ABSTRACTS (MASTER THESIS)

A transport engineering approach to synthetic biology for artepillin C production in yeast

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Propolis is a resinous substance that honeybees prepare by collecting wax-rich part from buds and other aerial parts of different plant species in order to seal physical damages (e.g., cracks and holes) of beehives, to prevent invasion of their enemies [1]. This honeybee product has been sold as natural medicines and food supplements worldwide because of its broad pharmaceutical and health-promoting activities attributed to its complex chemistry of over 500 constituents [2,3]. The chemical composition of propolis is highly diversified depending on its botanical sources, geological locations and bee species, which gives unique spectrum of bioactivities for each type of propolis [2]. Brazilian green propolis is one of the most globally spread types for commercial purposes. It is characterized by the presence of bioactive prenylated derivatives of *p*-coumaric acid, such as drupanin and artepillin C, the latter of which is a major constituent exceeds 10% at highest levels in the Brazilian propolis [3]. It is to be noted that this main compound exhibits its activities by oral administration as reported, for instance, suppression of colon and pulmonary carcinogenesis chemically induced in mice [4,5]

Despite the high value of artepillin C, this compound is mainly accumulated only in Brazilian plants belonging to *Baccharis* species, such as *B. dracunculifolia*, a bush distributed in South America. Because of the Nagoya protocol, applied sciences with the Brazilian plant contain potential risks of benefit share. We have thus searched domestic plants that have productivity of artepillin C, namely diprenyltransferase for *p*-coumaric acid. As the results, we identified AcPT-1 from *Artemisia capillaris*, which was then subsequently applied to produce artepillin C in yeast [6].

In the production procedure, we have realized that the produced artepillin C remains at the cellular level, while non-prenylated substrate, *p*-coumaric acid, is almost exclusively secreted to the medium leading to the inefficient usage as the enzyme substrate. This observation encouraged us to identify transporter molecules responsible for the secretion of artepillin C in the intact plant. Then, we have thoroughly listed candidate transporter genes that may be involved in the excretion of artepillin C in the native plant.

References

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