Global epithelial cell transcriptional responses reveal Streptococcus pyogenes Fas regulator activity association with bacterial aggressiveness.

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Abstract

The bacterial human pathogen Streptococcus pyogenes (group A streptococci, GAS) is able to adhere to, internalize into and cross-talk on multiple levels with its host cells. To gain insight into the Fas function in pathogenesis we used Affymetrix human genome DNA-arrays to measure temporal and global transcriptional responses of HEp-2 cells infected with M49 S. pyogenes wild-type bacteria and DeltafasX, an isogenic S. pyogenes two-component-signal-transduction system mutant. A modified stringent statistical analysis method identified a total of 86 HEp-2 cell genes as differentially transcribed upon infection over the investigated time course. Increased expression of genes encoding proteins involved in GAS host cell adherence and internalization (fibronectin, integrin-alpha5) was found as a common response. In contrast to earlier reports investigating other GAS serotype strains, Ras superfamily and RhoA pathways are exploited by M49 GAS, suggesting serotype specific interactions with the host cell cytoskeleton. Despite transcriptional induction, secreted IL-8 levels of deltafasX mutant infected cells were below those of non-infected

cells, indicating an absence of Fas expression could be important for GAS tissue colonization and long-term intracellular persistence. Oppositely, activity of the S. pyogenes Fas-system apparently promotes high adherence and internalization rates, massive cytokine gene transcription and cytokine release, host cell apoptosis via a caspase-2 activation pathway, and cytotoxicity. Thus, the S. pyogenes Fas two-component signal transduction system could be involved in local tissue destruction and general bacterial aggressiveness towards host cells.

Beteiligte Forschungseinheiten

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