...resistant to p38, an inhibitor of the mitogen-activated protein kinase. We observed that treatments with p38 inhibitors reduced parasitoid emergence. Our findings suggest that p38 signaling plays a role in the regulation of parasitoid emergence. Further research is needed to elucidate the mechanisms involved.

**REFERENCES**


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Hawkins et al. (1) demonstrate a significant and robust relationship between the outcome (success or failure) of a potential biocontrol program and the maximum percentage parasitism achieved by the parasitoid agent following its initial release. They propose that this relationship illustrates the size of a "ref-
The question of whether parasitoids that are rare in their introduced locations can reduce host densities after introduction was not addressed in our report, but it is an important issue. If by “rare,” we mean that the parasitoid occurs at low densities, then it is indeed possible that it is an effective agent, because by keeping its host at low densities, it also occurs at low densities. If “rare” means that parasitism rates are very low, this may not have anything to do with the host if competition among parasitoids in a multispecies complex or hyperparasitism keeps that particular species rare. Either way, rarity does not tell us anything about host refuges. However, a related issue is whether low rates of maximum parasitism in the host’s native range can be used to predict whether any parasitoid can affect control in exotic locations. If the current data are representative, they suggest that hosts that never suffer parasitism of more than 30% in their native ranges will not be amenable to biological control by using parasitoids. Thus, an additional test of the hypothesis would examine maximum (not mean) parasitism rates by all parasitoid species in native locations and success rates in exotic locations.

Refuge theory assumes that parasitoids are climatically adapted to the region of introduction. If not, our theory of host-parasitoid interactions based on dynamic constructs is not applicable. Examples of high maximum parasitism rates that do not lead to reductions in pest densities because of climatic mismatch have been given (1).

Williams and Hails raise the issue (from a theoretical perspective) of variability in parasitism rates resulting from density-dependent forces. As they summarize, much of the theory of parasitoid-host dynamics, including our own, suggests that this variability is important. Even so, our principal result indicates that quantifying this probabilistic refuges may not be critical in practice. Maximum percentage parasitism reflects more than just parasitoid establishment (which, although essential, provides no guarantee of successful control). It is an estimate of the minimum fraction of hosts escaping parasitism, or of the proportional refuge.

Finally, refuge theory offers a parsimonious explanation for a wide range of patterns found in parasitoid-host interactions, including success in biological control (3). Further empirical research will tell us the extent to which proportional refuges can serve as a predictor of these patterns.

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Calcium and Inositol 1,4,5-Trisphosphate–Induced Ca2+ Release

One of the pathways that regulates cytosolic free Ca2+ is that of inositol 1,4,5-trisphosphate (InsP3) inducing intracellular stores to release Ca2+ (1). It has been suggested that the dependence of this release on the concentration of free Ca2+ in the cytoplasm comprises Ca2+-induced activation of the InsP3-gated channel in the presence of submicromolar concentrations of cytosolic Ca2+ (2, 3). The immediate positive feedback control of InsP3-induced Ca2+ release resulting from such activation would be important in the regulation of store discharge, and this control has been incorporated into different models describing the spatiotemporal aspects of Ca2+ signaling, for example, hormone-induced oscillation in cellular Ca2+ and propagation of Ca2+ waves (1-3).

Nevertheless, as the buffering of free Ca2+ at low concentrations generally involves the use of Ca2+-chelators, the validity of such experiments may be doubted if the chelators have any activity other than chelating. Recently, Richardson and Taylor showed that several chelators interfered with the InsP3 receptor (4). In their experiments, the Ca2+-free forms of the Ca2+ chelator BAPTA and the related fura-2 dye proved to be competitive antagonists of InsP3 binding to its receptor. In contrast, EGTA [another Ca2+ chelator that has been widely used in most of the experiments supporting Ca2+ activation of the InsP3-gated channel (2)] was found by Taylor and Richardson to have virtually no effect on InsP3 binding to its receptor, as measured at low temperature under alkaline conditions (4).

We further investigated the effect of EGTA by directly measuring InsP3-induced 45Ca2+ efflux from micromolar stores derived from cerebellum, a tissue rich in InsP3 receptors. We found that 1 mM EGTA greatly reduced the amount of 45Ca2+ released during 2 s (Fig. 1). The dose dependence of InsP3-induced 45Ca2+ release was studied in two different media buffered at pH 6.5 (20°C, pH 7.1), which contained either 30 mM Ca2+-free EGTA and 30 mM Ca2+ EGTA or 1 mM Ca2+-free EGTA and 1 mM Ca2+ EGTA. In the presence of the higher concentration of EGTA, the dose-response curve for InsP3 was shifted upwards by one order of magnitude, which implies inhibition by EGTA. Arterial effects of EGTA or CaEGTA on different systems are well documented (5).

Preliminary experiments suggested that when the inhibitory effect of EGTA was taken into account, free Ca2+ was a poor activator of InsP3-induced Ca2+ release (not shown), which is consistent with previous results by Meyer and co-workers (6). They found no influence of free Ca2+ in the range of 150 to 800 nM on the kinetics of Ca2+ release from permeabilized basophilic leukemia cells into Ca2+-depleted media in which the only buffer for Ca2+ was fluo-3, present at a small concentration, around 1 μM. Do these results negate the activating effects of Ca2+ on InsP3-induced Ca2+ release described previously? At least, they call for reexamination of the possible arterial effects of Ca2+ chelators or Ca2+ probes in these experiments, as such effects likely account for part of the previously observed activation by Ca2+. The Ca2+ sensitivity of the InsP3 receptor might well have been overestimated.

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Response: After examination of Combettes and Champel’s legitimate concerns, we conclude that artificial effects of Ca che-