The term METABOLOME describes the complement of all metabolites expressed in a cell, tissue or organism during its lifetime. Already at the 19th century it was suggested that two classes of metabolites exist; primary (or basic) and secondary. Secondary metabolism refers to compounds that are not needed for the cell survival and propagation but are believed to be of importance to continued existence in particular environmental conditions. Secondary metabolites (SMs) are derived from primary metabolites (e.g. amino acids and carbohydrates), through modifications, such as methylation, hydroxylation, and glycosylation. Evolutionary processes directed towards enhancing plant fitness most probably stimulated formation of new structures. SMs are formed both as part of normal plant developmental pathways and upon diverse endogenous and environmental stimuli. Examples of SMs are fruit flavor and aroma compounds, flower and fruit pigments and "sun screen" metabolites such as the flavonols. Up to date, a few hundred thousand different SMs structures have been identified in plants, the largest of them are the Phenylpropanoids, Isoprenoids and Alkaloids.

The main interest of our lab is in the regulation of plant metabolic pathways, in particular those associated with secondary metabolism and its coordination with developmental and stress response programs.

Metabolomics: A Complementary tool in Systems Biology and Functional Genomics

The capacity to measure and identify metabolites is an essential component of the lab research activity and we are currently setting-up a Metabolomics platform that could generate a detailed metabolic profile for any given organism, tissue or cell type. In its current state, Metabolomics requires robust methodology development before it can be fully integrated with genomics, transcriptomics and proteomics. Metabolomics holds great promise as an effective tool in numerous applied fields of research such as in metabolic engineering of crop plants, identification of target molecules of toxicity and diagnostic biomarkers, and establishing a functional basis for defining the contribution of genetic polymorphism to individual susceptibility to environmental conditions and diseases. Three interrelated components of Metabolomics technology development are currently addressed in the lab: (a), sample collection, extraction, recovery and validation for specific classes of metabolites; (b), analyte detection, identification, quantification, and structure elucidation; and (c), integrating metabolomics and transcriptomics to obtain a "birds eye" view of metabolic response. High-end analytical hyphenated instruments are employed (LC-Q-ToF-MS-MS and GC-MS) and integrated into a computational infrastructure, which includes software for interpreting and visualizing the flood of data (Figure 1).

The Primary-Secondary Metabolism Interface

An estimated 20% of all carbon fixed in the leaves passes through the Shikimate pathway and 30% of the plants dry weight comes from this pathway products, the aromatic amino acids Phenylalanine, Tryptophan and Tyrosine. These amino acids are the primary source of carbon for the formation of a myriad of SMs in both plants and microorganisms (Figure 2). For example, the insects deterring glucosinolates are products of Phenylalanine and Tryptophan metabolism and the phytohormone Salicylic acid is produced from Chorismate, the final product of the Shikimate pathway. We are interested in how plants tune the flow of carbon through the Shikimate pathway to the different branches of the downstream pathways during its development and under stress conditions.

Two Arabidopsis proteins that might be transcriptional regulators of the Shikimate pathway and its downstream branches are currently being characterized. The particular expression of one of them points to its possible role in directing the flux of carbon to the biosynthesis of lignin in stem tissue undergoing secondary cell wall formation. Directing the exact amount of carbon to lignification is crucial for plants since formation of the lignin polymer requires large quantities of carbon skeletons and they cannot re-use it. Our aim is to identify additional components of the network of proteins controlling the
The cuticle plays multiple roles in plants, including the regulation of epidermal permeability, non-stomatal water loss and protection against insects, pathogens, UV light, and frost. It also functions in the prevention of post-genital organ fusion, pollen-pistil interactions and cell-to-cell communication.

Generation of cuticular components in epidermal cells involves four major independent biosynthetic pathways, namely those for the synthesis of cutin monomers, aliphatic wax components, triterpenoids, and aromatic metabolites (e.g. flavonoids). Our lab is interested in the regulation of the different pathways constructing the cuticle and how the secretion of their end products to the cuticle is executed. We recently identified an Arabidopsis ATP Binding Cassette type transporter gene that is potentially involved in the transport of cuticle components, (e.g. wax), from the epidermal layer to the cuticle. Its down-regulation by RNAi resulted in a dramatic effect on plant morphology. Most strikingly, fusions of leaves and floral organs to leaves were observed. We are also conducting an in-depth characterization of the recently identified SHINE/WIN clade of AP2/EREBP transcription factors from Arabidopsis. Overexpression of either one of the three factors resulted in the same phenotype, primarily, a six fold increase in total cuticular wax. Strong developmental defects were also observed including increased leaf glossiness, growth retardation, leaf curling, and altered epidermal cell differentiation.

In parallel to the study of cuticular metabolism in vegetative tissues we are also investigating the cuticle in reproductive organs such as tomato fruit skin. Metabolic and expression profiling of the skin tissue is underway to identify key enzymes, transporters and transcriptional factors mediating cuticle metabolism in this tissue.

**Selected publications**


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