among tissues with varying concentrations of the toxin within a plant. Whereas physiological resistance in insects to pesticides and plant resistance (biotypes) is well documented (*2*), inherent behavioral capabilities of insects to discriminate in a toxin mosaic superimposed on their host or habitat is not well understood (*3*). Insect-resistant transgenic plants appear to provide an ideal substrate in which entomologists can explore this previously recalcitrant and otherwise neglected subject. Nonlethal repellency of preadapted populations from human-valued resource tissues to yield insensitive tissues offers the prospect of conserving the extant insect genome by these intraplant refugia and of increasing mortality in cannibalistic species by concentrating populations in smaller areas. Realization of such possibilities would be accelerated if prepared minds were combined with proprietary technology in a context of production agriculture.

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It is regrettable, but not surprising, that *Bt* cotton in its initial year of commercialization has fallen victim to the bollworm. During 1994, when bollworm numbers were extremely high in North Carolina, peak boll damage and yield reductions in two of our *Bt* cotton tests exceeded 20% (*1*).

Our data (*1*, *2*) were summarily ignored in favor of data acquired when there were low numbers of "wild" bollworms or from test sites artificially infested with laboratory-cultured larvae. The wave of euphoria created by *Bt* cotton swept across the cotton-belt and carried many entomologists with it.

In *Bt* cotton, biotechnology has provided cotton farmers with a most powerful tool to assist in the management of insect pests; however, for success and sustainability the tool must be strategically integrated with other management tactics into systems designed for specific areas.

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HIV Fusion

Recently, an assemblage of evidence (*1*, *2*) demonstrated that any one of four β-chemokine receptors can act as human immunodeficiency virus (HIV) cofactors. In some interpretations (R. Weiss, "HIV receptors and the pathogenesis of AIDS," Viewpoints, 28 June, p. 1885) (*1*), these host cell receptors have been prematurely assigned HIV coreceptor function. Back-to-back reports drew contradictory conclusions about the specificity of one such HIV cofactor, suggesting the complicity in HIV infection of additional unaccounted variables.

For a component to be classified as a receptor, three criteria must be met: the component must demonstrate (i) saturable binding of the ligand to the receptor; (ii) specific binding of the ligand to the receptor that is competitively inhibited at the binding site; and (iii) a rate-dependent biologic response to the ligand (*3*). When the meth-

ods used to characterize and identify β-chemokine receptors as candidate HIV co-receptors (*1*, *2*) are stacked up, only one of three criteria has been addressed—biologic response. One controversial assumption made in the recent studies is that HIV infectivity is mirrored by fusion between surrogates for both host cells and virus in a format that lacks the full complement of possible molecular events.

The loose application of the term "receptor" in virology might be an accepted practice. However, the characteristics implicit in the definition (for example, specificity) cannot be assumed as a bonus. In only one study (*4*) have the binding parameters between HIV envelope proteins and potential co-receptors been measured. An alternative host membrane protein was demonstrated to have saturable, reversible, and specific binding to the fusion domain of HIV (*4*). In the presence of nontoxic concentrations of inhibitors with specificity for this HIV interactive host protein, infectivity of peripheral blood mononuclear cells with primary isolates of HIV-1 was inhibited. This protein fulfills all three criteria of the definition of HIV receptor.

The strategy of targeting β-chemokines in the design of interventive modalities is still premature, but the fusion receptor might serve as an appropriate therapeutic target, because specific inhibitors have already demonstrated the potential to diminish HIV infectivity in vitro.

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Response: Bristow is right that the term "receptor" in virology commonly relates less strictly to biochemical criteria than to functional penetration of the host cell by the virus. Almost every retrovirus receptor, including CD4 for HIV, was first identified functionally and only later by the binding criteria that she says are paramount (*1*). So it is with the new findings on chemokine receptors, and no doubt critical binding sites will in due course be unravelled. In the meantime their identification through gene transfer and functional HIV entry represents a landmark in AIDS research.

Bristow writes that any one of four β-chemokine receptors can act as HIV co-factors, but they show specificity for HIV strains of differing cellular tropisms; one of them (fusin or CXCR-4) allowing entry of syncytium-inducing HIV strains, more closely resembles an α-chemokine receptor, for which the natural ligand has just been shown to be stromal cell–derived factor 1 (*2*). New data show that persons inheriting defective CKR-5 receptors are resistant to infection by macrophage-tropic, nonsyncytial HIV (*3*), further strengthening the relevance of these receptors to AIDS.

Bristow states that only her study on a cell surface protease fulfills the criteria of an HIV co-receptor. Yet before Bristow's paper, Kido *et al.* (*4*) showed binding of HIV gp120 to a protesae, while Bhat and Harouse (*5*) demonstrated a much higher binding affinity of the HIV envelope to galactosyl ceramide. However, neither "receptor" provides an efficient means of HIV entry. The role of proteolysis therefore remains in doubt (*1*, *6*). I remain a little skeptical about the function of a molecule showing saturable, apparently specific binding of HIV until it can be demonstrated that the molecule is required for infection. A number of charged oligopeptides and sulfated polysaccharides inhibit HIV infection in a spuriously specific manner, because they also inhibit other enveloped viruses that use quite distinct receptors.

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Letters to the Editor

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