

Endophytic community biosynthesis

Plant compound maytansine has a microbial biosynthetic origin

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*Given the central role of chemical crosstalk in plants and endophytes, it is compelling that certain compounds or their precursors formerly believed to be synthesized only by plants or exclusively considered plant metabolites can be produced by endophytes or other plant-associated microorganisms. The basic objective of our work was to verify whether the important anticancer and cytotoxic compound maytansine is produced entirely by *Putterlickia* plants or by their endophytic microflora.*

Endophytes are a diverse group of microorganisms that colonize the internal tissues of plants without any manifestation of disease and engage in mutualistic association with the host plants. The main objective of our work was to experimentally prove whether maytansine is produced by *Putterlickia verrucosa* and *Putterlickia retrospinosa* plants, or by the endophytic microbial community harbored in them. We evaluated the fermentation products of endophytic community harbored in different tissues of *Putterlickia* plants by a combination of high performance liquid chromatography high-resolution mass spectrometry (HPLC-HRMSⁿ), matrix assisted laser desorption ionization imaging high-resolution mass spectrometry (MALDI-imaging-HRMS) and gene discovery methods to characterize the production of maytansine.

After isolating the endophytic community from different tissues of *Putterlickia* plants, we used the combination of HPLC-HRMSⁿ and MALDI-imaging-HRMS, a maytansine-specific selective microbiological assay, and gene discovery methods to elucidate the source and site of maytansine biosynthesis. Initially, HPLC-HRMSⁿ analysis revealed the production of maytansine by root endophytic community. This was further coupled to a microbiological assay (bioautography) using maytansine-sensitive type strain *Hamigera avellanea*. Finally, the presence of AHBA synthase gene in the root endophytic communities of *Putterlickia* plants coupled to its absence in host plants confirmed that maytansine is a biosynthetic product of root endophytic community. Additionally, MALDI-imaging-HRMS demonstrated the accumulation of maytansine produced by endophytes in the root cortex of both the host plants.

Thus far, our study reveals maytansine is actually a biosynthetic product of root-associated endophytic microorganisms and opens up further questions about the broad ecological role of maytansine in nature and the endophytes residing in distinct ecological niches.

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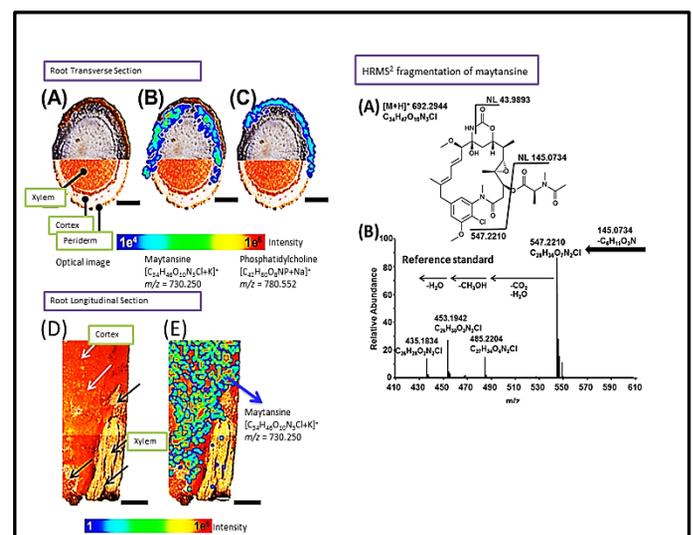


Figure 1: Maytansine produced by the endophytes is typically accumulated mainly in the root cortex of both plants, but not in other tissues

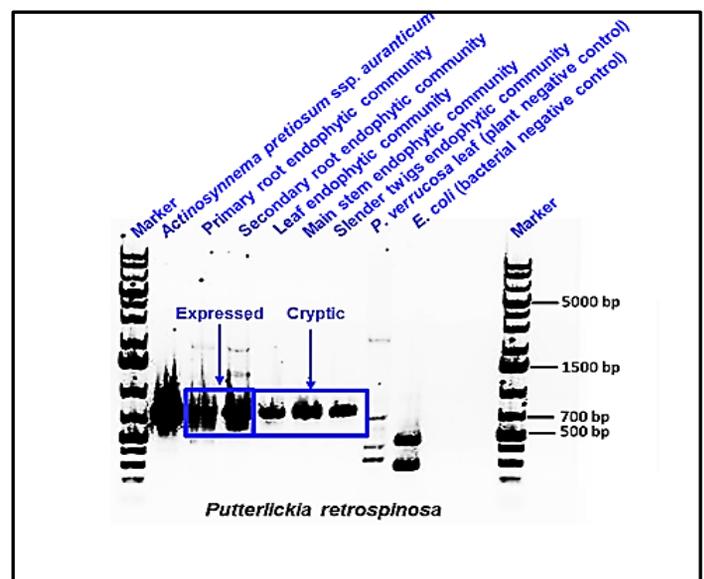


Figure 2: Confirmation of maytansine production by root bacterial endophytic community by gene discovery

Publications:

[1] Kusari S., Lamshöft M., Kusari P., Gottfried S., Zühlke S., Louven K., Leistner E., Hentschel U., Kayser O., Spiteller M. (2014) Endophytes are hidden producers of maytansine in *Putterlickia* roots. *J Nat Prod* 77:2577-2584