Engineered transfer of the PKS/NRPS biosynthesis pathway of albicidin: a promising approach to overproduce this potent antibiotic

Cociancich S[1], Vivien E[1], Pitorre D[1], Duplan S[1], Pieretti I[1], Gabriel DW[2], Rott P[1] and Royer M[1]

[1]CIRAD, UMR BGPI « Biologie et Génétique des Interactions Plante-Parasite », TA 41/K, Campus International de Baillarguet, F-34398 Montpellier Cedex 5, France. [2]Department of Plant Pathology, Univerity of Florida, Gainesville, Florida 32611.

Xanthomonas albilineans, which causes leaf scald disease of sugarcane, produces a highly potent pathotoxin and antibiotic called albicidin that was shown to inhibit DNA replication in both sugarcane proplastids and *Escherichia coli*. Low yields of albicidin production in slow growing *X. albilineans* have slowed studies of its chemical structure and potential therapeutic applications. Albicidin is synthesized by a unique hybrid PKS/NRPS (polyketide synthase/nonribosomal peptide synthase) pathway that does not resemble any other described to date. We report here the transfer of the entire 49 kb albicidin biosynthetic gene cluster from *X. albilineans* into *X. axonopodis* pv. *vesicatoria* and the subsequent production of an antibiotic active against *E. coli* that shows cross-resistance with albicidin. The yield of this antibiotic in *X. axonopodis* pv. *vesicatoria* is 6 times higher than in *X. albilineans*. This study demonstrates the feasibility to transfer the albicidin pathway into an heterologous host and offers a promising strategy to overproduce, characterize and explore potential therapeutic applications of this potent antibiotic.