Letters Response

Response to Pichersky *et al.*: Correcting a misconception about the screening hypothesis

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It is unfortunate that Eran Pichersky, Thomas Sharkey and Jonathan Gershenzon's comment [1] on our Letter [2] ascribes ideas to us that we do not actually hold. Although they seem to accept the basic tenet of the Screening Hypothesis (that potent biomolecular activity is a rare property for any chemical structure to possess) they claim that we implied that some secondary products '...are nevertheless produced because of the future advantages that they might bring' [1]. Pichersky *et al*. rightly note that this offends evolutionary theory but we do not hold the view ascribed to us, nor have we ever ascribed to such a view. Furthermore, if they carefully read our original and recent papers (http://www-users.york.ac.uk/~drf1/sh/) they will see that our model is based on the postulate that it is the overall metabolic capacity to make natural product diversity that is shaped by evolution. At any moment in evolutionary time, an individual plant will make a mix of natural products and the net cost–benefits must be positive if that metabolic capacity is to be selected for. Many natural products found in that plant will, as Pichersky *et al*. accept, bring no benefits. Hence the selection pressure to reduce the production of such inactive chemicals will depend on the magnitude of the costs of producing those compounds, and the degree to which it is possible to reduce the production of any inactive compounds without eliminating active compounds (this is less easy where metabolic matrices, branching or long pathways are involved). The Screening Hypothesis proposes ways of reducing the cost of producing and maintaining chemical diversity. Such cost savings will reduce the rate with which inactive compounds are lost from a genotype but it does not follow that such compounds are retained for some unspecified future benefit. We hope that Pichersky *et al.* accept that our model is based on somewhat more robust evolutionary thinking than they imply.

Pichersky *et al*. [1], in criticizing Susan Owen and Josep Peñuelas's [3] views on the role of volatile terpenes, can be accused of over generalization in that they ascribe properties to whole groups of chemicals when the reality is that only a few members of that group possess the properties in question. 'For terpenes, for example, a number of interesting functions have been demonstrated in recent years...indirect defense...and direct defense...against herbivores, resistance to abiotic stress...and wound-activated signaling' [1]. Terpenes as a group undoubtedly have individual members that possess each of these properties but it is not true that all individual terpenes possess any of these properties. Indeed, all available evidence suggests that the majority of terpenes have no assigned function. Although (and in some sense trivially) this is a consequence of inadequate study, even Pichersky *et al*. seem to agree with us that some terpenes might be members of a transient population of chemicals that might never serve an evolutionary role; these chemicals are made because evolution is selecting for the overall metabolic capacity to produce the optimum mix of chemicals.

We would also question the basis for Pichersky *et al*.'s apparent optimism that new knowledge will confirm roles for most natural products. New knowledge is actually revealing the opposite. The rate at which new chemical diversity is being discovered far outstrips the rate at which roles are being found for these new chemicals. Such a disparity is likewise explainable by the Screening Hypothesis.

Finally we point out that the Screening Hypothesis has a clear parallel in animal immunology, where the machinery that makes antibodies is the important feature, not the ability to make any one antibody. Most of the antibodies that an individual makes never benefit that individual. The immune system is neither forward-looking nor is every antibody shaped perfectly to current circumstance. Like secondary metabolism, it is in some ways a Panda's Thumb [4] – tuned and shaped by natural selection.

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Letters

Plant volatiles: a lack of function or a lack of knowledge?

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We read with interest the recent exchange between Richard Firn and Clive Jones [1] and Susan Owen and Josep Peñuelas [2] regarding the specific roles of volatile plant secondary metabolites. We became concerned when it appeared that both pairs of authors agreed that many of these substances have no function for the emitting plant. Firn and Jones ([1] and references therein) aver that '...potent biomolecular activity is an inherently rare property for any chemical structure to possess...' and '...organisms have to generate substantial chemical diversity for a few compounds to have any likelihood of possessing biomolecular activity'. Hence, they propose that the majority of so-called 'secondary compounds' do not make a contribution to the fitness of the plant but are nevertheless produced because of the future advantages that they might bring. We agree that any particular secondary compound might not confer a selective advantage at present and in some cases might cost too little to have a measurable negative impact on fitness. But to argue that most secondary compounds have no current function and yet the plant pays no penalty (in terms of fitness) for making so many of them is inconsistent with our understanding of population genetics. Basic evolutionary theory posits that selection operates on existing fitness and not on future potential. Over time, small differences in fitness will result in corresponding changes in the frequency of alleles responsible for such differences (with rare exceptions such as when random drift occurs in small populations), with selection favoring alleles that currently confer an advantage, not those that might confer an advantage in the future. Given that new alleles arise by random mutations and therefore initially their frequency in the population is low, their frequency would be unlikely to increase and reach fixation in the population if they did not confer a selective advantage and particularly if they cost the plant unnecessary expenditure of energy.

Owen and Peñuelas [2] make the interesting claim that many volatile secondary metabolites of the terpene class might be side products produced and emitted as a consequence of flux through the pathway to produce primary metabolites that are needed. This argument might have some merit but here too it is important not to conclude that function is lacking when it has rarely been investigated in detail. Secondary metabolites were historically defined as 'secondary' because we did not know why plants made them. Often, for lack of a better explanation, they were hypothesized to be 'waste products'. As more and more compounds have been investigated in detail, more and more functions have been found. For terpenes, for example, a number of interesting functions have been demonstrated in recent years [3], including indirect defense [4,5] and direct defense [6] against herbivores, resistance to abiotic stress [7,8] and wound-activated signaling [9]. To propose that most secondary compounds have no current function and are produced by forward-looking plants for future use or as side products of the formation of other metabolites that are required is not only contrary to our understanding of how evolution works but also ignores a multitude of recent papers on the varied and fascinating functions of secondary compounds.

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Response to Pichersky *et al.*: Plant volatile isoprenoids and their opportunistic functions

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We thank Eran Pichersky, Thomas Sharkey and Jonathan Gershenzon for their interest and their response [1] to our communication with Richard Firn and Clive Jones [2]. The scientific community (including ourselves) is, of course, thoroughly aware of the many important, fascinating and diverse roles of volatile isoprenoids for the plant species that emit these compounds. We made this clear in our Opinion article published in the September 2005 issue of *Trends in Plant Science* [3], where we refer to some of our own papers reporting different functions of plant volatiles. We agree with Firn and Jones [4], as do Pichersky, Sharkey and Gershenzon [1], that 'any particular secondary compound might not confer a selective advantage at present and in some cases might cost too little to have a measurable negative impact on fitness'. Our Opinion article [3], and our response to Firn and Jones [2] say no more than this. Neither our own articles, nor those of Firn and Jones [5,6] suggest that plants are explicitly or actively 'forward-looking'. Neither do we suggest that there is no current role for most volatile isoprenoids because there are many important roles for this large group of compounds (e.g. Refs [7–9]). We do not say that most volatile isoprenoids are redundant because nobody knows (as Pichersky and co-authors point out). Conversely, we do not know that a function will be found for all secondary isoprenoid compounds.

We do suggest that volatile isoprenoids cannot be generally essential for plant health and survival (as are the higher molecular weight isoprenoids) because not all plant species produce and emit them. We assume that in evolutionary terms, synthesis of isoprenoids such as carotenoids and chlorophyll side chains were of prime importance for the survival of plants. We hypothesize that during the process of evolution, volatile isoprenoid production occurred as a fortuitous accident of essential isoprenoid production and that their many roles and functions might also be fortuitous and thereafter retained.

Following on from this, we further hypothesize that control and synthesis of the higher molecular weight isoprenoids might have some effect on the control and synthesis of the lower molecular weight volatile isoprenoids. Firn and Jones's hypothesis is far more general and wide-ranging than our own but generally supports our ideas. Our hypothesis, in return, goes some way to supporting theirs. However, we did not intend our hypothesis to become involved in what we believe is a specialized and long-standing debate on secondary metabolism theory. Our 'opportunist hypothesis' refers to volatile isoprenoids, and to the exploration of mechanisms and controls that might not have been considered before by the volatile isoprenoid research community [3].

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