VeA, a Global Regulator of Secondary Metabolism, Can Increase Production of Secondary Metabolites

Published date: March 14, 2017

Technology description

Microorganisms, such as fungi, produce a variety of secondary metabolites. These secondary metabolites display a broad range of activities, including antibiotic, immunosuppressant, phytotoxic and mycotoxic activities, and are useful for drug or technological development. For example, the antibiotic penicillin and the cholesterol-lowering drug lovastatin are secondary metabolites.

However, producing large amounts of secondary metabolites is difficult, and available techniques often provide unpredictable results. Because they are formed from a relatively small number of metabolic pathways, identifying the genes that control these pathways may provide an alternative method of generating secondary metabolites.

The inventors previously identified a global regulator of secondary metabolism, called LaeA, in fungi (see WARF reference number P02379US). Overexpression of thelaeAgene upregulates production of secondary metabolites, greatly increasing penicillin production inAspergillus nidulansand lovastatin production inA. terreus. On the other hand, deletion oflaeAinA. fumigatuseliminates the production of gliotoxin and other secondary metabolites, decreasing the virulence of this human pathogen. UW-Madison researchers now have identified another global regulator of secondary metabolism, called VeA. VeA is a conserved protein that interacts with LaeA in an as yet unknown mechanism. Overexpression ofveAupregulates secondary metabolism inA. flavusto a greater degree than overexpression oflaeA. This gene could be used to increase the production of important natural products, including novel products with medicinal value.
The Wisconsin Alumni Research Foundation (WARF) is seeking commercial partners interested in developing methods of using VeA, a newly identified global regulator of secondary metabolism, to increase or decrease production of secondary metabolites in fungi.

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Application area

Increasing production of useful secondary metabolites, such as penicillin or lovastatin
Decreasing production of toxic secondary metabolites, such as aflatoxin

Advantages

Provides a simple method of increasing or decreasing secondary metabolite production
Upregulates secondary metabolism to a greater degree than LaeA
May enable new treatments for fungal infections
May be used to identify new secondary metabolite biosynthesis gene clusters

Institution

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