Identity and effects of quorum sensing inhibitors produced by Penicillium species

Quorum sensing (QS) communication systems are thought to afford bacteria with a mechanism to strategically cause disease. One example is Pseudomonas aeruginosa, which infects immunocompromised individuals such as cystic fibrosis patients. The authors have previously documented that blockage of the QS systems not only attenuates Ps. aeruginosa but also renders biofilms highly susceptible to treatment with conventional antibiotics. Filamentous fungi produce a battery of secondary metabolites, some of which are already in clinical use as antimicrobial drugs. Fungi coexist with bacteria but lack active immune systems, so instead rely on chemical defence mechanisms. It was speculated that some of these secondary metabolites could interfere with bacterial QS communication. During a screening of 100 extracts from 50 Penicillium species, 33 were found to produce QS inhibitory (QSI) compounds. In two cases, patulin and penicillic acid were identified as being biologically active QSI compounds. Their effect on QS-controlled gene expression in Ps. aeruginosa was verified by DNA microarray transcriptomics. Similar to previously investigated QSI compounds, patulin was found to enhance biofilm susceptibility to tobramycin treatment. Ps. aeruginosa has developed OS-dependent mechanisms that block development of the oxidative burst in PMN neutrophils. Accordingly, when the bacteria were treated with either patulin or penicillic acid, the neutrophils became activated. In a mouse pulmonary infection model, Ps. aeruginosa was more rapidly cleared from the mice that were treated with patulin compared with the placebo group.