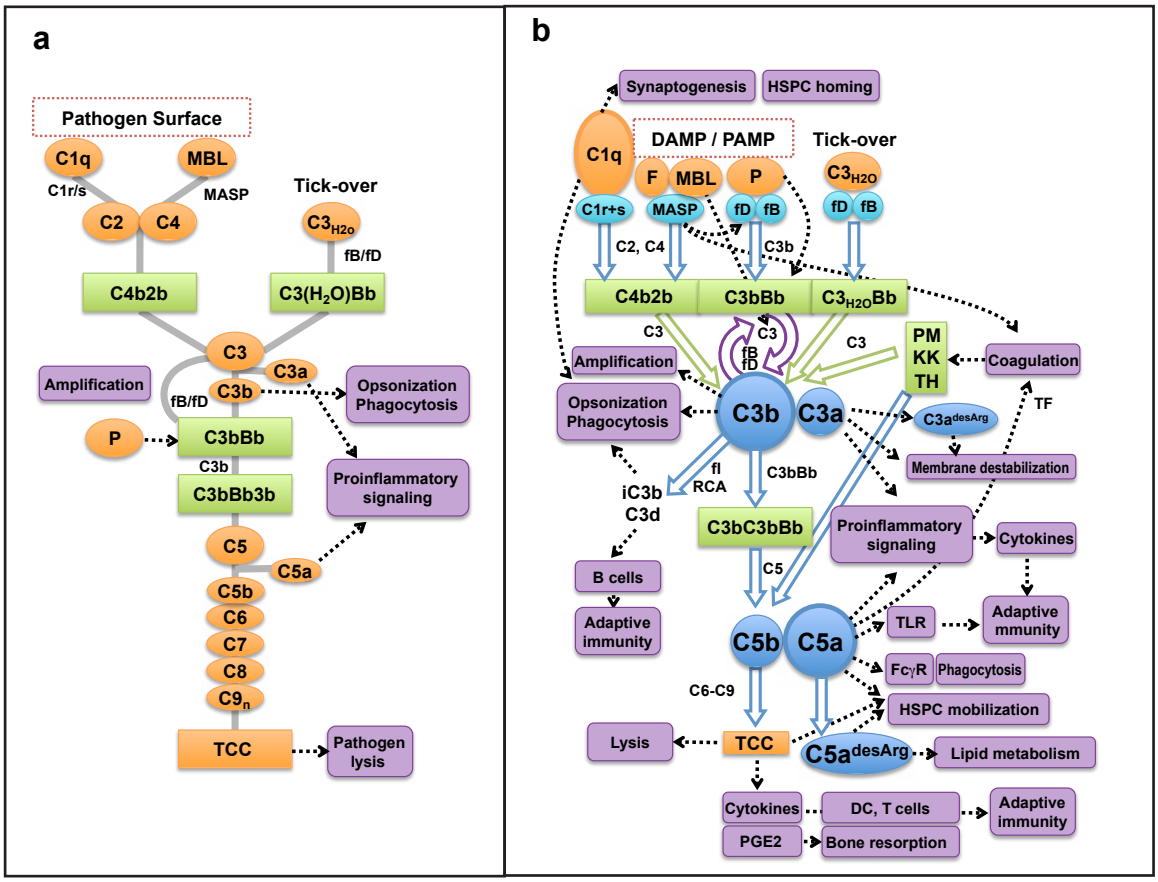
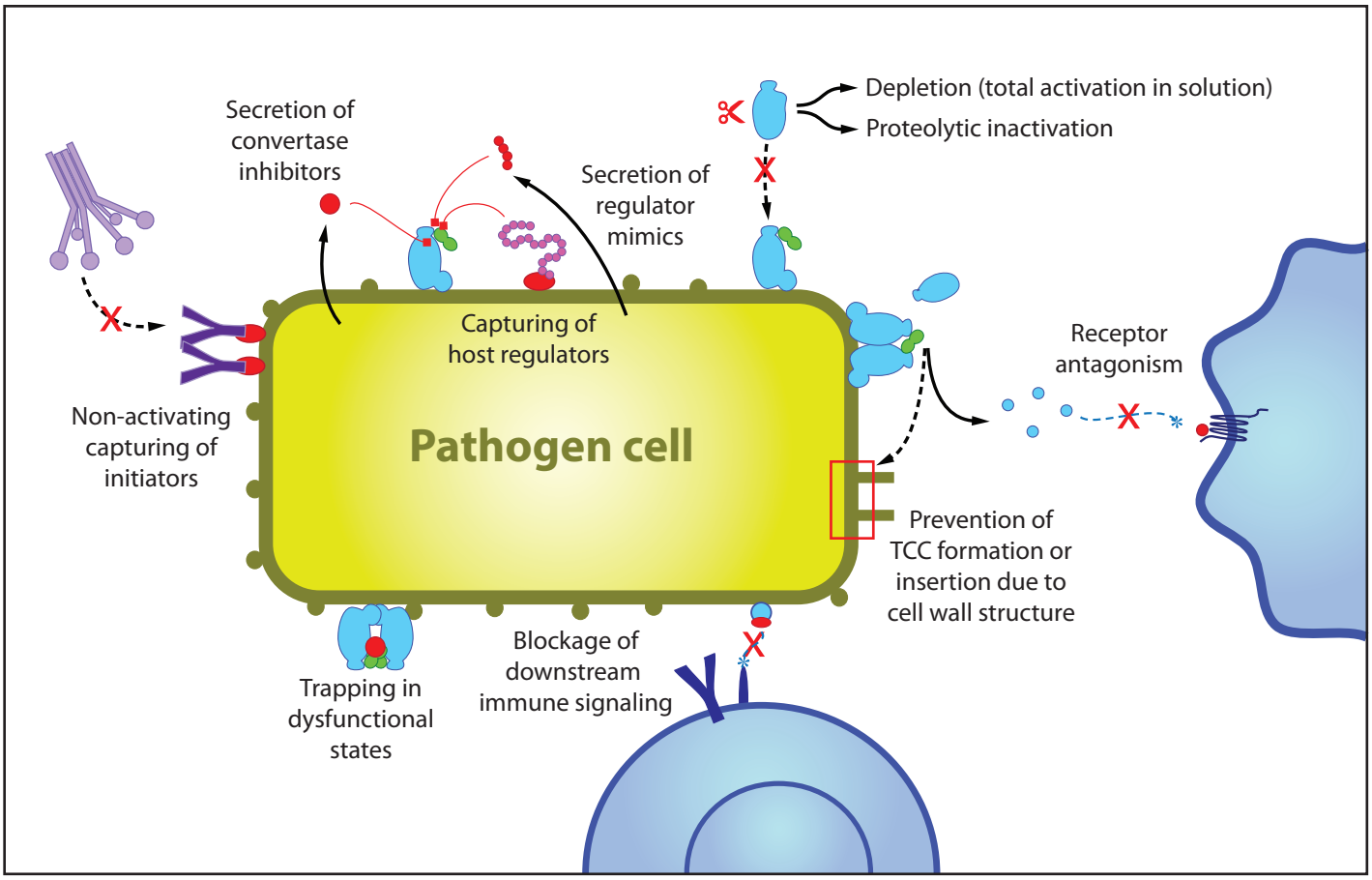
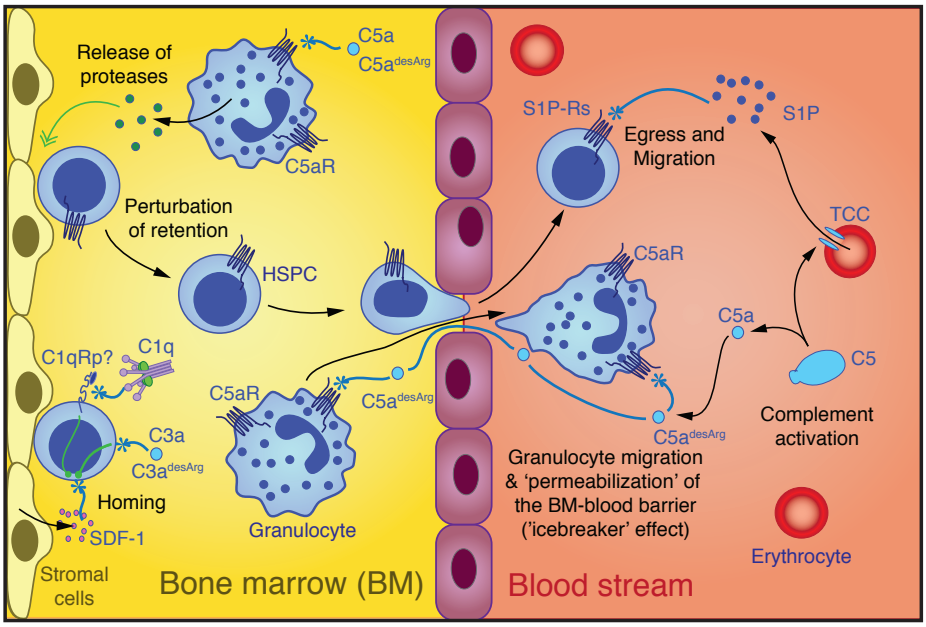
Supp. Fig. 1 (Ricklin, Hajishengallis, Yang & Lambris: Complement - a key system for immune surveillance and homeostasis)



Supplementary Fig. 1. Change of perspective on the complement system. (a) The traditional view regards the complement system as a linear cascade of equal components, with the primary aim of eliminating pathogenic intruders by phagocytosis and lysis. (b) In our current perception, complement acts more like a dynamic network that contains several key functional hubs like C1q, C3b, or C5a that are primarily involved in versatile function in both immune surveillance and cell homeostasis by close crosstalk with other pathways. Both representations depict highly simplified arrangements to illustrate the change in paradigm. No individual complement regulators are shown for the purpose of clarity. Abbreviation of complement proteins can be found in Table 1. Additional abbreviations: DAMP, damage-associated molecular pattern; DC, dendritic cell; FcγR, Fc gamma receptor; KK, plasma kallikrein; HSPC, hematopoetic stem/progenitor cell; PAMP, pattern-associated molecular pattern; PM, plasmin; TF, tissue factor; TH, thrombin; TLR, toll-like receptor.



Supplementary Fig. 2. Concepts of complement evasion strategies by human pathogens. As part of their survival strategy, most human pathogens have developed elaborate mechanism to help them escaping the fatal grip of complement. Though each pathogen has a highly specific arsenal of evasion protein, most of them can be explained by some general concepts. The capturing of complement initiators (*e.g.*, immunoglobulins) in a manner that shields signaling sites affects both phagocytosis and activation of the cascade. While pathogen cells lack complement regulators on their surface, they often express surface proteins that recruit host regulators, or they secrete regulator mimics. Secretion of specific inhibitors may impair convertases directly or trap them in non-functional states. Whereas some inhibitors mask important sites for downstream immune signaling on complement fragments, other act as antagonists for complement receptors on immune cells. Furthermore, several pathogens secrete proteases that either cleave complement proteins to result in inactive fragments, or deplete complement response by consuming C3 in solution rather than on the pathogen surface. Finally, pathogens may avoid certain complement activities in a more passive way: for example, the cell wall chemistry of Gram-positive bacteria prevents insertion of the TCC.



Supplementary Fig. 3. Effect of complement on hematopoetic stem/progenitor cells (HSPC). In the current model of the involvement of complement in HSPC mobilization, various complement components exert distict roles. Complement activation (*e.g.*, during infection or inflammation) generates C5a and $C5a^{desArg}$, which act on granulocytes in the bone marrow (BM) to release proteases that perturb the retention of HSPC. $C5a^{desArg}$ also provides a chemoattraction signal for granulocytes from the BM to the blood stream. The accompanied 'permeabilization' of the BM-blood barrier paves the way for the subsequent egress of HSPC into the blood stream ('icebreaker effect'). The necessary attraction gradient is likely provided by lysis of erythrocytes through TCC(as a product of the complement activation) and release of sphingosine-1-phosphate (S1P), which is known to attract HSPC via binding to S1P receptors. On the other hand, complement is also involved in retention or homing as both C3 activation products (C3a, $C3a^{desArg}$) and C1q have been described to strengthen the retention of HSPC in the BM.