Thaxtomin A: a promising alternative to synthetic herbicides

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Thaxtomins are natural phytotoxins produced by pathogenic *Streptomyces sp.*

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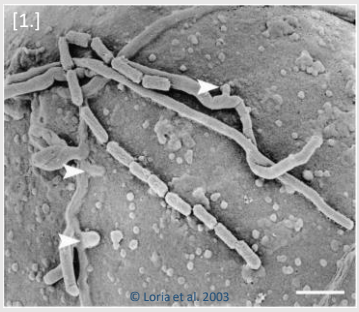

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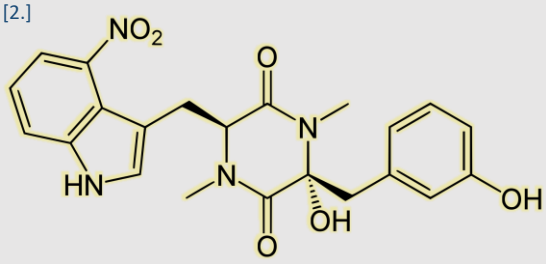

[3.]

Streptomyces scabies is the model and most widely-studied pathogenic *Streptomyces* species. It is responsible for the common scab (CS) disease affecting tuber crops and notably potato (*Solanum tuberosum*) cultures causing significant yield losses. Thaxtomin A is the main virulence determinant produced by *S. scabies* and other related species. Its yellow pigmentation is used as a natural reporter system for the phytotoxin production. **[1.]** Electron microscope view of a growing *S. scabies* mycelium perforating the surface of a potato tuber; **[2.]** Chemical structure of thaxtomin A; **[3.]** Potato tubers showing surface lesions caused by the CS disease upon infection by a pathogenic *Streptomyces sp.*

A promising bioherbicide interfering with cellulose biosynthesis mechanisms

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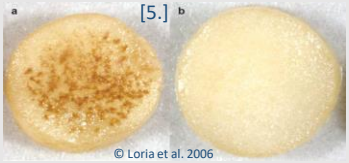

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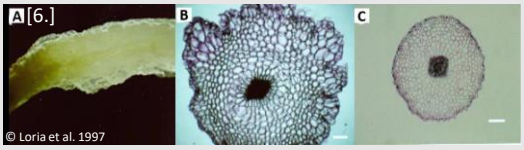

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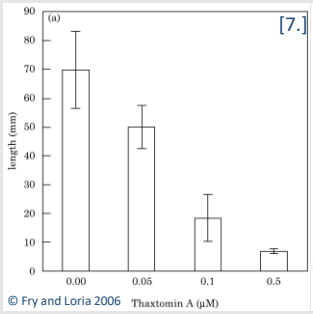

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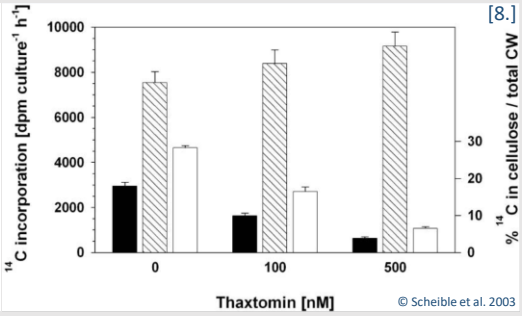

Thaxtomin A was shown to be active at very low concentrations (0.4 – 40 ppb), causing symptoms such as cell hypertrophy, root/shoot stunting and tissue necrosis at higher concentrations. Although its precise action mechanism is still unclear, standard phytotoxicity assays have shown that thaxtomins induce symptoms similar to isoxaben, a well-known cellulose inhibitor. **[4.]** Developmental impact of thaxtomin A treatment (1 µM, right) on *Arabidopsis thaliana* seedling compared to control untreated seedling (left); **[5.]** Potato tuber tissue treated (a) or not (b) with 100 nM of thaxtomin A. The treated slice displays necrosis induced by thaxtomin; **[6.]** Thaxtomin A causes cell hypertrophy on a radish hypocotyl (lateral view in (a) and cross section in (b)) compared to an untreated hypocotyl (c); **[7.]** Length of onion seedlings exposed to increasing concentrations of thaxtomin A (0.05 – 0.5 µM); **[8.]** Thaxtomin inhibits ^{14}C-glucose incorporation into the cellulosic cell wall fraction of *A. thaliana* seedlings. Black bars: Cellulosic (acid-insoluble) cell wall fraction ; Cross-hatched bars: Acid-soluble cell wall fraction; White bars: Percentage of label in the cellulose fraction relative to the amount of total label in the cell wall.

How computational predictions helped improving thaxtomin yields

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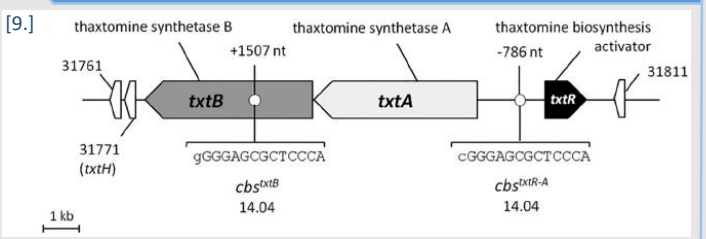

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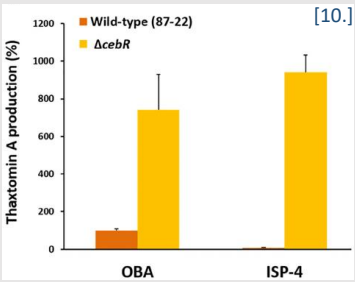

Using the PREDetector software, two CebR-binding sites (cbs) have been highlighted in the gene cluster involved in thaxtomin biosynthesis **[9.]**. CebR, the master repressor of cellulose utilization has been deleted to generate a new *S. scabies* (*ΔcebR*) strain capable of producing thaxtomin A constitutively **[10.]**. This strain also produces significantly more thaxtomin A without requiring the addition of expensive cello-oligosaccharides (CebR allosteric effectors) to the culture medium.

Unexpected constitutive thaxtomin production after deletion of a β-glucosidase

bglC is a gene located in the *ceb* operon which controls the import and processing of cellulose oligo-saccharides. BglC is a β-glucosidase that processes cello-oligosaccharides into glucose (Glc) **[11.]**. As $[Glc]_2$ and $[Glc]_3$ are inducers of thaxtomin biosynthesis, deleting an enzyme responsible for their depletion was expected to increase thaxtomin production compared to the wild-type strain. Indeed, *S. scabies* Δ*bglC* produced more thaxtomin A, but this mutant was also shown to be a constitutive producer **[12.]**. This unexpected phenotype is valuable because this strain is even more efficient than the Δ*cebR* mutant for thaxtomin production. Understanding the mechanisms responsible for this thaxtomin A overproduction in the Δ*bglC* mutant could help us improving production strains.

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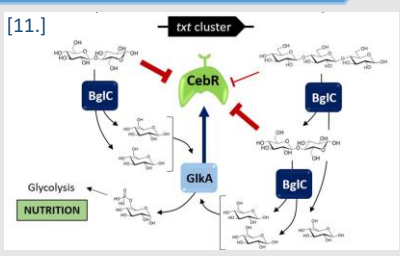

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