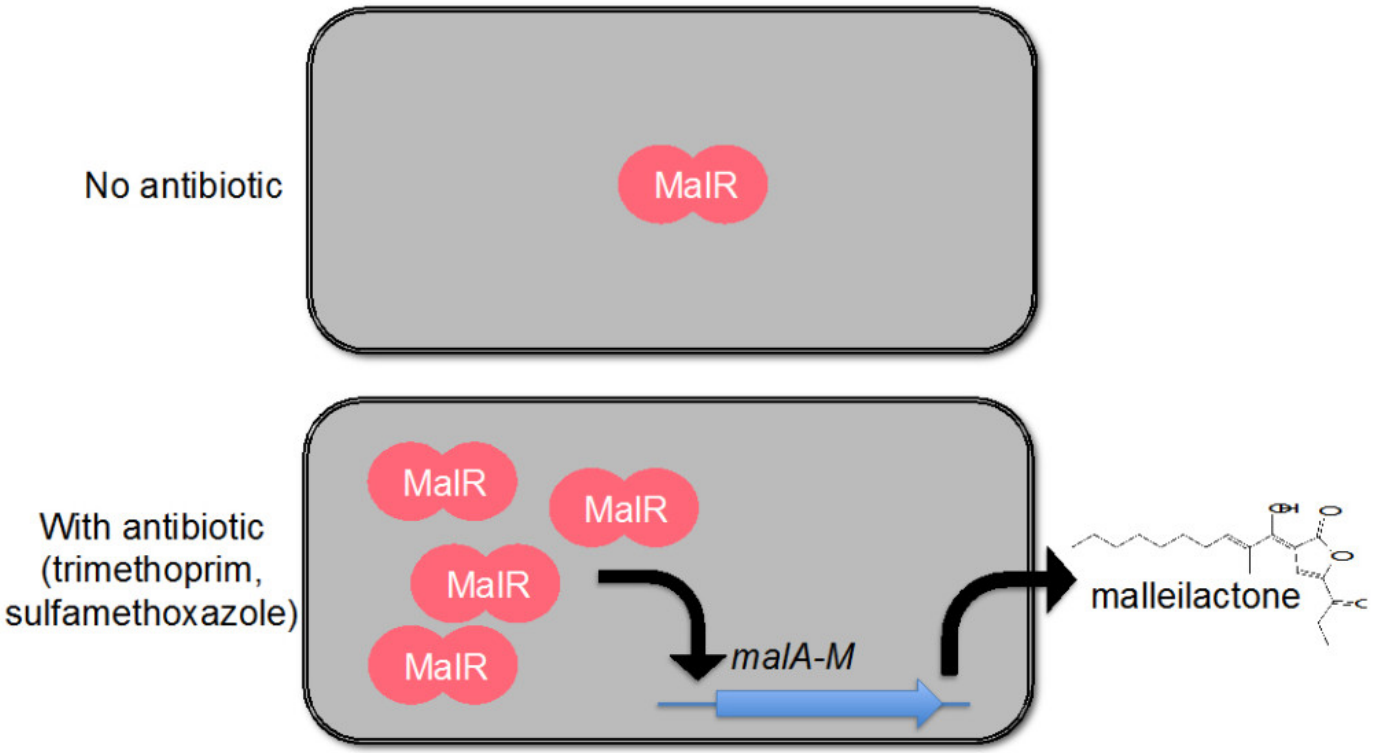
Antibiotic sensing by a bacterial communication system

Bacteria compete using antibiotics. Bacteria compete with one another using an array of destructive compounds and strategies. For example antibiotics, used to treat infections, are produced by bacteria and other microbes and can kill competitors in mixed microbial environments. However, antibiotics are expensive to produce and often only made when necessary. It is important to understand when and how bacteria induce the production of antibiotics for the discovery of new antibiotics, and to understand how antibiotics are used by bacteria in their natural environments.



Malleilactone regulation by MalR, an orphan quorum sensing regulator in the bacterium Burkholderia thailandensis. In the presence of antibiotics, such as those that might be produced by competing bacteria, MalR synthesis is increased in the cell triggering the expression of the genes malA-M, involved in production of the cytotoxic antibiotic malleilactone.

Antibiotics are regulated by bacterial 'quorum-sensing' systems. A single bacterium probably cannot produce enough antibiotics to kill other bacteria. However, many different species of bacteria have a way to count themselves using a system called quorum sensing. When the population count gets high enough, the quorum sensing system turns on production of antibiotics. These quorum-sensing systems may reduce the overall expense of making the antibiotic, because

they delay antibiotic production until there are enough bacteria to produce a killing antibiotic dose.

A bacterial quorum sensing receptor that senses antibiotics. Quorum sensing involves communication between bacteria using small diffusible signals. Quorum sensing requires only two proteins; the signal producer, and the signal receptor. The signals are produced at a low level, and when the population reaches a critical concentration the accumulated signal binds to the receptor and causes many changes in the cell, such as the production of antibiotics. In some cases the signal-producing protein is missing. Receptors with no signal-producing partner are called 'orphan' quorum-sensing receptors. Our current understanding of orphan receptors is limited compared with classic quorum sensing receptors. Our work describes the discovery of an orphan quorum-sensing receptor in the soil bacterium Burkholderia thailandensis. This receptor does not appear to respond to typical quorum sensing signals. Instead, the receptor responds to certain antibiotics, such as trimethoprim and sulfamethoxazole. These antibiotics increase synthesis of the orphan receptor, which triggers *B. thailandensis* to produce an antibiotic called malleilactone. Malleilactone is not produced in cells grown without antibiotics or that lack the receptor protein.

Our results show that *B. thailandensis* uses an orphan quorum-sensing receptor to sense and respond to certain antibiotics, which triggers production of a cytotoxic antibiotic called malleilactone. This regulatory pathway may be important for *B. thailandensis* to sense and and respond to competitors in multispecies soil communities. We can imagine this is a way for *B. thailandensis* to fight back against other bacteria that make things like trimethoprim. This work expands our current view of orphan quorum sensing receptors and their role in regulating antibiotics.

Publication

A Burkholderia thailandensis Acyl-Homoserine Lactone-Independent Orphan LuxR Homolog That Activates Production of the Cytotoxin Malleilactone.
Truong TT, Seyedsayamdost M, Greenberg EP, Chandler JR.
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