

# **Dođal bađıřıklık ve kompleman sistemi**

# ***Thioester-containing proteins (TEPs)***

$\alpha$ 2makroglobulinler  
- multimerik panproteaz  
intihar substratları

Kompleman proteinleri  
- yüzeylerde toplanma...

Marni Williams and Richard Baxter. The structure and function of thioester-containing proteins in arthropods. *Biophys Rev.* 2014 Dec; 6(3-4): 261-272.

### Complement, pre-activation

C3 (human) (Janssen et al. 2005)	2A73
C3 (bovine) (Fredslund et al. 2006)	2B39
C4 (Kidmose et al. 2012)	4FXK,4FXG
C5 (Fredslund et al. 2008)	3CU7
C5-SSL7 (Laursen et al. 2010)	3KLS,3KM9
C5-CVF (Laursen et al. 2010)	3PVM,3PRX



### Complement, post-activation

C3b (Janssen et al. 2006)	2I07
C3b-CR1g (Wiesmann et al. 2006)	2ICF
C3b-fH (Wu et al. 2009)	2WII
C3bBb (Forneris et al. 2010)	2XWJ
C3bBbD (Forneris et al. 2010)	2XWB
C3c (Janssen et al. 2005)	2A74
C3c-CR1g (Wiesmann et al. 2006)	2ICF
C3d (Nagar et al. 1998)	1C3D
C3d-CR2 (Szakonyi et al. 2001; van den Eisen and Isenman 2011)	1GHQ,3OED
C5b6 (Hadders et al. 2012)	4A5W



### A2M structures

A2M MG2 (Doan and Gettins 2007)	2P9R
A2M RBD (human) (Jenner et al. 1998)	1AYO
A1M RBD (rat) (Xiao et al. 2000)	1EDY
A2M(MeNH2) (Marrero et al. 2012)	4ACQ



### iTEP structures

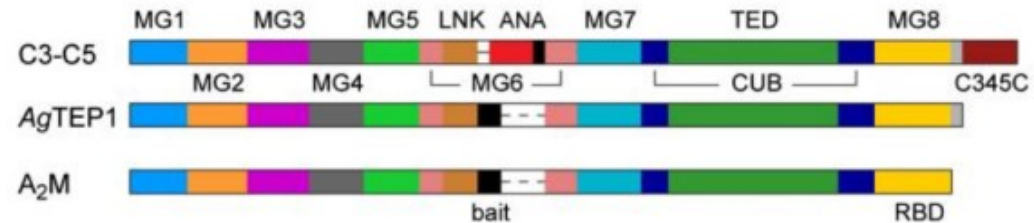
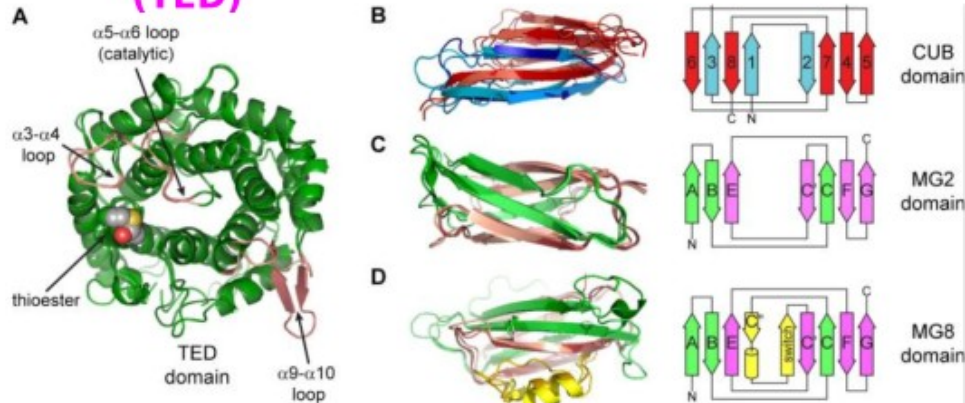
AgTEP1*R1 (Baxter et al. 2007)	4D94
AgTEP1*S1 (Le et al. 2012)	4LNV



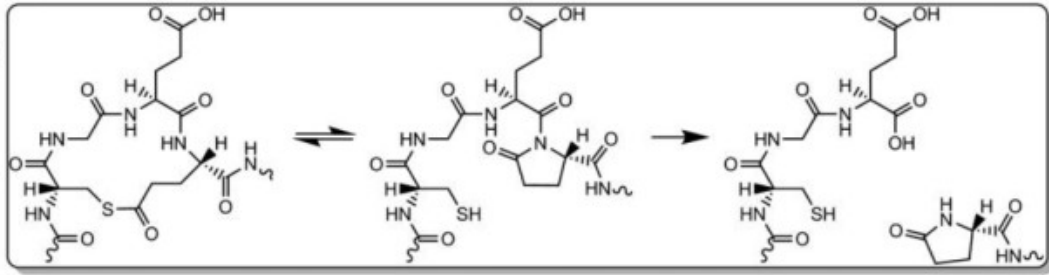
# Proteoliz ile tetiklenmiş konformasyon değişiminin regülasyonu

- > doğal bağışıklık
- > gelişimsel biyoloji
- > ahücre ölümü

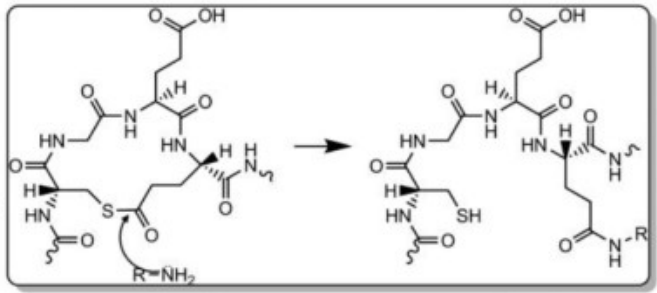
## thioester domain (TED)



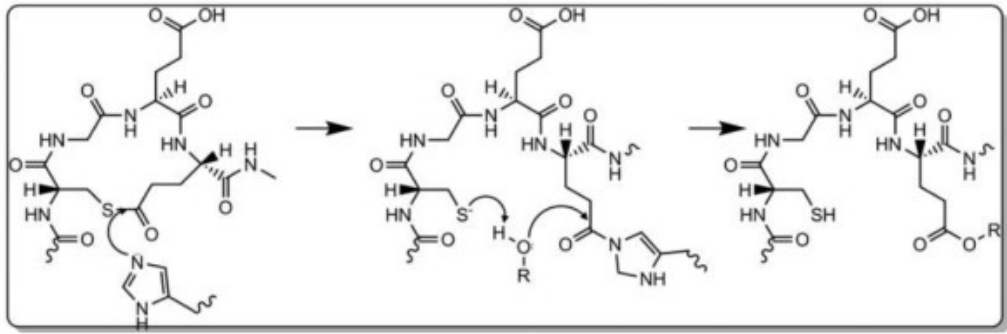
autolytic cleavage



nucleophilic substitution



nucleophilic catalysis



TEP geni #

5



*Drosophila melanogaster*

2

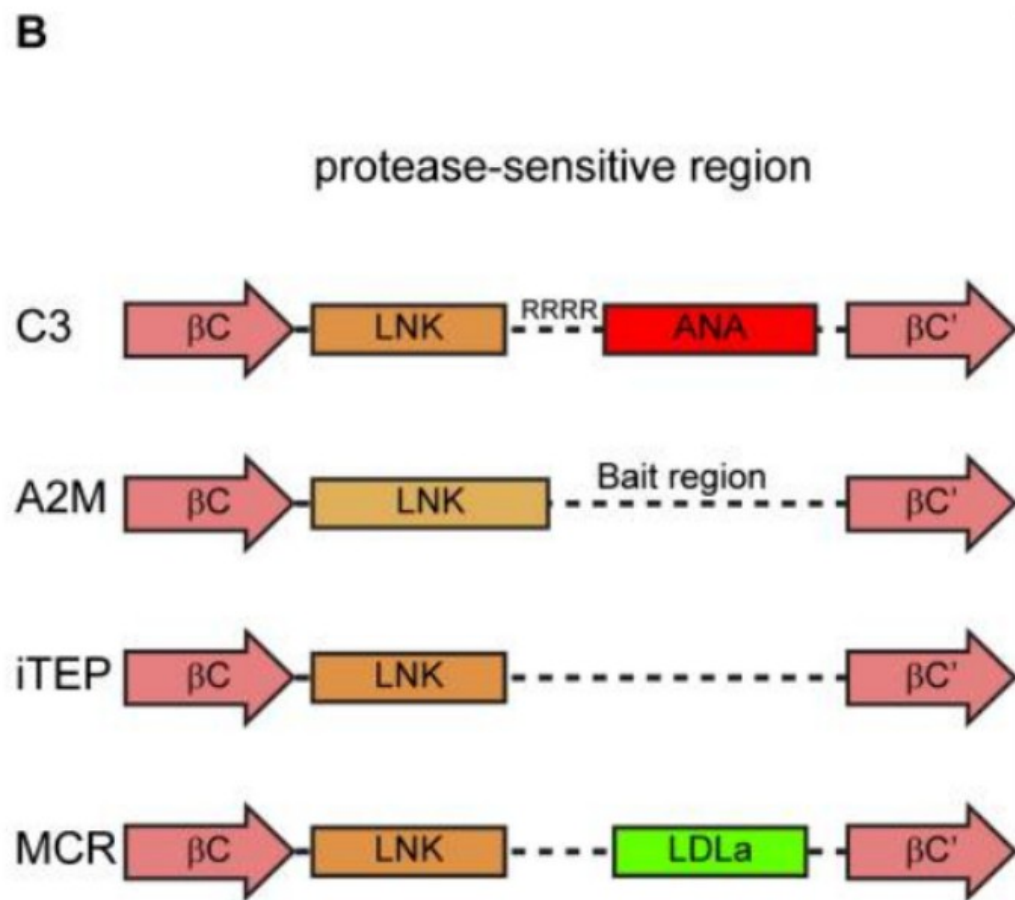
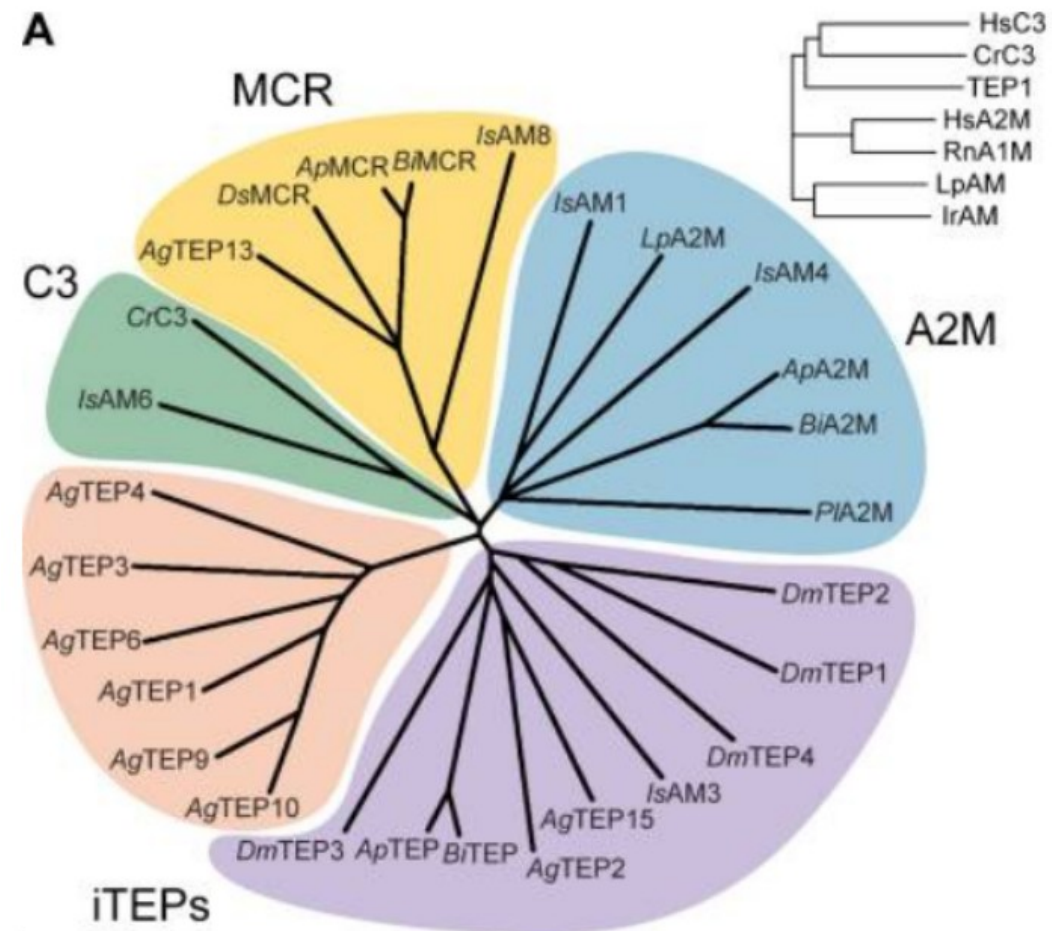


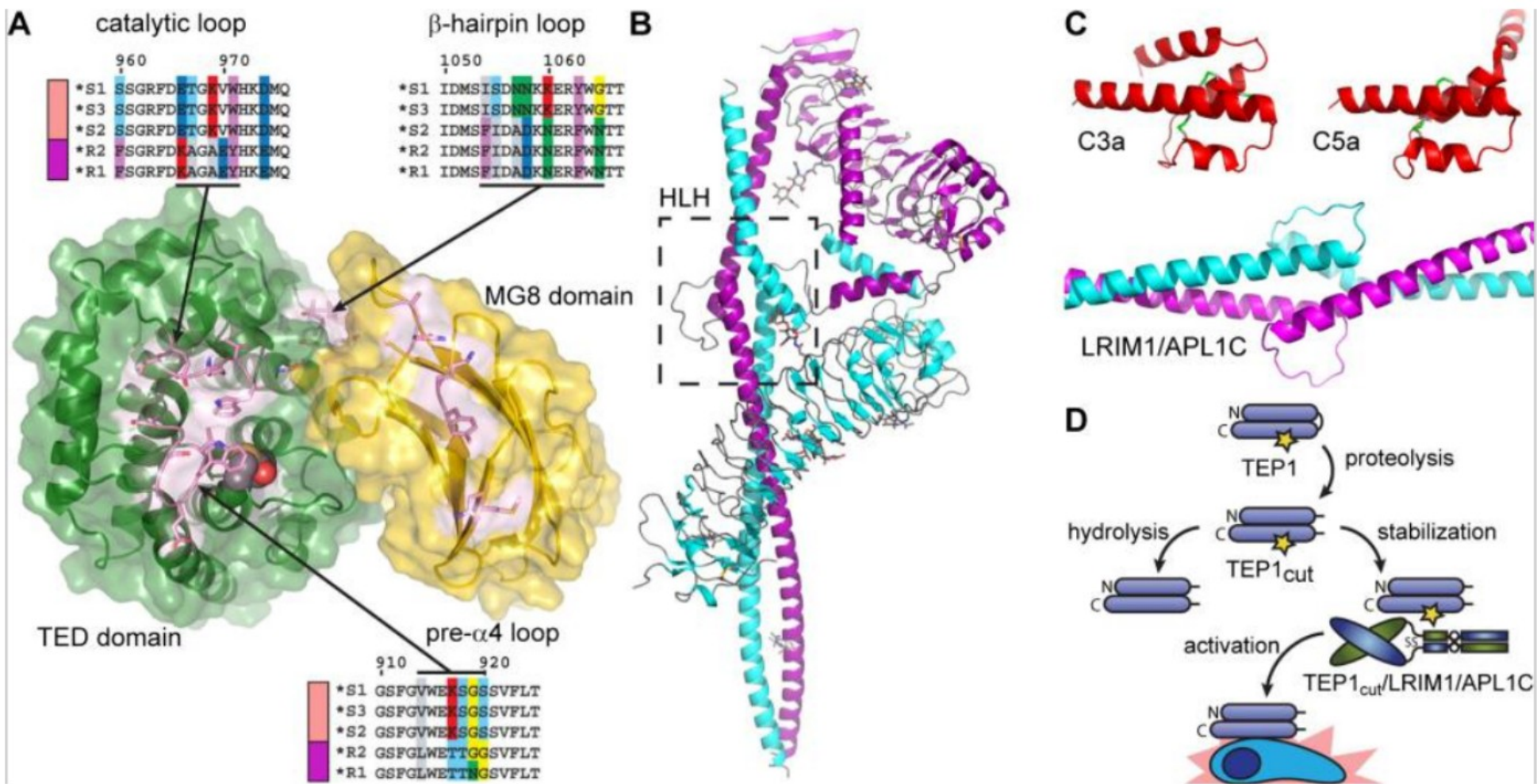
*Apis mellifera*

> 12



*Anopheles*





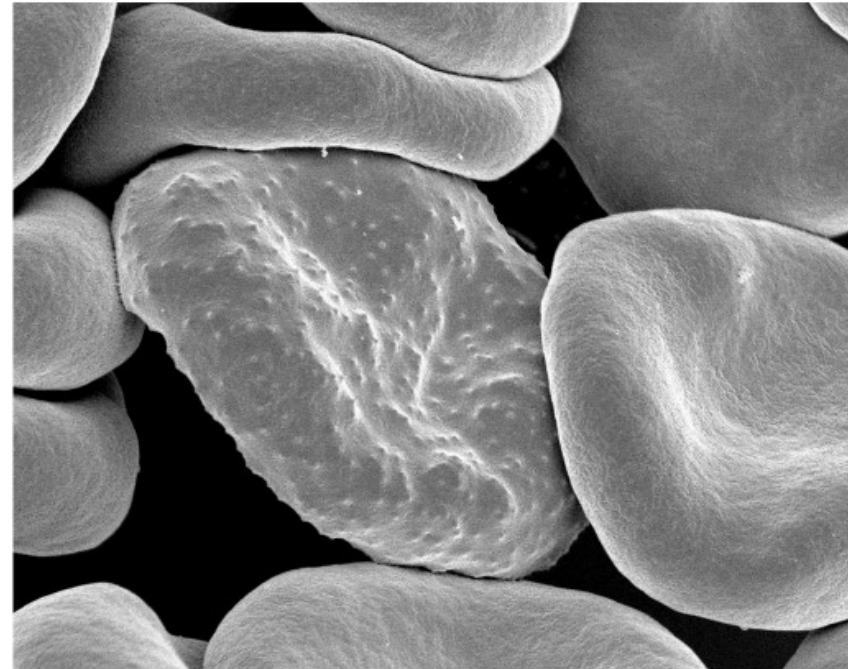
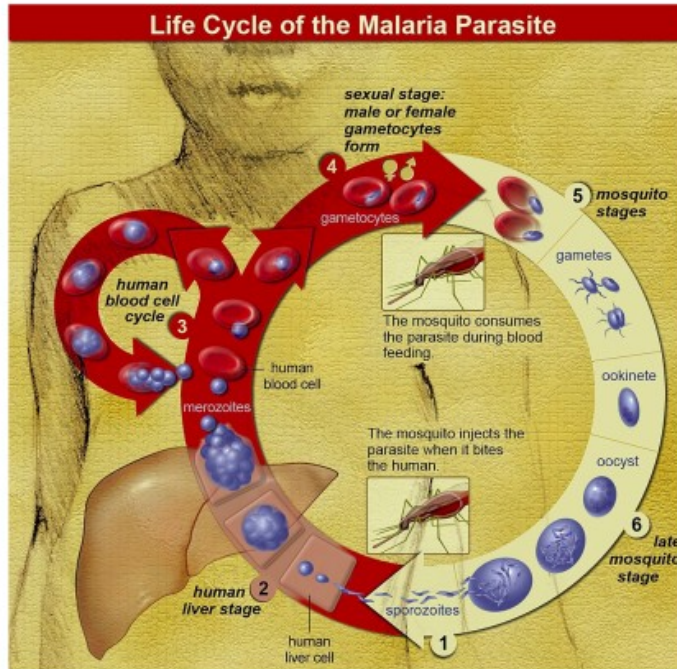
Marni Williams and Richard Baxter. The structure and function of thioester-containing proteins in arthropods. *Biophys Rev.* 2014 Dec; 6(3-4): 261-272.

# AgTEP ---> AgTEP1 + AgTEP1cut

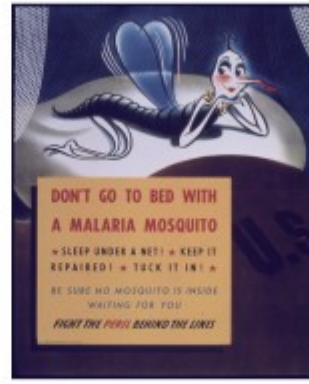
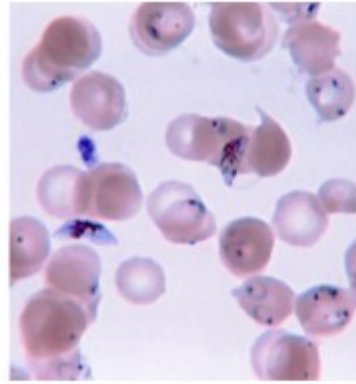
AgTEP1\*S

>90% identical

AgTEP1\*R







<https://en.wikipedia.org/wiki/Malaria>



*Aedes aegyptii*

## AgTEP1

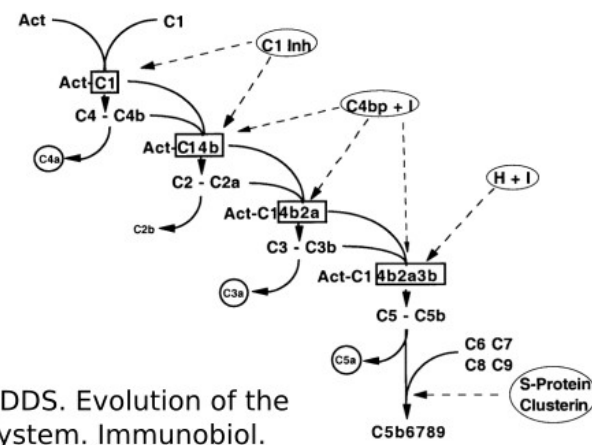
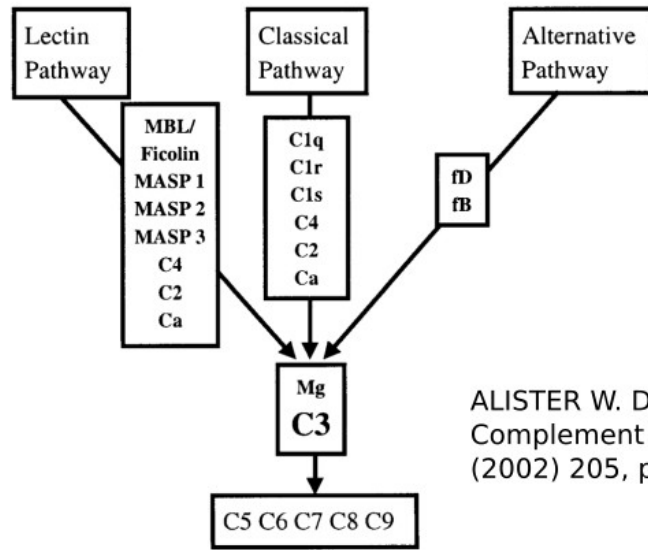
Flavivirus  
enfeksiyonu



*Drosophila melanogaster*

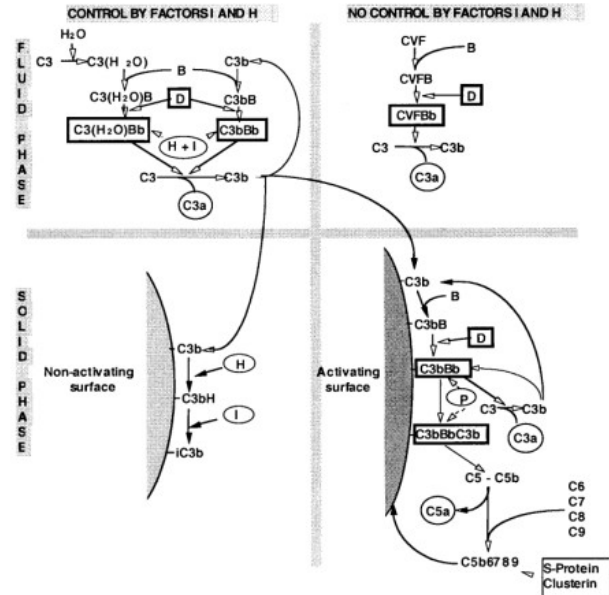
**DmTEP2 KO** -  
E. coli fagositozu

**DmTEP3 KO** -  
Stafilokok fagositozu

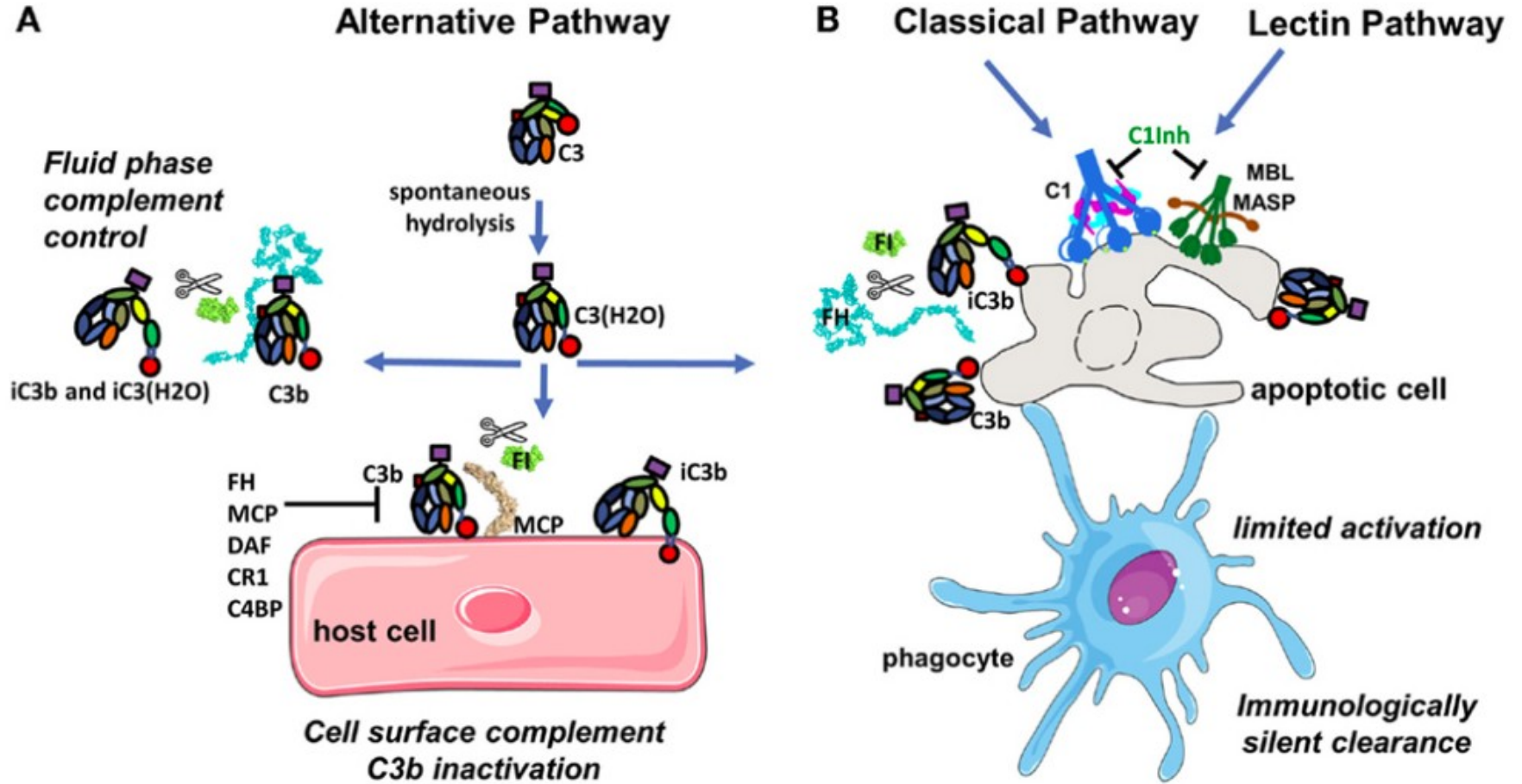


ALISTER W. DODDS. Evolution of the Complement System. Immunobiol. (2002) 205, pp. 340 - 354

	Mammals	Birds	Reptiles	Amphibians	Bony fish	Cartilaginous fish	Agarthaous	Arthropods	Ascidians	Echinoderms	Arthropods
<b>RECOGNITION</b>											
C1q	+	+		+	+	+					
MBL	+	+									
Ficolin	+										
<b>PROTEASES</b>											
C1r/C1s	+			+	+	+					
MASP	+	+		+	+	+					
C2/Factor B	+	+		+	+	+					
Factor D	+			+	+	+					
Factor I	+			+	+	+					
<b>THIOESTER</b>											
C4	+	+		+	+	+					
C3	+	+	+	+	+	+					
C5	+			+	+	+					
<b>MAC</b>											
C6	+	+		+	+	+					
C7	+	+		+	+	+					
C8	+	+		+	+	+					
C9	+	+		+	+	+					
<b>CONTROL</b>											
Factor H	+			+	+	+					
CR3	+										
CD59	+										

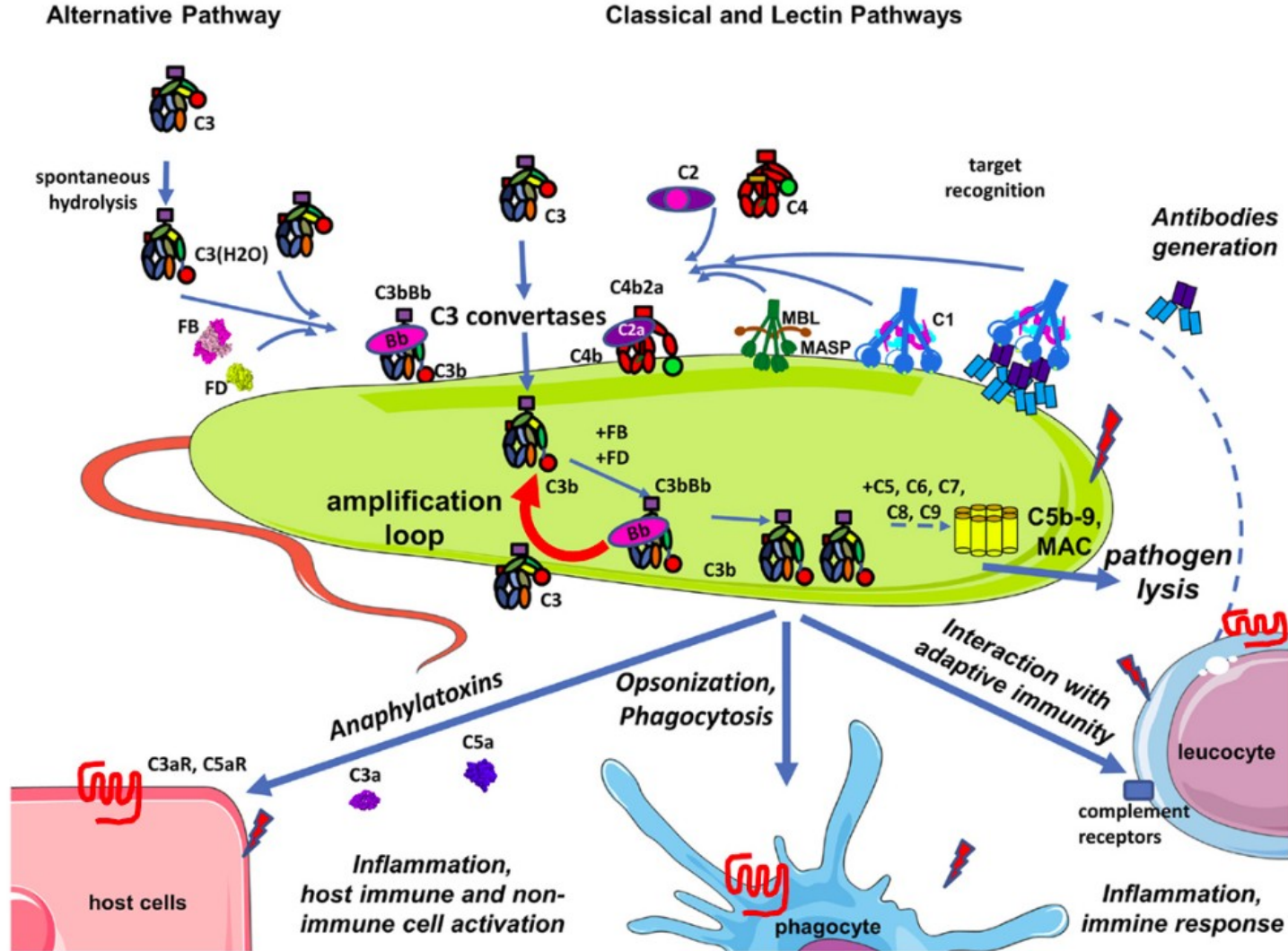


# FIZYOLOJİK KOŞULLAR

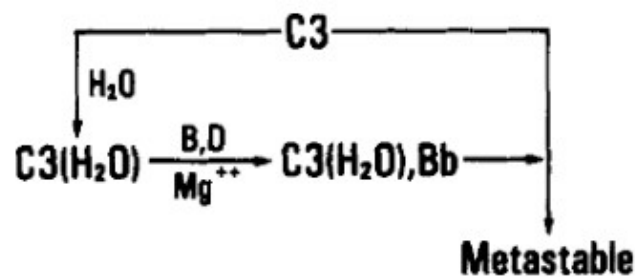


Nicolas S. Merle, Sarah Elizabeth Church, Veronique Fremeaux-Bacchi, Lubka T. Roumenina. Complement system part I - molecular mechanisms of activation and regulation. Front. Immunol., 02 June 2015 | <https://doi.org/10.3389/fimmu.2015.00262>

# ENFEKSİYON



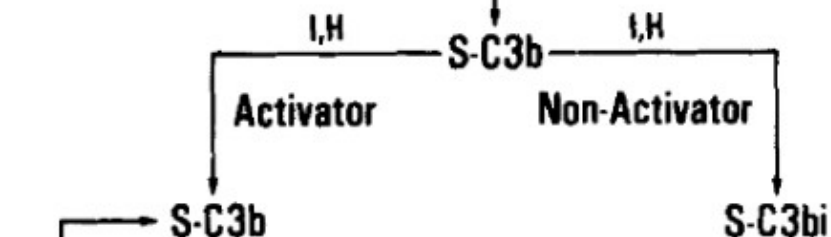
Initiation



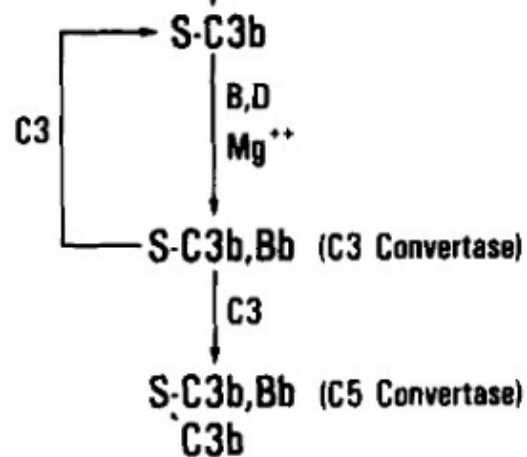
Depositon of C3b

Metastable  
C3b

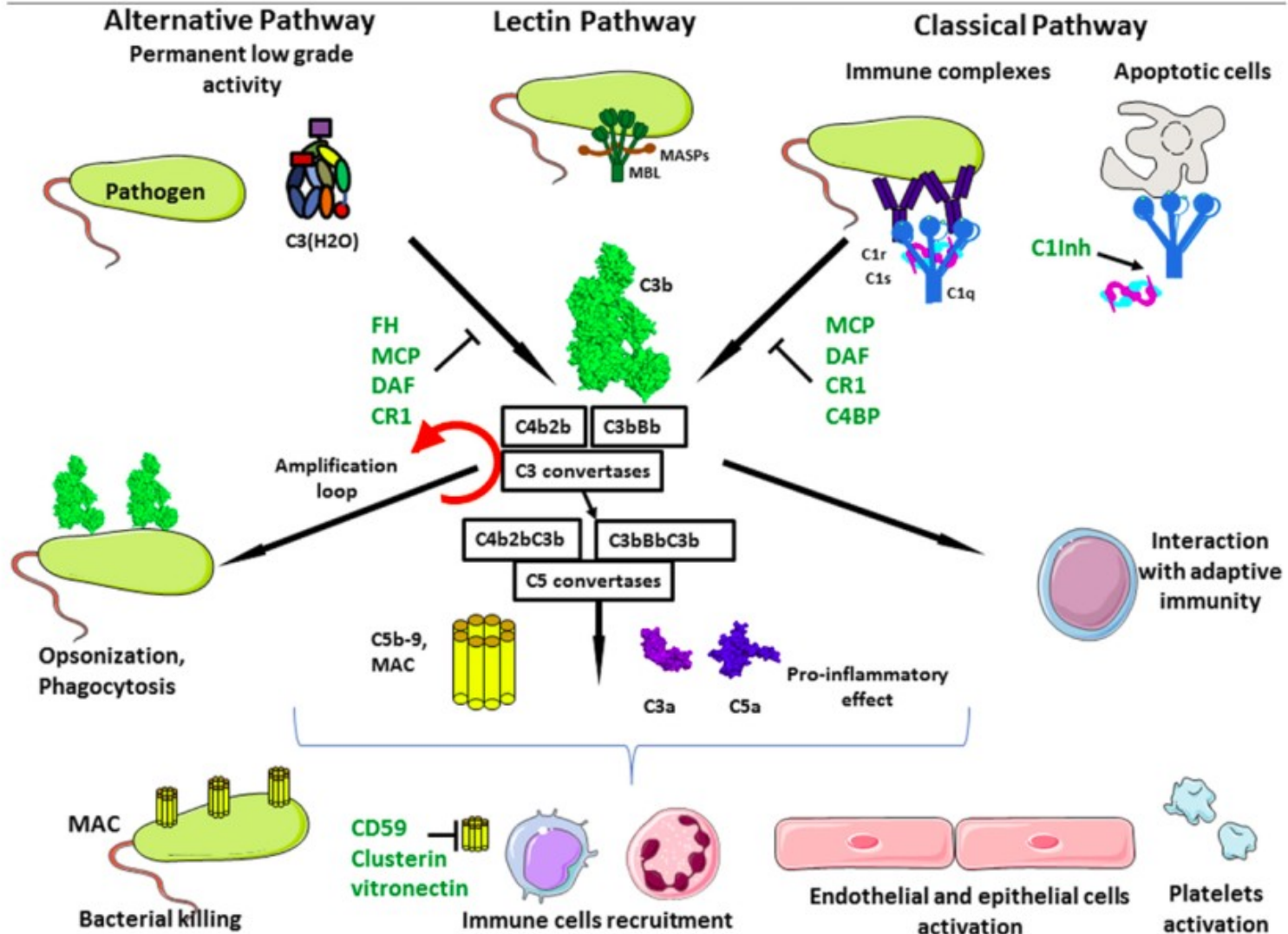
Recognition



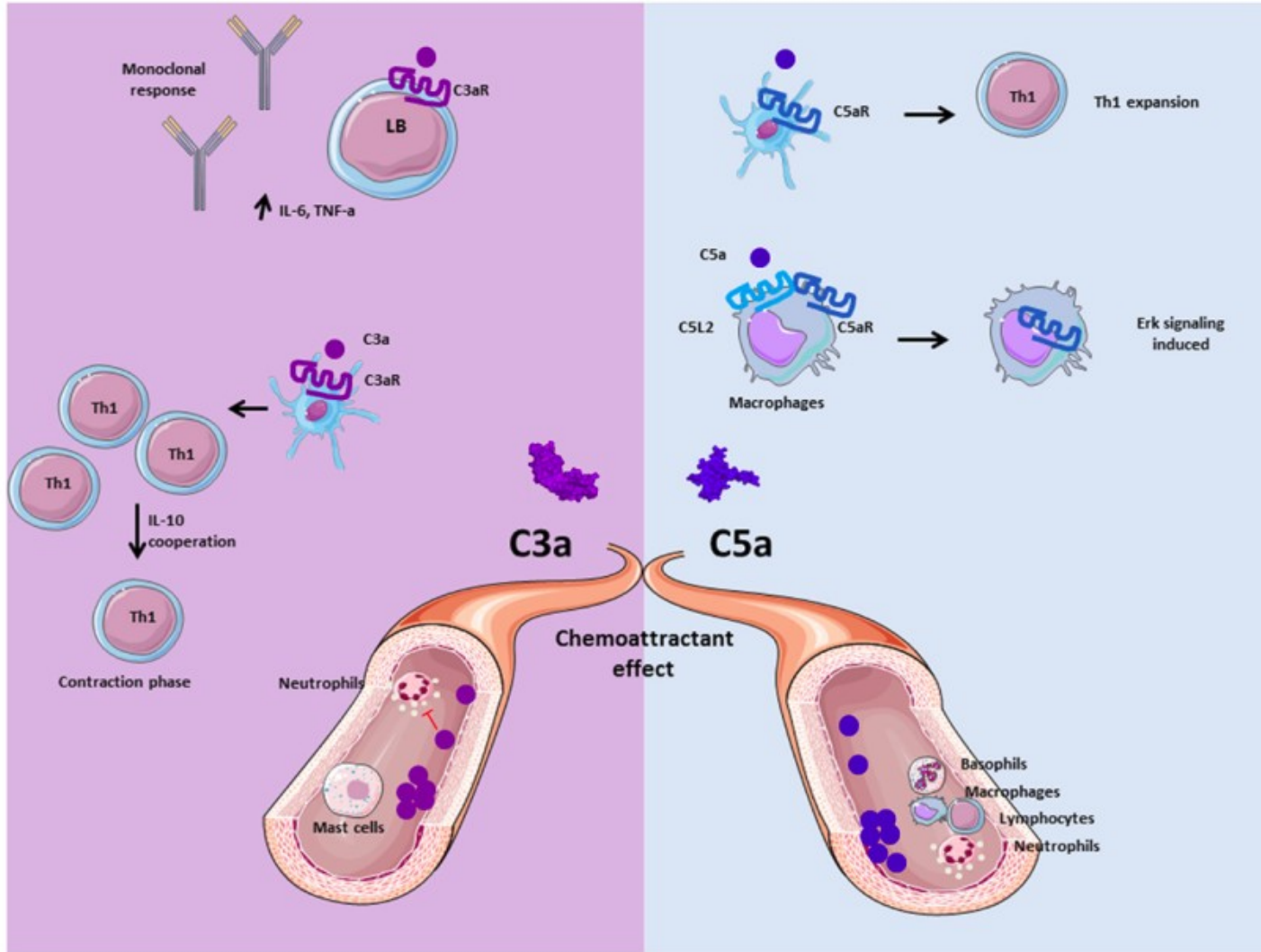
Amplification

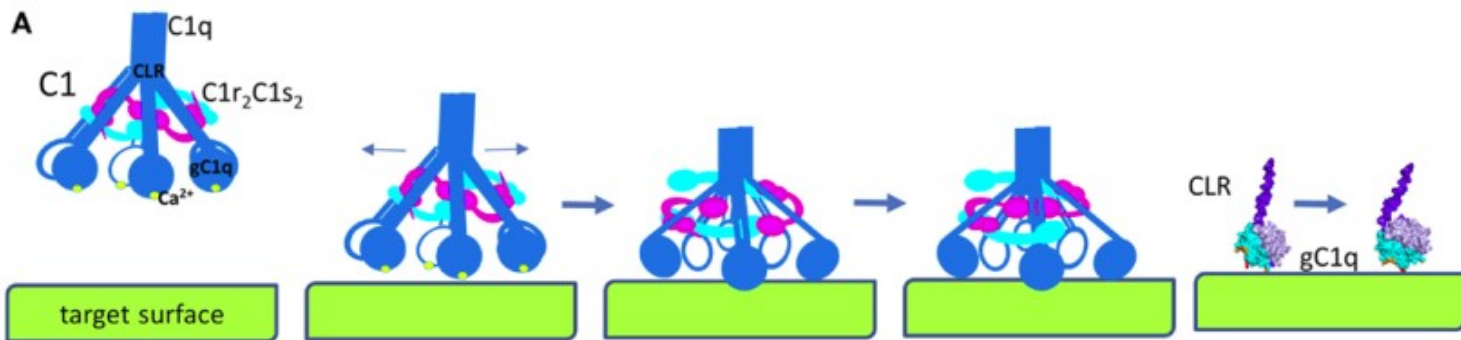


M K Pangburn, R D Schreiber, H J Müller-Eberhard. Formation of the initial C3 convertase of the alternative complement pathway. Acquisition of C3b-like activities by spontaneous hydrolysis of the putative thioester in native C3. J Exp Med (1981) 154 (3): 856-867. <https://doi.org/10.1084/jem.154.3.856>

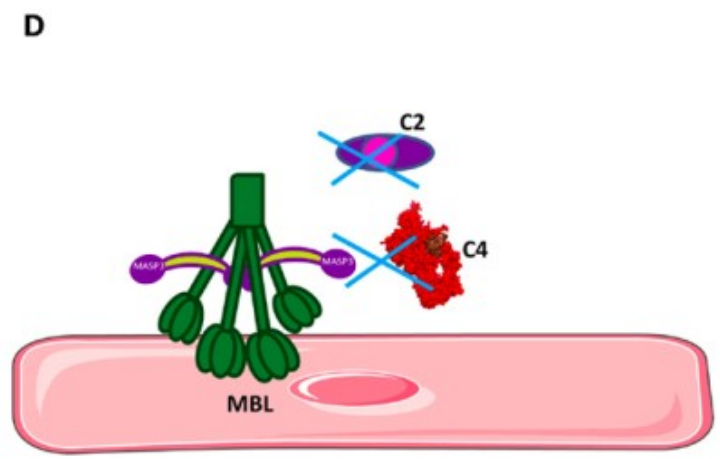
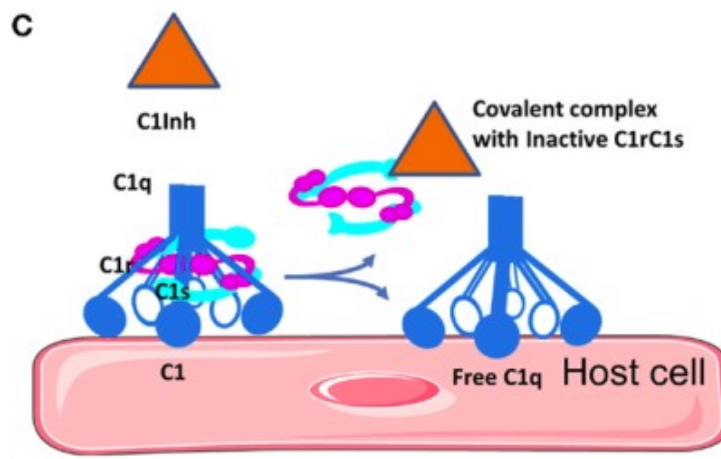
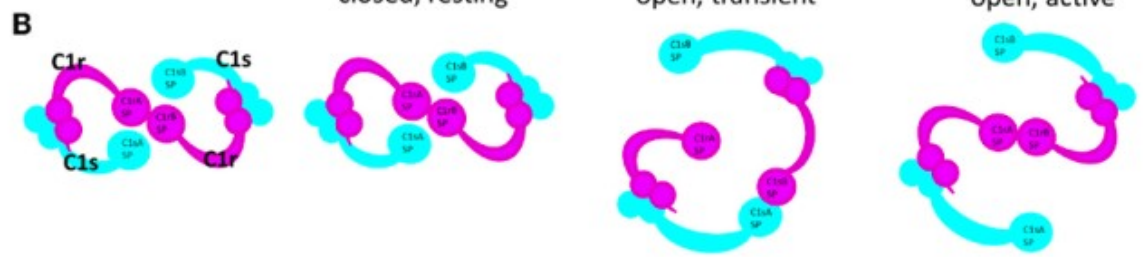


# Anaflatoksinler

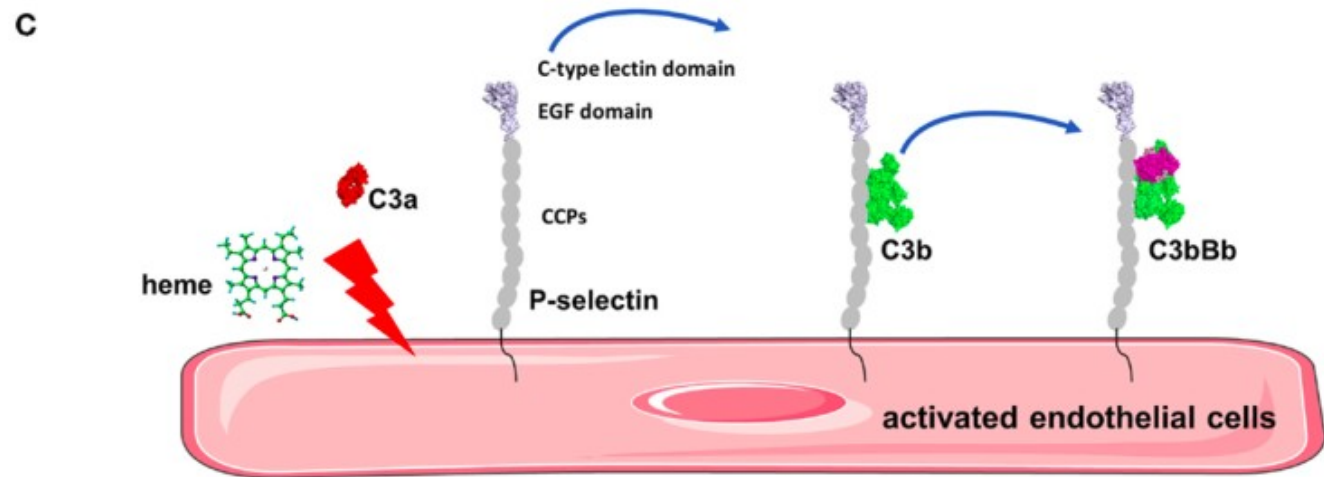
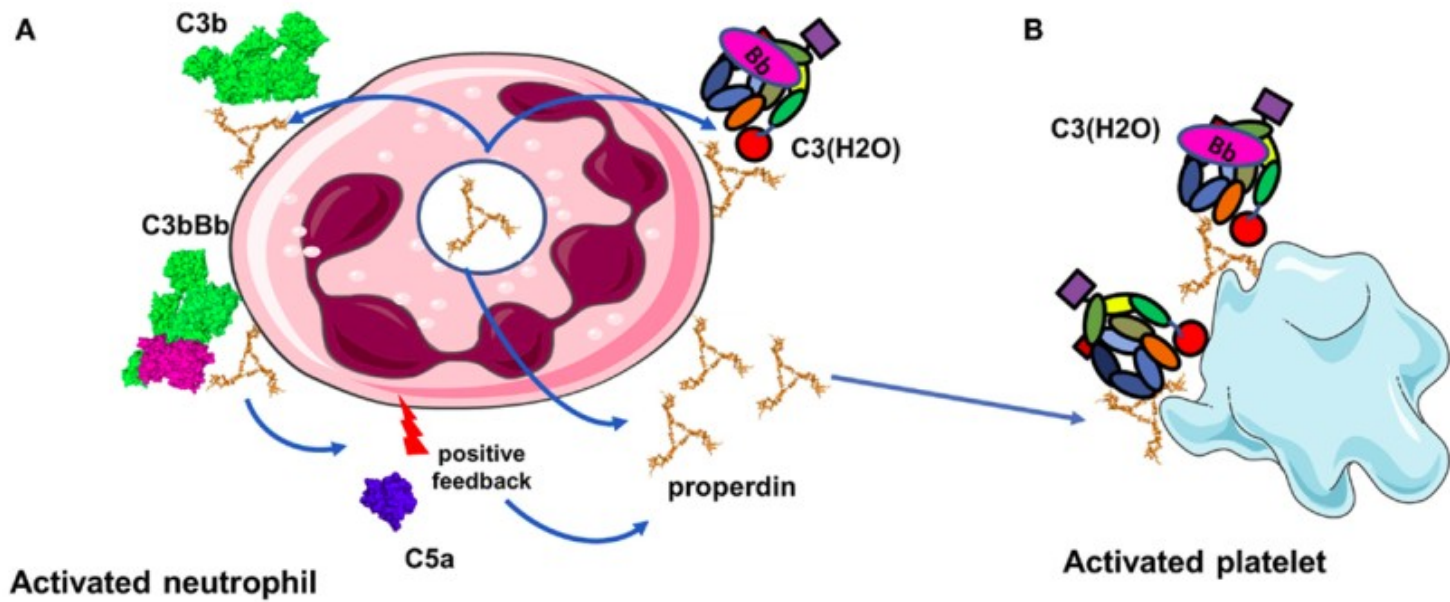


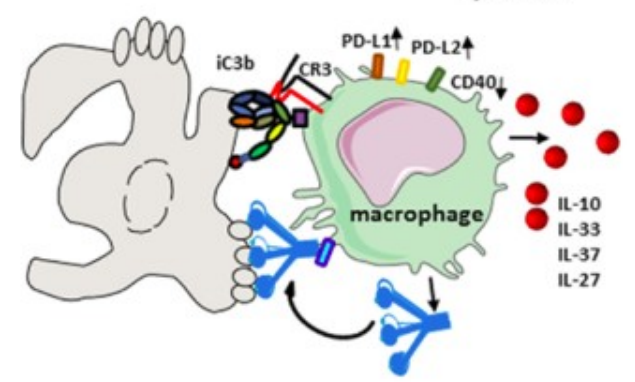
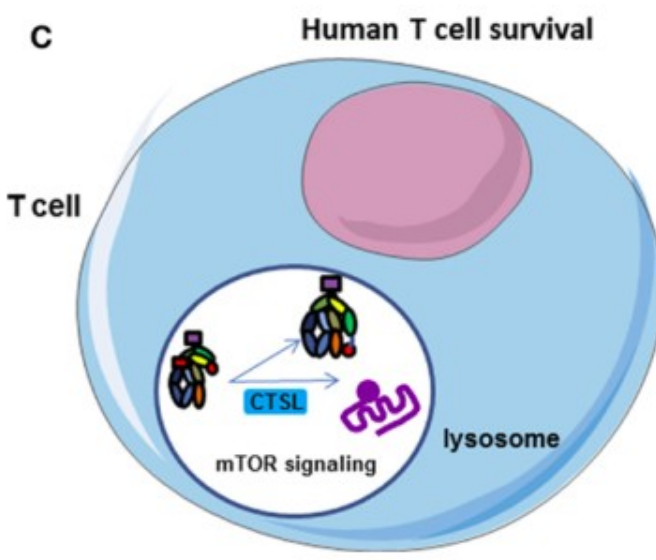
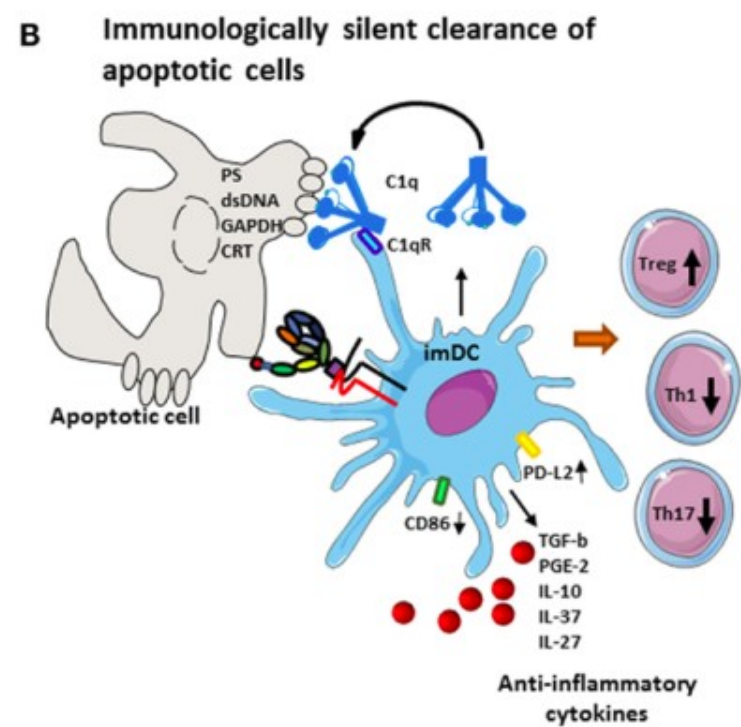
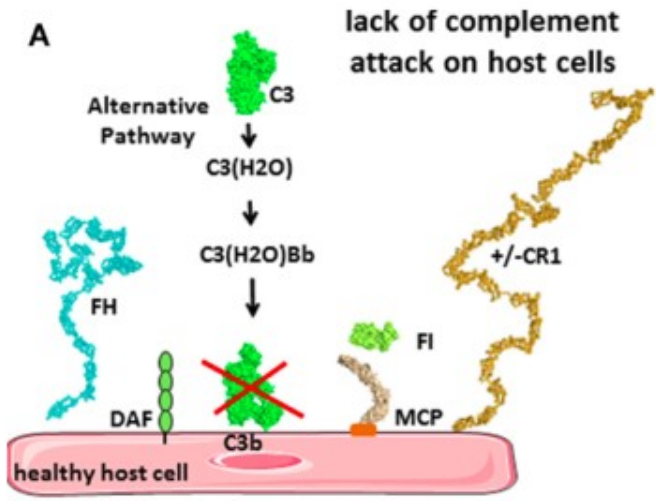


closed, resting      open, transient      open, active

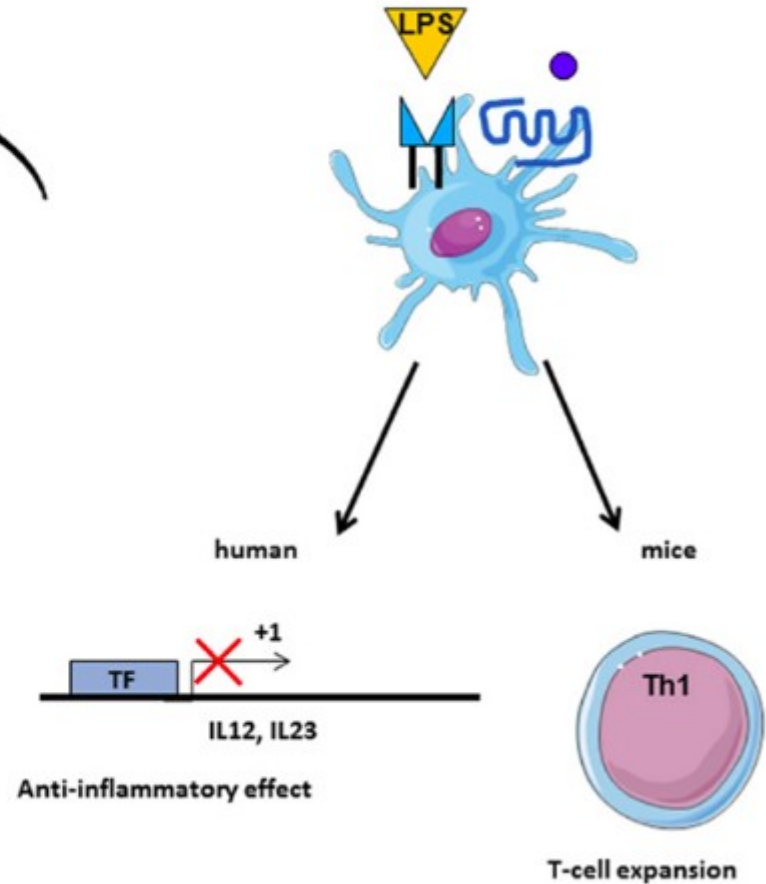
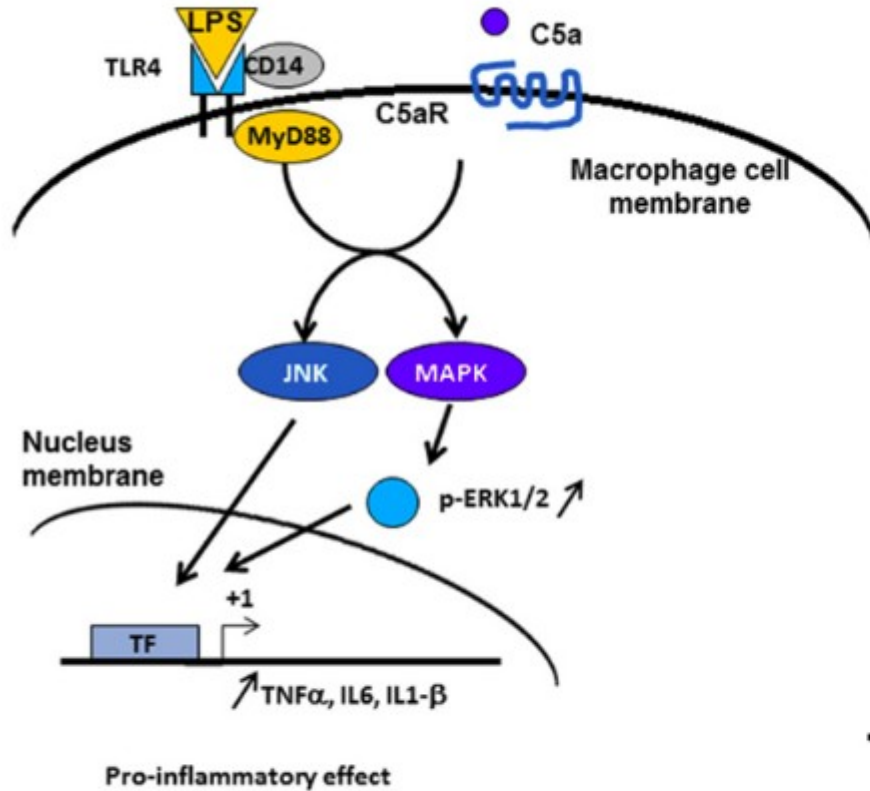




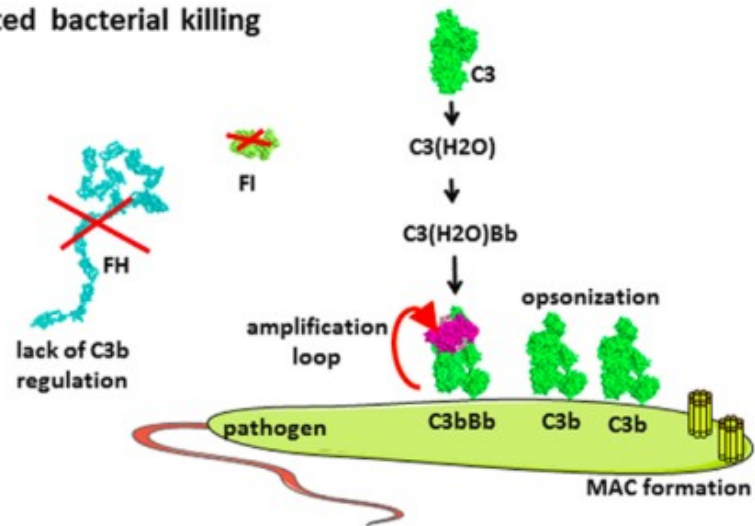




# Kompleman - TLR etkileşimi



### A Complement-mediated bacterial killing



### B Engulfment of C3 fragments-opsionized pathogens

