P123

Global Gene Expression Changes by Caffeic Acid Phenethyl Ester in Human Colorectal HCT116 Cells

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Caffeic acid phenethyl ester (CAPE) is one of bio-active components of propolis derived from honeybee. In the present study, we investigated whether caffeic acid phenethyl ester (CAPE) could affect cancer cell viabilities, human colorectal HCT116 cells were treated with CAPE in a dose-dependent manner. CAPE decreased cancer cell viabilities and induced apoptosis detected by MTS assay and FACS analysis, respectively. To understand the molecular mechanism of cell death in response to resveratrol treatment, we performed oligo DNA microarray analysis. We found that 39 genes were up-regulated more than 2-folds, whereas 21 genes were down-regulated more than 2-folds by 24 hr treatment of 20 μM CAPE. Among the up-regulated genes, we selected non-steroidal anti-inflammatory drug-activated gene-1 (NAG-1) for further experiment. Because NAG-1 belongs to a TGF-β superfamily gene associated with pro-apoptotic and anti-tumorigenic activities. The results of quantitative real-time PCR indicate that CAPE can induce NAG-1 expression in a time- and concentration-dependent manner in HCT116 cells. This result implies that NAG-1 induction is highly associated with apoptosis induced by CAPE. Overall, these results may be helpful in understanding the molecular mechanisms of the pro-apoptotic and anti-tumorigenic activities by CAPE in human colorectal cancer.

Key words: Caffeic acid phenethyl ester, gene expression, NAG-1, colorectal cancer

P124

Computational Approaches to the Post-PKS Modification

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Polyketides are a large family of natural products with diverse chemical structures and a broad range of pharmacological effects, including antibacterial, antifungal, antiparasitic, anticancer and immunosuppressive activities. The area of biosynthetic engineering of the enzymes (i.e. polyketide synthases : PKSs) involved in polyketide biosynthesis has advanced recently to obtain various compounds of polyketide origin. The post-PKS tailoring steps catalyzed mainly by oxidoreductases and group transferases are crucial for the addition of important functional groups to polyketide skeletons and are key to the structural diversity and biological activity of this class of natural products. Among group transfer reactions, glycosyltransfer ones are perhaps the most important biotransformation. Glycosyltransferases are responsible for the attachment of sugar moieties, often deoxysugars, which add important features to the shape and the stereo-electronic properties of a molecule and often play an essential role in the biological activity of many natural product drugs. In this respect, our study focuses on the computational approaches for the substrate prediction of a given glycosyltransferase (GT) and the biosynthetic pathway prediction of a deoxysugar which is synthesized by diverse biosynthetic enzymes and functions as a substrate of GTs. A directed and weighted graph is introduced to represent and predict the biosynthetic pathway. In addition, specificity and homology based clustering method is used to predict the GT's substrate. This study may be useful to the rational design of polyketide natural products.