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INSIGHTS INTO MANUFACTURING OF *CATHARANTHUS ROSEUS* ALKALOIDS IN RELATION TO PLANT GROWTH AND DEVELOPMENT

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The remarkable diversity of plants is in part based on their unlimited capabilities to make small molecules with biological activity. Plant based chemicals have been used for a variety of human activities that include their use as poisons, hallucinogens, stimulants, pigments and most importantly to cure diseases. Our studies focus on the molecular events during growth and development of plants that stimulate certain cells in the organism to become specialized for making such molecules. These 'cell factories' have appeared through evolution and natural selection to make certain classes of molecules that are characteristic to the 'species' and that impart certain biological characteristics.

For example, *Catharanthus roseus* (Madagascar Periwinkle) has been the source of unique alkaloid drugs with powerful anticancer properties that have revolutionized the fight against cancers like infantile leukemia and Hodgkins disease. Vinblastine and vincristine drugs have saved countless numbers of lives over the last 30 years. Recent research activities have created a new generation of less toxic, more powerful and more effective analogs of vinblastine that will be introduced commercially in the next few years.

This renewed commercial interest together with the our interest in complete identification of the pathways leading to the biosynthesis of *Catharanthus* alkaloids has prompted us to apply the new and versatile techniques of laser capture micro-dissection and carborundum abrasion technology to produce cell-type specific cDNA libraries (leaf epidermis, idioblast, laticifer, mesophyl and vasculature-specific cells) for EST analyses. This new technology is being combined with large-scale sequencing, plant transformation and RT-PCR to complete our identification of the entire pathway for biosynthesis of monoterpenoid indole alkaloids, like vindoline and to determine the the exact sites of MIA biosynthesis. The results of cell-type EST sequencing will be presented to show that we have identified the cell type responsible for assembling the majority of the vindoline molecule in *Catharanthus* and that genes for the entire pathway have been obtained. In the broader context, this new knowledge about biochemical specialization for manufacturing plant secondary metabolites will also be harnessed to increase production of commercially relevant secondary metabolites or to transfer whole biochemical pathways into specialized plant cells of crop plants.