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No to Neocosmospora: Phylogenomic and Practical Reasons for Continued Inclusion of the *Fusarium solani* Species Complex in the Genus *Fusarium*

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**ABSTRACT** This article is to alert medical mycologists and infectious disease specialists of recent name changes of medically important species of the filamentous mold *Fusarium*. *Fusarium* species can cause localized and life-threatening infections in humans. Of the 70 *Fusarium* species that have been reported to cause infections, close to one-third are members of the *Fusarium solani* species complex (FSCS), and they collectively account for approximately two-thirds of all reported *Fusarium* infections. Many of these species were recently given scientific names for the first time.
by a research group in the Netherlands, but they were misplaced in the genus *Neocosmospora*. In this paper, we present genetic arguments that strongly support inclusion of the FSSC in *Fusarium*. There are potentially serious consequences associated with using the name *Neocosmospora* for *Fusarium* species because clinicians need to be aware that fusaria are broadly resistant to the spectrum of antifungals that are currently available.

**KEYWORDS** clinical mycology, evolution, fungi, phylogenetics, taxonomy

Robust taxonomy facilitates communication and should be cogent and consider the scientific and practical ramifications. As presently circumscribed, the monophyletic genus *Fusarium* comprises over 300 phylogenetically distinct species (i.e., phylospecies) distributed among 23 evolutionary lineages referred to as species complexes (1; D. M. Geiser, A. M. S. Al-Hatmi, T. Aoki, T. Arie, et al., submitted for publication). Over 70 *Fusarium* species distributed among 12 of these complexes have been implicated in mycotic infections of humans and other animals (Fig. 1A) (2, 3). Of these, members of the *Fusarium solani* species complex (FSSC) account for approximately two-thirds of all reported fusarioses and at least 23 of the clinically relevant phylospecies (Fig. 1B). There has been a consensus for over a century that the FSSC is part of *Fusarium*, which was affirmed by molecular phylogenetic analyses (4) and codified in a proposal to recognize *Fusarium* as a monophyletic group that includes the FSSC (5). However, there has been a recent push to divide *Fusarium* into seven genera and specifically to move the FSSC, the most important group of fusarial human pathogens, into the genus *Neocosmospora* (6–8).

In this paper, we demonstrate that these nomenclatural changes were based on the incorrect interpretation of the phylogenetic data regarding the Geiser et al. (5) circumscription of *Fusarium* that includes the FSSC. In addition, these papers published an additional 31 FSSC species and 18 new combinations under the genus *Neocosmospora* (7, 8). A new 19-locus phylogeny, however, removes all doubt about inclusion of the FSSC in a taxonomically sound and historically consistent concept of *Fusarium* (Geiser et al., submitted). Thus, Aoki et al. (9) recombined these species in *Fusarium*, as the more robust phylogeny reaffirmed the Geiser et al. (5) circumscription of *Fusarium*. Here, we correct the record and argue that support for inclusion of the FSSC in *Fusarium* is more definitive than ever. We also cite concerns of medical mycologists if human-pathogenic fusaria are unnecessarily fragmented into multiple genera and urge continued use of the genus name *Fusarium* for human pathogens in the FSSC, along with the *F. dimerum* and *F. ventricosum* species complexes (10).

Fusarial infections most frequently encountered in healthy individuals include onychomycoses and keratitis; the latter often occurs after a traumatic introduction to the eye or is associated with soft contact lens wear (11). *Fusarium* keratitis outbreaks that occurred in 2005 and 2006 in the United States, Singapore, and Hong Kong were associated with the use of Bausch & Lomb’s ReNu with MoistureLoc contact lens solution (12, 13). The finding that most of these infections were caused by FSSC species/multilocus sequence types (MLSTs) that are common in and apparently adapted to plumbing systems (14) suggests that patients inadvertently contaminated their contact lenses through poor hygiene. Though relatively rare compared to invasive candidiasis and aspergillosis (15), fusaria can cause life-threatening disseminated opportunistic infections in persistently neutropenic immunocompromised and immuno-suppressed patients (16). Mortality among this patient population is high because fusaria are resistant to the broad spectrum of antifungals currently available and dissemination frequently occurs (17). Successful treatment of these patients often requires antifungal drug combinations in addition to the patient recovering from neutropenia (18).

Prior to the introduction of MLST-based diagnoses and recognition of phylospecies based on genealogical exclusivity (19), mycoses caused by members of the FSSC were typically reported as *F. solani* (20), due to a lack of diagnostic micromorphological
characters among FSSC species. The first robust MLST-based species-level studies on the FSSC, however, revealed two important facts: (i) the FSSC comprises at least 45 phylospecies distributed among three clades and (ii) all of the clinically relevant species were nested within clade 3, one of three major evolutionary subgroups that comprise the FSSC (21, 22). Because Latin binomials were not available for most of the species, Chang et al. (12) adopted an ad hoc species/multilocus haplotype nomenclature for the FSSC, in which species and multilocus haplotypes were distinguished, respectively, by Arabic numerals and a lowercase Roman letter. This informal nomenclature was subsequently extended to 35 species in FSSC clade 3 (e.g., FSSC 2-d denotes haplotype d of *F. solani* species complex undescribed species 2) to facilitate accurate communication within the clinical microbiological and phytopathological scientific communities (22).

FIG 1 (A) Partitioned maximum likelihood bootstrapped (ML-BS) phylogeny of *Fusarium* inferred from exonic sequences of 19 housekeeping genes totaling 54.99 kb; 20.3 kb of characters were parsimony informative characters (PIC). The phylogram was rooted on sequences of two outgroup species, *Beauveria bassiana* and *Trichoderma brevicaespum*. Evolutionary relationships among the 12 species complexes that contain clinically relevant fusaria were completely resolved based on ML-BS values between 91 and 100%. The node identified by F1, which represents the generic limits of *Fusarium*, received 100% ML-BS support based on 5,000 pseudoreplicates of the data conducted with IQ-TREE (27). (B) ML-BS phylogeny of clade 3 of the *Fusarium solani* species complex (FSSC) inferred from portions of three loci (TEF1, RPB2, and the internal transcribed spacer [ITS] ribosomal DNA [rDNA]). All 23 species implicated in fusarioses of humans and other animals are nested in FSSC clade 3. Numbers on nodes represent ML-BS support based on 5,000 pseudoreplicates of the data. FSSC numbers in brackets represent the ad hoc nomenclature previously used to distinguish species (22). T, ex-type strains; IT, ex-isotype strain; NT, ex-neotype strain.
Following the work of Short et al. (23), where names were assigned to two of the most important human-pathogenic FSSC species, *F. petroliphilum* (FSSC 1) and *F. keratoplasticum* (FSSC 2), Sandoval-Denis and Crous (7) and Sandoval-Denis et al. (8) provided names and types for almost all of the remaining phylogenetically diagnosable species. However, these species were described under the name *Neocosmospora*. These authors went to great lengths to promote the use of this genus name but with arguments that either fail to address or inaccurately represent the work of O’Donnell et al. (4) and Geiser et al. (5). In addition, they recombined species originally described in *Fusarium* in this teleomorphic genus, thus promoting a *de facto* dual nomenclature that obscures the fact that *Neocosmospora* is nested phylogenetically within a monophyletic *Fusarium* (5, 24; Geiser et al., submitted). There are potentially serious consequences associated with this because clinicians need to be aware that these fungi are broadly resistant to the spectrum of antifungals that are currently available (25). An identification as *Neocosmospora* would thus fail to connect a case to this crucial knowledge, thereby disregarding the valuable clinical information that distinguishes it from an identification as *Fusarium*. Therefore, we are strongly opposed to this taxonomy because it will confuse stakeholders and may have negative ramifications in clinical microbiology and medicine.

The present article and a companion submission to *Phytopathology* (Geiser et al., submitted) are nearly unanimously supported by the global *Fusarium* research community. Here, we set the record straight by pointing out that the justification of Sandoval-Denis and Crous (7) for describing members of the FSSC as *Neocosmospora* was based on four errant conclusions (i to iv below).

**Errant conclusion i.** The molecular phylogenetic circumscription of *Fusarium* in the work of Geiser et al. (5) and, by extension, of O’Donnell et al. (4) is polyphyletic.

**Response.** The claim that the Geiser et al. (5) delimitation of *Fusarium* is polyphyletic is not supported by published data. Indeed, we know of no published data that even suggests this conclusion. The monophyletic circumscription of *Fusarium* presented by Geiser et al. (5) was based on a two-locus phylogeny published by O’Donnell et al. (4); similar clades have been resolved in many other publications (e.g., the “Terminal *Fusarium* Clade” [26]), including that of Lombard et al. (6). In fact, Geiser et al. (5) conservatively and critically evaluated the phylogeny presented in the work of O’Donnell et al. (4), which was based on sequences of the largest (*RPB1*) and second-largest (*RPB2*) RNA polymerase II subunit genes, to ensure that the delimitation of *Fusarium* was robustly connected to a monophyletic group. Two nodes in the *RPB1/RPB2* tree (named F1 and F2) were identified as potential taxonomic hypotheses for *Fusarium*, with F1 better representing longstanding use but receiving inferior statistical support compared to that of F2. It is important to note that both F1 and F2 included the FSSC, but F2 excluded the two most basal lineages (i.e., the *F. dimerum* and *F. ventricosum* species complexes). The Geiser et al. (5) hypothesis provisionally retained these species complexes in *Fusarium* (hypothesis F1 in Fig. 1A) until their inclusion or exclusion could be assessed by a more robust comparative phylogenomic data set.

The 19-gene phylogeny recently presented in the paper of Geiser et al. (submitted) and presented here in modified form (Fig. 1A) is such a data set. Both the F1 and F2 taxonomic hypotheses from Geiser et al. (5) received strong statistical support (i.e., 100% maximum likelihood [ML] bootstrap) in the 19-gene analysis. Details of the partitioned ML phylogenetic analysis of the 55.1-kb 19-gene data set conducted with IQ-TREE (27) are presented in the paper by Geiser et al. (submitted) and illustrate the power of comparative phylogenomics for discovering novel phylogenetically informative marker loci. In summary, the phylogenetic uncertainty openly considered by Geiser et al. (5) has been resolved in support of a taxonomic concept for *Fusarium* that includes the FSSC, consistent with longstanding use by medical mycologists and phytopathologists.

**Errant conclusion ii.** Segregation of the FSSC as *Neocosmospora* represents a “more natural classification.”
Response. The term "natural classification" means that all members of a taxon share an ancestor; in other words, they should be monophyletic. Based on our response to errant claim i, *Fusarium*, inclusive of *Neocosmospora*, is monophyletic. The claim that separation of *Neocosmospora* from *Fusarium* represents a more natural classification is without merit because the concept of *Fusarium* that includes the FSSC is defined based on its monophyly, and monophyly is the principal criterion for taxon recognition in modern taxonomy. Even prior to the demise of the dual nomenclature system on 1 January 2013, when teleomorph genera had taxonomic priority, the FSSC had a longstanding taxonomic place within *Fusarium*, with virtually no controversy among stakeholders, especially among medical mycologists and plant pathologists. Certainly, there is great value in continuing to recognize the >90 species in this clade as the “*Fusarium solani* species complex,” representing its status as a distinct clade within a monophyletic *Fusarium*, and maintaining continuity of use. In contrast, use of “*Neocosmospora*” creates an unnecessary communication barrier between the FSSC and over a century of *Fusarium* research. Also note that because *Fusarium* was typified close to a century before *Neocosmospora* (1809 versus 1899), the name *Fusarium* has nomenclatural priority (https://www.iapt-taxon.org/nomen/pages/main/art_11.html).

*Fusarium* is by far the most widely used name applied to the FSSC, as reflected by a simple Google search. “*Fusarium solani*” received 100 times more hits than “*Neocosmospora*” (~3,190,000 to ~31,600; search conducted 27 May 2020). The longstanding status of the FSSC in *Fusarium* has also been reinforced by annual *Fusarium* educational workshops offered around the world since the 1970s, in particular, the Fusarium Laboratory Workshop (28) and the Tropical *Fusarium* Workshops. Highlighting the natural connection between the FSSC and *Fusarium*, in both of these workshops, the FSSC and *F. oxysporum* species complex (FOSC, which Lombard et al. [6] retains in *Fusarium*) are presented in tandem due to the ecological, genomic, morphological, and clinical connections that exist between these two groups.

Errant conclusion iii. Substantial molecular evidence indicates *Fusarium* and *Neocosmospora* are not congeneric.

Response. Absolutely nothing has been published to date to suggest that “*Neocosmospora*” is not nested phylogenetically within *Fusarium* as we define it (4) (Fig. 1). This unassailable fact reflects the central logic of the Geiser et al. (5) taxonomic hypothesis. Lombard et al. (6) hypothesize that *Fusarium* and *Neocosmospora* are two equally ranked clades within a broader clade consisting of at least seven genera, all of which have an established taxonomic history as *Fusarium* species. These competing hypotheses are supportable by the same phylogenetic evidence but are readily distinguished based on their relative practical merits. In fact, the phylogeny can be used as the basis for any number of taxonomic hypotheses within node F1 (Fig. 1A), either as a single genus as it has been treated for over a century, as seven genera, or as potentially dozens of genera.

Errant conclusion iv. Support of the *Fusarium* research community for the Geiser et al. (5) conservation of *Fusarium* in a way that includes the FSSC, with its adherents referred to as “some researchers,” has been understated.

Response. To the contrary, 66 scientists from 16 different countries spanning 6 continents, representing virtually all of the world leaders in *Fusarium* research and the disciplines of medical mycology, plant pathology, molecular biology and genomics, mycotoxicology, and other fields, coauthored Geiser’s proposal to circumscribe a monophyletic *Fusarium* such that it preserves longstanding use (5) (Fig. 1). Now that there is overwhelming statistical support for hypothesis F1 (Fig. 1A), the Geiser et al. (5) circumscription of *Fusarium* will gain even more support from end users.

Just prior to the demise of dual nomenclature, two scholarly studies opened the door to dividing *Fusarium* along teleomorph lines (26, 29), using competing genus names that would require breaking *Fusarium* up into at least seven genera. However, both studies also referred to the clade associated with the F1 node as “The Terminal *Fusarium* Clade” (italics theirs), raising the question, “Why did they use that name if that
clade represented something other than the ideal circumscription of *Fusarium*? These papers also presented phylogenetics that provided a framework for a monophyletic *Fusarium* that includes the FSSC, as presented here. The FSSC is an integral part of FUSARIUM-ID (30; http://isolate.fusariumdb.org/blast.php) and *Fusarium* MLST (31; http://fusarium.mycobank.org/), two websites dedicated to identification of fusaria via the Internet. We urge the people who maintain these sites to respect the will of the *Fusarium* community and retain the FSSC in *Fusarium* and their databases. Formal recombinations of the newly proposed *Neocosmospora* names in *Fusarium* were registered in *Index Fungorum*, where they are now validly published (9; Geiser et al., submitted). In addition, we updated our nucleotide accessions in GenBank to reflect the current taxonomy.

End users will ultimately decide what names to use for these fungi (32), and we urge the clinical microbiological community to continue to refer to these etiological agents by their *Fusarium* binomials (see clade 3 in Fig. 1B for binomials of the 23 FSSC members of clinical relevance) or as a member of the FSSC when an identification is made only to the species complex level (33). Using the name “*Neocosmospora*” obscures rather than facilitates communication among basic and applied scientists and regulatory agencies in medicine and agriculture by promoting a taxonomy governed by *de facto* dual nomenclature. When infectious disease specialists need to access clinically relevant literature to manage fusarial infections, they will need to use “*Fusarium*” or “fusariosis,” not “*Neocosmospora*” or “neocosmosporosis,” as the search terms. With 191,000 Google hits (search conducted on 27 May 2020), fusariosis is well embedded in the medical/clinical literature, whereas “neocosmosporosis” failed to recover even a single clinically relevant record. Applying the work of Hawksworth (34) to this case, the name “*Fusarium*” is crucial for accessing the accumulated knowledge in clinical, medical, and other scientific literature.

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