DISCOVERING MORE EFFICIENT PRODUCTION PATHWAYS OF PLANT SECONDARY METABOLITES THROUGH RETROSYNTHESIS

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ABSTRACT

Plant secondary metabolites constitute a useful array of natural ingredients, especially for therapeutics, the food additives industry, and many other industrial fields. Thereby, metabolic engineers are looking for alternative strategies that may be more efficient for the enhancement of valuable secondary metabolite production quality and quantity. However, the knowledge of production pathways and related enzymes of secondary metabolites is quite scarce. In this study, we aim to build a biochemical reaction networkstoring paths between source and target molecules where intermediates are known metabolites of a given organism (plant and/or *Escherichia coli*), besides related reactions, enzymes, and genes data.

The tool that is predominantly used in this study to reveal the unknowns of production pathways is RetroPath2.0 workflow on KNIME analytics platform. It is a rule-based retrosynthesis tool that can suggest possible production pathways for a given molecule along with precursor and intermediate molecules and enzymes by processing reaction rules and available compounds in the environment. The output of RetroPath2.0 contains possible pathways ranked according to feasibility.

The RetroPath2.0 tool is being executed for 16 valuable secondary metabolites to discover their possible production pathways in a common plant metabolites pool (based on metabolic models of *Arabidopsis thaliana*, *Oryza sativa* and *Zea mays*) and *E. coli* metabolites pool. The resulting pathway suggestions are integrated into the metabolic database. This procedure serves as a promising method to uncover the unknowns of plant metabolome and propose new feasible production pathways of valuable plant secondary metabolites. Thus, it has the potential to make industrial production of these economically important plant secondary metabolites more efficient in terms of production quality and quantity. This study is supported by Yildiz Technical University Scientific Research Projects Coordination Unit with the project number FBA-2021-4698.

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