The Rise of *Candida auris*: a Drug-Resistant Fatal Fungus

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Background:

Candida auris is a fungus that is creating a significant public health threat, causing severe healthcare associated infections. Commonly misidentified in laboratories, *C. auris* is extremely resistant to most antifungal medications. *C. auris* infections are most commonly identified through a culture of the blood or other bodily fluid, but can be misidentified for other *Candida* strains. The most reliable way to accurately identify *C. auris* is through matrix-assisted laser desorption/ionization time-of-flight mass spectroscopy (MALDI-TOF MS). One of the biggest challenges of managing *C. auris* is differentiating it quickly enough from other *Candida* species in order to treat it appropriately. *C. auris'* resistance to antifungal medications makes it an urgent threat that can cause severe infections with high death rates. The death rate of patients with *C. auris* remains between 45-55%. Although this is concerning, the fungus is not generally a threat to healthy people. The fungus is the most dangerous to the immune systems of patients during long or frequent stays in healthcare facilities or to those patients with already weakened immune systems. The main finding in patients diagnosed with this deadly fungus is a bloodstream infection with symptoms such as a fever, chills, sweating, and low blood pressure. *C. auris'* ability to live on surfaces for several weeks makes it that much more dangerous to hospital residents through contaminated surfaces and equipment.

Source: CDC

Immune Evasion:

Figure 1 by Nett *et al* shows that *C. auris* is not successfully killed by human neutrophils. Neutrophils failed to produce neutrophil extracellular traps (NETs), structures made of DNA, histones, and proteins with antimicrobial action. Numerous invasive disease outbreaks have been caused by the newly discovered fungus *Candida auris* in hospitals all over the world. According to this research, *C. auris* is more resistant to neutrophil killing than the most prevalent *Candida* species, *C. albicans*. Although neutrophils create NETs (neutrophil extracellular traps) when they come into contact with *C. albicans*, they do not develop in response to *C. auris*. According to Nett's research done in zebrafish model, *C. auris* attracts neutrophils unsuccessfully and escapes immunological response.

Resistance:

This organism can become resistant through mutations in some genes, positive regulation of the efflux pump genes, and single nucleotide polymorphisms (SNPs) at different places throughout its genome. Figure 2 A and B show phenotypic switching from yeast to filamentous forms via passage through mice. Filamentous cells are more invasive ane penetrate host tissues.

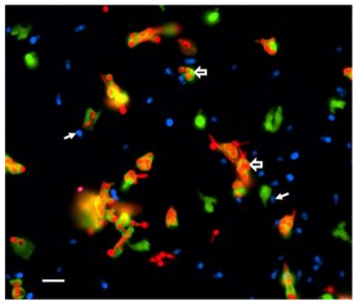


Figure 1:. Source: Nett, J. E. (2019). *PLoS Pathogens, 15*(4) (2019)

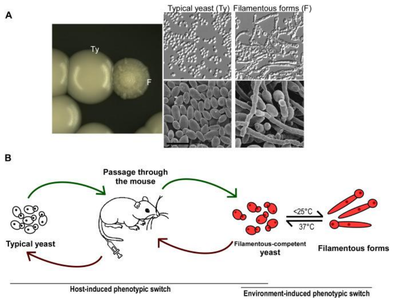
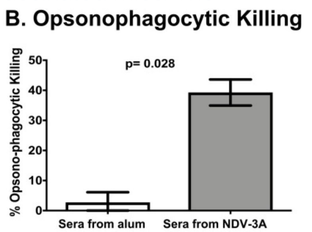


Figure 2. Source: : Du, H. et al. PLoS Pathog 20 Oct 22

Vaccine:

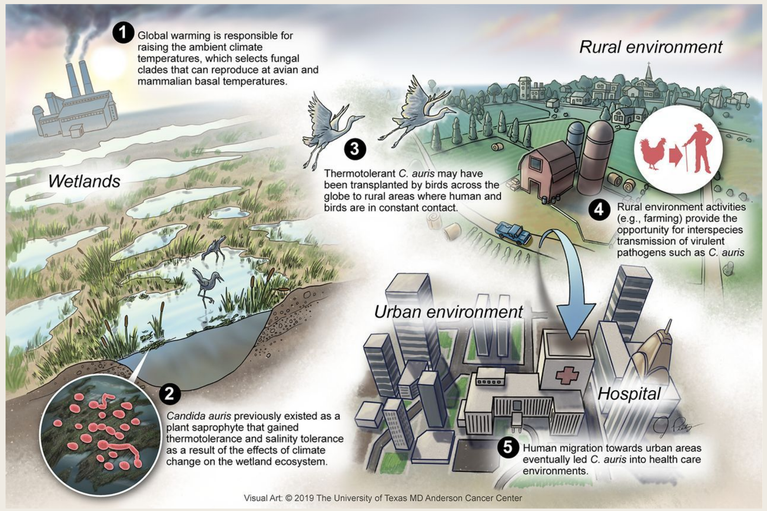
A study done at the Division of Infectious Disease at the Los Angeles Biomedical Research Institute shows *C. auris'* ability to adhere to polymeric surfaces and form highly drug-resistant biofilms. Anti-Als3 proteins formulated with alum were able to recognize *C. auris* in vitro, blocking its ability to form its deadly biofilm. NDV-3A vaccination - already known to be effective in treating other candida species - was found to induce significant levels of *C. auris* cross-reactive humoral and cellular immune responses and protected the immunosuppressed mice from lethal amounts of inseminated *C. auris* compared to the control alum-vaccinated mice. The mechanism of protection found attributes to the anti-Als3p antibodies and CD4+ T helper cells activating the tissue macrophages.



Source: Singh, S. (2019). The serum from NDV-3A-vaccinated mice significantly enhanced yeast OPK compared to alum group.

Surface Disinfection:

Candida auris has the ability to survive on surfaces and can resist environmental stressors, which can create challenges for eradicating it from hospitals and clinics. An in-vitro study was done by the School of Medicine in the UK, to evaluate how the *C. auris* clinical isolates would survive on different surface environments against the standard disinfectant sodium hypochlorite and the high-level disinfectant peracetic acid. The results convey that *C. auris* does selectively tolerate the relevant concentrations commonly used in hospitals and clinics. The activity between polymer and steel surfaces are also important to note as the way the general ability of the *Candida* species can adhere and develop biofilms that are innately more resistant. To conclude, using the peracetic acid on plastic polymers showed a significant and more of an effective reduction compared to stainless steel. Nevertheless, due to it's multidrug resistance capabilities it's ability to persist is still an ongoing concern.



Casadevall et al 10 (2019) *mBio* Proposed scheme for the emergence of *C. auris*.

Climate Effects:

It is hypothesized that *Candida auris* might have previously existed as a plant saprophyte in specialized ecosystems, such as the wetlands. The state of its emergence is likely linked to human induced global warming and through its ecological niche caused a consequence of fungus's combined thermal and salinity tolerance. The effects of higher UV radiation in combination with the warm earth may contribute to such mutagenic events that caused the sudden increase of fitness for survival in a host. It is also important to note that birds can serve as reservoirs for indirect transmission of the drug-resistance *Candida* species to humans. The effects of climate change induced by the growing human population can drive the fungal evolution. Therefore this should be an area of intense research in the future to come.

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