

## Editorial

## Evolution of metabolic diversity

Plant and microbial secondary metabolites form an immense reservoir of natural chemical diversity. The structures of more than 200,000 secondary metabolites have been elucidated to date, providing us with an enormous diversity of unique carbon skeletons and functional group modifications. In contrast to primary metabolism, which is essential to the growth and development of an organism, secondary metabolism is not essential to these processes. Secondary metabolites are, however, required for the interaction of an organism with its environment. Fascinating examples of this exist in the area of defense against herbivores and microbial pathogens. The dynamic exchange between competing organisms further reflects the functional variety found in secondary metabolism. The ability to produce such an abundance of chemicals is based upon the continual evolution of new genes brought about by gene duplication and subsequent recruitment and adaptation to the diverse demands of secondary metabolism. This natural plasticity of secondary metabolism underlies the ease with which microorganisms develop resistance to antibiotics and with which parasites and insects resist long-term chemical control. The obvious demand of plant secondary product diversity drives evolution of genetic diversification leading to multigene families. Moreover, the manifold survival strategies of organisms have resulted in an arsenal of natural products with specific toxic, antimicrobial and deterrent properties that since the emergence of mankind are utilized in herbal folk medicine and today's phytotherapy and provide valuable pharmaceuticals and leads for rational drug development.

Each biosynthetic route of secondary metabolism derives from primary metabolism and involves complex and often highly specific reactions that lead to defined end products. In many cases, the first reaction that deviates from primary metabolism is pivotal to the formation of a new secondary biosynthetic pathway. If the resultant new gene product (enzyme) can form a secondary product that is advantageous to the plant in its generally hostile environment, the trait is inherited under selection

pressure. There is increasing evidence that duplications of essential genes of primary metabolism are an important basis for gene recruitment in secondary metabolism. In the course of evolution, these duplicated genes acquired new functions and were optimized and diversified for their role in new pathways. Our understanding of these phenomena is still rudimentary, however, and more research in this area is necessary to get a deeper insight into the strategies of natural product evolution.

We are witnessing the beginning of a worldwide revolution in plant science, the understanding of the evolution of metabolic diversity. Powerful new techniques in molecular genetics, biochemistry and analytical chemistry now enable us to address exciting questions about, and to accelerate our understanding of molecular evolution. In Germany plant scientists, microbiologists and chemists initiated a collaborative program with the aim to investigate the evolution and diversity of secondary metabolite formation. Since 2003 these activities have been supported by the DFG priority program 1152, "Evolution of Metabolic Diversity" (EvoMet).

This special issue of PHYTOCHEMISTRY presents a collection of papers submitted by colleagues working on various aspects of plant research covering evolutionary aspects of metabolic diversity on the three major molecular levels: genes, proteins (enzymes) and metabolites. Gene duplication and recruitment of the duplicates for new functions in secondary metabolism are involved in the biosynthesis of gramine and DIBOA in *Hordeum* as well as pyrrolizidine alkaloids in *Crotalaria* (Fabaceae). Gene duplications and functional diversification of the duplicated genes are exemplified with 2-oxoglutarate-dependent dioxygenases involved in flavonoid biosynthesis of the Apiaceae, serine carboxypeptidase-like acyltransferases involved in sinapate ester formation in Brassicaceae, and, presumably, floral benzenoid methyltransferases. Another facet concerns convergent evolution of pathways in phylogenetically unrelated organisms such as of the gibberellins in plants and fungi, the tropane alkaloids

in Solanaceae and Erythroxylaceae, and  $\beta$ -lactam antibiotics in Ascomycetes and Streptomyces. The latter even discusses horizontal gene transfer and recruitment of regulatory elements. Several studies are performed to understand the mechanisms behind diversification on the metabolite level: The rich diversity of polyketides in lichenized fungi is mirrored by a high sequence diversity of the respective polyketide synthases. The diversity patterns of ergot alkaloids found in different strains of *Claviceps purpurea* is caused by sequence variations confined to the non-ribosomal peptide synthase modules of the respective ergot alkaloid gene cluster. The diversity of lignans in the genus *Linum* is apparently partly related to changes in the stereoselective function of biosynthetic enzymes. Structural diversity of biologically active secondary metabolites is exemplified by a new bridged angucyclinone from *Streptomyces griseus* and carotenoid-derived trisporoids and trisporoid analogues from *Mucor mucedo*. From different points of view geographic and evolutionary diversification within a phylogenetic framework is illustrated by the glucosinolates in *Arabidopsis* and its relatives, the pyrrolizidine alkaloids within the *Senecio* section Jacobaeae as well as the benzyloquinoline alkaloids in Angiospermae.

We hope that you enjoy reading this special issue on evolution of metabolic diversity as much as we

have enjoyed putting it together. These are certainly exciting times in the study of plant secondary metabolism as we are not only able to address topics on metabolite structure and function, but also the fundamental question on how these very special metabolites came to be.

Guest Editor

Thomas Hartmann

*Institute of Pharmaceutical Biology, TU Braunschweig*

*Mendelssohnstr. 1, D-38106 Braunschweig, Germany*

*E-mail address:* [t.hartmann@tu-bs.de](mailto:t.hartmann@tu-bs.de)

Guest Editor

Toni M. Kutchan

*Department of Natural Product Biotechnology, Leibniz*

*Institute of Plant Biochemistry, Weinberg 3*

*D-06120 Halle (Saale), Germany*

*E-mail address:* [kutch@ipb-halle.de](mailto:kutch@ipb-halle.de)

Editor

Dieter Strack

*Department of Secondary Metabolism, Leibniz Institute*

*of Plant Biochemistry, Weinberg 3*

*D-06120 Halle (Saale), Germany*

*E-mail address:* [dstrack@ipb-halle.de](mailto:dstrack@ipb-halle.de)

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