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BACTERIAL DEVELOPMENT

Streptomyces' cue to leave

> a previously unknown growth mode in *S. venezuelae* that enables cells to explore their environment

The lifestyle of *Streptomyces*, which is a genus of Gram-positive bacteria, is complex and has been described as involving three developmental stages: branching vegetative hyphae, non-branching aerial hyphae and spores. Classic developmental studies have been carried out using single-species cultures, and, in light of the intricate interactions between microorganisms in polymicrobial communities, Jones *et al.* co-cultured *Streptomyces venezuelae* with the yeast *Saccharomyces cerevisiae* and investigated the effect on developmental behaviour. The authors found that the yeast triggered a previously unknown growth mode in *S. venezuelae* that enables cells to explore their environment.

In contrast to the normal-sized colonies that are observed for bacteria grown alone, *S. venezuelae* colonized the entire surface of an agar plate after 14 days of co-culture with *S. cerevisiae*. Intriguingly, *S. venezuelae* could effectively spread across both biotic and abiotic surfaces, as growth was not obstructed by rocks or polystyrene barriers. The authors termed this phenomenon 'exploratory growth' and named the spreading cells 'explorers'. To investigate the morphology of explorers, they used scanning electron microscopy and showed that these cells adopt a non-branching vegetative hyphal conformation. When the authors co-cultured mutant bacteria that lacked known developmental regulators (that is, *bld* and *whi* genes, which regulate the formation of aerial hyphae and spores, respectively) with yeast, they unexpectedly found that these mutant bacteria showed the same exploratory behaviour as the wild-type cells. Based on these findings, they concluded that exploratory growth is distinct from the canonical life cycle of *Streptomyces*.

This novel developmental behaviour seems to be widespread, as several *Streptomyces* species exhibited exploratory growth, which was triggered by several fungal species.

Next, the authors investigated how the fungi can induce this growth behaviour in bacteria. They found that mutant fungi that had defective tricarboxylic acid (TCA) cycle function were unable to induce exploratory growth in *S. venezuelae*, which suggests that glucose uptake or consumption have a role. Indeed, *S. venezuelae* that was grown in glucose-depleted medium exhibited exploratory growth. Moreover, the authors showed that alkaline conditions were required for the exploratory behaviour of *S. venezuelae* and that the bacteria themselves mediate the increase in pH in the environment. To combat these conditions, explorer cells induce the expression of genes that are involved in the alkaline stress response. But how does *S. venezuelae* induce this increase in pH? To answer this question, the authors used a two-compartment assay, in which the compartments were separated by a polystyrene barrier. Measuring the pH in the agar revealed that exploratory cultures increased the pH in the adjacent non-inoculated compartment, which suggests that the cells alkalinize the medium by producing a volatile organic compound (VOC). Using the same experimental set-up, the authors showed that *S. venezuelae*, as well as a wild *Streptomyces* isolate, grown in one compartment exhibited exploratory growth when *S. venezuelae* explorers were cultured in the adjacent compartment. This suggests that the produced VOC functions as an exploration-promoting signal for physically separated and unrelated colonies. The VOC was identified as trimethylamine (TMA), which is a volatile nitrogen-containing metabolite. In agreement with the above results, further experiments showed that TMA increased the pH of agar plates and induced exploratory growth in *S. venezuelae*. Not only did TMA elicit an exploratory response in distant *Streptomyces* species it also inhibited the growth of other bacteria, which suggests that this airborne signal provides a fitness advantage to the TMA-producing bacteria.

In summary, this study identifies a novel inter-kingdom interaction that alters microbial behaviour. Two key metabolic cues, glucose depletion and increased pH, promote a new growth mode in *S. venezuelae*. Bacteria produce a volatile compound that can induce exploratory growth in distant colonies and other *Streptomyces* species, thus promoting communication over a long range. This new growth strategy provides *Streptomyces* with an alternative means of colonizing new habitats.

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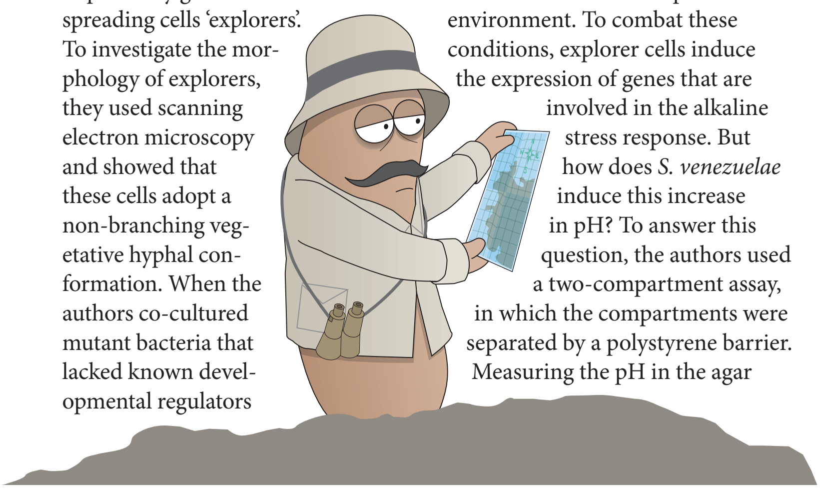
ORIGINAL ARTICLE Jones, S. E. *et al. Streptomyces* exploration is triggered by fungal interactions and volatile signals. *eLife* **6**, 21738 (2017)



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