Letter to the Editor

Possible Role of Nuclear Structure in Disease Resistance of Plants

Lee A. Hadwiger

Department of Plant Pathology, Washington State University, Pullman 99164-6430.
Supported in part by Washington Sea Grant RX-10 PPNS0003, Washington State University, College of Agriculture and Home Economics, Research Center.
I thank R. A. Allan, Catherine Daniels, and Roland Line for reviews of the manuscript, and Ruby Latham for manuscript preparation.
Accepted for publication 2 June 1988 (submitted for electronic processing).

No single gene product, attributable to a single Mendelian trait for disease resistance in plants as designated in the gene-for-gene hypothesis of Flor (15), has been biochemically characterized or had its structural gene cloned. However, considerable progress has occurred in locating and characterizing avirulence genes in the pathogen (17,63). Efforts to resolve unique plant gene products by two-dimensional separations of proteins synthesized by or contained in lines possessing single Mendelian traits for disease resistance have been unsuccessful (18). Similarly, cascade hybridization, transposon mutagensis, and other recombinant techniques potentially able to uncover such unique gene sequences have not yet been successful (38). However, the presence of such Mendelian traits in a genotype can be shown to be associated with pleiotropic effects involving the increased activation of multiple host genes (9,25). Some of the single dominant traits for disease resistance have been mapped to certain chromosomal loci, on the basis of their linkage in segregation ratios of progeny possessing the resistant phenotype (15,48) (Table 1). Although the locus may constitute a unique DNA sequence, it may or may not code for a given protein. Therefore, the traits associated with these loci will henceforth be referred to as single "Mendelian traits" to distinguish them from single structural genes coding for an enzyme or other protein products.

How can the Mendelian traits influence the pleiotropic resistance response observed biochemically, cytologically, or symptomologically? The subsequent discussion will relate aspects of nuclear structure to the following molecular explanations of gene-for-gene interactions, some of which have been discussed elsewhere or were devised from other eucaryotic systems.

1. Avirulence gene product/resistant gene product interaction. A single plant locus may code for a single protein that is a receptor for a given product of the avirulence gene produced by the incompatible race (70). The avirulence gene product/dominant gene product complex in some way promotes a cascade of effects in the host and subsequently causes retardation of pathogen growth. A receptor protein for an avirulence gene product has not yet been found, but it has been demonstrated that a single host protein can confer sensitivity to a fungal toxin (12).

2. Gene product is an enzyme of a secondary pathway. A single dominant gene of the resistance locus may code for the rate-limiting enzyme in the production of a major secondary plant metabolite.

3. Single resistance locus contains multiple genes. The Mendelian disease-resistance trait mapped to a single locus contains multiple genes, as do the histocompatibility loci of mice and humans (40). When one or more separate genes or gene codons react with avirulence gene product(s), there is a transcription of multiple genes, which in concert develop a response that retards fungal penetration.

4. Single gene product is a transcription-influencing factor. A single dominant resistance trait may be a single gene that codes for a transacting transcription factor (71). This factor may enable the transcription of multiple genes throughout the genome, which in concert develop resistance.

5. Single disease-resistance gene has a threshold-surpassing function. The major dominant locus, which segregates as a single trait, may be an entity with a specific promoter or enhancer sequence. Similar such sequences of DNA would exist throughout the genome. When such sequences are confronted directly or indirectly with the unique avirulent gene product(s), there is a multiple gene response. However, the threshold-surpassing trait has the intensity adequate to raise the total host response to the threshold level required for complete, rather than only temporary, resistance. Thus, disease resistance would depend on, but not be attributable in total to, a single gene product.

6. Resistance genes are a manipulated rearrangement of evolutionarily attained cell-regulation systems. Disease-resistance genes may constitute evolutionary deviations from normal cell-control mechanisms. Such genes may have developed because quirks in transcriptional states for "normal" developmental processes have occurred via translocations, deletions, and other mutations (32). Such alternations would influence the location of blocks of genes with respect to nucleosomes, heterochromatin regions, chromatin loops, scaffold attachment regions, nuclear membrane attachment sites, telomeres, or centromeres, and thus would also influence the control of genes within large regions of chromatin.

It is possible that some role exists for all of these explanations. I would like to relate these explanations to what is presently known about nuclear structure and gene regulation. Genome rearrangements, such as those described in explanation 6, have been reported to influence the regulatory control of multiple genes

TABLE 1. Distribution of some disease-resistance traits on wheat chromosomes after McIntosh (48)

Chromosome	Arm[a]	Resistance trait[b]
1A	S	Pm3a
1B	S	Bt4, (Bt5, Bt6), Yr10, (Sr14*)
1D	L	Sr18,* Sr33,** Lr21
2A	S	Lr17**
	L	Sr21, Pm4b**
2B	S	Sr36, Lr23, Lr19, (Sr28)
	L	Sr9a, Sr9b, Sr9d, Sr9g, Sr19, Sr20, Sr28, Sr16, Yr7
2D	···	Sr6, Lr22, Lr2a, Lr22b, Lr15
3A	···	Sr35
4Aβ	···	Lr25, Pm7, Lr12, Lr16 [Lr12, Lr16]e
4B	L	Sr7a, Lr28, Lr30
5B	L	Lr18**
5D	S	Pm2
5D	L	Sr30**, Lr1
6A	···	Sr8, Sr13
6B	S	Lr9*
6B	L	Sr11, Lr3
6D	···	Sr5, Sr29
7A	L	Pm1, Sr22, Lr20, (Pm9), (Sr15) [(Pm9), (Sr15)]e
7B	L	Pm5, Lr14a, Sr17
7D	L	Sr25, Lr19

[a] Arm designations are S = short; L = long; ··· = not designated.
[b] Symbols are Bt = bunt; Lr = leaf rust; Pm = powdery mildew; Sr = stem rust; Yr = yellow rust. (Genes in parentheses indicate the chromosome arm was not designted.) * = no detectable e crossing-over percentage with centromere; and ** = assortment independent from centromere.

in eucaryotic genomes. The genes in or adjacent to such regions are subject to external influences as a type of position effect. Their new chromosomal position may be beneficial to rapid transcription. For example, the *c-myc* locus in humans is involved in the control of cell proliferation (32). When located on chromosome 8, it responds to normal transcriptional control mechanisms. However, when juxtaposed to an immunoglobulin gene on chromosome 14, it is transcribed constitutively at elevated levels. Thus, the immunoglobin locus contains genetic elements capable of activating *c-myc* transcription in *cis* over considerable chromosomal distances (32).

Such highly transcribed chromatin has been described as being poised for transcription (7). Some portions of the genome, e.g., the locus of some dominant Mendelian trait with a potential for disease resistance, could also be located near the nuclear circumference or some such site especially influenced by the influx of unique cell wall fragments elicitors or elicitor-released second messengers. The systematized screening for disease resistance among natural plant populations or within the progeny of genetic crosses may have brought into focus chromosomal regions adept at bolstering resistance. Within such activated regions would reside the message for certain functions (e.g., β-glucanase, chitinase) with the potential to destructively suppress fungal growth (47). Such transcripts may also code for repair functions required by all cells, such as those involved with membrane replacement, cell wall regeneration, and nuclear structure. Additionally, the enhancement of constitutively expressed genes may result in excessive accumulations of polymers such as callose and lignin, beneficial in limiting colonization by the pathogen. The host genome that could most rapidly sequester or maintain such a transcriptional state following pathogen challenge would be symptomatically resistant. Responses in a susceptible reaction would be short lived either because of a less optimal transcription initially or because the potential for an optimized response is reduced by suppressors, inhibitors, toxins, hydrolytic enzymes, etc. released by the pathogen. Or simply, the chromatin with time becomes less poised for transcription. Thus, the chromosomal rearrangements and alterations required for the quirks of transcriptional states may be the DNA sequences we have come to know as those disease-resistance traits, heritable in genetic crosses.

Recent information (50) indicates how specific sequences central to nuclear structure can regulate processes in eukaryotic cells. I will review this information and relate it to the explanations listed above. This information, along with what is known about biotic elicitors, may provide useful clues as to the function and regulation of genes involved with disease resistance.

The pathogen's potential to alter the plant's transcriptional state with elicitors, inducers, etc. There is an amazing array of natural and synthetic compounds that induce responses in plant cells mimicking to varying degrees induction by an intact pathogenic organism. Although it is possible for the plant to accumulate secondary products simply by alterations in intermediate metabolism, recent work indicates major changes often occur as a result of changes in the rate of transcription or translation (1) of key enzymes in secondary metabolism. The inductions of hydrolytic enzymes, enzymes of secondary metabolism, phytoalexins, lignin, hydroxyproline-rich glycoprotein, and other disease-resistance response genes and their proteins that occur following pathogen challenge can be mimicked by individual components released from cells of the pathogen or of the host itself.

Processes such as phytoalexin induction can occur following treatment of plant tissue with foreign substances as diverse as detergents, heavy metals (8,24), DNA base analogs (60), DNA intercalators (29), DNA cross linkers (20), thymidine-specific agents (30), or thymidine dimerization per se (56). Naturally occurring plant and fungal components also induce phytoalexins (27,58).

What is the common molecular denominator for such inductions? Since the early work of Ruth Allen, and possibly before, pathologists have noticed changes in plant nuclei following infection. The plant nucleus, the ultimate location of transcriptional change (50), is quickly influenced by invading fungal cells (21). I propose the action of natural elicitors can directly or indirectly influence nuclear structure.

Elicitors and their formation. The natural elicitors important to the induced transcription of certain plant-defense genes most likely develop in the generated debris of both pathogen and plant walls (27). The debris of the fungal cell wall is often a more potent elicitor than that derived from plant cell walls (58,66). The live pathogen cell in the unique environment of the host may be continually producing an optimal elicitor component following the plant challenge. The induction potential can change as the pathogen wall or culture filtrate components are extracted and purified (13). Products released from pathogens in artificial culture can be quite different from those released in nature (6).

Cell wall components can be changed as they are being synthesized or deposited. For example, chitosan, a component of fungal walls, is produced via chitin (10). The sugar precursor for both compounds, UDP-N-acetylglucosamine, is incorporated first into chitin fibrils, which can then be deacetylated to produce the glucosamine polymer, chitosan.

Stress components can also influence the deposition of cellulose into plant walls. It has been shown that cellulose (β-1,4-linked glucose) deposition can be shifted to callose formation, which is mostly β-1,3-linked glucose with some fraction of the polymer being β-1,4-linked (11).

A potential for altering the biosynthetic composition of both plant and fungal walls, along with some precisional enzymatic degradation of plant and fungal walls in host parasite interactions, provides a cell debris source. The content of such debris can be consistent for a given interaction (64). The digestion products of pectolytic material from one plant source does not yield the same biological entity as that from other plant species (58). Also, debris that activates a response in one plant may not do so in another (51,66). Thus, the consistency of the debris reflects the genetics of the parent organisms involved in the interaction.

Some of the genes that function as avirulence or pathogenicity genes might blueprint the carbohydrate, glycoprotein, etc. polymer structures from which the wall and elicitor fragments are ultimately derived (27). Logically, this debris cannot traverse the plant membrane and cytoplasm without some initial disruption, which in itself could induce host responses via a release of second messenger components. For example, β-glucan polymers reportedly localize in the plant membrane fraction (58). Additionally, some of the pathogen wall debris may directly or indirectly influence the transcription of genes by somewhat specific effects ultimately on the nucleus of the plant cell. Given the recent information on the structure and function of nuclear components reviewed by Newport and Forbes (50), the potential for direct influence on nuclear structure and transcription may no longer be farfetched. The macro molecular traffic into and out of the nucleus is highly controlled and is developmentally regulated to meet the major needs of the cell throughout plant development (14).

In addition to size (100-110 A) limitations of the nuclear pore, nuclear localization also depends on signal sequences of proteins that may enable nuclear entry at other locations. Signal protein sequences for nuclear entry differ from those that target proteins to the endoplasmic recticular, mitochondria, Golgi, vesicles, and extracellular destinations (14,55). It has been found recently that major nuclear proteins, when complexed to nonnuclear proteins or even large gold particles, allow rapid entry of the entire complex into the nucleus. Although there are some similarities among the known signal sequences of proteins allowing entrance to the nucleus, the nuclear localized proteins need not share additional similarities in the remaining portion of the protein. The most potent nuclear transport signal sequence contains a positively charged block of amino acids (Pro-Lys-Lys-Lys-Arg-Lys-Val)(50). This suggests an entry potential for many compounds possessing a series of positive charges. For example, positive charged proteins produced in the cytoplasm (such as protamine and histone) end up in the nucleus.

Conversely, in vitro transport into the nucleus can be blocked by other types of molecules; e.g., wheat germ agglutinin was shown to bind to the nuclear pore and inhibit completely the transport of

nucleoplasmin into the nucleus. Competition by N-acetylglucosamine, the sugar recognized by wheat germ agglutinin, relieved all inhibition of this nuclear transport (50). Thus, cell debris containing an array of polymers when entering the cytoplasm has a potential to influence nuclear transport, depending on charge, size, and structure of the debris.

The fungal wall component chitosan, a positively charged polymer, enters the plant cell and its nucleus during infection (23). Chitosan is positively charged because of the amino groups on glucosamine residues (22). Other derivatized glycosamine polymers, such as those containing N-acetylglucosamine and muramic acid, are major components of bacteria wall polysaccharides (52). Polygalacturonic acid polymers with an overall negative charge may not reach the nucleus, but have the potential to complex with and delay positively charged compounds destined for nuclear transport. Also, certain glycoproteins can enter the Golgi for processing and then be transported back to the endoplasmic recticula or to the nucleus (36).

Components of nuclear structure and function subject to change. Although changes in structure of plant nuclei have been reported (21) following challenge by fungal pathogens, the manifestation of these alterations and their subsequent consequences within the cell have been difficult to visualize. The organization of the interphase nucleus (50) is now better understood and will be summarized as background for discussing potential effects of plant-pathogen interactions related to nuclear change. First, the chromosomes are oriented with centromeres attached to the nuclear envelope at one pole of the nucleus and telomeres attached to the envelope at the opposite pole (37). The chromosome arms are maintained in separate spatial domains. The chromosomes are highly contorted and very closely packed within the nucleus but do not loop around each other. Certain specific chromosomal loci are frequently found attached to the nuclear envelopes. In polytene chromosomes such loci occur almost exclusively at positions of intercalary heterochromatin. These sites are relatively evenly distributed along each chromosome arm, on the average every 10^6 base pairs (46). Chromatin itself is organized in loop domains. Following removal of the majority of chromatin's proteins with high salt, the nuclear DNA remains anchored to a residual proteinaceous scaffold that retains the basic morphological organization of the nucleus (5).

Two proteins, *ScI*, a 170-Kd protein (topoisomerase II), and *ScII*, a 135-Kd protein, are major components of the scaffold of the interphase nuclei (2). The DNA (a single duplex strand) is attached to this scaffold at numerous sites, forming loops (19). The organization of chromatin into loop domains is a stable and conserved feature of interphase and metaphase chromosomes (50) and is identifiable from generation to generation. Laemmli and co-workers (19) used restriction enzymes to remove DNA sequences unattached to nuclear structures, thereby leaving the DNA of attachment, called scaffold attachment regions. This DNA was found to possess specific sequences.

Such nuclear binding sequences have been identified in association with the histone gene repeat, heat shock protein 70 gene, alcohol dehydrogenase gene, mouse Kappa immunoglobulin gene, and ribosomal RNA genes (50). The spacings of these specific sequences along the genome range from 5,000 to 112,000 base pairs apart. These sites are not homologous in sequence. Their similarity is that they are approximately 200 base pairs long and are A-T rich (50). There is estimated to be 10,000 scaffold attachments regions per nucleus. An enrichment of sequences related to the consensus of the topoisomerase II cleavage sequences ($GTN^{A}_{T}A^{T}_{C=}$ $ATTNATNN^{G}_{A}$) has recently been found in the scaffold attachment region of a small DNA loop containing the chicken lysozyme domain (53). Topoisomerase II, a major enzyme of the nucleus, may regulate the topology of a loop by regulating the supercoiling density (4). The scaffold attachment regions also co-map with or near (3) some upstream enhancer-like regulatory regions. Thus, scaffold attachment or detachment and variation in topoisomerase II activity are likely to regulate some functions in addition to assisting in the formation and maintenance of loop domains. For example, novobiocin, which blocks topoisomerase II activity, also blocks the heat shock response (34). Nuclei with different activities organize their chromatin differently (50).

Chromatin and nuclear envelope attachment. The number of segments of chromatin that interact with the nuclear envelope is estimated as high as 1,500 attachments per interphase nuclei in salivary gland chromosomes (50). Attachments involve the centromeric region, telomeric region, and several unique heterochromatic regions within each chromosome. There is also evidence for interactions between chromatin and the nuclear lamina of the nuclear membrane, which would provide a stable organization of the chromosome within the nucleus. It is generally observed that some rearrangement of nuclear components occurs during mitosis. The chromatin condensation occurring during mitosis is accompanied by the inactivation of RNA transcription. Thus, the conformation of the chromatin is important in gene regulation even at the level of chromatin segments.

Nuclear chromatin. More insight on the potential for function of the nucleus is available from information on its formation from protein-free DNA (50). DNA is first assembled into nucleosomes, then rearranged to form a distinctive, highly condensed sphere. The condensation process resulting in this sphere involves formation of a scaffold, and topoisomerase is a part of this condensation process. After chromatin is fully condensed, lamin and membrane components begin to assemble around the DNA. Nuclear envelope formation may be mediated by specific chromatin-bound receptors (probably proteins).

Plant nuclear structure in plant-pathogen interactions hypothesis. How then might the structure of the plant nucleus relate to host-pathogen interactions? I speculate that some of the sequences specific for the attachment of chromatin to scaffold, lamin, nuclear envelope, etc. may constitute a part of the DNA within the linkage group containing a specific Mendelian disease-resistance trait. These sequences enable both specific and nonspecific responses to be generated as compounds foreign to the nucleus to enter the nucleus. Further, genes functioning in maintaining host cell viability become more active when these sequence-specific attachments undergo change.

Origin of Mendelian traits and disease resistance. Breeders originally searched for and found disease resistance that was often controlled by single dominant traits (15). These genes or collective minor genes provide resistance. Because resistance can be preinduced in lines that do not possess the specific Mendelian traits for resistance (42), it may be necessary to look for explanations other than those proposing a single gene (single protein) function (explanations 1 and 2).

How can genotypes, inherently without major gene resistance, develop resistance? A considerable amount of work is available to explain how alterations in the expression of certain traits occur by changes in chromosome structure and arrangement, such as the translocations that converts prooncogenes to oncogenes. Also, it has been shown that the activity of genes transfected into a plant genome is widely variable depending on the chromosomal environment in which it resides (43). Thus, rearrangement or genetic alteration of a given plant genotype may be ample to enhance the selective expression of a subset of gene products that function to develop resistance. As a result of specific chromosomal perturbations, the genome may respond or fail to respond to a given set of elicitors entering the host cell.

How might transcription be influenced by chromosomal perturbation? Several lines of evidence suggest that transcriptionally poised chromatin is under torsional stress (4,39). Nuclease probes that detect transcription promoting regions (33) often selectively react with regions in active chromatin that are preferential targets in supercoiled, but not relaxed, naked DNA. Also, transcription of DNA, when injected into *Xenopus oocytes*, is influenced by template topology (35). That is, circular DNA is transcribed, linearized DNA is not. Minichromosomes enriched in transcriptionally active material possess an elastic torsional strain in supercoiled DNA (45,59). Linear chromosomal DNA molecules must be anchored in the nucleus to impede free rotation to allow this torsional stress to be introduced into chromatin domains. Nontranscripted spacer regions of some genes have been shown to

be localized at the bases of loop domains (49), the same area of some reported topoisomerase attachments sites. Gene-specific gyration of this loop structure has been demonstrated in response to transacting factors. Thus, the transcriptionally poised loop structures can be influenced by factors external to the gene-containing domain. I propose that plant genes within these loop structures can be influenced directly or indirectly by elicitors released from the pathogen.

Direct influences of abiotic elicitors on loop structures. We have shown that many planar multiple ring structures that intercalate in between base pairs of DNA can induce increases in phenylalanine ammonia lyase activity and pisatin accumulation in peas (26,29). Intercalators influence circular DNA by removing the condensed state (by reversing right-hand coils) to open ring structures and, with additional intercalation, can reverse the helical structure (by developing left-hand coils) and achieve a condensed state again (68). It has been shown that when DNA intercalating agents act on preparations of eukaryotic DNA, which are devoid of a majority of proteins but are still bound to the scaffolding thus still forming a loop, they undergo sedimentation changes (3) similar to those of supercoiled circular plasmid DNA (68). These findings may indicate the potential of intercalating agents, bifunctional alkylating agents, DNA strand binding agents, etc. to alter the conformation of loop DNA that could either induce or suppress the genes within these domains (50). Many other DNA-altering compounds and treatments have been shown to elicit phytoalexin accumulations (26) and some to enhance transcription in vitro and in vivo (34,60). Further, these compounds with differing DNA-influencing actions also induce other disease-resistance-related responses (31,44).

Scaffold attachment regions. The AT-rich (70%) scaffold attachment regions may have been involved in Reilly and Klarman's (56) demonstration that phytoalexin induction in soybean was associated with thymidine dimerization of DNA that occurs when cells are exposed to 260 nm of UV light. Psoralen compounds, which also preferentially link the pyrimidine base thymidine, induce pisatin in peas (20). These psoralen compounds in the presence of UV 366-nm light can covalently bind to the pyrimidine base to form a monoadduct or, with additional UV light intensity, can cross link DNA strands. The latter action can promote DNA repair (65), which could further influence the torsional stress of the loop domain. Psoralen and other DNA-specific compounds, including the fungal wall component chitosan, have been shown to mimic the inducing action of the pathogen *Fusarium solani* f. sp. *phaseoli* by enhancing the accumulation of mRNA for the same disease-response proteins or RNA species homologous with the disease-resistance response genes (44). Sequence analyses of the DNA in the vicinity of these structural genes will eventually determine if scaffold attachment regions or other chromosome structural features are involved in their regulation. Clusters of topoisomerase cleavage sites and indications of scaffold attachment regions have been recently discovered (C. Chiang and L. A. Hadwiger, unpublished) in regions 5′ to the disease-resistance response gene PG49.

Possible relationship of specific nuclear structural changes to the six molecular explanations of gene-for-gene resistance. The discovery that multiple scaffold attachment regions prevail in the heterochromatic component (50) of the nucleus may provide insight into the functional makeup of major Mendelian disease-resistance traits. For example, the locus of a Mendelian resistance trait might be enriched with scaffold attachment regions or other nontranscript sequences rather than sequences for enzyme-coding structural genes (explanation 6). Little is known about the locus size of any Mendelian trait in kilobases of DNA, because estimates are based only on linkage data. In the absence of evidence indicating a single gene product exists as the function of the single Mendelian trait controlling resistance (explanation 1 and 2), alternate possibilities should be entertained. For example, one could visualize that some resistance loci may represent heterochromatic regions encompassing one or more scaffold attachment, and others envelope attachment regions. Fungal elicitors entering the cell could indirectly (or directly) introduce change in the torsional stress of these transcriptionally poised chromatin regions, thus generating the pleiotropic gene activation responses that are typically observed (9,16). The pleiotropic aspect may sometimes be essential. For example, multiple gene enhancement is often associated with pathways of secondary metabolites. Unfortunately, it is difficult to decipher which gene or spectra of genes is functioning to develop complete resistance. Because DNA sequences similar to those in scaffold attachment regions can be associated with multiple eucaryotic genes (explanations 3 and 5), DNA sequence analyses of the 5′ and 3′ regions of genes active in resistance responses should be extended to determine how far the scaffold attachment and nuclear membrane attachment regions reside from structural genes.

Model for poising the chromatin within loops. Figure 1 provides a scheme demonstrating the proposed role of chromosomal loops in the regulation of genes associated with the resistance response. Constitutive levels of the enzymes β-glucanase and chitinase with a potential to digest β-glucans and chitin of the fungal wall appear to be ubiquitous to plants. The enzymatically released cell debris entering the cytoplasm is distributed in the cell on the basis of reactive groups. For example, basic polymers can enter the nucleus; hydrophobic compounds will likely reside in membranes; agglutinating proteins will attach to their specific sugars; substrates, co-factors, and inhibitors will complex with enzymes, etc. The total action of the debris can be to interfere with cellular function directly or indirectly through second messengers (54,58). The loop structure of the nucleus may also change when positively charged compounds complex with the negatively charged phosphate groups on DNA or when negatively charged compounds interfere with the nuclear accumulation of the cell's native compounds that are positively charged (e.g., histones). For example, we have shown that positively charged chitosan can alter circular dichroism spectra and restriction enzyme digestion of DNA segments (25). Others have found the more negatively charged polygalacturonic acid residues to be effective elicitors of phytoalexins (57,67).

Nuclear structure changes possible early in the host-parasite interaction. The specificity of a foreign substance entering a plant cell would be dependent on the relay function of receptors or the alteration of the transcriptionally poised state of the chromatin. Fungal components entering the plant nucleus or components present in normal chromatin assembly might temporarily change the internal organization of the chromatin by altering heterochromatin, telomeres, nuclear lamina, scaffold, or centromere attachment regions of the chromatin. Major changes to these regions could in turn affect the multiple gene functions

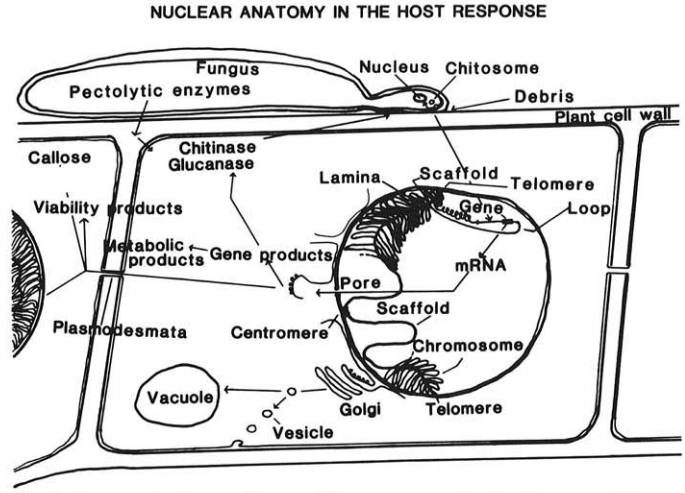

Fig. 1. A general scheme of some of the components of a disease-resistance response, designating the following nuclear regions proposed to be sensitive to elicitor (cell debris) action: Lamina associated with the nuclear membrane, scaffold attachment region, centromere attachment region, telomere attachment region, chromosomal loops, and enhancer/promoter regions.

within a loop domain or possibly the entire chromosome. Distal changes affecting transcription could occur, in addition to the local control of 5′ elements (61) and transcription factors directly affecting individual genes (explanation 4). As a result, multiple genes may be induced (or suppressed) at various levels.

Chromosomal position. A generation of researchers using mutagenesis for crop improvements (41) have shown the potential for genetic alterations in improving resistance within genotypes that previously were not regarded as resistant. Resistance may have been influenced as a result of rearrangement of genes in a manner reminiscent of the early observed position effects. Table 1 includes the chromosomal locations for some resistance traits in wheat and demonstrates that resistance loci can be scattered over a majority of the chromosomes. A locus on a given chromosome often contains multiple alleles capable of responding incompatibly to different races of the same pathogen. Genetic traits that control the resistance for one pathogen seldom perfectly overlap with those of a related pathogen (e.g., leaf- and stem-rust resistance). Some disease-resistance traits map indistinguishably from the centromere. Are these located within the centromeric attachment region? Other traits can be assigned to a given linkage group, even though the traits may exceed 50% crossing over. Are these traits located at the extremity of a chromosome and possibly near a telomeric membrane attachment site?

If the single Mendelian trait for disease resistance represents a unique DNA sequence responsible for developing a given transcriptional state receptive to influence by a given pathogen, then no single unique product of the resistance traits will be found. The mechanism allowing such a region within the nuclear structure to influence distal transcription may be similar to that of DNA elements that serve as enhancers significantly distal from the structural gene being regulated. As with enhancer action, nuclear structural changes may be more likely to augment than to supersede the regulation of genes that occurs via DNA elements proximal to the structural genes (explanation 4).

Although some of the explanations discussed in this paper depart at times from the dogma of earlier hypotheses for gene-for-gene interactions, they encompass some recent information on gene regulation and nuclear structure in eukaryotic cells. It is hoped that the attention drawn to nuclear structure will encourage researchers to examine more closely the information contained within the nontranscript regions of chromosomal DNA that may not code for products, in addition to examinations of the transcribed regions that code for protein products.

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