

Biofilm-associated molecular patterns

Bacteria may exist as single cells in the planktonic mode or as communities of aggregated bacteria embedded in a common extracellular matrix in biofilms. The biofilm lifestyle may protect bacteria from host immunity and contribute to chronic infections by hyperinflammation. This hyperinflammatory response is largely driven by excessive neutrophil activity, which can contribute to tissue damage and reduce susceptibility to antibiotics.

The innate neutrophil responses to bacteria are mediated by pattern-recognition receptors (PRRs) recognizing pathogen-associated molecular patterns (PAMPs). To explain the exaggerated neutrophil response to biofilms, we hypothesized that biofilms express a distinct subset of PAMPs at immunostimulatory levels specifically during biofilm growth. We term these **biofilm-associated molecular patterns (BAMPs)** and present evidence supporting their existence.

This evidence includes: **1)** neutrophils exhibit a stronger respiratory burst in response to biofilm-forming *Pseudomonas aeruginosa* than to planktonic bacteria at low bacterial densities; **2)** hyperexpression of the biofilm matrix components alginate and Psl enhances the neutrophil respiratory burst. These hyperexpressing clones display a mucoid phenotype which is associated with accelerated lung function decline during chronic *P. aeruginosa* pneumonia, highlighting the potential clinical relevance of BAMPs; and **3)** biofilm growth confers BAMP-like properties on *P. aeruginosa* LPS, as indicated by enhanced pro-inflammatory cytokine production by responding human monocytes. This demonstrates that biofilm-associated changes can enhance innate immune activation beyond neutrophils.

Together with other recently described BAMP-like properties of biofilms, these findings support the existence of BAMPs as a distinct, biofilm-associated subset of PAMPs. BAMPs may therefore represent potential therapeutic targets for reducing detrimental hyperinflammation while preserving the host's ability to control dissemination by planktonic bacteria.