Influence of Niche-Specific Nutrients on Secondary Metabolism in Vibrionaceae - DTU Orbit (09/11/2017)

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Many factors, such as the substrate and the growth phase, influence biosynthesis of secondary metabolites in microorganisms. Therefore, it is crucial to consider these factors when establishing a bioprospecting strategy. Mimicking the conditions of the natural environment has been suggested as a means of inducing or influencing microbial secondary metabolite production. The purpose of the present study was to determine how the bioactivity of *Vibrionaceae* was influenced by carbon sources typical of their natural environment. We determined how mannose and chitin, compared to glucose, influenced the antibacterial activity of a collection of *Vibrionaceae* strains isolated because of their ability to produce antibacterial compounds but that in subsequent screenings seemed to have lost this ability. The numbers of bioactive isolates were 2- and 3.5-fold higher when strains were grown on mannose and chitin, respectively, than on glucose. As secondary metabolites are typically produced during late growth, potential producers were also allowed 1 to 2 days of growth before exposure to the pathogen. This strategy led to a 3-fold increase in the number of bioactive strains on glucose and an 8-fold increase on both chitin and mannose. We selected two bioactive strains belonging to species for which antibacterial activity had not previously been identified. Using ultrahigh-performance liquid chromatography-high-resolution mass spectrometry and bioassay-guided fractionation, we found that the siderophore fluvibactin was responsible for the antibacterial activity of Vibrio furnissii and Vibrio fluvialis These results suggest a role of chitin in the regulation of secondary metabolism in vibrios and demonstrate that considering bacterial ecophysiology during development of screening strategies will facilitate bioprospecting. A challenge in microbial natural product discovery is the elicitation of the biosynthetic gene clusters that are silent when microorganisms are grown under standard laboratory conditions. We hypothesized that, since the clusters are not lost during proliferation in the natural niche of the microorganisms, they must, under such conditions, be functional. Here, we demonstrate that an ecology-based approach in which the producer organism is allowed a temporal advantage and where growth conditions are mimicking the natural niche remarkably increases the number of *Vibrionaceae* strains producing antibacterial compounds.

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