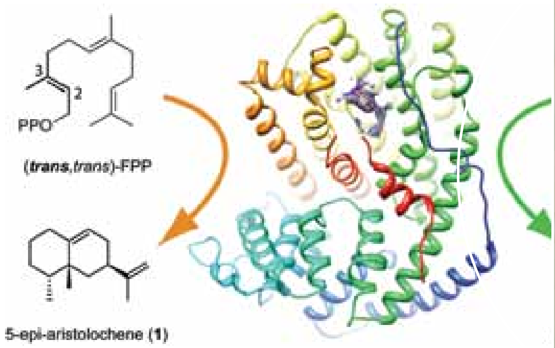

Joseph P. Noel

Howard Hughes Medical Institute Investigator
Professor and Director, Jack H. Skirball Center for Chemical Biology and Proteomics

"Most people are familiar with the word *biodiversity*, but 'chemodiversity'—the extraordinary tapestry of natural chemicals found in all organisms—is just as important for life and the survival of many different ecosystems on the earth. I am particularly interested in the chemical systems or biosynthetic pathways that give rise to these vital molecules."

Trying to make the best of their real estate, plants dispatch an impressive arsenal of small molecules to communicate and interact with the outside world. Among them, terpenes—the oldest and probably most widespread group of natural products synthesized by plants—play a particularly important role. Examples of common terpenes are pine resins and the essential oils of myrrh, rosemary, and thyme, but two of the best-known terpenes are probably cholesterol and taxol.

Despite their extraordinary diversity, all terpenes are assembled from the same five-carbon isoprene building blocks and then modified by an armada of terpene synthases in thousands of ways. Despite the great variety in the terpene synthases' substrate and product specificity, each enzyme falls squarely into one of two camps: cisoid or transoid, depending on how they prefer their raw material spatially configured. As a general rule, terpene synthases only produce cisoid products from cisoid substrates and transoid products from transoid substrates. In a recent study, however, Noel and his team discovered a notable exception: the transoid tobacco sesquiterpene synthase, which is in charge of catalyzing the first step in the biosynthesis of capsidiol, the main component of tobacco's natural antifungal chemical defense.

When fed a non-natural (*cis, trans*) version of the enzyme's natural (*trans, trans*) substrate, the enzyme very efficiently converted the alternative substrate into a new compound with a complex chemical structure and a pleasant woody scent. This finding hinted that the so-called non-natural version of the enzyme's substrate may not be so non-natural after all. In fact, there is now evidence that it is made in small amounts in all living systems. During its evolutionary history, this particular plant enzyme may have taken advantage of the presence of this alternative substrate to produce a new chemical, with a function selected for during the course of evolution. With the compound now in hand, the search for its role in the plant is under way. Nevertheless, this new compound not only might be of great interest to the fragrance industry, it could become an important starting point for the development of new pharmaceuticals to treat disease.

For more information, please visit
salk.edu/faculty/noel.html

Left to right:

Back row: Jing-Ke Weng, Nikki Dellas, June Brennan, Gordon Louie, Marianne Bowman, Kyle Merchant, Justin Pacheco, Tom Baiga

Front row: Ryan Philippe, Charisse Crenshaw, Yongxia Guo, Joseph Noel, Greg Macias, Charles Stewart, Hyun Jo Koo