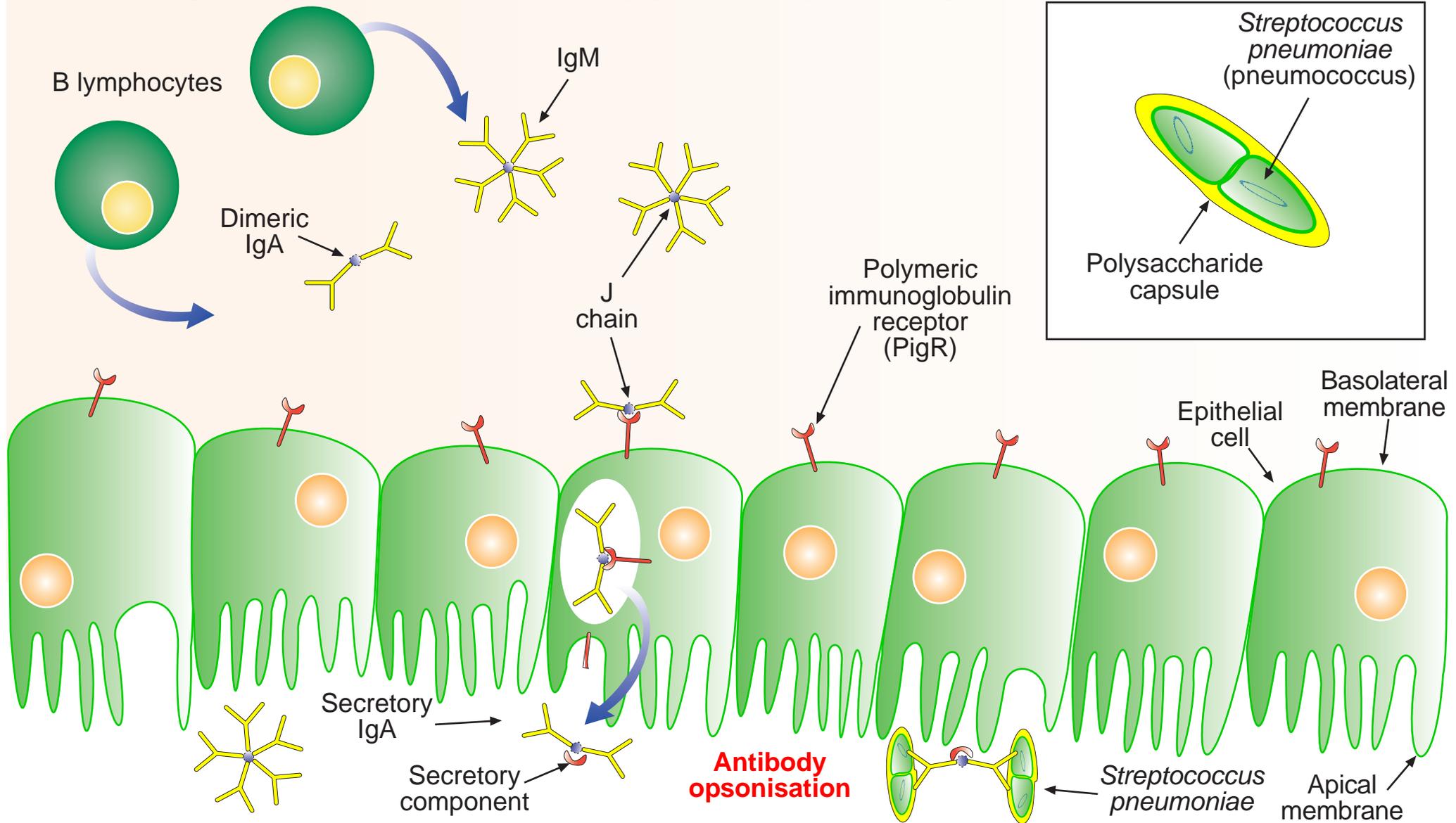
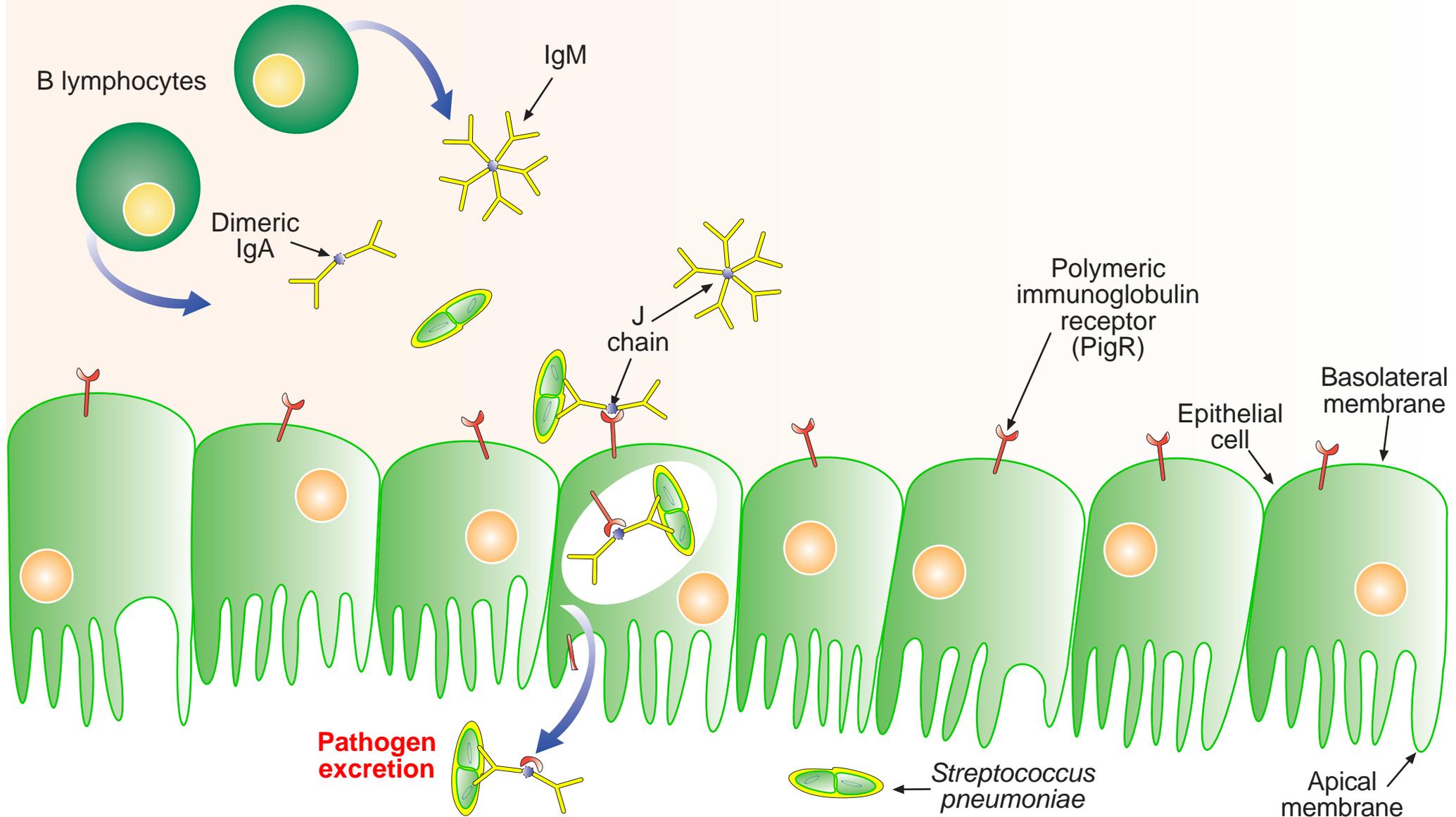


Secretory antibodies in the upper respiratory tract



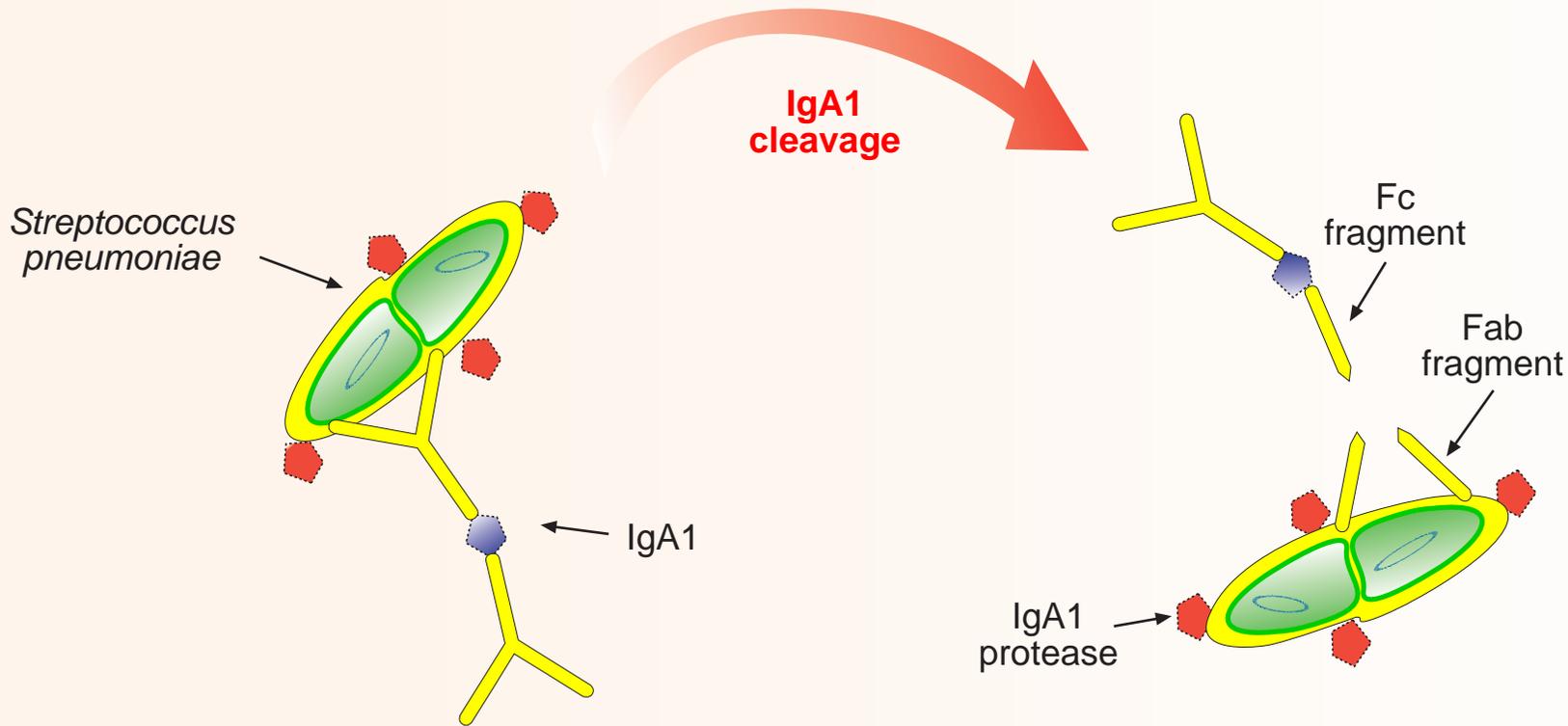
Anti-capsular antibodies play an important role in defense against invading *Streptococcus pneumoniae* species. The polysaccharide capsule, however, is variable between strains with more than 90 serotypes currently identified. The variability of the capsule allows a different bacterial strain to escape humoral responses generated against a previous infecting strain. In addition, the polysaccharide capsule masks epitopes and also interferes with phagocyte receptors due to the negative charge. This also prevents bacteria from entrapment in mucous. Colonisation of the upper respiratory tract is inhibited by IgM and IgA opsonising antibodies secreted across the epithelium mediated by the polymeric immunoglobulin receptor (PigR).

Excretion of pathogens across upper respiratory tract epithelium



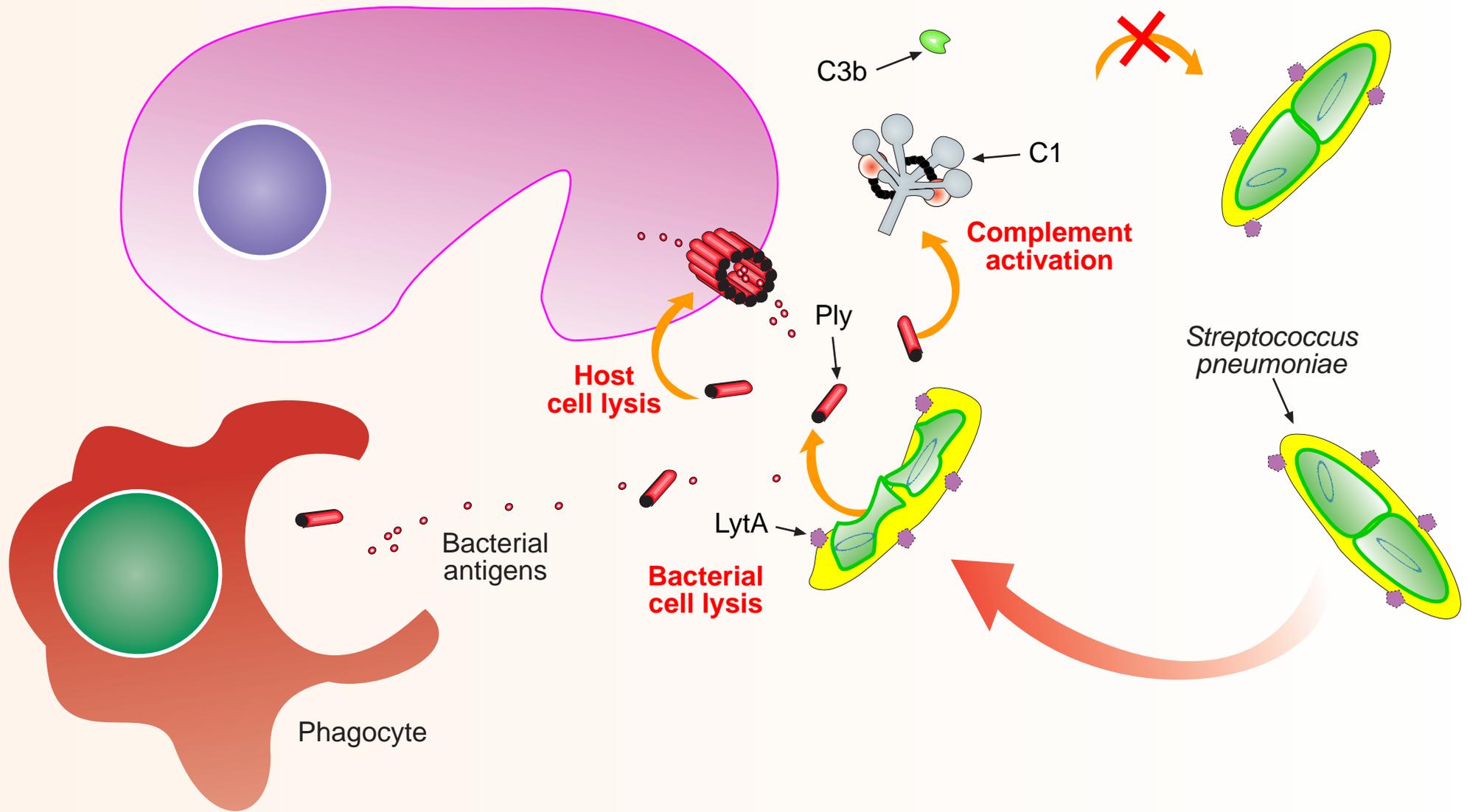
Penetration of bacteria into the submucosa can be reversed by opsonisation with IgM or dimeric IgA secreted by B lymphocytes. The polymeric immunoglobulin receptor (PigR) binds the J chain of antibodies already bound to antigen and thereby facilitates the excretion of pathogens by transcytosis.

Interference with IgA1 antibody efficacy



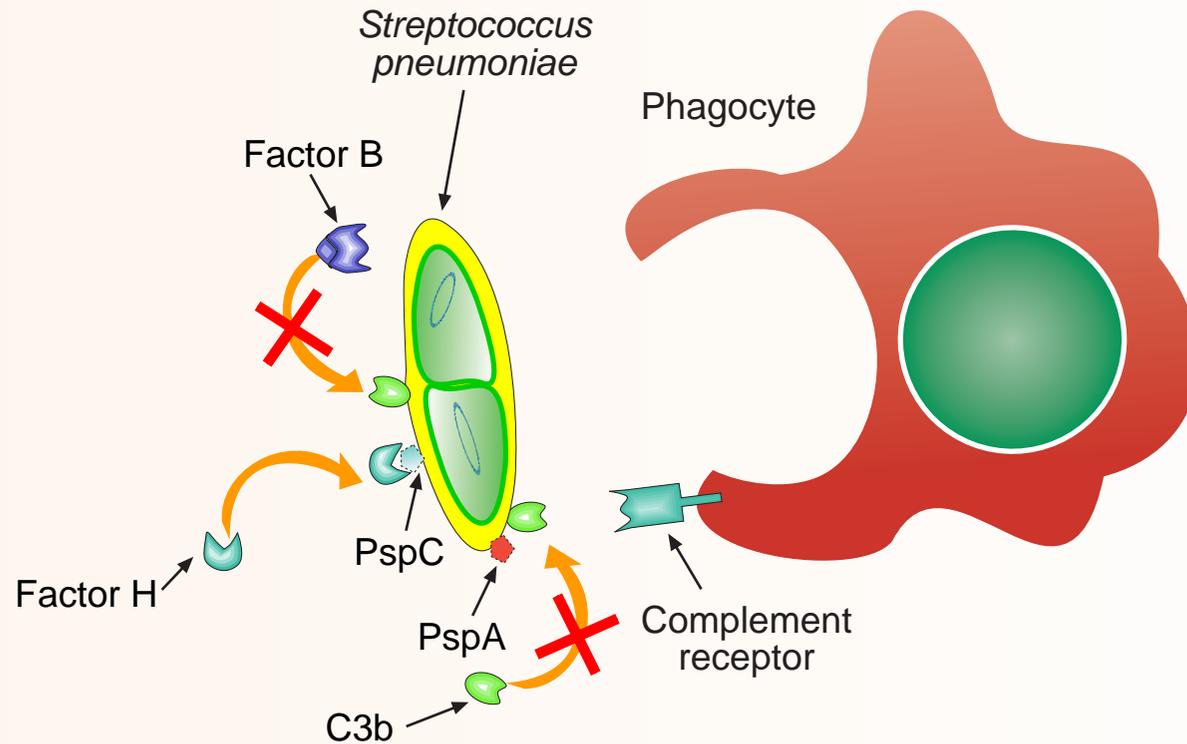
Streptococcus pneumoniae successfully colonises the nasopharynx in humans. The polysaccharide capsule varies between strains and has a negative charge that resists entrapment in mucus. The polymeric immunoglobulin receptor (PigR) transports IgM and dimeric IgA across the epithelium by transcytosis. These antibodies opsonise bacteria detected at mucosal surfaces and prevent attachment. Bacteria detected in the submucosa can also be excreted by antibody-mediated transcytosis. The IgA1 isoform is the most common type of secretory IgA. *Streptococcus pneumoniae* expresses a surface IgA1 protease that cleaves the Fc domain from IgA1 which inhibits receptor-mediated phagocytosis. The Fab fragments remain bound and serve to mask other epitopes.

Complement evasion and inhibition of phagocytosis



Streptococcus pneumoniae has evolved a number of survival strategies such as interference with effective complement attack and subsequent phagocytosis. In a self-sacrificing way some bacteria autolyse and divert immune attack away from living bacteria. The LytA molecule expressed on the bacterial cell surface, once activated promotes lysis of the bacterium which facilitates release of the intracellular toxin, pneumolysin (Ply). Ply activates complement and diverts the attack from other bacteria. In higher concentrations, Ply can form a pore in the cell membrane of host cells and promote lysis. Release of bacterial antigens excessively activate phagocytes via toll-like receptor engagement and allow bacteria to escape phagocytosis.

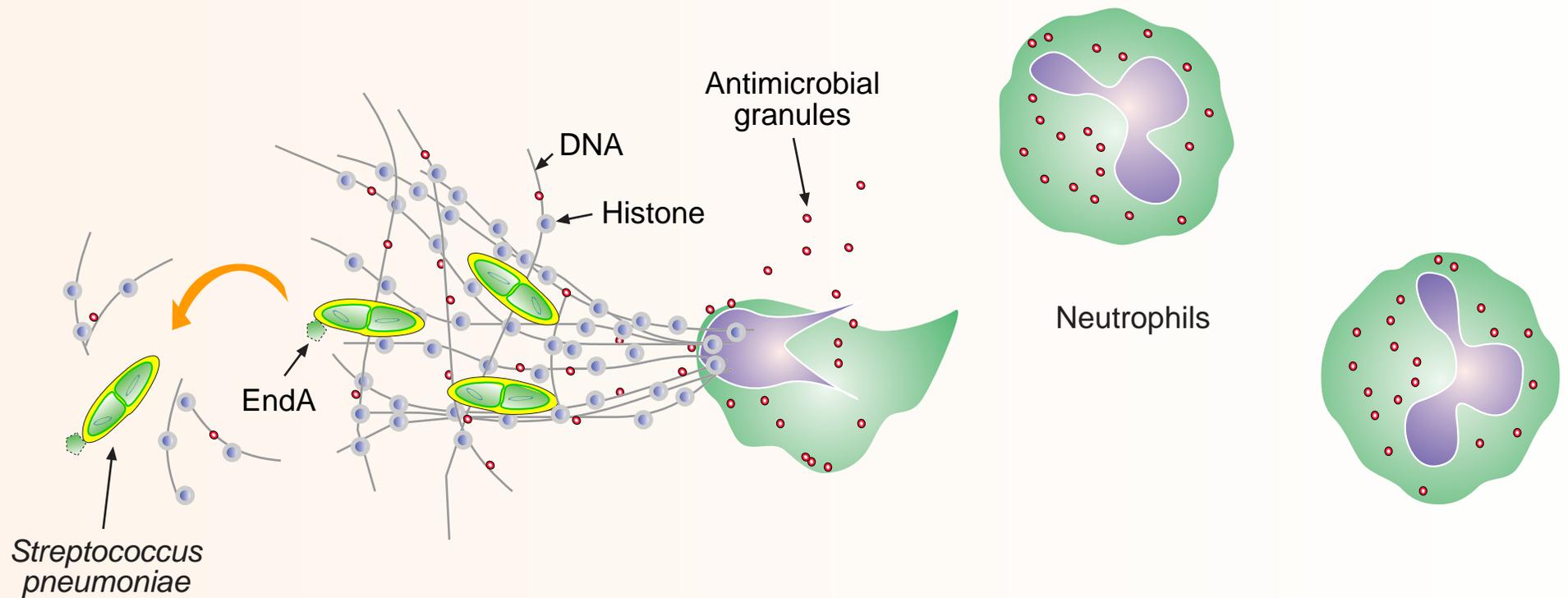
Complement evasion and inhibition of phagocytosis



Streptococcus pneumoniae also expresses cell surface molecules that disrupt complement protein binding. PspA prevents C3b surface deposition. C3b usually initiates the alternative complement cascade and is also produced as an opsonin by the classical and lectin complement cascades. Another surface protein, PspC, binds factor H, a negative regulator of the alternative complement system, which prevents factor B binding to C3b to assemble the C3 convertase. Phagocytes expressing complement receptors are thus inhibited from engulfing bacteria.



Escape from neutrophil extracellular nets



Neutrophils play an important role in innate immune control of bacteria, particularly *Streptococcus pneumoniae*. Neutrophils classically employ phagocytosis and release of antimicrobial granules to control extracellular pathogens. However, a recently discovered innate defense mechanism known as the neutrophil extracellular trap (NET) has been described. Chromatin (DNA and histone proteins) with attached antimicrobial granules is extruded from the neutrophil into the environment and serves to trap pathogens. The neutrophil dies during this process. However, *Streptococcus pneumoniae* evades capture by expressing a DNA endonuclease, EndA, that cleaves the DNA and permits escape from the trap.

