【Grant-in-Aid for Scientific Research (S)】

# Molecular dissection of plant specialized metabolism machineries


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## Purpose and Background of the Research

### ●Outline of the Research

Plants produce a diverse array of secondary metabolites called “specialized metabolites”. The structures of these metabolites can vary among plant species, with their diversity being estimated to exceed one million. These metabolites have many uses as pharmaceuticals, pigments, fragrances, and raw materials for chemical products, thereby contributing to the improvement of human welfare (Figure 1). Because plants have a remarkable ability to produce metabolites efficiently and with enormous diversity, they are often referred to as “miracle chemical factories”. However, it has not been fully clarified how such a remarkable metabolic capacity of plants is achieved *via* the acquisition of enzyme functions to appropriately control metabolism. As such, the methods for industrial production of specialized metabolites are mainly limited to extraction from plant materials. This research project will decipher its underlying mechanism.

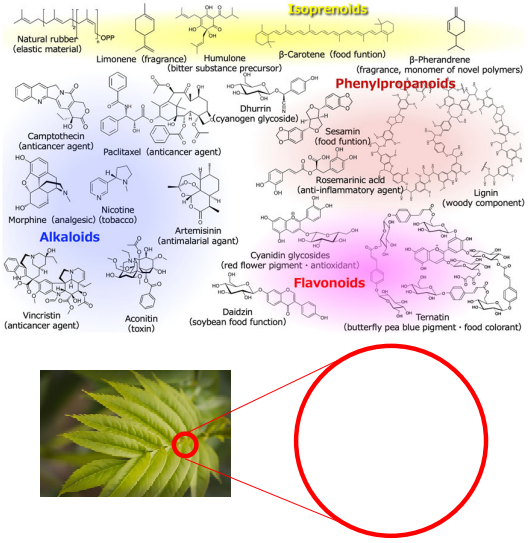


Figure 1. An image diagram of this research project. Plants are miracle chemical factories. The objective of this research project is to decipher its underlying mechanism.

### ● Catalytic promiscuity of enzymes involved in plant specialized metabolism

Despite the fact that specialized metabolism proceeds very efficiently in plant cells, the catalytic functions of enzymes involved in this process are highly promiscuous (*i.e.*, wasteful and incomplete in light of their physiological functions) in a test tube, as exemplified by chalcone synthase (CHS) (Figure 2, left) and the natural rubber synthase HRT1 of *Hevea brasiliensis* (Figure 2, right). There must be mechanisms within the cell to overcome the catalytic promiscuity of enzymes. Unless such mechanisms are clarified, the industrial production of plant specialized metabolites by metabolic engineering will not be achieved.

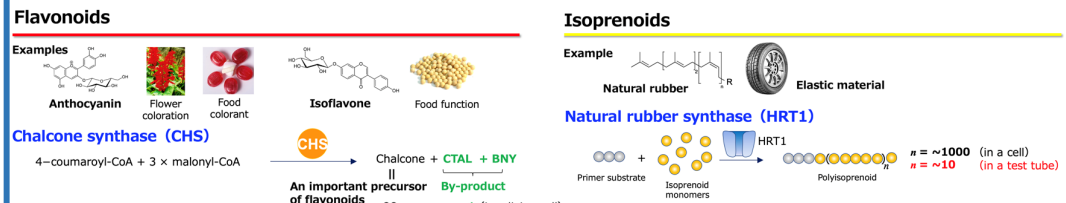


Figure 2. Catalytic promiscuity

### ● Plant specialized metabolism machineries

The principal investigator has reported many lines of evidence showing that membrane-bound, dynamic supramolecular complexes of enzymes (termed plant specialized metabolism machineries) form in plant cells. In these machineries, the enzymes and proteins involved in plant specialized metabolism interact with each other (Figure 3). Moreover, we have shown that the specificity of metabolic enzymes is narrowed through interactions with other proteins in the machineries to establish efficient metabolism. Thus, the key to the function of plants as “miracle chemical factories” may be the formation of such membrane-bound machineries.

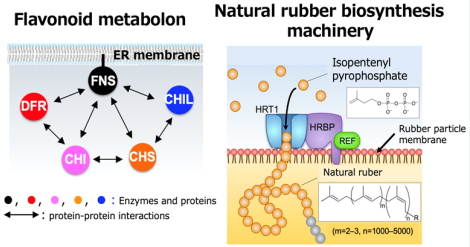


Figure 3. Proposed formation of plant specialized metabolism machineries involved in flavonoid biosynthesis (*left*) and natural rubber biosynthesis (*right*)

## Expected Research Achievements

### ●What this research reveals

This research project mainly focuses on flavonoid metabolons and the natural rubber biosynthesis machinery. Our aim is to investigate the structures of the enzymes and proteins that make up these machineries and their interactions, including interactions with biological membranes. By doing so, we will clarify the molecular mechanisms that permit highly efficient metabolism in plant cells, and establish a general theoretical basis for the formation and engineering of plant specialized metabolism machinery. This will make it possible to design metabolic engineering systems for the efficient production of specialized metabolites on an industrial scale. To achieve this, this research project comprises three research pillars—membrane assembly engineering (Research Pillar A) , multi-dimensional structural analysis (Research Pillar B), and functional analyses (Research Pillar C) .

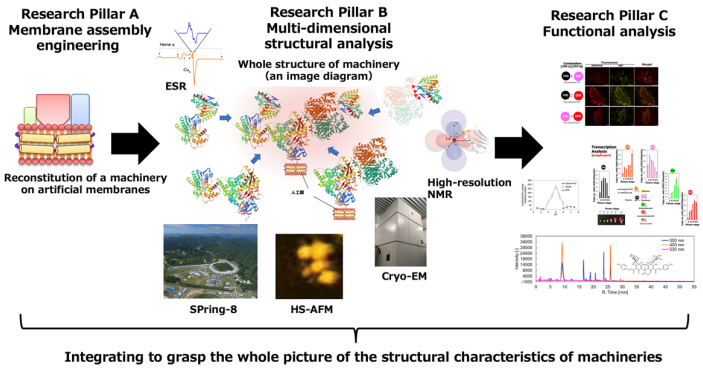


Figure 4. Research pillars

### ● Social benefits of the academic achievements

The establishment of a general theoretical basis for the formation and engineering of plant specialized metabolism machinery in this research project will not only provide a new understanding of the intracellular dynamics of metabolism, but also create a new academic field, namely “metabolic machinery engineering”. This will contribute to further progress in the fields of “synthetic biology” and “smart cell industries” to enhance human welfare through the realization of efficient industrial production and the use of plant specialized metabolites.


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