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Candida auris Biofilm Colonization on Skin Niche Conditions

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ABSTRACT *Candida auris*, an emerging multidrug-resistant yeast, has recently been associated with outbreaks of invasive infections in health care facilities worldwide. Its success as a nosocomial pathogen lies in its capability to sustain for prolonged periods in the intensive care unit (ICU), adeptly colonize skin, and spread among patients. Little is known of the mechanism behind the predilection of *C. auris* for skin or the extent of its resilience on it. Now, M. V. Horton, C. J. Johnson, J. F. Kernien, T. D. Patel, et al. (mSphere 5:e00910-19, 2020, https://doi.org/10.1128/mSphere.00910-19) demonstrate that in synthetic sweat medium designed to mimic axillary skin conditions, *C. auris* can grow into multilayers of cells called biofilms that can resist desiccation. *C. auris*' propensity to form biofilms was further elaborated using a novel *ex vivo* porcine skin model of skin colonization. These studies provide early evidence that *C. auris* biofilm cells persisting on skin could serve as source of continuing outbreaks in health care facilities. Interventions blocking *C. auris* biofilm growth on skin will help control the spread of this pathogen.

KEYWORDS *Candida auris*, biofilm, skin, porcine, sweat, nosocomial, fungi

Candida auris is an emerging multidrug-resistant fungal pathogen that can cause invasive infections predominantly in immunocompromised hospitalized patients (1, 2). First isolated in 2009 from the ear canal of a Japanese patient (3), *C. auris* has been reported to cause disseminated diseases associated with mortality rates as high as 60% (4). Of concern is that only within the past decade, *C. auris* pathogenic isolates have appeared in nine countries and four continents, including the Unites States (1, 5–7). In fact, a report from a referral hospital in sub-Saharan Africa revealed that incidence of *C. auris* candidemia surpassed that of cases of *Candida albicans*, the most successful human fungal pathogen (5). Given the simultaneous worldwide outbreak of *C. auris*, the Centers for Disease Control and Prevention has designated this fungal pathogen a global public threat and has recently published an alert for health care facilities to surveil and report new cases of *C. auris* patients (8).

Unlike other pathogenic *Candida* species such as *C. albicans* that predominantly exist as a part of the normal flora of humans, *C. auris* can persist and thrive in the environment of health care facilities (6, 9). Because of this, *C. auris* possesses characteristics representative of a pathogen that can cause nosocomial infections (10), such as its (i) propensity to cause outbreaks likely due to spread by horizontal transmission, (ii) ability to cause life-threatening disease in immunocompromised patients, and (iii) multidrug resistance profile. Indeed, *C. auris* transmission occurs primarily among patients with a prolonged hospital stay.

Recent reports have shown that *C. auris* can form a community of cells called biofilms on surfaces recovered from hospital rooms during outbreaks (9, 11). However, these biofilms on inanimate surfaces are found to be rudimentary and weaker than robust biofilms typically produced by *C. albicans* (11, 12). The extent and mechanism of colonization of *C. auris* on human skin has not been explored. Given that *C. auris* can spread like wildfire between hospital rooms and health care

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facilities, *via* human contact, it is important to understand how *C. auris* perseveres on skin.

To understand the mechanism of skin colonization, Horton and colleagues analyzed growth of *C. auris* in synthetic sweat medium designed to mimic axillary skin conditions *in vitro* (13) Under these conditions, *C. auris* grew as a multilayer biofilm composed of yeast cells, with cellular burden intriguingly 10-times greater than that formed by *C. albicans*, a fungus that is otherwise adept at robust biofilm growth. Conversely, as published previously, *C. auris* developed only a thin monolayer of cells in standard laboratory medium, indicating that components in the synthetic sweat medium such as high salinity, fatty acids, etc. may provide *C. auris* with a growth advantage over *C. albicans* (14). Indeed, this finding was further evidenced when *C. auris* (but not *C. albicans*) biofilms could persist under stress conditions representing desiccation. In concentrated sweat medium (mimicking evaporated sweat), *C. auris* biofilms continued to thrive for 14 days, while *C. albicans* biofilm cells succumbed to this dehydrated environment only within the first week of growth. It is no surprise, then, that robust biofilm growth and ability to withstand dry surfaces make *C. auris* a successful environmental pathogen.

To understand the interaction of *C. auris* directly with skin, Horton et al. (13) simulated *C. auris* growth on an *ex vivo* porcine skin model. This novel skin model shares several characteristics with human skin and thus is a clinically relevant model (15, 16). Additionally, this model specifically supports the scenario of fungal colonization rather than invasion, making it ideal to study persistence rather than infection. As witnessed *in vitro*, *C. auris* developed multiple aggregates and robust biofilms on porcine skin, while *C. albicans* showed little fungal growth. Together, the studies suggest that part of the reason that makes *C. auris* such a successful pathogen is its ability to adeptly colonize skin niches and withstand environmental stresses. Certainly, recent isolated reports on outbreak surveillance from hospitals in the United States have implicated skin colonization by *C. auris* as one of the risk factors for nosocomial infections (9, 14). The study by Horton et al. (13) reinforces this finding by showing that a biofilm architecture not only serves as a high-burden reservoir of cells that can be shed intermittently upon contact but also provides *C. auris* with an enhanced ability to withstand the vagaries of environmental stresses. The latter advantage is not surprising, considering that a biofilm phenotype is known to protect microbial cells from a number of stresses, including immune cell assault and antimicrobial drugs (17).

In summary, Horton et al. (13) have taken the first steps to understand the interaction of *C. auris* with the skin milieu by designing inventive *in vitro* assays and *ex vivo* experimental models of axillary skin colonization. These models are clinically relevant, considering that reusable axillary probes have been linked to *C. auris* outbreaks (18). A more serious implication of skin colonization by *C. auris* biofilms is perhaps intravenous catheter contamination by skin puncture, which can carry the pathogen directly into the bloodstream. Indeed, the presence of indwelling medical devices is a primary risk factor for persistent candidemia by *C. auris* (1, 4, 6). An important future direction of this research would be harnessing the experimental models of colonization to identify molecular pathways underlying adherence of *C. auris* to the skin and to discover genetic determinants of biofilm growth. This knowledge will be critical for the thoughtful development of new interventional strategies against *C. auris* biofilm growth and persistence on skin.

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