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## INTRODUCTION

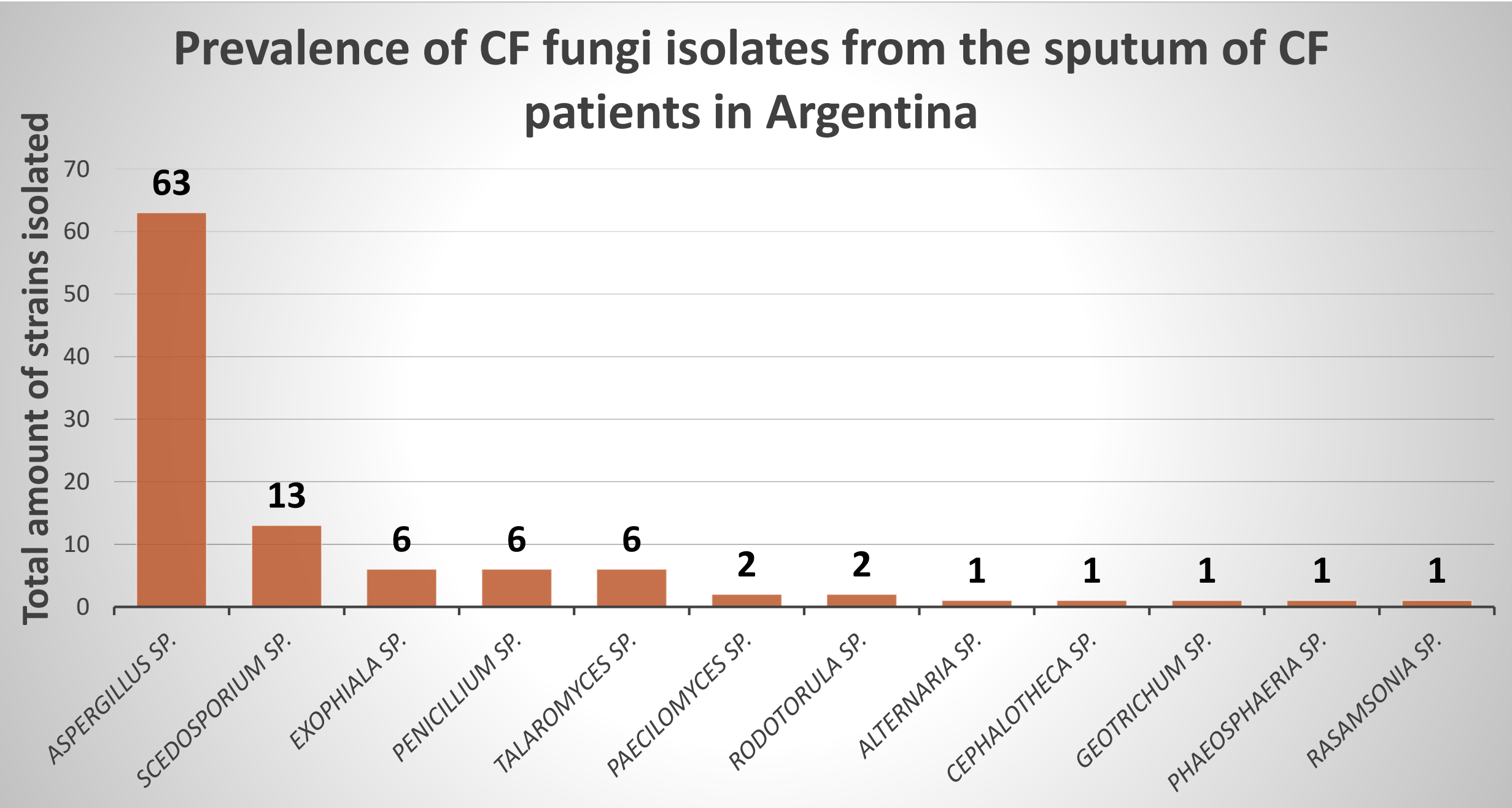
Cystic fibrosis (CF) is the major cause of pulmonary disease in children with an incidence of 1/2,000-1/3,500 live newborns. Chronic pulmonary infections caused by opportunistic pathogens affect more than 90% of patients suffering from CF. In addition to bacterial colonization, these patients are predisposed to fungal colonization, due to the capacity of environmental fungi to colonize the lower respiratory tract and to the prolonged therapy with antibiotics and corticosteroids, which leads to the alteration of the normal biota. Currently, the role of fungi in the course of CF is not clearly defined but there is evidence supporting that filamentous fungi may lead to the deterioration of lung function, as occurs in allergic broncho-pulmonary aspergillosis (ABPA) which is the most common fungal disease in this context. *Aspergillus fumigatus*, *Scedosporium apiospermum* and *Aspergillus terreus* are the main filamentous fungi associated with CF described worldwide. The prevalence of different fungi in CF patients from Argentina is unknown.

**Objectives:** To give an overview of the diversity and epidemiology of fungal species in CF patients from Buenos Aires, Argentina.

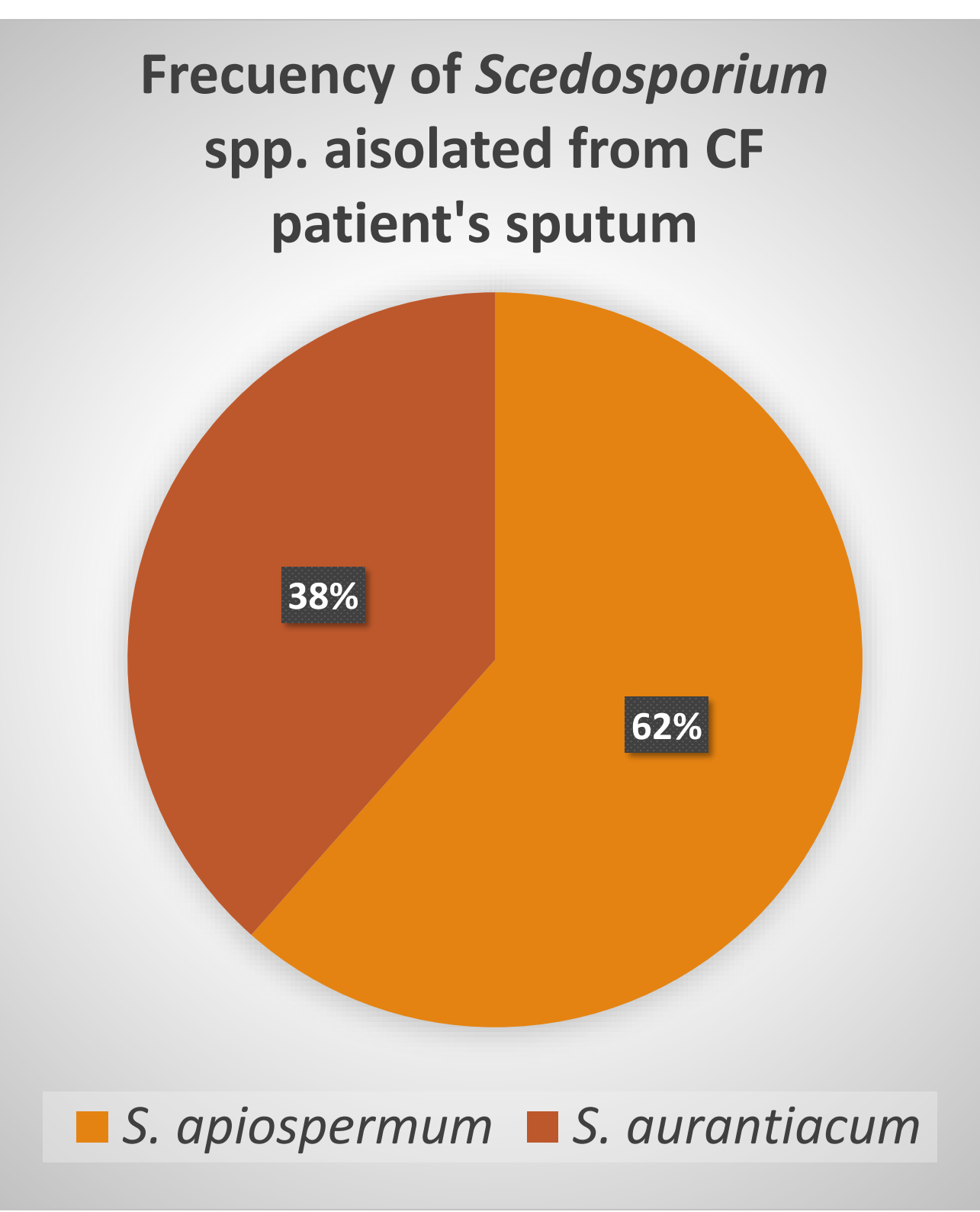
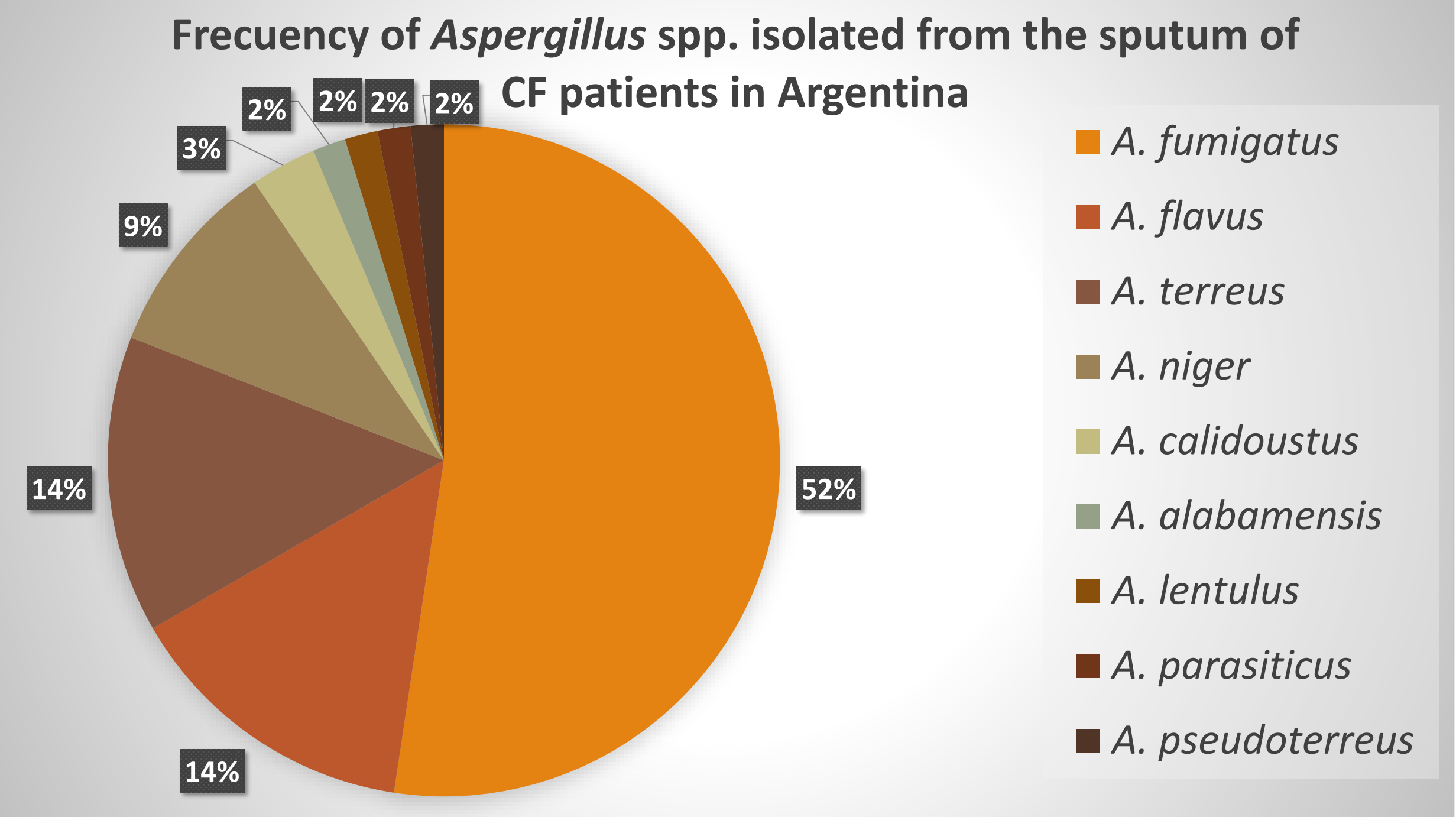
**Methods:** A total of 103 fungal strains isolated from sputa of 30 patients from Buenos Aires, Argentina, were investigated. Isolates were identified according to standard macroscopic and microscopic morphological criteria. In order to differentiate species, subspecies and strains of fungi, sequence analysis of the fungal ITS regions of the ribosomal DNA (primers ITS1/ITS4), the beta-tubulin region (primers Bt2a/Bt2b) and the calmodulin region (CMD5/CMD6) was performed.

## RESULTS

*Aspergillus* species were the most common filamentous fungi (61,2%) followed by *Scedosporium* spp. (12.6%), *Penicillium* spp. (5,8%), *Exophiala* spp. (5.8%), *Talaromyces* spp. (5.8%), *Rasamsonia* spp. (1%), *Geotrichum* spp. (1%) and *Paecilomyces* spp. (1%) (Fig. 1). Among the *Aspergillus* genera, *A. fumigatus* was the most prevalent, followed by *Aspergillus flavus*, *A. terreus*, *Aspergillus niger*, *Aspergillus calidoustus*, *Aspergillus alabamensis*, *Aspergillus lentulus*, *Aspergillus pseudoterreus* and *Aspergillus parasiticus* (Fig. 2). Among the genera *Scedosporium*, the most common species were *S. apiospermum* and *Scedosporium aurantiacum* (Fig. 3). In 20% of the cases, fungal co-infections were successively detected (eg: *A. fumigatus*, *A. niger* and *E. dermatitidis*; *A. terreus* and *S. aurantiacum*; *A. fumigatus*, *A. niger* and *A. pseudoterreus*; *A. fumigatus* and *Rasamsonia* sp.; *A. fumigatus* and *A. terreus*; *A. niger*, *A. calidoustus* and *Scedosporium* sp.) in the same patients.

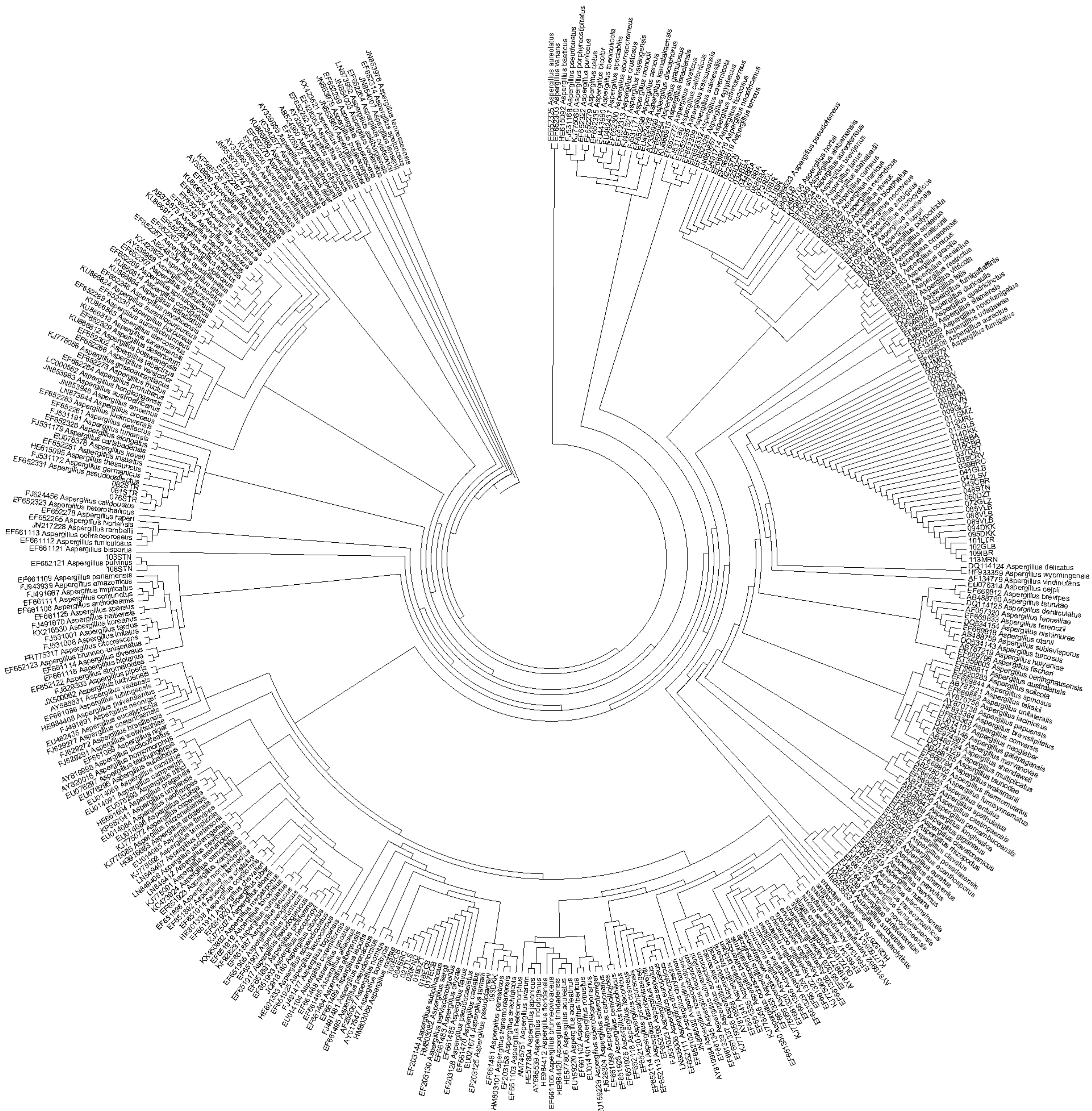


**FIGURE 1** – Diversity and frequency of fungi strains isolated from the sputum of Argentinean CF patients. Isolates were identified by morphological and molecular criteria.



**FIGURE 2 (Top)** – *Aspergillus* strains were classified into sections by macro and micro morphological criteria. Crypto-species were determined by sequencing *b-Tub* and *CaM* genes and using Blastn against a cured *Aspergillus* spp. specific database as reported by Samson et al. 2014.

**FIGURE 3 (Left)** – *Scedosporium* strains were identified by macro and micro morphological criteria. Later, identification was confirmed by sequencing ITS regions, *b-Tub* and *CaM* genes and using Blastn against the NCBI and Mycobank database.



**FIGURE 4** – Maximum Likelihood tree created with Mega v.7 using isolates' *BenA* sequences and those obtained from the cured *Aspergillus* spp. database by Samson et al. 2014 (Downloaded from [www.aspergilluspenicillium.org](http://www.aspergilluspenicillium.org) on July 2017). All sequences were aligned in Mega v.7 with ClustalW multiple sequence alignment. The tree was created by the Maximum Likelihood method using the Kimura 2-parameter model and default conditions, with 1000 bootstrap replications.

## CONCLUSIONS

This is the first report about fungal infections in patients with CF in Argentina. *A. fumigatus* was the most prevalent hyphomycete in CF samples. Although less common, several fungal species including *A. alabamensis* and *A. calidoustus* may be isolated transiently from CF respiratory secretions, while others such as *A. fumigatus*, *A. terreus*, *E. dermatitidis*, *S. apiospermum* and *S. aurantiacum* may chronically colonize the airways. Further studies are needed to evaluate the contribution of the different fungi to inflammation and clinical deterioration in CF patients and the clinical implications of fungal coinfections in the physiopathology of CF lung infection-colonization.

## References:

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