Low Invasiveness of Pneumococcal Serotype 11A Is Linked to Ficolin-2 Recognition of O-acetylated Capsule Epitopes and Lectin Complement Pathway Activation.

Background. The divergent epidemiological behavior of Streptococcus pneumoniae serotypes suggests that serotype-specific features such as capsule O-acetylation influence the propensity of a strain to cause invasive pneumococcal disease (IPD). We hypothesize that innate host factors mediate the observed negative association between IPD and the serotype 11A (ST11A) capsule O-acetyltransferase gene, wcjE. Methods. We evaluated the ability of ficolin-2, an initiator of the lectin complement pathway that was previously shown to bind ST11A pneumococci, to recognize and mediate complement-dependent opsonophagocytosis of different pneumococcal serotypes. We supplemented findings with an epidemiological meta-analysis comparing invasiveness of the 30 most prevalent pneumococcal serotypes. Results. Ficolin-2 bound ST11A capsule polysaccharide and other wcjE-containing pneumococcal serotypes, except ST9V and ST20B. Ficolin-2 did not bind wcjE-null serotypes, including the wcjE-null variant of ST11A, ST11E. We observed C1q-independent complement deposition and phagocytic killing of pneumococci expressing ST11A but not those expressing ST11E. Inhibition of ficolin-2 binding abrogated ST11A-associated complement deposition and phagocytosis. In children, invasiveness of ST11A was the lowest among serotypes tested in our meta-analysis, while ST9V was among the highest. Conclusions. Ficolin-2 mediates serum protection by recognizing specific O-acetylated epitopes of pneumococcal capsule polysaccharides, exemplifying a novel host-microbe interaction that innately offers serotype-specific immunity to IPD.

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