fully mobilizable luk-PV phage are so prevalent in other CA-MRSA.

Overall, this study shows that USA300 fails to overexpress luk-PV under stress, suggesting phage induction is not an important regulatory pathway for toxin expression in SSSI infection. Once again, the role of this toxin in disease remains elusive.

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Shielding, a new pathogen defence mechanism against PMNs

In an article published in this issue, Alhede et al. (2009) demonstrate that the opportunistic pathogen Pseudomonas aeruginosa can react to the presence of PMNs by producing abundant quantities of rhamnose-containing glycolipid biosurfactants, the rhamnolipids (Maier & Soberon-Chavez, 2000). PMNs are phagocytic cells and are important players in the innate immune response since they produce a range of antimicrobial molecules able to kill pathogens. Rhamnolipids are known to cause fast lysis of amoebae such as Dictyostelium discoideum (Cosson et al., 2002); they have previously been shown by the same research group to cause lysis of several cellular components of the human immune system, e.g. monocyte-derived macrophages and PMNs (Jensen et al., 2007; Van Gennip et al., 2009). In P. aeruginosa, rhamnolipid synthesis is under control of the quorum-sensing (QS) system, particularly via the RhII-RhIR C4-homoserine lactone synthase/LuxR regulator system (Williams & Camara, 2009). The control of rhamnolipid production by QS is necessary to avoid constant exposure of eukaryotic cells, including the components of the innate immune system, to these surfactants, which could lead to the triggering of a strong inflammatory response. To demonstrate the importance of rhamnolipids as a shield against PMNs, the authors tested the capacity of an rhlA mutant (unable to produce these biosurfactants) to survive in the lungs of infected mice and found a drastic reduction of colony-forming units compared to the wild-type.

Like other pathogens, P. aeruginosa is capable of forming biofilms (Parsek & Tolker-Nielsen, 2008). This is particularly the case in the lungs of cystic fibrosis patients, where P. aeruginosa forms biofilms in the thick mucus layer (Winstanley & Fothergill, 2009). In this study the authors measured the release of lactate dehydrogenase by PMNs in contact with in vitro P. aeruginosa biofilms, as an indicator of cell lysis. They demonstrated that a large fraction of the PMNs exposed to the wild-type biofilm rapidly lysed, while no PMNs lysed after exposure to the rhlA mutant, demonstrating the importance of rhamnolipid production as a strategy to aggressively respond to PMNs. However, in agreement with another study (Morici et al., 2007) Alhede et al. (2009) found that in vitro biofilms produce very little rhamnolipid, which at first seems to contradict the rapid lysis observed by the authors. In investigating this apparent anomaly, Alhede and colleagues demonstrated that exposure to PMNs acts as a signal triggering the fast production of rhamnolipids, which remain associated with the biofilm rather than being released in the surrounding fluid. This suggests that PMNs become eliminated by contact with the biofilm. This is in agreement with microscopic investigations of P. aeruginosa-infected tissue samples from the lungs of cystic fibrosis patients and chronic wounds, which suggest that PMNs stay in the periphery but do not reach inside the biofilm cell mass. Furthermore, lysis of the PMNs causes release of DNA, which is
used as a component of the biofilm matrix (Ma et al., 2009).

Collectively, the results presented by Alhede et al. (2009) suggest that biofilm P. aeruginosa cells can sense the presence of PMNs and respond by producing the rhamnolipid shield. A transcriptome analysis of the response of biofilm P. aeruginosa cells to exposure to PMNs confirmed the upregulation of QS-dependent genes (85% of upregulated genes), including the rhlA and rhlB genes for rhamnolipid production. The response to PMNs seems to be orchestrated by another QS signal molecule, the Pseudomonas quinolone signal (PQS), responsible for the induction of different virulence factors (Diggle et al., 2006). The biosynthetic pqs operon is indeed upregulated in the presence of PMNs, suggesting an increase in PQS signal production. Confirming the importance of the PQS signal molecule in the induction of rhamnolipid production upon exposure to PMNs, a pqsA (PQS-deficient) mutant was unable to produce the shield response.

A remaining major challenge is now to identify which signal(s) coming from the PMNs are able to trigger the rapid PQS-dependent response of P. aeruginosa cells. The authors have already excluded oxidative stress and dynorphin, which has previously been shown to enhance the production of virulence factors in a planktonic P. aeruginosa culture (Zaborina et al., 2007). P. aeruginosa cells can detect and react to mammalian effectors such as interferon-γ, which is sensed by P. aeruginosa via the OprF porin, triggering the production of QS-dependent virulence factors (Wagner et al., 2006; Wu et al., 2005). No doubt future research will unveil more interesting pathways leading to inter-kingdom interactions.

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