

Endophytes as a new source for gene and drug discovery

Exploring the potential of plant associated fungi to produce paclitaxel

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Endophytes are bacterial or fungal microorganisms colonizing intra- and extracellular host plants. Typically they are causing no apparent symptoms of diseases and some of these are known to synthesize natural products. These natural products are structurally identical or very closely related to the host pattern. From the genetic point of view, endophytes are a very interesting group of microorganisms because of clustering biosynthetic pathways known in the host plant. A better understanding of the genetic blueprint may provide chances to learn from endophyte to construct optimized producer organisms in pharmaceutical biotechnology.

In 1995 Strobel et al. Science (1993) published an extraordinary paper on the production of paclitaxel in the endophyte *Taxomyces andreanae*. Since this striking report no further information was provided about the genetic blueprint, physiology or yield of the important anticancer drug from this endophyte. To shed light on these questions *T. andreanae* from *Taxus baccata* and other endophytes from *Wollemia nobilis* were isolated and studied. *W. nobilis* is considered as living fossil from Australia and here again endophytes with paclitaxel producing properties were found.



Fig. 1 Taking endophytic samples from *Wollemia nobilis*

Highlight: Identification of biosynthetic genes from the plant paclitaxel pathway in *T. andreanae*. Based on known gene sequences for the first time the biosynthetic genes *taxadiene synthase* (txs) and *phenylpropanoyl transferase* (bapt) were found back by RT-PCR in *T. andreanae* but not in *W. nobilis*.

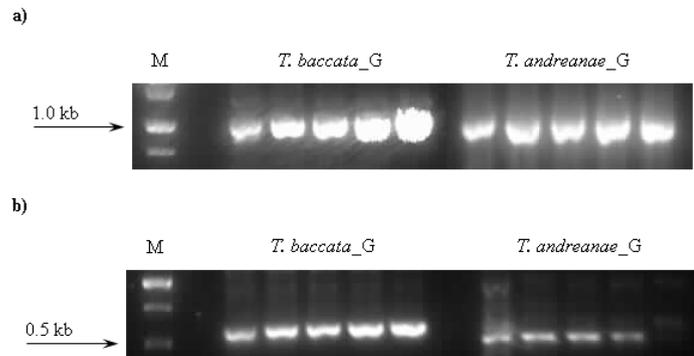


Fig. 2 PCR analysis for the presence of a) *taxadiene synthase* (~ 1.0 kb) and b) *phenylpropanoyl transferase* (~ 0.5 kb) in *Taxomyces andreanae*; *Taxus baccata* needles were a source of plant DNA samples, providing for a positive control of txs & bapt presence verification

Highlight: Despite the lack of evidence supporting taxane production in *T. andreanae*, the endophytic extracts show substantial anti-cancer activity. Unfortunately, the natural products being a source of the observed proliferation arrest are, as yet, unknown.

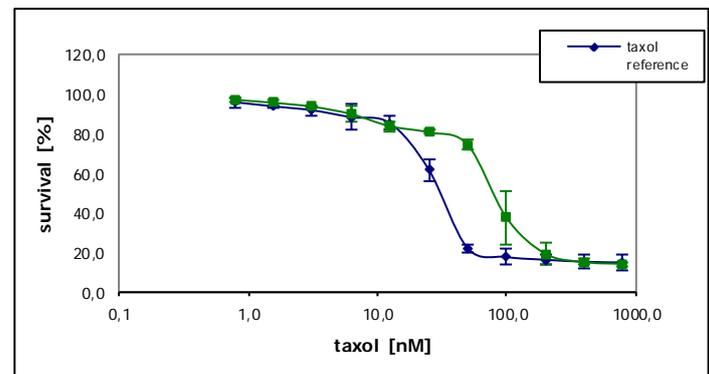


Fig. 3 MTS assay – dose response curves for taxol reference and plant extract

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Publications:

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