

SOLUCEL[®] - A FUNCTIONAL GENOMICS APPROACH TOWARDS THE UNDERSTANDING OF PLANT SECONDARY METABOLISM

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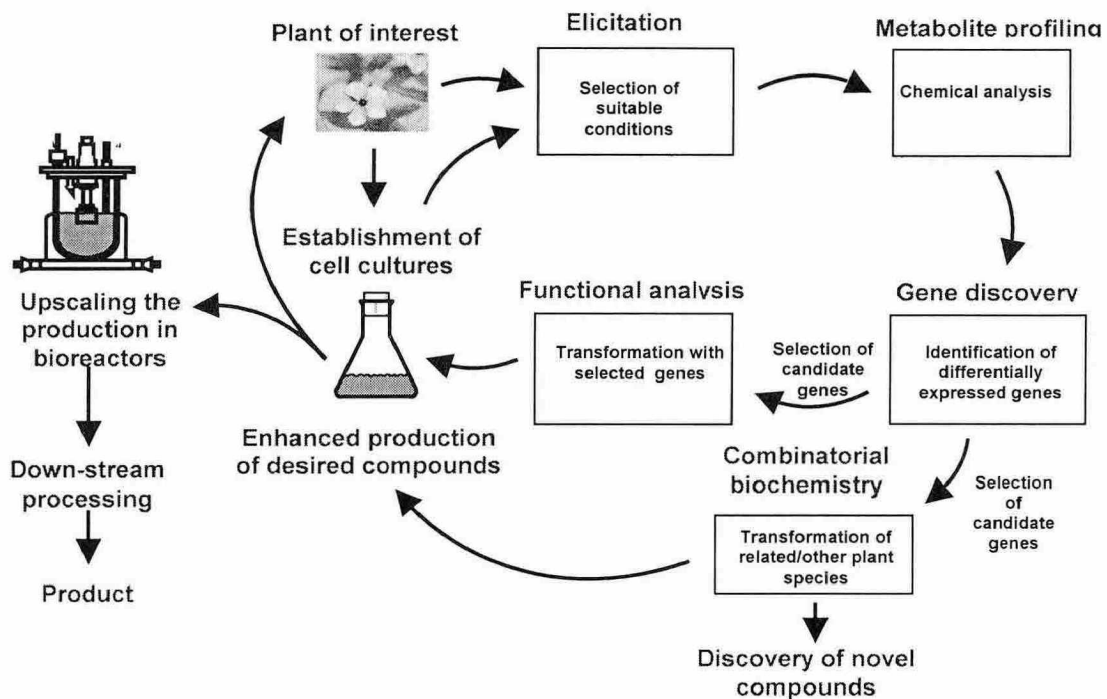
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Molecules derived from plants make up a sizeable proportion of the drugs currently available on the market. A quarter of all pharmaceuticals, either used as a pure compound or chemically engineered to form appropriate derivatives, are of plant origin. These include compounds such as morphine, codeine and several anti-cancer drugs, the monetary value of which is very high. At the present time small amounts of these compounds are isolated with some difficulty from natural vegetation or cultivated plants. Chemical synthesis of the molecules is difficult and economically unprofitable owing to their complex, often three-dimensional structure. Some substances can only be isolated from extremely rare plants.

Genetic knowledge on biosynthetic pathways and the regulation thereof is of crucial importance to bypass the low-product yield of various secondary metabolites in plant cells. To facilitate gene discovery in plant secondary metabolism, we have developed a comprehensive profiling approach that is based on functional genomics and can be applied on any plant system without a need for prior sequence knowledge. Jasmonate-induced changes have been monitored on the transcript and alkaloid profiles of tobacco and two other medicinal plants. Using cDNA-AFLP based transcript profiling, an inventory of hundreds of genes, potentially involved in plant secondary metabolism, has been built (1). A technology platform, especially driven towards the exploitation of plant cell cultures, for high-throughput isolation and functional analysis of these genes, has been established.

At present, 47 tobacco BY-2 full-length open reading frames, with the special interest in genes encoding putative protein have been isolated and are currently subjected to functional analysis. So far, of the genes assayed, three have shown clearly to result in an altered metabolite accumulation pattern compared to control cell line and those lines have been subjected for further studies.

So-called Combinatorial Biochemistry approach has also been used to transform genes from our BY-2 tobacco transcript profiling to either related or non-related plant species leading to the formation of transgenic hairy roots. Some of the hairy root clones of *Hyoscyamus muticus* and *Catharanthus roseus* showed besides altered metabolite profile also remarkable increase of main alkaloids or formation of compounds which were not at all present in the control clones.



We have developed a technology platform called SOLUCEL[®] that allows creating a novel toolbox for metabolic engineering of plant cells (2). It can be applied (i) to enhance the production of marketed high-value pharmaceuticals in plant cell cultures (ii) to develop reliable and reproducible sources of plant-derived molecules with potential pharmaceutical value, and (iii) to increase the chemical diversity of plant based molecules through Combinatorial Biochemistry thus offering new lead compounds of pharmaceutical interest for the industry.

References:

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2. Oksman-Caldentey, K.-M. & Inzé, D 2004: Plant cell factories in the post-genomic era - new ways to produce designer secondary metabolites. *Trends Plant Sci.* 9: 433-440.

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Education

BSc 1976 pharmacy, University of Helsinki, Finland
MSc 1980 pharmacy, University of Helsinki, Finland
PhD 1988 pharmacy, University of Helsinki, Finland
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Professional Experience

Technical Research Centre of Finland, VTT Biotechnology, Espoo, Finland
1998 - Present: Group Manager of Plant Biotechnology
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Editorial Experience

2000- Present: Member of the advisory board, Planta Medica
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