A review of German *Scedosporium prolificans* cases from 1993 to 2007

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*Scedosporium prolificans* is one of the most life-threatening fungal opportunistic pathogens due to its high resistance to common systemic antifungal agents. While a close relative of *Pseudallescheria boydii*, *S. prolificans* has a more limited geographic range being primarily found in Australia, USA and Spain. Infections have also been reported from several other European countries and from Chile. Twenty patients with *Scedosporium prolificans* infection or colonization from August 1993 to May 2007 were retrospectively reviewed in Germany. They had been identified at or reported to the Reference Laboratory for *Pseudallescheria Scedosporium* spp. in Berlin. Twelve of 13 patients with haematological disorders and/or on immunosuppressive therapy developed a fatal invasive scedosporiosis. Colonization of the respiratory tract was reported for one patient after heart-lung transplantation, all six patients with cystic fibrosis and one with chronic sinusitis. Molecular studies of the *S. prolificans* isolates confirmed that parts of the 18S, the Internal Transcribed Spacer (ITS) regions and the D1/D2 domain of the 28S region of rDNA are monomorphic. However, sequencing of parts of the translation elongation factor EF1-alpha (EF-1α) and the chitin synthase (CHS-1) genes revealed the presence of three and two distinct genotypes, respectively. Two informative mutations were found in EF-1α and a single nucleotide exchange in the CHS-1 gene.

**Keywords** *Scedosporium prolificans*, ITS, D1-D2 sequencing, genotype, translation elongation factor EF-1a, chitin synthase CHS-1, in vitro-susceptibility

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**Introduction**

*Scedosporium prolificans* Guého & de Hoog (formerly *Lomentospora prolificans* Hennebert & Desai and *Scedosporium inflatum* Malloch & Salkin), an emerging pathogen, is highly resistant to antymycotic agents [1,2].

Due to its dark conidia, it is considered to be the most common agent of disseminated phaeohyphomycosis [3]. The fungus is a member of the order Microascales and more specifically of the *Pseudallescheria/Scedosporium* species complex [4]. In contrast to the more common species *Pseudallescheria boydii* and *Scedosporium apiospernum*, *S. prolificans* has a somewhat more limited geographic distribution. According to current knowledge, the organism is distributed mainly in Australia, USA and Southern Europe, especially in Spain [5–10]. This geographic presence suggests an association with semi-arid climates. It is more rarely reported from other European countries, e.g., France [11], UK [12], Germany [13], The Netherlands [14], as well as from Chile [15].

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Given the emergence of this fungus in temperate climates, we conducted a review of the recovery of *S. prolificans* in Germany over a 14 year-period. An epidemiological typing system was developed by multilocus sequencing studies and the *in vitro* antifungal susceptibility of the strains was analyzed.

**Material and methods**

**Case reports**

Each case report associated with *Scedosporium prolificans*, documented at the Reference Laboratory for *Pseudallescheria boydii / Scedosporium prolificans* at the Robert Koch Institute in Berlin, Germany, was retrospectively evaluated. If possible, patients were analysed for: (1) their underlying disease, (2) the origin of the isolate, (3) the clinical relevance of *S. prolificans* (colonization versus infection), (4) whether the patient was already under antifungal treatment, (5) therapeutic strategies after identification of *S. prolificans*, and (6) clinical outcome. Infection was defined by the recovery of *S. prolificans* from a sterile body site of a patient who developed clinical symptoms compatible with a deep seated fungal infection and/or histopathologically proven hyphomycosis. Isolation of *Scedosporium prolificans* from only the respiratory tract (sputum, sinus maxillaris), without any histologically proven hyphomycosis, was defined as colonization.

**Strains**

All clinical isolates were identified on the basis of macro- and micromorphological criteria, temperature maxima, cycloheximide susceptibility [16] and by PCR with species-specific primers [17]. Reference strains from Spain, Belgium, UK, Australia and USA were included in the genotyping studies. Isolates were deposited in the fungal collection at the Robert Koch-Institut, Berlin. Stocks were stored on ceramic beads at −70°C (Microbank, MAST-Diagnostica, Reinfeld, Germany). All available isolates have also been studied by amplification and sequencing of parts of the 18S, the ITS regions and the D1/D2 domain of the 28S rDNA, the chitin synthase (CHS-1) and the translation elongation factor 1-alpha (EF-1α) [18] in order to determine diversity within the species, as well as their potential value in genotyping.

**DNA extraction**

Mycelia (approximately 50 mg, wet weight) were homogenized in 300 μl of cetyltrimethylammoniumbromide (CTAB) buffer containing glass beads (0.45–0.50 mm in diameter; B. Braun, Melsungen, Germany) as previously described [17]. After 15 min of sonication in a water bath, followed by an incubation step at 65°C for 10 min, then 300 μl ethanol were added and samples were homogenized by vortexing. Total DNA was purified on silicagel columns (Qiamp Mini Kit, Qiagen, Hilden, Germany), according to the manufacturer’s instructions and stored at −20°C.

**Amplification**

Fragments of rDNA were amplified with the primer pairs NS7-ITS2, ITS4-ITS5 [19], ITS3-R635 and F63-R635 [20], EF 1-728 F [CAT CgA gAA gTT CgA gAA gg] and EF 1-986 R [TAC TTg AAg gAA CCC TTA CC] and CHS-79 [Tgg ggc AAg gAT gCT Tgg AAg AAg] and CHS-354 [Tgg AAg AAC CAT CTg TgAg gAg TTg] [18] in a reaction mixture containing 25 μl distilled water, 5 μl of PCR buffer (MgCl2, 10 ×), 8 μl 0.25 mM dNTP (Roche Diagnostics GmbH, Germany), 1 μl of each primer and 1.25 U of Taq BioTherm DNA polymerase (Rapidozym, Germany). The PCR reaction (in brackets for the amplification of the translation elongation factor EF1-α and CHS-1) started with an initial denaturation step at 96°C, 5 min (95°C, 10 min) followed by 30 cycles 96°C, 30 s (35 cycles 95°C, 15 s); 52°C, 30 s (55°C, 20 s); 72°C, 75 s (72°C, 60 s). The last elongation step at 72°C was prolonged with 3.5 min (5 min).

**DNA sequencing**

The amplified products were purified by QIAquick Gel Extraction Kit (Qiagen). Direct sequencing was performed with an ABI PRISM 3130 XL Sequencer (Applied Biosystems).

Sequences obtained were aligned with the computer program BioEdit sequence alignment editor version 7.0.5.

**Antifungal susceptibility testing**

Susceptibility testing was performed according to Clinical and Laboratory Standards Institute methods [21]. The combined effects of voriconazole/terbinafine and voriconazole/caspofungin were studied by a checkerboard microdilution method with 17 and 15 isolates, respectively. Briefly, the spore suspensions were adjusted spectrophotometrically to yield a final inoculum of 1 × 10⁴ to 5 × 10⁴ CFU/mL. Testing was done in 0.165 M MOPS-buffered RPMI medium (pH 7.0) in microtiter plates, incubated at 35°C for 48 h. Final concentrations ranged from 0.03–16 μg/ml for voriconazole and from 0.25–16 μg/ml for terbinafine and for caspofungin.
caspofungin. MIC studies were conducted in duplicate, with at least one rerun. Results were read visually with the help of a reading mirror by two laboratory persons acting independently of each other.

MICs of voriconazole and terbinafine were defined as the lowest concentrations that completely inhibited growth (score of 0, growth inhibition of 100%). A partial inhibition (score of ≤2, growth inhibition greater than or equal to 50%) was considered for the MIC of caspofungin. For comparison with published data and for antifungal combinations, a score of ≤2 was also used. The combination effects were calculated by the fractional inhibitory concentration index (FIC-Index) [22] and interpreted according to Odds: ≤0.5 synergy, >0.5-4.0 no interaction and >4.0 antagonism [23].

Results

Patients

Twenty *S. prolificans* positive patients were identified and/or registered at the Reference Laboratory (Table 1) from 1993 to 2007. Thirteen out of the 20 patients had a hematologic malignancy and/or underwent bone marrow or solid organ transplantation or received long-term corticosteroids. Twelve of these 13 patients developed proven invasive fungal infections, 8 of which involved fungemia. Ten of the patients died of sepsis or two others died as a result of their underlying diseases associated with their disseminated fungal infections. The lungs of one patient who underwent heart-lung transplantation seven years prior to the present studies were colonized with *S. prolificans* for nearly three years, but without the development of proven infection. He died after the development of a motile thrombus in the heart from a non-sclerotic cardiac infarction. Colonization of the respiratory tract was noted with all 6 CF patients and one with chronic sinusitis. In some patients with CF, *S. prolificans* was isolated once, while in others it was repeatedly recovered without signs of invasive infections. The longest period of colonization as revealed by repeated isolation of the fungus from the respiratory tract was 3 years. Instances of locally invasive infections due to *S. prolificans* were not found in our CF-patients. Diagnosis of sepsis in the patients was made by positive blood culture in 8/12 (66%) of the patients with proven invasive fungal infection and in 50% of them this occurred less than a week before death.

Molecular results

A total of 35 isolates (23 clinical isolates from 18 patients in Germany and 12 reference strains, Table 2) were included in these investigations. Analysis of sequences of nearly 1,500 basepairs (bp) from the 11 terminal regions of the SSU, the ITS 1, 5.8S and ITS 2 regions to the D1/D2 domain of LSU rDNA were monomorphic for all isolates. The alignment of the 326 to 328 bp long sequences of an intron of the translation elongation factor EF-1α revealed three clusters (genotypes). The first type, EF-1α A, differed from type EF-1α B by 2 nucleotide exchanges (C/T) and (T/G) at position 104 and 233 and from type EF-1α C by 5 nucleotide exchanges at five different positions (28, 48, 82, 247-8 and 266). The nucleotides C at position 104 and T at position 233 were specific for genotype EF-1α B. Type EF-1α A was associated with 9 German patients, 4/6 reference strains from Spain, as well as in WCH 07-201141 from Australia and CBS 114.90 from the USA. Type EF-1α B was found in 8 German patients, as well as in the *S. prolificans* type strain CBS 467.74 from Belgium, FMR 6643 from Spain, NCRI 7685 from the UK and WCH 07-201137 from Australia. Type EF-1α C was found in isolates from another 4 German patients, as well as in FMR 6641 from Spain and WCH 07-327433 from Australia. Genotypes were identical in sequential isolates from the same patient, i.e., three from one patient and four isolates from one patient. The alignment of 254 bp long sequences of the chitin synthase gene (CHS-1) revealed a single nucleotide exchange (C instead of T) at position 27, which was detectable in three isolates from Germany, one from Australia, and the one from USA, but not in isolates from Spain (Table 2). The nucleotide sequences of each EF-1α genotype and of the two CHS-1 genotypes (CHS-1 A and CHS-1 B) were deposited in GenBank (Accession numbers EU596512-EU596513-EU596514 and FJ179541-FJ179542).

In-vitro susceptibility testing

Ranges of MICs (µg/ml) as score 0 (score of ≤2 in brackets) were 16 to >16 (2 to 16) for voriconazole, 8 to >16 (2 to >16) for terbinafine and (4 to >16) for caspofungin. Synergy of voriconazole and terbinafine was observed in 11/17 (65%) of the isolates but no interaction was observed in the remaining 6/17 (35%) isolates. Using the score of ≤2, synergy increased to 82% (14/17) and indifference (no interaction) was seen in 18% of the isolates. The voriconazole MIC (score of ≤2) of three isolates was 2 µg/ml, whereas the geometric mean MIC of voriconazole against the other
14 isolates was 5.1 µg/ml (data not shown). The highest synergistic effect of voriconazole plus terbinafine was noticed in the three isolates with the lowest MIC. For the combination of voriconazole and caspofungin, synergy was found in only 2/15 isolates (13%), independently from the endpoint used (score of 0 or ≤2). Antagonism was not observed in any of the combinations.

**Discussion**

Since 1993, reports have documented the importance of *Scedosporium prolificans* as the cause of life threatening hyphomycosis in the temperate climate of Germany. Development of an infection after exposure to *S. prolificans*, as with other opportunistic fungi, clearly depends on the immunological status of the host. As published previously, *S. prolificans* may colonize the respiratory tract for months or even years, especially in patients with cystic fibrosis (CF) [10,24,25], without becoming invasive. This colonization can be transient, as noted in two of our patients, not requiring antifungal therapy. Neither the CF patients nor the patient with chronic sinusitis developed a scedosporiosis. Nevertheless the risk of developing an infection after long term colonization by *S. prolificans* cannot be excluded.

Abbreviations: AIDS, acquired immunodeficiency syndrome; AMB, amphotericin B; AML, acute myelogenous leukemia; BAL, bronchoalveolar lavage; BMT, bone marrow transplantation; CAS, Caspofungin; CF, cystic fibrosis; CML, chronic myelogenous leukemia; FLZ, fluconazole; HLTX, heart-lung transplantation; ITZ, itraconazole; LTX, lung transplantation; MCZ, micafungin; PCZ, posaconazole; RTX, renal transplantation; TRB, terbinafine; TS, tracheal secretion; VCZ, voriconazole.

*This case report has been published [13].
### Table 2: Analyzed strains, their genotypes and geographical origin

<table>
<thead>
<tr>
<th>First isolation of <em>S. prolificans</em></th>
<th>Patient No.</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Underlying disease</th>
<th>Site of isolates</th>
<th>Clinical manifestation</th>
<th>Antifungal treatment before isolation of <em>S. prolificans</em></th>
<th>Antifungal treatment after isolation of <em>S. prolificans</em></th>
<th>Outcome following diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1993</td>
<td>1</td>
<td>54, F</td>
<td>RTX</td>
<td>Blood</td>
<td>Blood</td>
<td>Fever, pneumonia, sepsis, skin</td>
<td>None</td>
<td>AMB liposomal + 5FC; MCZ</td>
<td>Died d 9</td>
</tr>
<tr>
<td>1993</td>
<td>2</td>
<td>52, M</td>
<td>AML</td>
<td>Sepsis, skin biopsy</td>
<td>Skin biopsy</td>
<td>Sinusitis maxillaris, disseminated skin lesions</td>
<td>FLZ, AMB + 5-FC</td>
<td>none</td>
<td>Died d 1</td>
</tr>
<tr>
<td>1994</td>
<td>3</td>
<td>53, F</td>
<td>AML</td>
<td>Blood (5x)</td>
<td>Blood</td>
<td>Pneumonia, sepsis, endophthalmitis, skin</td>
<td>AMB + 5FC</td>
<td>AMB + 5FC</td>
<td>Died d 7</td>
</tr>
<tr>
<td>1995</td>
<td>4*</td>
<td>60, M</td>
<td>AIDS, Burkitt lymphoma</td>
<td>Brain</td>
<td>Sepsis (lung, spleen, kidney, heart, cerebrum)</td>
<td>Colonized 54 month</td>
<td>FLZ 100 mg</td>
<td>diagnosis post mortem</td>
<td>Died</td>
</tr>
<tr>
<td>2000</td>
<td>5</td>
<td>20, F</td>
<td>HLIX</td>
<td>Sputum</td>
<td>Sputum</td>
<td>Colonized 34 month</td>
<td>ITZ, AMB per inhalation</td>
<td>AMB per inhalation, VCZ</td>
<td>Died of cardiac infarction</td>
</tr>
<tr>
<td>2000</td>
<td>6</td>
<td>61, F</td>
<td>Long term corticosteroids</td>
<td>TS, blood</td>
<td>Fever, pneumonia, multi organ failure</td>
<td>Colonized</td>
<td>AMB per inhalation, VCZ</td>
<td>Died of cardiac infarction</td>
<td></td>
</tr>
<tr>
<td>2001</td>
<td>7</td>
<td>15, M</td>
<td>CF</td>
<td>Sputum</td>
<td>Sputum</td>
<td>Sepsis, endophthalmitis</td>
<td>Colonized</td>
<td>AMB per inhalation, VCZ</td>
<td>Died d 5</td>
</tr>
<tr>
<td>2001</td>
<td>8</td>
<td>15, M</td>
<td>CF</td>
<td>Sputum</td>
<td>BAL, urine, catheter, blood</td>
<td>Pneumonia, sepsis</td>
<td>FLZ, CAS</td>
<td>none</td>
<td>Died d 5</td>
</tr>
<tr>
<td>2002</td>
<td>9</td>
<td>44, F</td>
<td>CML, BMT</td>
<td>Sputum</td>
<td>Routine CF screening</td>
<td>Colonized</td>
<td>n.a.</td>
<td>n.a.</td>
<td>S. p. not invasive</td>
</tr>
<tr>
<td>2002</td>
<td>10</td>
<td>12, F</td>
<td>CF</td>
<td>Sputum</td>
<td>Blood</td>
<td>Sepsis, endophthalmitis</td>
<td>Colonized</td>
<td>AMB per inhalation, VCZ</td>
<td>Died d 5</td>
</tr>
<tr>
<td>2003</td>
<td>11</td>
<td>n.a., M</td>
<td>BMT</td>
<td>BAL</td>
<td>Sputum</td>
<td>Sepsis, lung, heart, spleen, kidney</td>
<td>Colonized</td>
<td>VCZ</td>
<td>Died d 5</td>
</tr>
<tr>
<td>2004</td>
<td>12</td>
<td>55, M</td>
<td>AML</td>
<td>Blood</td>
<td>BAL</td>
<td>Sepsis, multi organ failure</td>
<td>Colonized</td>
<td>AMB</td>
<td>Died d 0</td>
</tr>
<tr>
<td>2004</td>
<td>13</td>
<td>40, M</td>
<td>AML</td>
<td>Blood</td>
<td>Blood</td>
<td>Sepsis, multi organ failure</td>
<td>Colonized</td>
<td>AMB</td>
<td>Died d 0</td>
</tr>
<tr>
<td>2004</td>
<td>14</td>
<td>64, M</td>
<td>AML</td>
<td>Blood</td>
<td>Sputum</td>
<td>Sepsis, multi organ failure</td>
<td>Colonized, routine CF screening</td>
<td>AMB</td>
<td>Died d 0</td>
</tr>
<tr>
<td>2005</td>
<td>15</td>
<td>9, M</td>
<td>CF</td>
<td>Sputum</td>
<td>Sputum</td>
<td>Sepsis, multi organ failure</td>
<td>Colonized</td>
<td>AMB</td>
<td>Died d 0</td>
</tr>
<tr>
<td>2005</td>
<td>16</td>
<td>n.a., M</td>
<td>CF</td>
<td>Sputum</td>
<td>Sputum</td>
<td>Sepsis, multi organ failure</td>
<td>Colonized</td>
<td>AMB</td>
<td>Died d 0</td>
</tr>
<tr>
<td>2006</td>
<td>17</td>
<td>10, F</td>
<td>CF</td>
<td>Sputum</td>
<td>Blood</td>
<td>Sepsis, multi organ failure</td>
<td>Colonized</td>
<td>AMB</td>
<td>Died d 0</td>
</tr>
<tr>
<td>2006</td>
<td>18</td>
<td>60, M</td>
<td>Chronic idiopathic myelofibrosis, BMT COPD, LIX</td>
<td>BAL, blood</td>
<td>Sepsis, endophthalmitis</td>
<td>Colonized</td>
<td>AMB, VCZ</td>
<td>Died d 16</td>
<td></td>
</tr>
<tr>
<td>2007</td>
<td>19</td>
<td>47, F</td>
<td>BAL, vitrues body</td>
<td>BAL, LIX</td>
<td>Sepsis, endophthalmitis</td>
<td>Colonized</td>
<td>AMB</td>
<td>Died d 19</td>
<td></td>
</tr>
<tr>
<td>2007</td>
<td>20</td>
<td>18, F</td>
<td>Allergic rhinopathia, sinusitis maxillaris</td>
<td>Sinus maxillaris</td>
<td>Sinusitis maxillaris</td>
<td>None</td>
<td>None</td>
<td>S. p. transient</td>
<td>Died d 19</td>
</tr>
</tbody>
</table>


*Isolates with single nucleotide exchange in the CHS 1 gene (genotype CHS-1 B).*
in this patient population. This was indicated recently in an S. prolificans-infected patient with double lung transplantation (LTX) and GVHD [26], although it was not documented with certainty whether or not the patient had been colonized by S. prolificans prior to LTX. Serological tests to detect S. prolificans specific antibodies are not routinely performed, although they could assist in the diagnosis of allergic bronchopulmonary mycosis and the early detection of an invasive infection due to S. prolificans. The question of whether colonization of the respiratory tract by S. prolificans is a contraindication for lung transplantation in CF patients remains under discussion. One of the reported CF patients (patient 15) developed a dramatic respiratory failure at the same time as the first isolation of S. prolificans after treatment which included voriconazole and terbinafine. This young boy finally developed a fungus ball in the lung, but investigation is still ongoing to identify the infectious agent.

All but one of the patients receiving immunosuppressive therapy developed fatal, disseminated scedosporiosis. Nearly all of them were receiving antifungal treatment, but none received a combination therapy of voriconazole (or posaconazole) plus terbinafine. The short survival period of most of the patients with deep infection is alarming. In eight patients with haematological disorder and documented onset of invasive scedosporiosis, the survival period, on average, was 5.6 days. This observation underlines the need for earlier detection, e.g., with molecular methods.

Fever was one of the main clinical symptoms and was used as an indicator for the collection of blood samples for culture. The high percentage of successful isolation of S. prolificans from blood cultures, as reported previously [6,8], is remarkable when compared to other hyphomycoses. The detection of S. prolificans obviously is nearly unaffected by ongoing antymycotic treatment. Breakthrough Scedosporium infections are frequently found in patients with neutropenia under antifungal prophylaxis [7]. This reflects the extreme resistance of this species to these drugs as opposes other opportunistic hyphomycetes, e.g., P. boydii and S. apiospermum. Scedosporium prolificans is known to be multi-drug resistant, especially to amphotericin B, 5-flucytosine, and most azoles. While there is limited data on the successful treatment of patients with deep seated S. prolificans infection, the combination of voriconazole plus terbinafine appears to be the most effective [27–29]. The in vitro studies of S. prolificans isolates from Germany may underline the recommendation for the use of this therapeutic regimen. Interestingly, three isolates recovered from patients who had not receive prior voriconazole therapy showed their MICs to be significantly lower than those from other patients. The susceptibility of S. prolificans isolates susceptible to voriconazole have been reported rarely [30,31], which suggests that there is a need for further studies on susceptibility and resistance mechanisms of S. prolificans.

Due to inadequate surveillance of systemic fungal infections, an assessment of the incidence of this particular mycosis in Germany is not possible. A recent telephone survey at three University institutes for microbiology with mycological expertise revealed that isolation of S. prolificans is still rare or has never been noticed. However, we have to take into account the fact that about 50% of the clinical isolates arriving at the Reference Laboratory had been sent as 'unidentified hyphomycetes'. Thus one can speculate that S. prolificans is an underdiagnosed in many laboratories or even neglected as a contaminant. Analysis of all clinical Scedosporium isolates at the Reference Laboratory during the period 1993–2007 revealed that 18% of patients were colonized or infected by S. prolificans. In CF patients the rate was even higher, 6/18 (33%) of CF patients at an ambulatory clinic in Muenchen, Bavaria, 2001–2005, being colonized by S. prolificans.

The sequencing results presented here confirm the high homology within S. prolificans, which is known to be highly conserved in the ITS1/2 region [17,32] and the D1/D2 domain of the large rDNA subunit. In contrast, molecular typing by random amplification of polymorphic DNA (RAPD) and PCR-fingerprinting [33] and especially by inter-simple-sequence-repeat polymerase chain reaction [34] revealed so many diverse molecular patterns that the appropriate method for epidemiological studies in S. prolificans is still under discussion. Our data document the existence of different genotypes in Scedosporium prolificans. Three EF-1α genotypes and two CHS-1 genotypes were found in isolates from patients in Germany, Spain and Australia. Until now only one CHS-1 genotype was found in the limited number of Spanish isolates. So far no correlation of these genotypes to the clinical outcome and antifungal susceptibility has been found. Further studies will be necessary to determine if there is a correlation between the CHS-1 genotypes and the geographical origin of the isolates.

The EF-1α genotypes in S. prolificans are distributed on a worldwide basis, similar to the airborne species Aspergillus fumigatus [35]. However, marked differences in regional prevalence of Scedosporium species are observed [10,36] which is probably explained by prevailing environmental conditions. The mechanism of dispersal of S. prolificans and the route of transmission are still poorly understood, since the slimy conidia
are only rarely detected in studies of airborne fungi. In species with low effective dispersal, such as Penicillium marneffei [37] and Fonsecaea species [38], whose conidia are supposed to travel only small distances, populations tend to show regional structuring.

The observation of differing EF-1α and CHS-1 genotypes may be helpful in further epidemiological studies on S. prolificans and especially in the development of a MLST scheme, to explore the question of S. prolificans population structures, as well as species epidemiology.

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