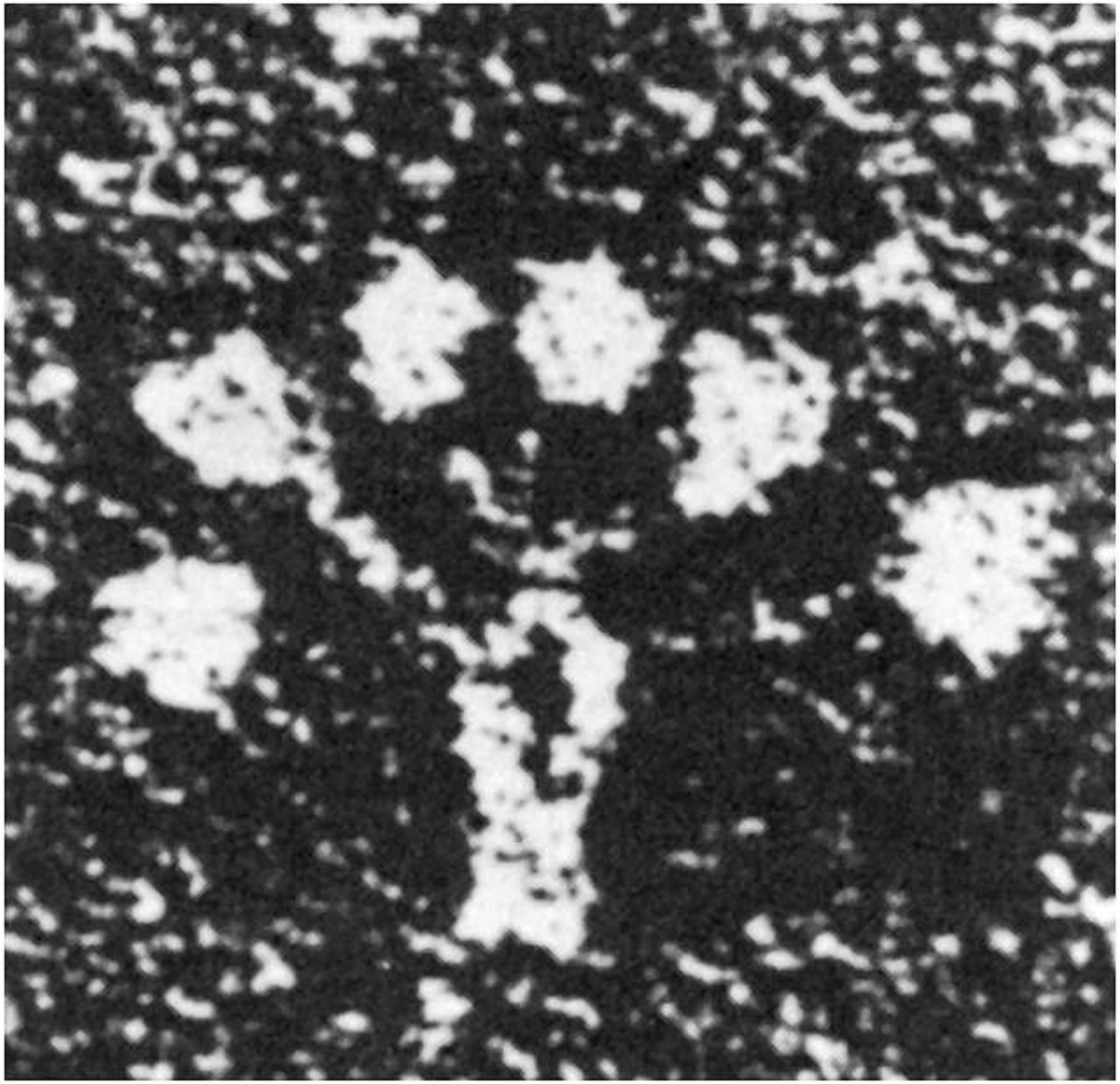
Parazitler (trypanosomes)

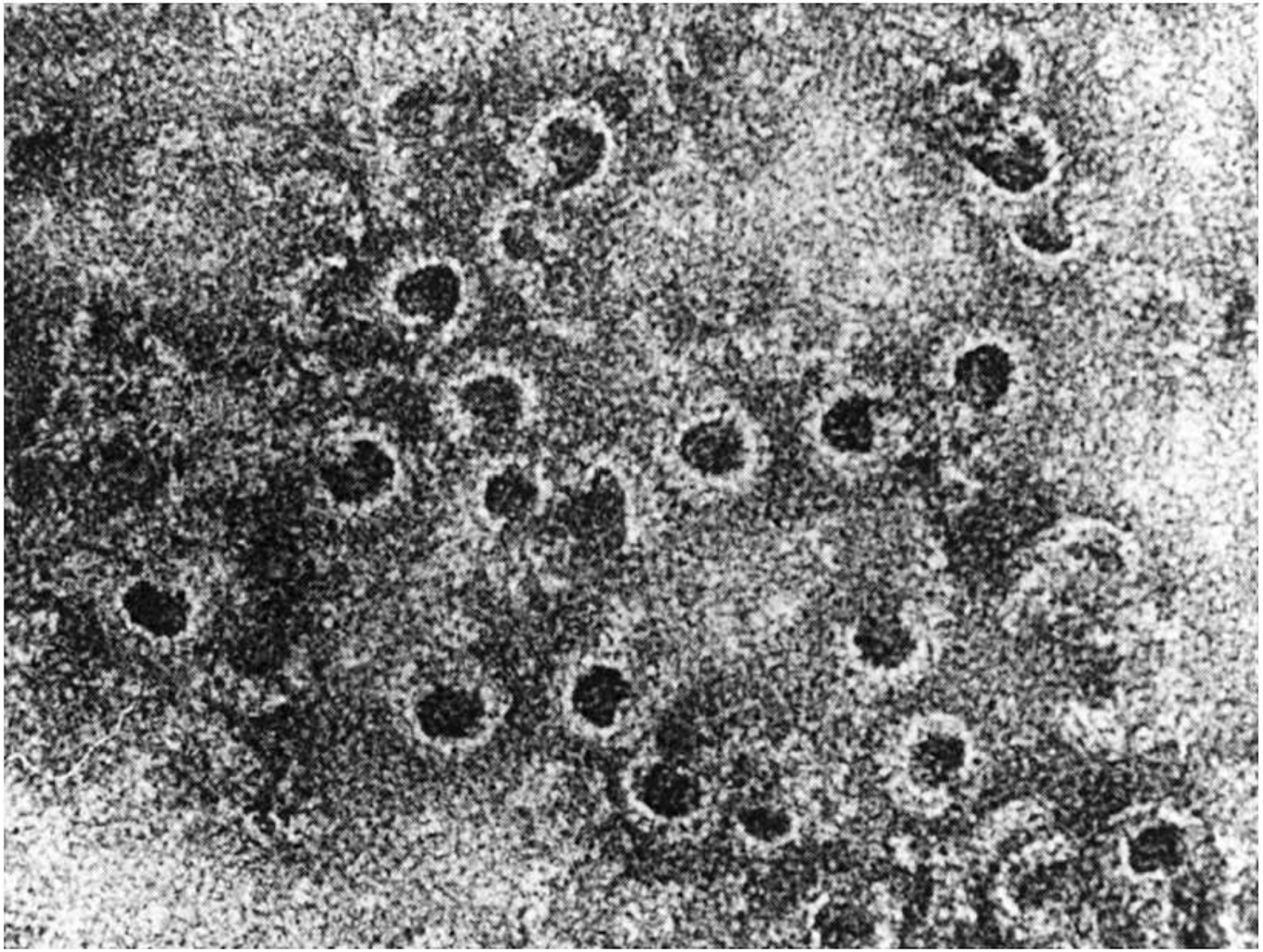

C3
C3b
+
C3a
Factor B
Factor D
C3bBb
+
Properdin
C3 convertase
C3
+
C3bBb3B
C5 convertase
C5
C5b
+
C5a
Membrane
attack
complex


C6
C7
C8
C5b
C567
C5b678
C5b678
C9
Poly-C9
Membrane attack complex

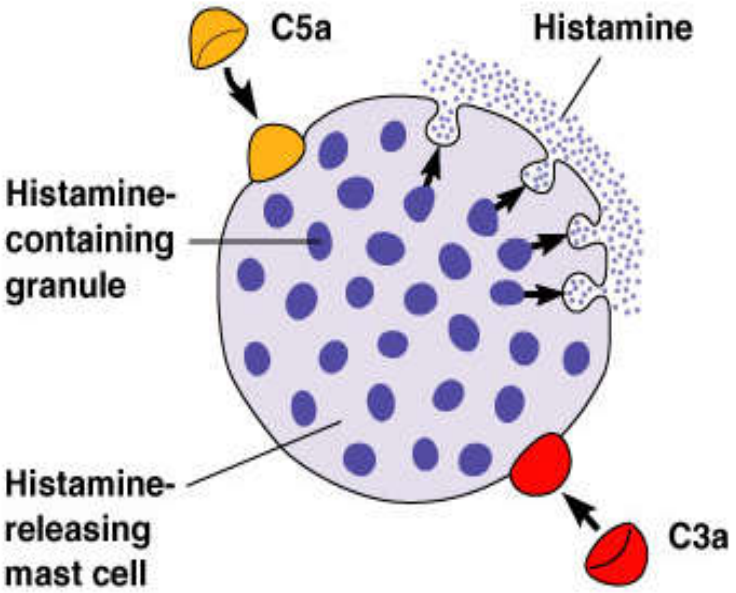


C9 kompleksi

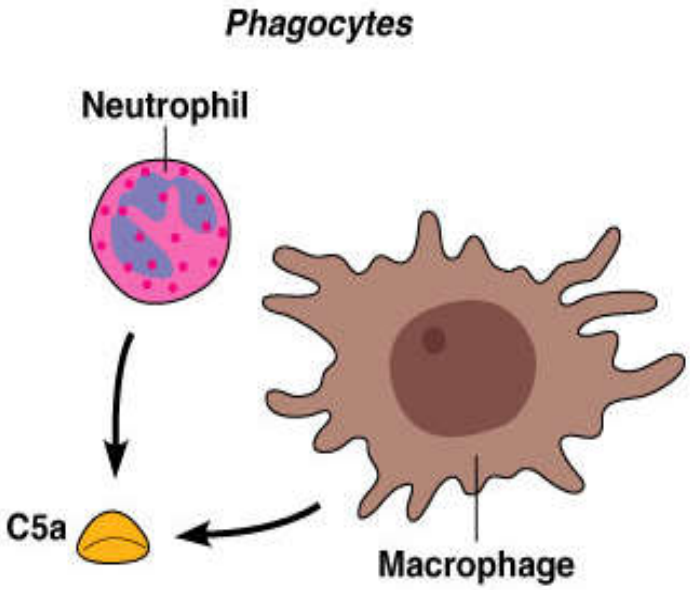




Diğer komplement faktörleri



(a)



(b)

Komp. sisteminin zararlı etkileri Tablolarda (Tablo 13-2) ve Şekilde gösterilen proteinler ile kontrol edilmektedir.

TABLE 13-2 KOMPLEMENT SİSTEMİNİ KONTROL EDEN PROTEİNLER

Protein	Type of protein	Pathway affected	İmmunolojik fonksiyonu
C1 inhibitor (C1Inh)	Soluble	Classical	Serine protease inhibitor: causes $C1r_2s_2$ to dissociate from C1q
C4b-binding protein (C4bBP)*	Soluble	Classical and lectin	Blocks formation of C3 convertase by binding C4b; cofactor for cleavage of C4b by factor I
Factor H*	Soluble	Alternative	Blocks formation of C3 convertase by binding C3b; cofactor for cleavage of C3b by factor I
Complement-receptor type 1 (CR1)* Membrane-cofactor protein (MCP)*	Membrane bound	Classical, alternative, and lectin	Block formation of C3 convertase by binding C4b or C3b; cofactor for factor I-catalyzed cleavage of C4b or C3b C3bBb
Decay-accelerating factor (DAE or CD55)*	Membrane bound	Classical, alternative, and lectin	Accelerates dissociation of $C4\overline{b2a}$ and $C3\overline{bBb}$ (classical and alternative C3 convertases)

*An RCA (regulator of complement activation) protein. In humans, all RCA proteins are encoded on chromosome 1 and contain short consensus repeats.

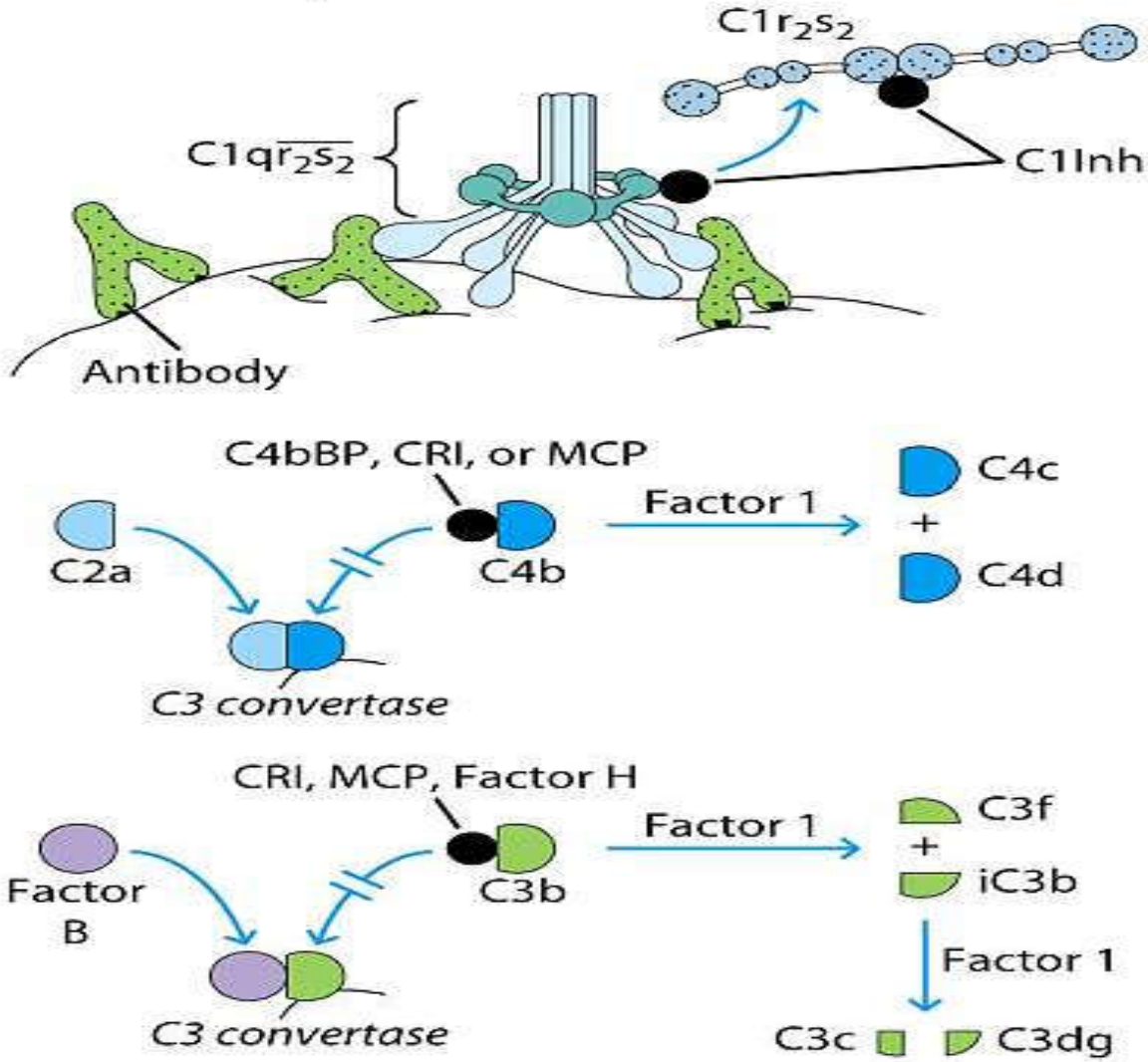
TABLE 13-2 Proteins that regulate the complement system

Protein	Type of protein	Pathway affected	Immunologic function
Factor-I	Soluble	Classical, alternative, and lectin	Serine protease: cleaves C4b or C3b using C4bBP, CR1, factor H, DAE, or MCP as cofactor
S protein	Soluble	Terminal	Binds soluble C5b67 and prevents its insertion into cell membrane
Homologous restriction factor (HRF) Membrane inhibitor of reactive lysis (MIRL or CD59)*	Membrane bound	Terminal	Bind to C5b678 on autologous cells, blocking binding of C9
Anaphylatoxin inactivator	Soluble	Effector	Inactivates anaphylatoxin activity of C3a, C4a, and C5a by carboxypeptidase N removal of C-terminal Arg

*An RCA (regulator of complement activation) protein. In humans, all RCA proteins are encoded on chromosome 1 and contain short consensus repeats.

Regulation of the Complement System

(a) Before assembly of convertase activity



Komplement fonksiyonları hücrelerdeki reseptörleri ve aktivitelerine göre ifade edilir.

Burada ve diğer Tablo'da (Tablo 13-3) komplementin fagositik, opsonik, B hücre aktivatörü ve anaflatoksik rolleri gösterilmektedir.

TABLE 13-4 *KOMPLEMENT RESEPTÖRLERİ*

Receptor	Major ligands	Activity	Cellular distribution
CR1 (CD35)	C3b, C4b	Blocks formation of C3 convertase; binds immune complexes to cells	Erythrocytes, neutrophils, monocytes, macrophages, eosinophils, follicular dendritic cells, B cells, some T cells
CR2 (CD21)	C3d, C3dg,* iC3b	Part of B-cell coreceptor; binds Epstein-Barr virus	B cells, follicular dendritic cells, some T cells
CR3 (CD11b/18) CR4 (CD11c/18)	iC3b	Bind cell-adhesion molecules on neutrophils, facilitating their extravasation; bind immune complexes, enhancing their phagocytosis	Monocytes, macrophages, neutrophils, natural killer cells, some T cells
C3a/C4a receptor	C3a, C4a	Induces degranulation of mast cells and basophils	Mast cells, basophils, granulocytes
C5a receptor	C5a	Induces degranulation of mast cells and basophils	Mast cells, basophils, granulocytes, monocytes, macrophages, platelets, endothelial cells

*Cleavage of C3dg by serum proteases generates C3d and C3g.

TABLE 13-3 *Komplement ürünlerinin biyolojik etkileri*

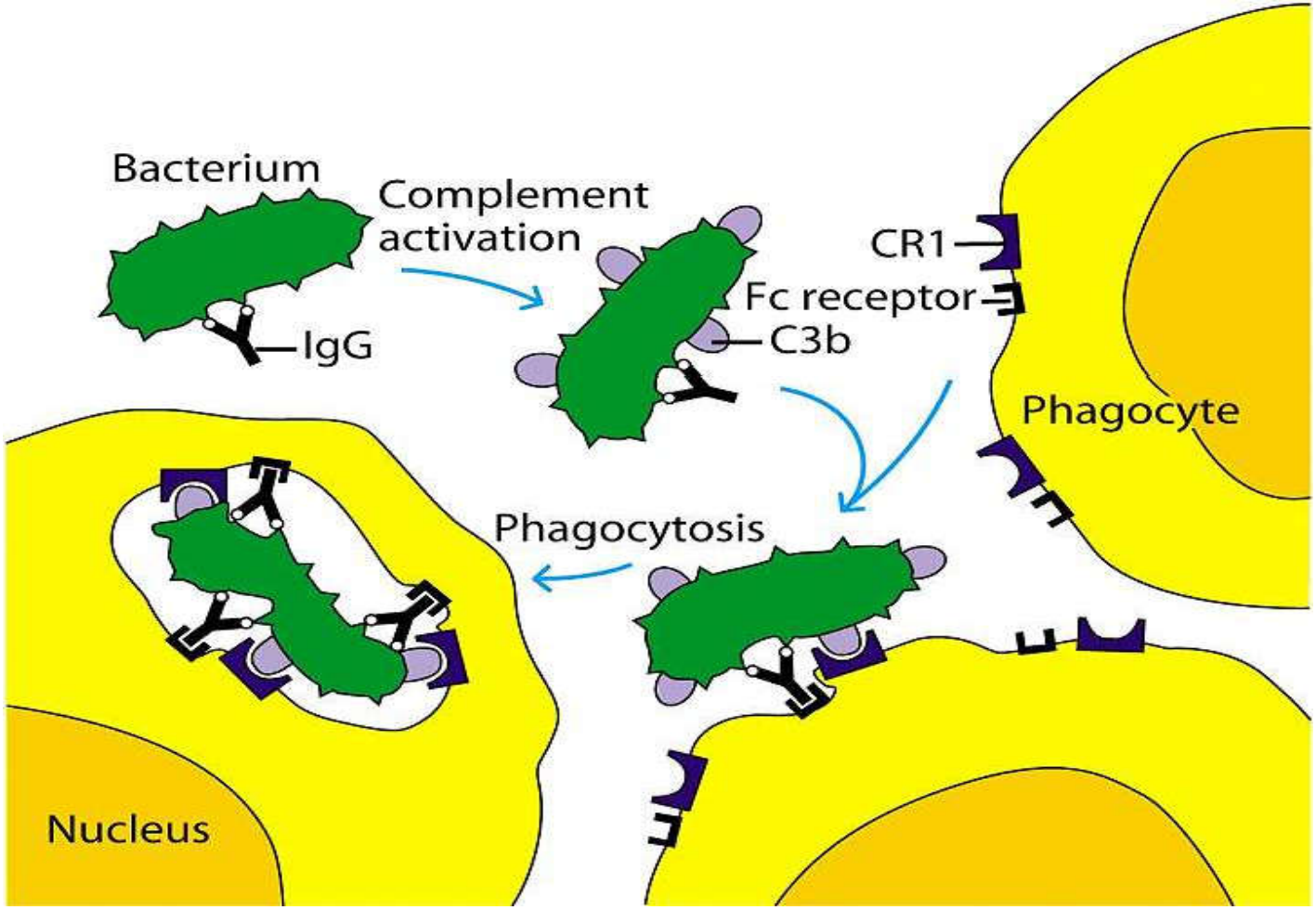
Etki	*Aracılık eden komplementler*
Hücre lizisi	C5b–9, the membrane-attack complex (MAC)
Yangısal yanıt	
Degranulation of mast cells and basophils†	C3a, C4a, and C5a (anaphylatoxins)
Degranulation of eosinophils	C3a, **C5a**
Extravasation and chemotaxis of leukocytes at inflammatory site	C3a, **C5a**, C5b67
Aggregation of platelets	C3a, C5a
Inhibition of monocyte/macrophage migration and induction of their spreading	Bb
Release of neutrophils from bone marrow	C3c
Release of hydrolytic enzymes from neutrophils	C5a
Increased expression of complement receptors type 1 and 3 (CR1 and CR3) on neutrophils	C5a
Opsonization of particulate antigens, increasing their phagocytosis	**C3b**, C4b, iC3b
Viral neutralization	C3b, C5b–9 (MAC)
Solubilization and clearance of immune complexes	C3b

*Boldfaced component is most important in mediating indicated effect.

†Degranulation leads to release of histamine and other mediators that induce contraction of smooth muscle and increased permeability of vessels.

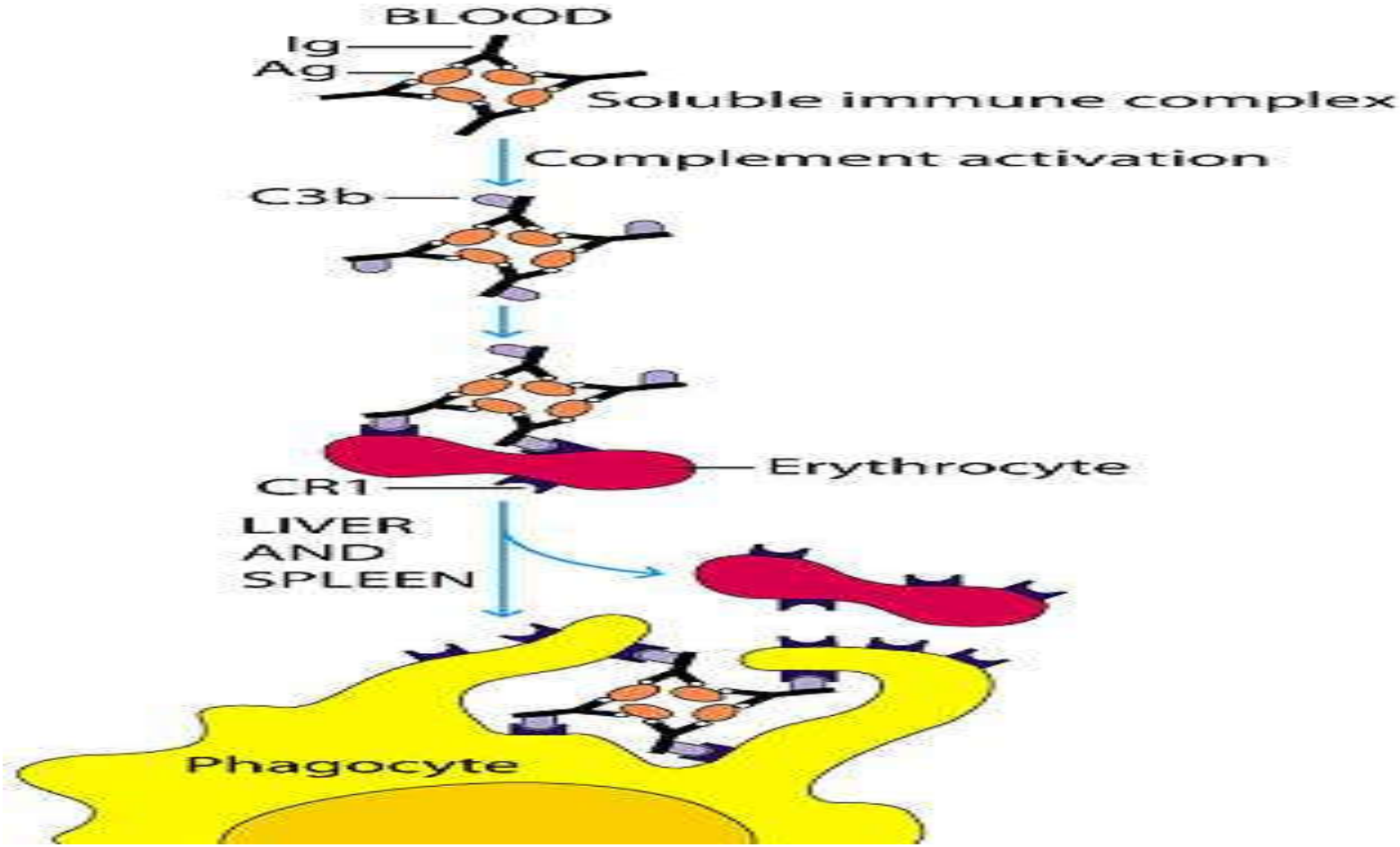
Opsonizasyon

Fagositik hücreler, CR1 ve IgG reseptörü taşırlar. Kapsül gibi hidrofilik yapılar ancak IgG ve komplement ile fagositoza uygun olurlar.



İmmün komplekslerin (antijen-antikor kompleksi) uzaklaştırılmasında komplementin rolü (klasik yol komplement aktivasyonu)

Eritrosit ve fagositik hücrelerin işlevi

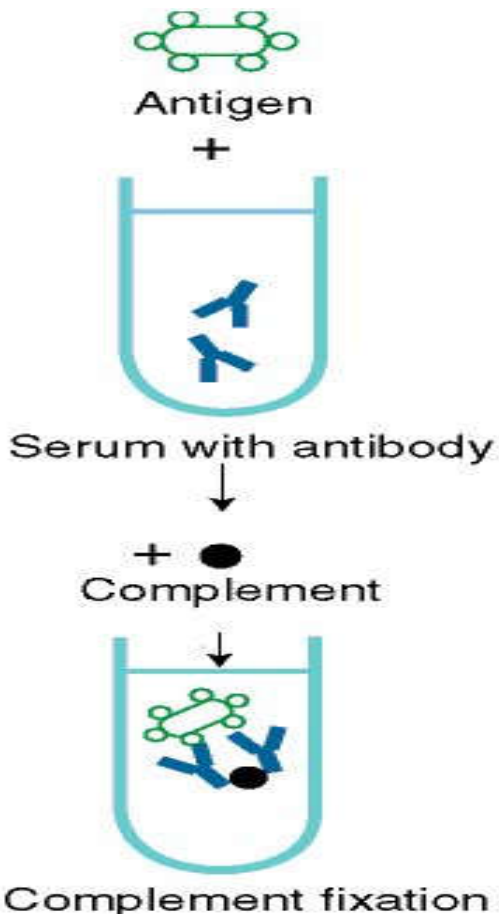


Komplement Fikzasyon Testi (KFT)

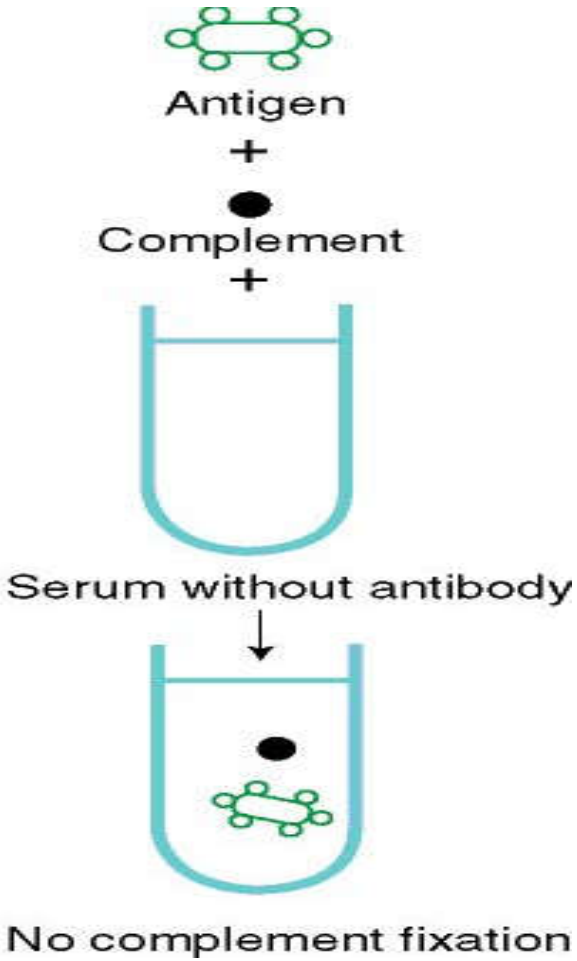
- **Referans olduğu hastalıklar**
- Bruselloz
- Q Fever
- Klamidiyoz
- Paratüberküloz

KFT Mekanizması

Serumda **antikor varsa**



Antikor yoksa



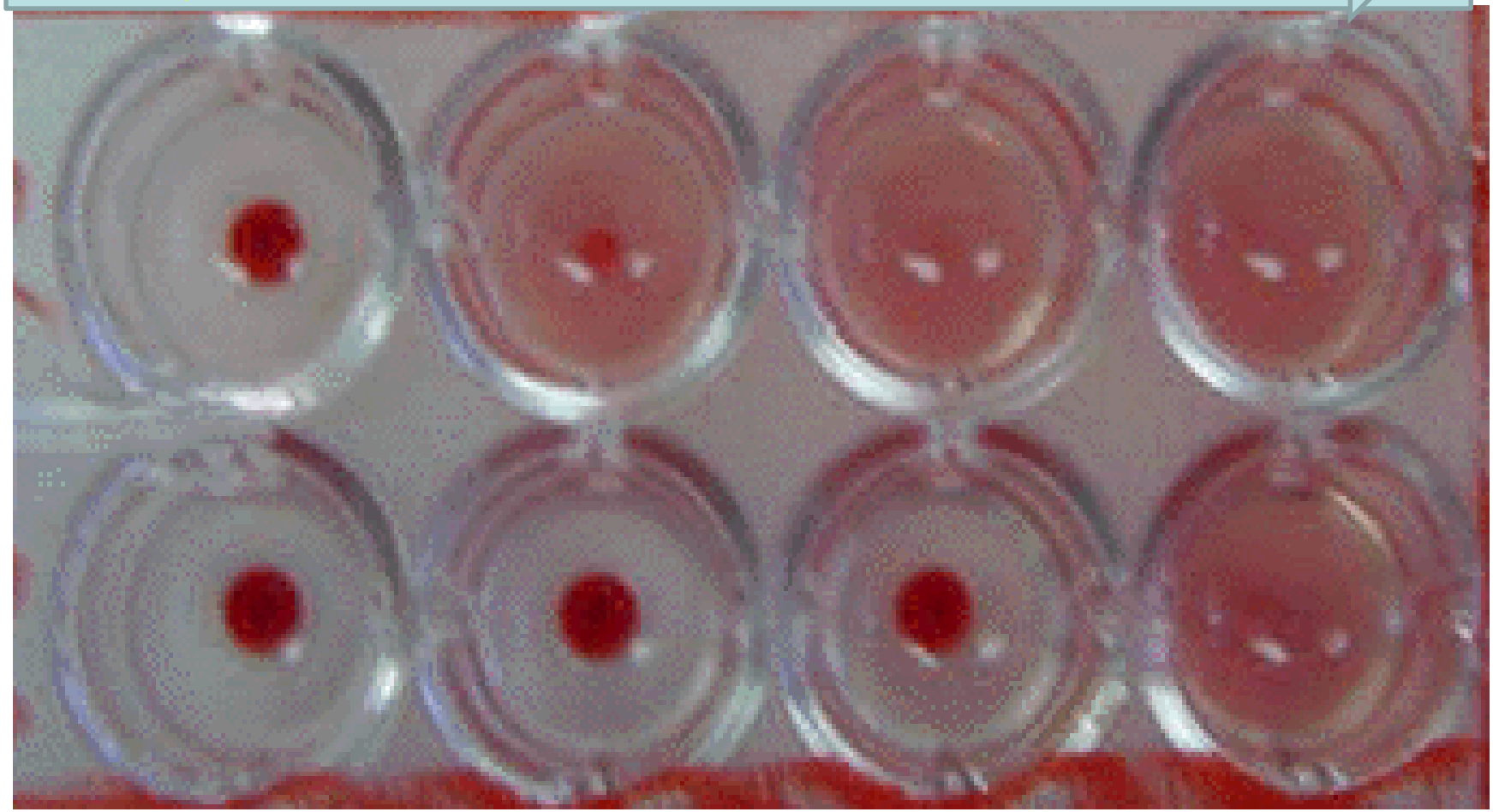
antikor varsa **antikor yoksa**

İndikatör sistem: koyun eritrositi ile tavşanlarda koyun eritrositine karşı üretilen antikor içeren serum

Serumda antikor varlığında, antijen-antikor kompleksi oluşur. Teste sonradan ilave edilen komplement (taze kobay serumu) kompleksdeki antikorun Fc bölgesine bağlanır ve ortamda serbest komplement kalmaz.
Sonradan ortama indikatör veya hemolitik sistem ilave edildiğinde (Şekil-2) Serbest komplement kalmadığından hemolitik sistemde bağlanamaz ve hemolitik sistem yıkımlanmadan çöker. Hemoliz olmaz. Antikor yokluğunda ise serbest komplement hemolitik sistemdeki anti-eritrosit antikorlarına bağlanarak eritrositi yıkımlar. **Yani hemoliz pozitif serumda antikor olmaz.**

KFT (Mikropleytte)

Hemoliz yok hemoliz var

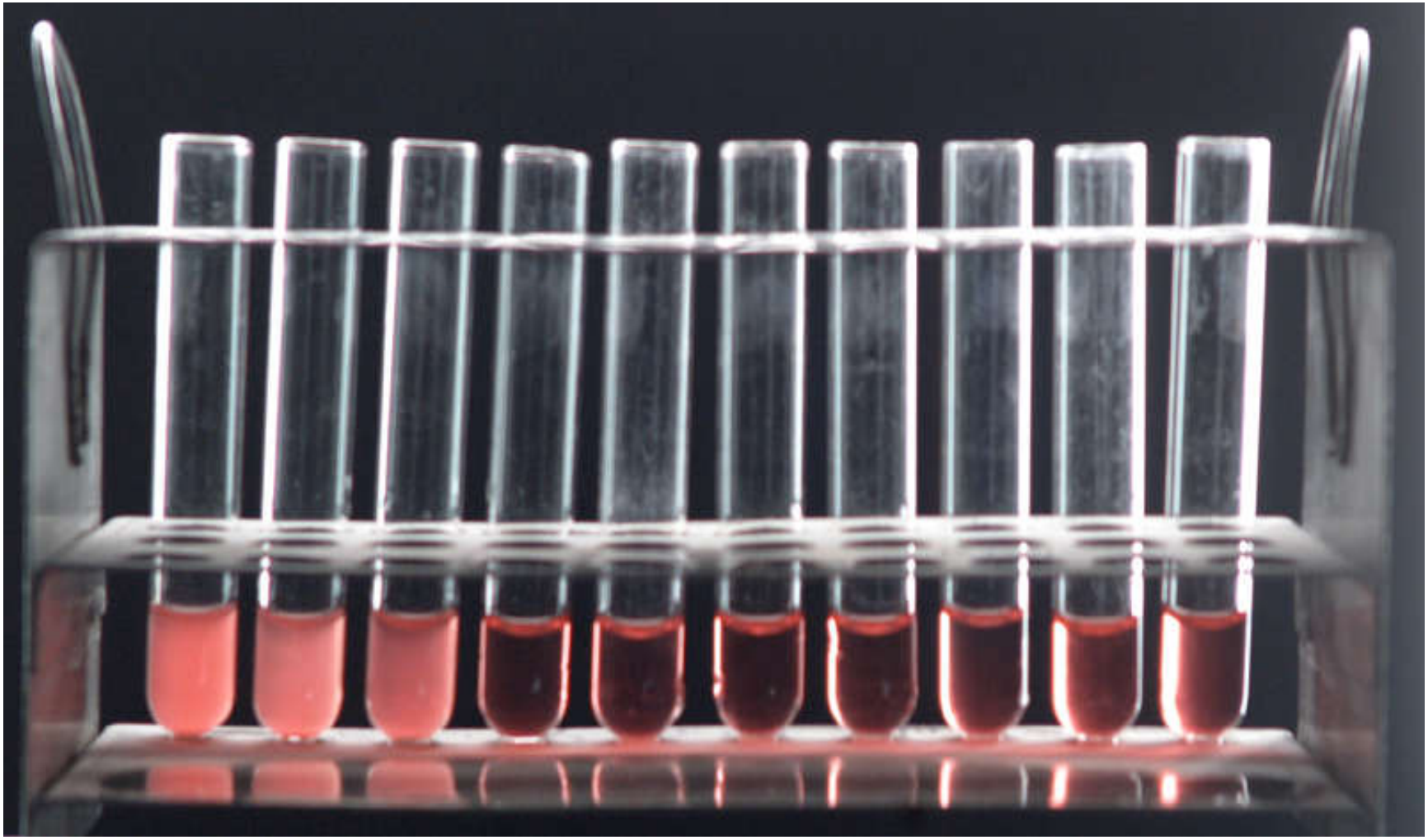


Hemoliz yok hemoliz var

KFT (Tüpte)

Tüpler ters konumdadır.

Değerlendirme ters çevrilerek yapılır.



Konu ile ilgili sorular

- 1- Komplementin tanımı, fonksiyonları
- 2- Komplement aktivasyon yolları ve aktivatörler
- 3- Komplement faktörlerinin biyolojik fonksiyonları ?
- 4- Komplement reseptörleri ve önemleri ?
- 5- Komplement eksikliğinde gözlenecek durumlar ?
- 6- KFT'in referans olduğu hastalıklar nelerdir?
- 7- KFT'i serumda antikor durumuna göre değerlendiriniz?