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Research Focus

Geminivirus disease complexes: the threat is spreading

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Symptom-modulating DNA satellites associated with geminiviruses have come to our attention only recently but have proven to be widespread, associated with many diseases throughout the Old World, and economically significant, particularly in developing countries. Recent developments are elucidating the role played by these novel molecules in pathogenicity and in overcoming host plant defense. Further investigation into the promiscuous nature of these satellites and their ability to recruit further begomoviruses indicates that regions not yet affected by such begomovirus-satellite complexes are at great risk.

Geminivirus disease complexes are widespread in the Old World

Viruses of the family *Geminiviridae* are insect-transmitted pathogens of plants that have small, circular, single-stranded (ss)DNA genomes. The economically most important and most numerous of these are the whitefly-transmitted geminiviruses (genus *Begomovirus*), which have emerged as major pathogens of crops worldwide [1]. The majority of begomoviruses have genomes consisting of two components, DNA A and DNA B; these are the only begomoviruses native to the Americas. A few truly monopartite begomoviruses, with genomes consisting only of homologs of the DNA A components of bipartite viruses, have been identified – these occur almost exclusively in tomato and in the Old World. Following the identification of a novel ssDNA satellite (referred to as DNA β) associated with ageratum yellow vein disease [2], the vast majority of begomoviruses previously assumed to be monopartite have been shown to be satellite requiring. The number of begomoviruses species associated with DNA β is likely to increase.

DNA β satellites depend on their helper viruses for replication, movement in plants and, by trans-encapsidation in the coat protein, insect transmission, but share no significant sequence similarity. Since they were first reported in 2000, many DNA βs have been cloned and sequenced (>100 full-length sequences are available in databases). Analysis of their diversity has shown that they group both by host and geographical origin (Figure 1). The most prominent division of DNA β molecules is into those originating from species within the *Malvaceae* and those originating from non-malvaceous hosts. DNA β satellites have a highly conserved structure consisting of a single conserved (in both sequence and position) open reading frame (termed βC1), a sequence highly conserved between all DNA βs [the satellite conserved region (SCR)] and a region of sequence rich in adenine [3]. Recent studies have addressed the evolution of new complexes and elucidated the role of DNA β in viral pathogenicity [4–7].

βC1 is a symptom and pathogenicity determinant

The monopartite begomoviruses that require DNA β are characteristically able to infect their hosts in the absence of the satellite but induce either no, or mild or atypical symptoms and with low virus titers [2,8]. This finding suggested that DNA β has a role in pathogenicity, an unusual feature for a satellite. The work of three groups has shown this phenomenon to be mediated by βC1 [4–7]. The βC1 of distinct satellites were shown to induce virus-like symptoms expressed either transiently or as a stably integrated transgene, demonstrating that, for begomovirus-satellite complexes, the satellite determines pathogenicity and symptom phenotype. This provided an explanation for the observation that distinct begomoviruses interacting with the same satellite induce identical symptoms [9].

βC1 is a suppressor of gene silencing

RNA silencing is a ubiquitous plant defense mechanism against viruses and most viruses have been shown to encode factors (suppressors) that are capable of overcoming silencing [10]. Several begomoviruses have been shown to encode suppressors of RNA silencing. Phenomena, such as recovery from infection and synergism, which were described even before the geminiviruses were first identified, have recently been shown to involve modulation of gene silencing-mediated defense [11]. Two begomovirus proteins, the transcription activation protein (TrAP) and AC4, were shown to have suppressor activity that mediates these phenomena. Furthermore, the suppressor activity of these proteins differs significantly between species. Only weak suppressor activity could be demonstrated for the DNA β-associated monopartite begomovirus *Tomato yellow leaf curl China virus*, which was unable to overcome systemic silencing [12]. Instead, the major suppressor of RNA silencing of this virus-satellite complex is encoded on DNA β, specifically by βC1. This work also demonstrated that βC1 binds both double-stranded and ssDNA and localizes to the nucleus. Although the precise mechanism by which βC1 affects the RNA silencing pathway remains unclear, the severe phenotype developed by plants transformed with the βC1 gene, or with dimeric constructs of DNA β molecule, suggest that the protein interferes with normal plant developmental processes. Recently, Padmanabhan

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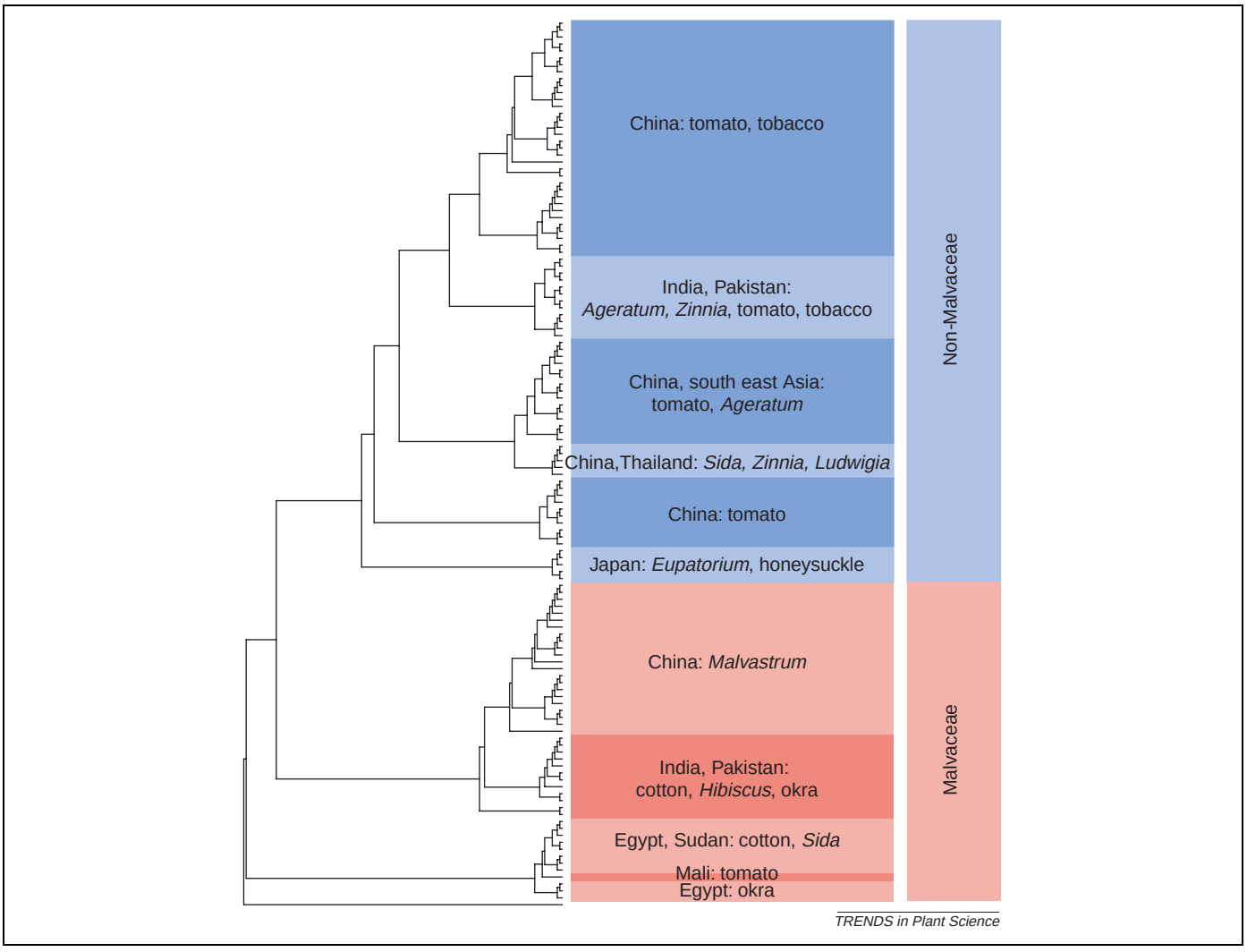

Figure 1. Diversity of begomovirus associated DNA β satellites. The phylogenetic dendrogram is based upon an alignment of all full-length DNA β sequences available in the databases. The tree was rooted on the sequence of a molecule (CLCuD DNA1) of a similar size but sequence unrelated (the lowest branch of the tree). The geographic and host origins of the DNA β molecules are indicated. The two major groups of DNA β molecules, the *Malvaceae* and non-*Malvaceae* types, are shown in pink and blue, respectively.

Chellappan *et al.* [13] demonstrated that the silencing suppressing AC4 protein of a bipartite begomovirus binds microRNAs (miRNAs): noncoding RNAs that, at the post-transcriptional level, negatively regulate target mRNAs involved in development [14]. It is likely that βC1 similarly can affect the miRNA pathway, possibly before it splits from the small interfering (si)RNA pathway that mediates RNA silencing. If this proves to be the case, it would be a major difference between DNA βs and satellite RNAs, the majority of which do not encode proteins and probably influence symptoms by directing RNA silencing against physiologically important host genes [15].

Diverse begomoviruses interact with DNA β

In contrast to the interaction of DNA B components with their cognate DNA A, which is highly specific, the interaction of DNA β components with their helper begomoviruses is much less stringent. For example, *Ageratum yellow vein virus* (AYVV) is able to interact with the majority of DNA βs, at least in the experimental host *Nicotiana benthamiana*. Keith Saunders *et al.* [16] have shown that the AYVV associated DNA β can interact with the DNA A of the bipartite Sri Lankan cassava mosaic virus in the natural host of AYVV, the widely occurring weed *Ageratum conyzoides*. This was an important demonstration of the determinative nature of DNA β with regards symptoms phenotype: the infected plants showing typical yellow vein disease symptoms. More significantly, Barbara Alberter *et al.* [17] have shown that the monopartite begomovirus *Tomato leaf curl virus* (ToLCV) can interact with the DNA β associated with cotton leaf curl disease originating from the Indian subcontinent. ToLCV occurs in Australia, a continent with low diversity of begomoviruses (only ToLCV has been reported) and from which DNA β has, to date, not been reported. The molecular basis for the promiscuity of DNA β components remains obscure. For ToLCV and its satellite (a defective non-symptom modulating molecule derived from DNA β), initiation of DNA replication does not to require high-affinity binding of the virus-encoded, rolling-circle replication initiator protein to recognition sequences within the origin of replication [18], in contrast to all other geminiviruses investigated where such an interaction is essential [19]. It remains to be established whether this is also the case for initiation of DNA replication for DNA βs and their helper begomoviruses.

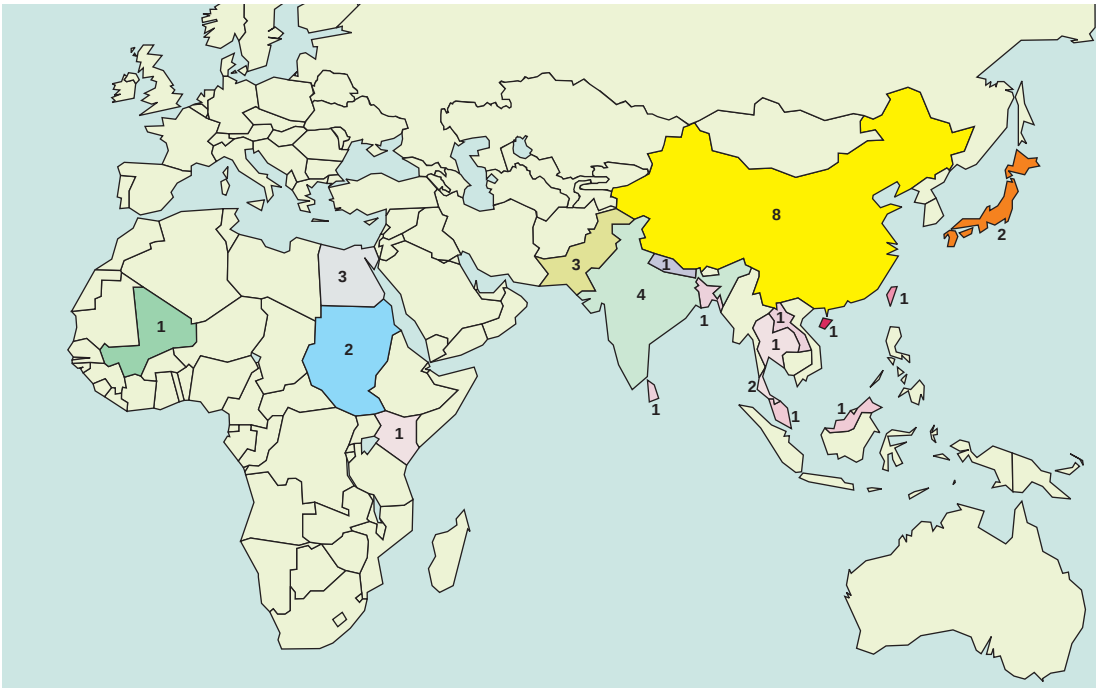

Figure 2. Geographic distribution of satellite DNA β-associated begomovirus disease complexes. Countries in which complexes have been identified, and the approximate numbers of distinct DNA β identified in each country, are indicated.

The origins of DNA β remain obscure, most likely they were 'captured' from another group of as yet unidentified or extinct viruses: a mechanism that resulted in the association of a second group of molecules (referred to as DNA 1) with begomovirus complexes (having been 'captured' from a nanovirus). That such complexes have been around for some considerable time is illustrated by the earliest description of the symptoms of a plant virus that were probably describing the infection of *Eupatorium makinoi* by the eupatorium yellow vein disease begomovirus complex [20]. The present limited geographic distribution of DNA βs (Figure 2), the center of diversity of which appears to be in southern Asia, is consistent with an origin (capture by a begomovirus) in Asia and subsequent divergence and geographical spread eastwards to Japan and westwards through the Middle East to northern and central Africa. They did not come to our attention in these areas until intensive agriculture (monoculture) and susceptible crops and varieties, such as tomato and tetraploid cotton species, were introduced. The large numbers of begomovirus complexes identified in all major dicot crops and the increasing global trade in produce means that no region is immune from them and that greater efforts to control their spread need to be made.

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Erratum

Erratum: Chromosomal histone modification patterns – from conservation to diversity

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In the review article by Jörg Fuchs, Dmitri Demidov, Andreas Houben and Ingo Schubert in the April issue of *Trends in Plant Science* [Fuchs, J. *et al.* (2006) Chromosomal histone modification patterns – from conservation to diversity. 11, 199–208], '*Saccharomyces pombe*' in paragraph 3 and in Table 1 should read '*Schizosaccharomyces pombe*'. We apologize to the authors and to our readers for this error.

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