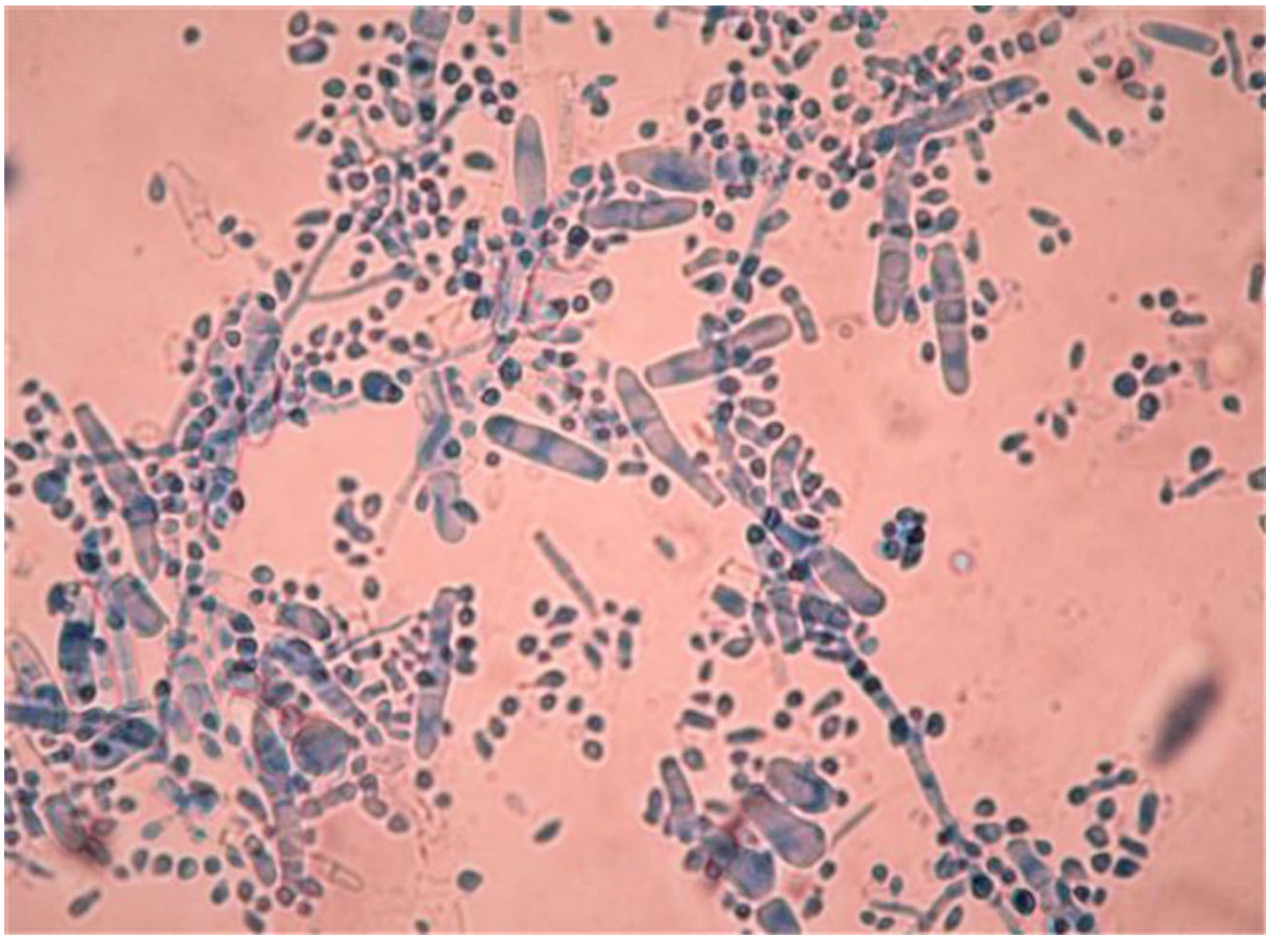

S6.3c
Adaptive dynamics in experimental populations of *Aspergillus nidulans*

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S6.3 Fungal adaptation and evolution, September 22, 2022, 4:45 PM - 6:15 PM

A total of 12 replicate populations initiated with a laboratory strain of the ascomycete fungus *Aspergillus nidulans* evolved on synthetic minimal glucose agar medium for 1 year, using weekly transfers of 1% of the produced asexual spores to fresh medium. This *Aspergillus* short-term evolution experiment (ASEX) was designed to understand how filamentous fungi adapt to growth on limited carbon in a spatially structured environment. We observed no systematic improvement in the fitness components tested and neither in the competitive fitness relative to the ancestor. Instead, we observed the repeated evolution of at least two morphotypes, with a fluffy-like (FL) or an ancestor-like (AL) colony morphology, leading to non-transitive fitness interactions among isolates in two selected populations. The genomic analyses of clones from all 12 populations at an early (week 10) and the final time point (week 52), show a clear role of natural selection during ASEX. We also observed a shared genetic basis and different timing of adaptation of AL and FL types. In addition, in most populations, both morphotypes do not form monophyletic groups, but they frequently disappear and re-evolve from ancestral forms of both types. Reduction in asexual spore yield, the most evident parallel phenotypic change found in all our evolved populations, is not due to the direct selection of genes involved in asexual reproduction. Instead, we argue that reduced spore yield is a pleiotropic effect of adaptive changes in metabolism.

S6.3d
***Candida albicans* commensalism in the oral mucosa is favored by limited virulence and metabolic adaptation**

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S6.3 Fungal adaptation and evolution, September 22, 2022, 4:45 PM - 6:15 PM

Objectives: As part of the human microbiota, the fungus *Candida albicans* colonizes the oral cavity and other mucosal surfaces. Commensalism is tightly controlled by complex fungus-host interactions that preclude fungal elimination but also fungal overgrowth and invasion that would result in disease. As such, defects in antifungal T cell immunity render individuals susceptible to oral thrush due to interrupted immunosurveillance. The factors that promote commensalism and ensure persistence of *C. albicans* in a fully immunocompetent host remain less clear. In this study, we aimed at identifying determinants of *C. albicans* commensalism in the oral cavity.

Methods: We used an experimental model of *C. albicans* oral colonization in mice, profiled the transcriptome of the fungus in the mucosal tissue, and conducted functional studies with the prototypical commensal isolate 101 in host-free and host-involving conditions.

Results: *C. albicans* commensalism is associated with a characteristic metabolic profile tailored to the nutrient-poor conditions in the stratum corneum of the epithelium where the fungus resides. Metabolic adaptation of the commensal isolate 101 was also reflected in enhanced nutrient acquisition when grown on oral mucosa substrates. Persistent colonization of the oral mucosa by *C. albicans* also correlated inversely with the capacity of the fungus to induce epithelial cell damage and to elicit an inflammatory response. These immune evasive properties of isolate 101 are explained by a strong attenuation of numerous virulence genes, including those linked to filamentation. De-repression of the hyphal program by deletion or conditional repression of the transcriptional repressor NRG1 abolished the commensal behavior of isolate 101.

Conclusions: This study establishes a central role of NRG1 in the commensal lifestyle of *C. albicans* in the oral niche of the host.

S6.4c
Primary cutaneous implantation coccidioidomycosis

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S6.4 One health approach for endemic mycoes in the Americas, September 22, 2022, 4:45 PM - 6:15 PM

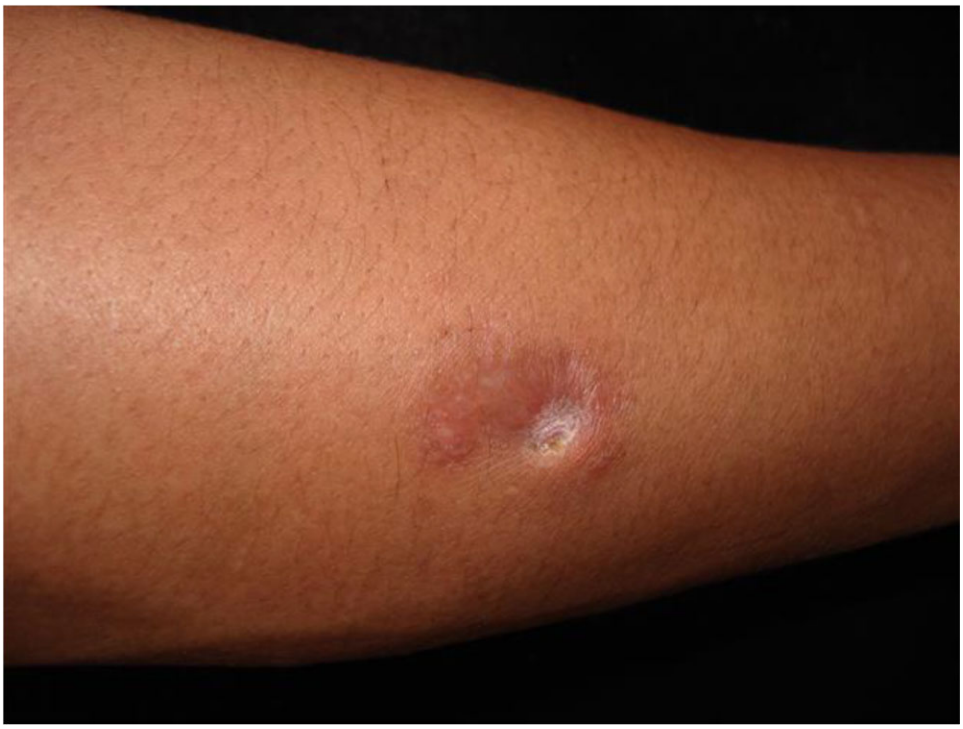
Objective: To present a series of cases of primary cutaneous coccidioidomycosis, to highlight this mycosis that can start as cutaneous implantation, after trauma, and to emphasize the classification criteria.

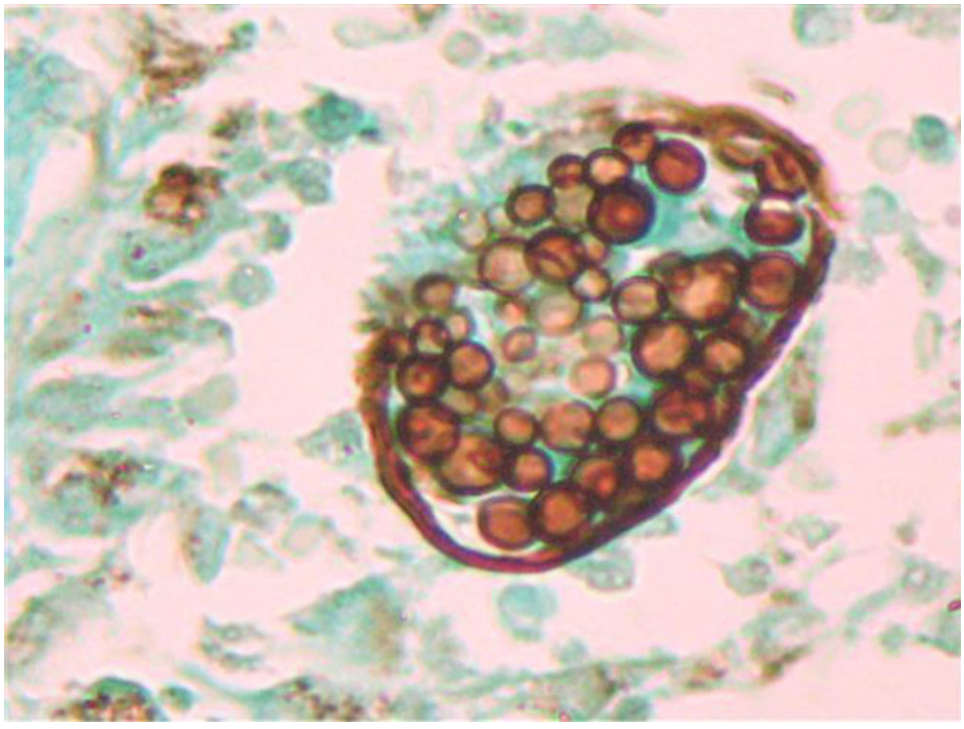
Methods: A series of cases of primary cutaneous coccidioidomycosis will be presented, all of them confirmed by mycological studies, fresh examinations, stains, and cultures, as well as their molecular identification; also confirmed by histopathology.

Results: A series of 22 cases of primary cutaneous coccidioidomycosis is presented, 16 (72.8%) in men, 6 (27.2%) in women. With an average age of 35.2 years, with the lowest case in a 14-year-old child and the highest at 72 years. All from rural and endemic areas. A total of 11 (50%) with fieldwork and the rest due to various injuries. The etiological agent was isolated in all of them: *Coccidiodes posadasii* in 16 (72.8%), *C. immits* in 3 and one by *Coccidiodes* sp. 20 cases were managed with itraconazole, with an average of 8 months and two more with a cycle of amphotericin B and subsequent itraconazole. Clinical and mycological cure was obtained in all.

Discussion: Primary cutaneous coccidioidomycosis, is considered an implantation mycosis, similar to other endemic ones, it occurs between 2%-10% of cases. It begins after trauma that inoculates the fungus, such as a primary chancre. To confirm that it is a primary form, Wilson's criteria must be met: the presence of skin trauma, regional lymphadenopathy, no evidence of pulmonary involvement, positive intradermal reaction, and low antibody titers. It may present auto involution and in immunosuppressed patients, it can spread.

Conclusion: The initial cutaneous form of coccidioidomycosis is rare, usually seen in patients living in endemic areas, and usually present in patients with rural occupations. It has a variety of clinical forms, being confused with many diseases. Its diagnosis is simple, being the biopsy the most used, and it must be confirmed by mycological tests. It has a good prognosis and its main management is with itraconazole.





6.5b
Genomics and metagenomics of *Madurella mycetomatis*

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S6.5 Efforts of improving the management of mycetoma: working towards the 2030 goals, September 22, 2022, 4:45 PM - 6:15 PM

Mycetoma is a debilitating disease recognized as a neglected tropical disease by the World Health Organization. The etiology of mycetoma is poorly understood; ~ 60% of cases are caused by fungi and the rest are bacterial, although this varies by region. The pathogenic fungus, *Madurella mycetomatis*, is most frequently identified in mycetoma cases. Here, we present a high-quality genome assembly of *M. mycetomatis* and the results of the whole genome sequence analysis of 25 isolates from Sudan. We demonstrate evidence of at least seven genetically diverse lineages and extreme clonality among isolates within these lineages. Shotgun metagenomic analysis of DNA from mycetoma grains confirmed that *M. mycetomatis* was the predominant causative agent of eumycetoma Sudan; however, 10% of grains also contained bacterial reads suggestive of secondary infections. A thorough understanding of the genetic structure and diversity of fungi causing mycetoma is essential for the development of new diagnostic methods and for identifying potential drug targets.

S6.5c
MycetOS: identifying drugs which can penetrate the mycetoma grain

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S6.5 Efforts of improving the management of mycetoma: working towards the 2030 goals, September 22, 2022, 4:45 PM - 6:15 PM

Mycetoma is a neglected tropical disease characterized by large subcutaneous swellings and the formation of grains. *Madurella mycetomatis* is the most common causative agent. Currently, mycetoma is treated with a combination of itraconazole