Innovative Approach for Targeting Plant Pathogens

-Development of Potent Anti-bacterials with a Novel Mode of Action

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TECHNOLOGY

Drs. Yang and Chen have synthesized several novel chemical compounds which inhibit the expression of the Type III Secretion System (T3SS) virulence genes of the plant pathogens *D. dadantii* 3937, *P. syringae* pv *tomato* DC3000, and *Erwinia amylovora* as well as the human pathogen *Pseudomonas aeruginosa*. The compounds do not affect the viability of the bacteria. The T3S apparatus is not necessary for survival of the pathogenic bacteria; therefore these inhibitors are unlikely to lead to selective pressure and trigger resistance to the compounds in the pathogens. The inhibitors also should not harm normal, non-pathogenic microbial flora. Lead compounds have been tested in field trials on apple blossoms for prevention of infection by *E. amylovora.* The results have shown that our novel lead compounds prevent infection similar to that seen for kasugamycin, an antibiotic currently used in crops, but prone to antibiotic resistance.

Limited options are available for the control of bacterial disease in plants, animals, and humans. Many commercially available antimicrobials lead to death of the pathogen. This pressure leads to the natural selection of microbes that develop mutations enabling them to resist the compound or drug and survive. Most antimicrobials used for fighting pathogenic bacteria also eliminate beneficial natural microbes. Loss of the natural symbiotic microbes leaves plants more vulnerable to future disease attacks due to a lack of competition against the pathogenic bacteria. Many pathogenic bacteria found in animals and plants utilize a type III secretion system (T3SS) which releases proteins into the host organism that are essential for pathogenesis. The T3SS is an attractive target for the development of antimicrobial compounds, since it is present in numerous plant, human, and animal pathogens, but is not found in their nonpathogenic counterparts.

FEATURES/BENEFITS

- **Novel** - Multiple new compounds (not commercially available) that inhibit plant and human bacterial pathogens
- **Safer** - Does not target natural microbial flora of treated organism; analogs of natural plant compounds
- **Better for environment** - Reduces risk of resistance emergence in bacterial pathogens
- **Multiple targets** - Potential effects on many plant, animal, and human pathogens
- **Broad applications** - Agriculture, food safety, biofilm prevention, household products, and pharmaceuticals

INTELLECTUAL PROPERTY

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This technology is licensed to T3 Bioscience, LLC and is part of an active and ongoing research program. The company is seeking partners for development of the final product.

MARKETS/APPLICATIONS

Plant diseases cause billions of dollars' worth of direct and indirect losses every year, but the options for bacterial disease control in plants are limited. The worldwide pesticide industry was $52 billion in 2008, and the market is expected to grow annually at a rate of 7% between 2008 and 2013 (SBI reports). Major cash crops that are affected by bacterial infections include: rice, barley, wheat, tomato, pepper, cabbage, onion, soybean, potato, carrot, lettuce, cucumber, and eggplant. Besides crop protection, antimicrobials are also utilized in agricultural applications such as feed additives, veterinary medicine, and aquaculture. Unfortunately, the non-therapeutic use of antimicrobial compounds is a major factor in the emergence of antimicrobial resistant pathogens worldwide.

The T3SS inhibitory compounds designed by the inventors specifically target an infectious component of the pathogenic bacteria that is non-essential for normal growth and survival. This feature greatly diminishes the chance of the pathogens acquiring resistance to the compounds. T3S components are conserved in numerous pathogens that infect plants, humans, and animals suggesting a broad range of applications for these compounds. Potential applications include control and prevention of plant disease in agriculture, application on vegetable surfaces to reduce the risk of co-contamination by human pathogens, prevention of post-harvest infection in storage crops, household antimicrobial products, veterinary medicine, and pharmaceuticals.

INVENTORS

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PUBLICATIONS

Li Y., Peng Q., Selimi D., Wang Q., Charkowski A.O., Chen X., Yang C.H. (2009) The plant phenolic compound p-coumaric acid represses gene expression in the *Dickeya dadantii* type III secretion system. Appl Environ Microbiol 75:1223-8.

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