Letter to the Editor

On the Question of 'Elicitors' or 'Inducers' in Incompatible Interactions Between Plants and Fungal Pathogens

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Studies of plant-fungal interactions have provided increasing evidence that fungitoxic compounds of host origin (phytoalexins) produced during infection may play a role in disease resistance. In addition to infection by fungi the production of phytoalexins can be caused by a wide variety of other agents such as ultraviolet light, salts of heavy metals, antibiotics, and numerous other compounds that are not related to one another by any evidently relevant properties. Therefore the evidence is overwhelming that a wide range of nonspecific stimuli can lead to phytoalexin production. Nevertheless, a high degree of specificity exists in the resistance of host cells to nonpathogens and to avirulent races of pathogens, which may differ from virulent races only in a single gene. Such incompatible interactions generally are manifested in a hypersensitive response which involves the rapid death of the invaded cells and frequently the associated production of phytoalexins.

In many instances the hypersensitive response to infection is the first visual manifestation of resistance. Parallel studies of the progress of the hypersensitive response and phytoalexin production suggest that the hypersensitive response occurs first (6, 7, 12). Thus, specificity in a host-fungus interaction logically must be associated either with the hypersensitive response or with some as yet unrecognized earlier event. Even though this should be obvious, the situation has become confused in recent years owing to attempts to determine the nature of the stimuli of fungal origin that give rise to incompatibility. Frequently they are referred to as inducers or elicitors of phytoalexin production per se without clarification as to whether the latter is a consequence of the hypersensitive response or other expression of resistance (2, 5, 8).

Arguments in support of specific induction by inducers or elicitors have been strongly advanced by Cruickshank and Perrin (2), Keen (8), and Albersheim and Anderson-Prouty (1) on the basis of evidence obtained from incompatible interactions in the Leguminosae. Some compounds, which are active as inducers in very low molar concentrations, have been described as peptides (2, 8) or carbohydrate-containing molecules (1). Albersheim and Anderson-Prouty (1) proposed that such molecules are present at the fungal wall surface and interact with specific receptors on the host-cell plasma membrane, triggering a hypersensitive response. For support, the authors cite examples of cellular interactions from other biological systems in which recognition is mediated by the interaction of carbohydrate-containing molecules and proteins. According to this proposal, small changes in the terminal structure of the elicitor molecules which might be brought about by gene mutation, would destroy the elicitor-receptor relationship, the host cell would fail to recognize the pathogen, defensive responses would not be set in motion, and the mutation would be from avirulence to virulence.

A major difficulty with any proposal based on the production of specific elicitors, however, was pointed out by Wood (16). Because avirulence or nonpathogenicity is the overwhelming rule among fungi, elicitor-receptor mechanisms for an almost infinite number of incompatible combinations must be envisaged. One might add, that if avirulence requires highly specific elicitor molecules and modification or absence of these confers virulence, then virulent forms should vastly outnumber avirulent ones. Also, there is the problem of accommodating such a highly evolved system in a scheme that also will account for the activity of unrelated and nonspecific chemical and physical agents.

Conceptually, it would be much simpler if specificity could be associated with the relatively exceptional virulent combinations. A simple alternative to the elicitor-receptor hypothesis would require only that the host recognize the virulent race as compatible and hence that virulent and not avirulent races produce molecules that effectively occupy or block receptor sites. Such situations appear to prevail whenever compatible cells come together. In fact, most of the examples cited by Albersheim and Anderson-Prouty (1) to support the proposition that recognition phenomena depend upon the interaction of carbohydrate containing macromolecules and proteins at the cell surface are taken from compatible interactions. Rejection or incompatibility, which in fungus-plant cell interactions result in a hypersensitive response and phytoalexin production, is associated in these examples with failure of the specific recognition process. We suggest that avirulent races of pathogens differ from genetically related virulent races simply in their inability to produce the same specifically recognizable molecule. Instead they may produce variants that do not fit the receptor site and hence for that reason impose stresses on the host cell. Such variants would be 'elicitors' and would account for the specificity of gene-for-gene relationships. Many less closely related molecules produced by nonpathogens of a particular host also would be 'elicitors' for the same reasons and hence account for the apparent paradox of both 'specific' and 'nonspecific' "elicitation" in the same system. Mutation of the host to resistance would require only a small conformational or other change in the receptor site. The system could embrace a wide range of host pathogen interactions.

According to this alternative view, lack of specificity in the induction of the hypersensitive response not only becomes understandable but essential. It is to be anticipated that all fungi, regardless of their virulence, will contain molecules that can function as elicitors. Thus, Varns et al. (13) found that sonicates of both avirulent and virulent races of *Phytophthora infestans* caused a

hypersensitive response in potato tubers. The demonstration by Király et al. (9) that virulent races, killed on their hosts by the application of antibiotics, gave rise to incompatible rather than compatible types of response, can be interpreted similarly. Virulent races must be exceptional in that in addition they produce molecules which specifically occupy host cell receptor sites. In homogenates of hyphae or spores, or in culture fluids, molecules of that kind (which to be effective presumably must be the first to make contact with the host cell) would be swamped by the abundance of 'nonspecific' molecules and lose their spatial advantage. The isolation from fungi of a homogeneous macromolecular fraction of appropriate specificity can be expected to be technically difficult owing to contamination by other molecules with possibly very minor differences. The latter would tend to obscure the ability of such a fraction to suppress a hypersensitive response (14), induce susceptibility (3), or accessibility (11), experimental criteria that might be used to test the efficacy of such preparations.

In conclusion, it is proposed that the available evidence logically supports a scheme in which the recognition of virulent races as compatible, rather than of avirulent races as incompatible, is the basis for specificity in host-parasite relations. If such recognition involves the interaction of molecular species from the pathogen with receptor molecules in the host cell plasma membrane it is the virulent race that produces the molecules that fit the receptors, avirulent races or nonpathogens produce variants or unrelated molecules that do not fit, and these have in the past been called elicitors or inducers. The recognition phenomenon is assumed to be the most fundamental aspect of the interaction, and the hypersensitive response may or may not be (10) a direct manifestation of this. Phytoalexin production is regarded as considerably more remote, and certainly without direct relation to specificity. In fact, there is evidence to support an early suggestion (4) that it represents only part of a major stimulation of secondary metabolic activity that follows a hypersensitive response, a part that has been recognized because its products are fungitoxic (15).

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