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Developing of trilobatin dihydrochalcone as a new-style of phytochemical agent

Mwafaq Ibdah, Bhagwat Nawade and **Mossab Yahyaa**
Newe Yaar Research Center Agriculture Research Organization, Israel

The increasing prevalence of several diseases, like Alzheimer's disease, obesity, cancer, and diabetes, in humans in recent decades worldwide, accompanied by rising concern regarding the safety of many synthetic chemistry-based pharmaceuticals, has raised public demand for phytochemical-based medicines. This in turn has led to increasing interest in metabolic engineering as an approach to produce such natural products on an industrial scale, which has the potential to decrease production costs of, e.g. desired dihydrochalcones. We note that fruits accumulating high level of phytochemicals including flavonoids and dihydrochalcones that may play a key role in reducing chronic disease risk. We have developed a novel concept to produce a new-style phytochemical agent of benefit for humans by genetic transformation of three characterized genes in plant cells, bacterial, and yeast systems. We have applied a set of molecular and biochemical tools to identified reactions and enzymes leading to the biosynthesis of dihydrochalcones. We recently cloned and biochemically characterized three key enzymes in the dihydrochalcone biosynthesis pathway; a p-coumaroyl-CoA double bond reductase that converts p-coumaroyl-CoA into p-dihydrocoumaroyl-CoA, chalcone synthase that accepted p-dihydrocoumaroyl-CoA, in the presence of malonyl-CoA, leading to production of phloretin, and a specialized phloretin-4'-O-glycosyltransferse which glycosylated phloretin in the presence of UDP-glucose into trilobatin. The production of the phytochemical trilobatin was achived by overexpression of these genes in microbial cell factory. The proof of our concept have open the possibility for developing new-style of natural phytochemical for a growing market of population suffering from "modern" diseases.