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Study of Plant Disease Uncovers New Class of Bacterial Enzyme Which May Lead to Useful New Products

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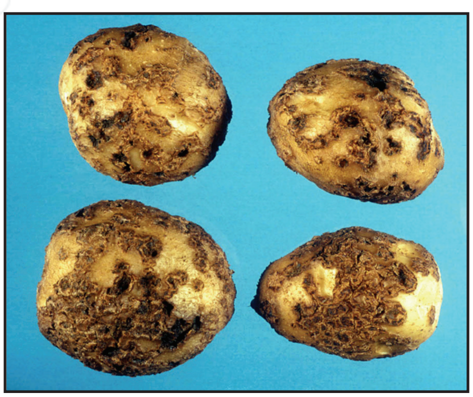
Most of the pharmaceutically important compounds used today came from a group of filamentous bacteria called streptomycetes. These bacteria live in soil and are veritable factories for biologically active chemicals. A few of these organisms cause diseases of plants, including the economically important disease known as potato scab. Potato scab is a source of significant crop losses to potato growers in most potato production regions in the United States. Research has shown that the several scab-causing Streptomyces species all produce an unusual chemical – thaxtomin – that is required for plant pathogenicity. The genes that enable these scab-causing streptomyces to produce thaxtomin is shared by all of these streptomyces. Thaxtomin is novel because it is decorated with a nitrate group; nitrate groups are extremely rare additions to natural products and the enzymes responsible for adding nitrate groups had never been described.



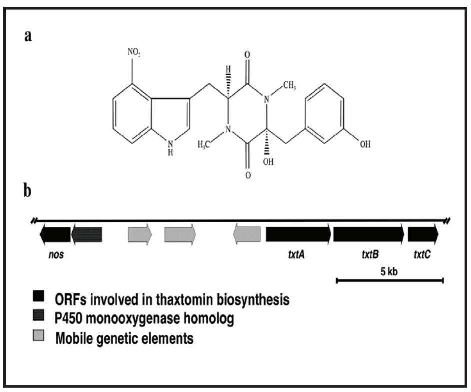
The potato scab disease is named for the corky raised or pitted lesions on potato tubers. This disease causes significant losses to farmers in the United States.

The goal of the research was to define the genes that make some species of Streptomyces cause potato scab. With help from the USDA's National Research Initiative, scientists at Cornell University and USDA-ARS identified the biosynthetic genes for thaxtomin and discovered a new class of enzymes responsible for nitration of microbial compounds. Surprisingly, this process involves the production of nitric oxide by a nitric oxide synthase (NOS). Nitric oxide synthases are well-studied enzymes in mammals which generate nitric oxide, a highly diffusible molecule used for cellular signaling. In mammals, nitric oxide mediates blood pressure, hormone release, and the immune response.

Discovery of a new class of enzymes in bacteria may lead to beneficial new drugs or other commercially useful products.

Researchers used the tools of genetics and chemistry to develop several independent lines of evidence for the role of the Streptomyces turgidiscabies NOS in nitration of thaxtomin. They found that disrupting the gene that codes for the NOS resulted in a dramatic drop in thaxtomin production. When a functional copy of the gene encoding the NOS was returned to the bacterium, thaxtomin production was restored.

Research showed that NOS inhibitors, developed for research in mammalian systems, could suppress thaxtomin production. Research also demonstrated that, in bacteria, nitric oxide synthases have a very different function than they do in animals; they are involved in the biosynthesis of nitrated compounds, including the toxin thaxtomin. It is surprising that mammalian nitric oxide signaling and bacterial biosynthetic nitration seem to share an evolutionary origin.



THAXTOMIN IS PRODUCED BY *STREPTOMYCES* SPECIES AND IS REQUIRED FOR PRODUCTION OF DISEASE SYMPTOMS. THE STRUCTURE OF THAXTOMIN IS UNUSUAL IN THAT IT HAS A NITRATE GROUP. THE NITRATION OF THE TOXIN IS CARRIED OUT BY A NITRIC OXIDE SYNTHASE (NOS), A NEW CLASS OF ENZYMES INVOLVED IN BIOLOGICAL NITRATION OF NATURAL PRODUCTS. RESEARCHERS DISCOVERED THE ROLE OF THE *STREPTOMYCES* NOS IN BIOLOGICAL NITRATION BY STUDYING THE GENETICS OF PLANT PATHOGENICITY.

Impact

This work may impact the development of plant disease control strategies, and may also have unexpected benefits in the development of new drugs or other commercially useful products. Since thaxtomin production is required for disease development, further research may find ways to inhibit its production and therefore prevent the development of potato scab. The discovery of the NOS is key in that non-nitrated versions of thaxtomin are inactive. Because bacterial NOSs have been identified in other bacteria, they may also participate in the production of yet-to-be discovered biological compounds. These compounds and their pathways can now be identified and hold the promise for discovery of new and useful biologically active compounds.

Research on the molecular basis for disease in plant-microbe interactions is a rich source of novel scientific discoveries. Microbes have been attacking plants for millennia and have devised novel strategies, including plant toxins, which allow them to penetrate plant defenses. Dissecting the disease-causing mechanisms invoked by microbes provides researchers with opportunities to use those mechanisms for other, more useful, purposes.

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