

Drug Development Considerations for the Prevention of Healthcare-Associated Infections - Virtual Public Workshop

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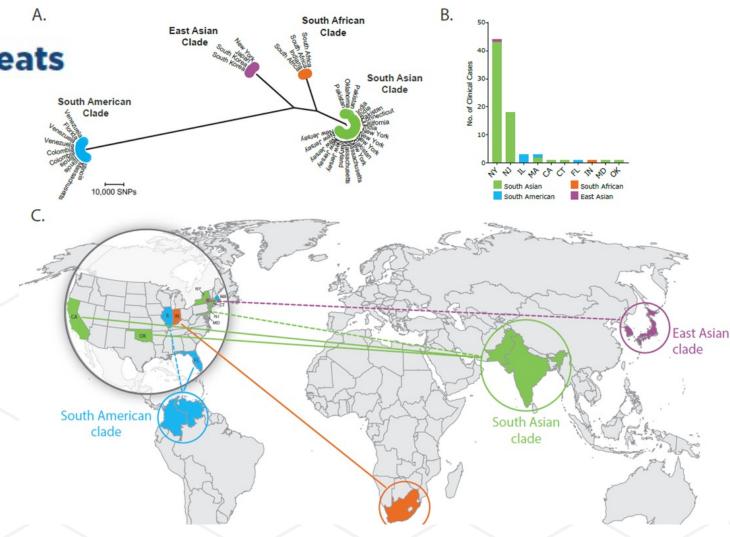
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THE PROBLEM

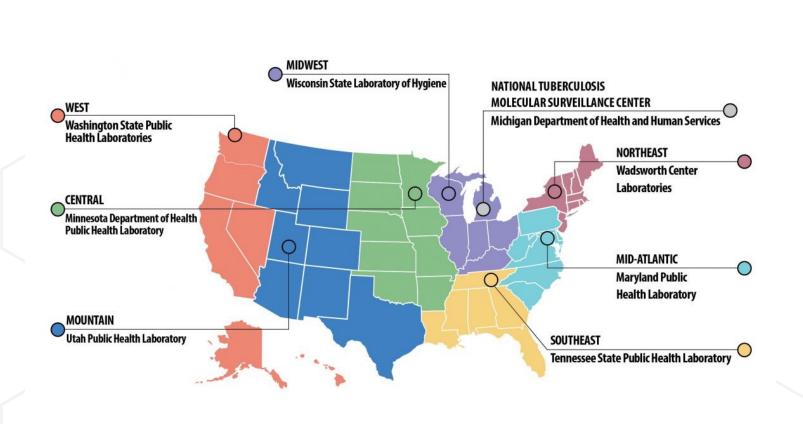
First described in 2009 - now an "Urgent" AR Threat

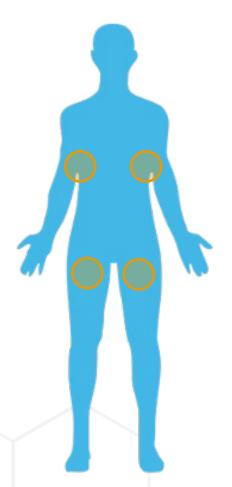
Urgent Threats

- C. auris is an emerging and multidrug resistant fungal pathogen identified in 2009
- C. auris heavily colonizes patients' skin, leading to outbreaks in healthcare settings
- There are no decolonization or pathogen reduction strategies for *C. auris* colonization



Tracking *C. auris* colonization through CDC's AR Lab Network







Why are we concerned about *C. auris*?

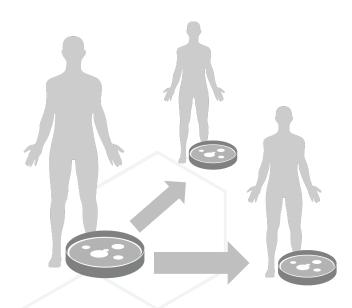


Only 3 classes of Antifungals

>80% isolates resistant to 1

>25% of isolates resistant to 2

Now over 30 total Pan R isolates



Colonization amplifies the problem

5-10% of colonized patients develop invasive infections

>45% mortality within 30 days

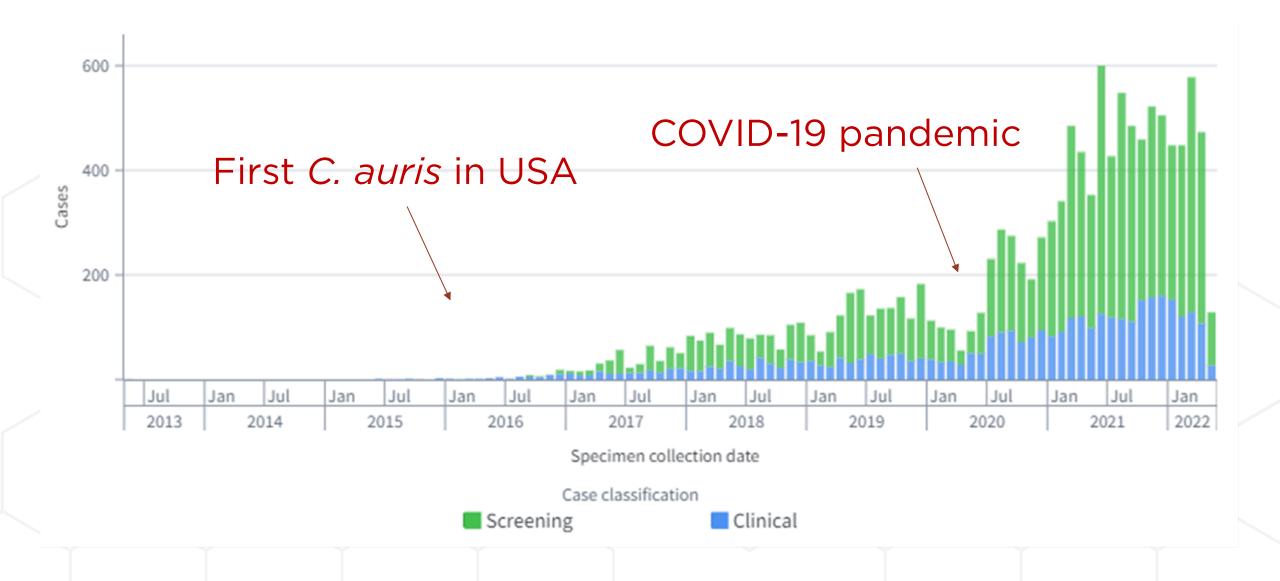


Large outbreaks in healthcare settings

>70% colonization prevalence

Outbreaks are difficult to control

C. auris cases are increasing



Who gets colonized by *C. auris?*

Known Risk Factors:

- Mechanically Ventilated
- Having ≥1 acute care hospital visit in the prior 6 months
- Carbapenem antibiotics in the prior 90 days
- Systemic fluconazole in the prior 90 days

Table 3. Multivariable Logistic Regression Models for Assessing Factors for Association With *Candida auris* Colonization, New York, 2016–2018

Factors	aOR	95% Confidence Interval	
		Lower	Upper
Mechanically ventilated ^a	5.88	2.25	15.37
Any ACH visit in the 6 months prior to PPS ^b	4.23	1.87	9.60
Received a carbapenem in the 90 days prior to PPS ^c	3.52	1.62	7.63
Received systemic fluconazole in the 90 days prior to PPS ^d	5.98	1.58	22.64
Received vancomycin in the 90 days prior to PPS ^e	1.65	.75	3.67
Any MDRO in the 90 days prior to PPS ^f	1.25	.56	2.76
Room with a colonized roommate ⁹	.37	.12	1.16
Room type at time of screening ^h			
In a room with 1 bed	Ref	Ref	Ref
In a room with 2 beds	1.44	.55	3.80
In a room with 4 beds	2.04	.54	7.70

Rossow et al, Clinical Infectious Diseases. 2021.

Challenges caring for patients colonized with *C. auris*

- Increased resources to implement robust transmission-based precautions and IPC program
- EPA's "<u>List P</u>" disinfectants
- Challenges discharging some facilities now rejecting patients colonized with *C. auris*
- Common question: "how do we decolonize patients"
- There are no options for decolonization or C. auris reduction strategies



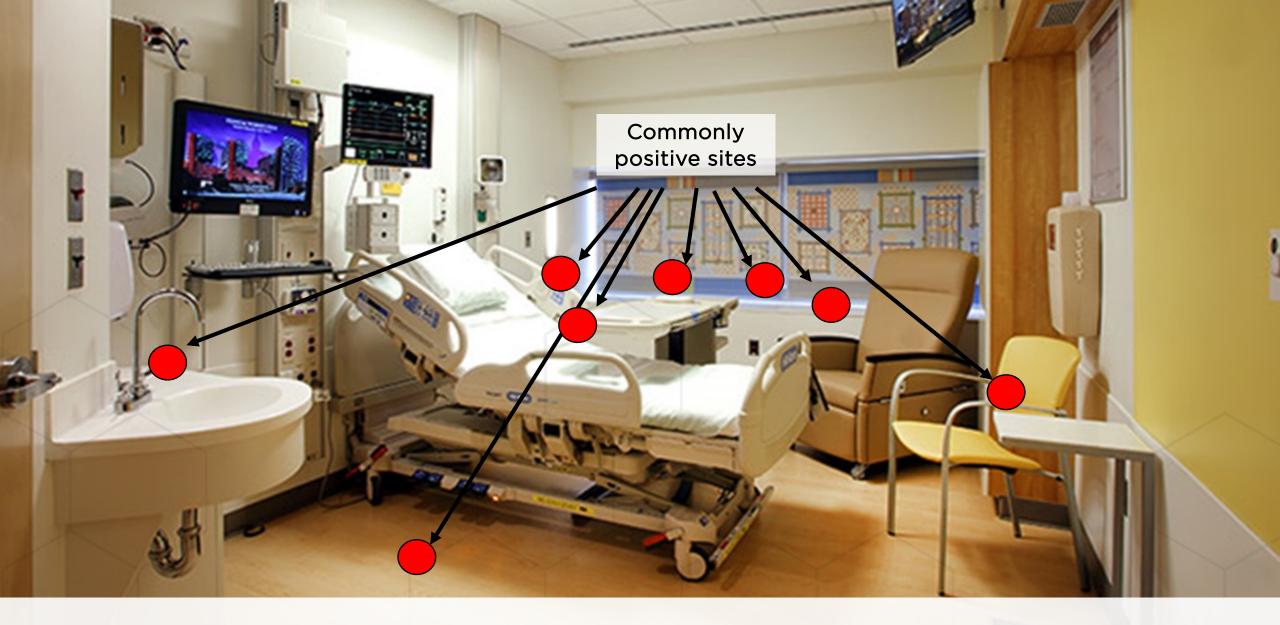






WHAT WE HAVE

Current tools, studies, and data gaps

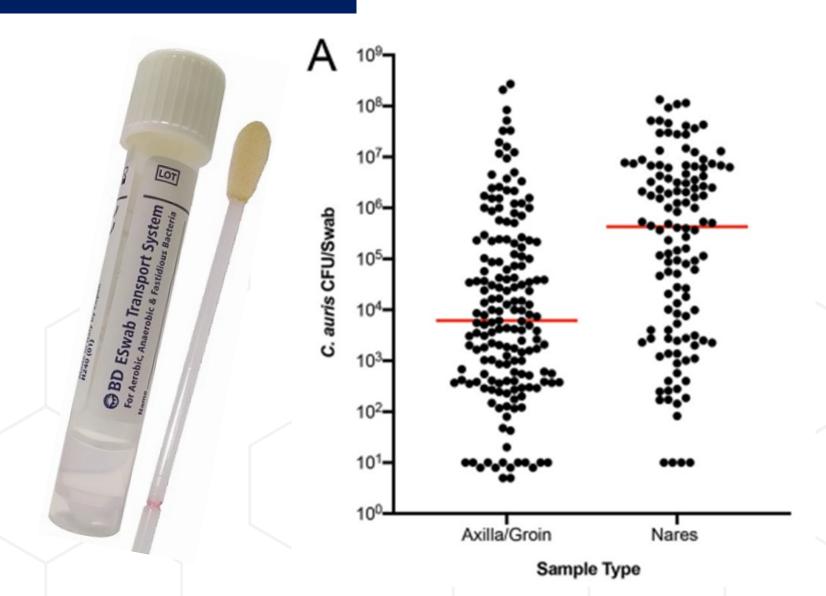


Candida auris contaminates and persists in the environment

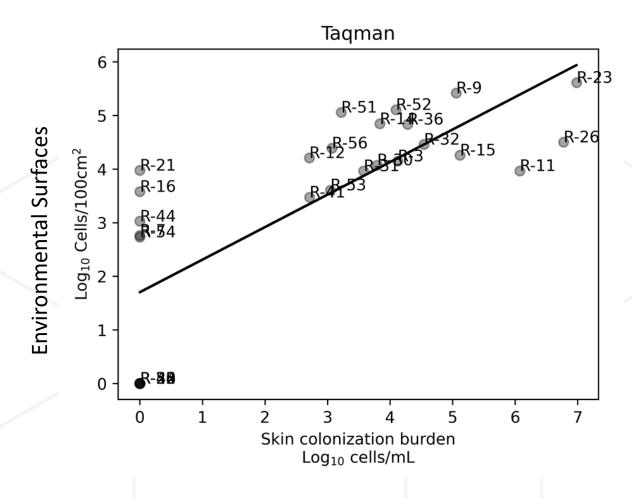
High concentrations of *C. auris* detected in colonization screening swabs

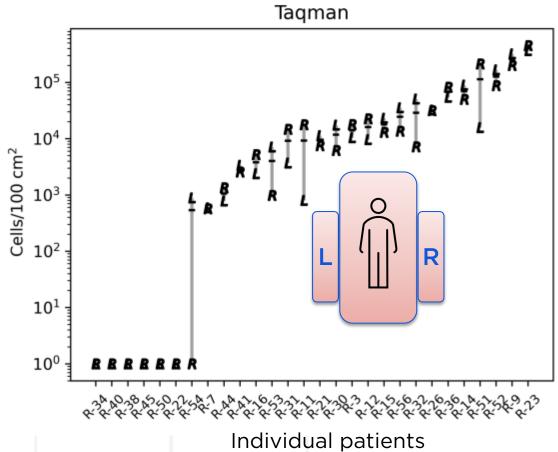
Notable Observations:

- Large range of colonization burdens, many very high (10¹ - 10⁸
 CFU)
- High C. auris
 concentrations observed
 in both axilla/groin and
 anterior nares



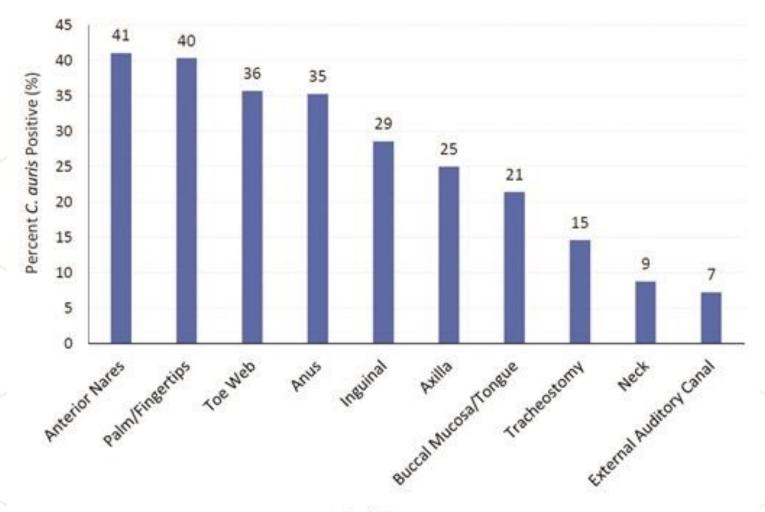
Patients with more *C. auris* on their skin have more *C. auris* in their environment

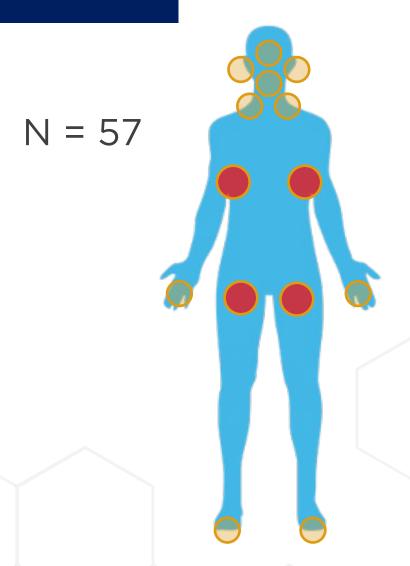




Frequency of *C. auris* colonization at specific body sites

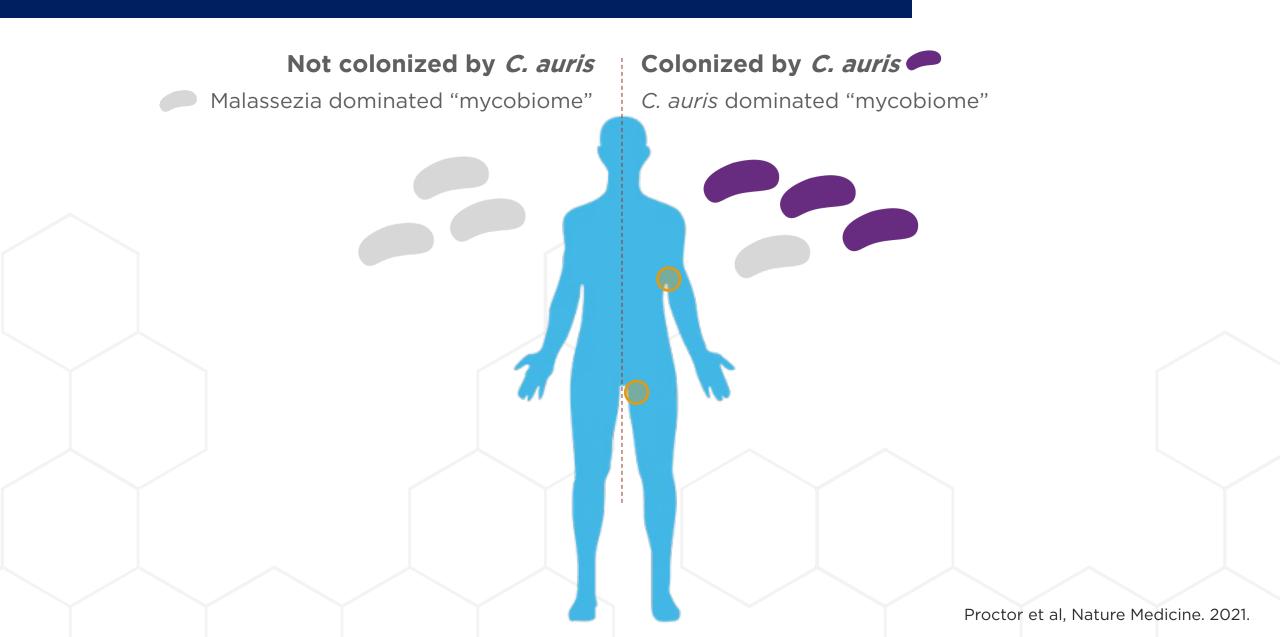
Figure 1: Proportion C. auris Positive Samples at first Survey by Body Site (N = 57 patients, 541 samples)





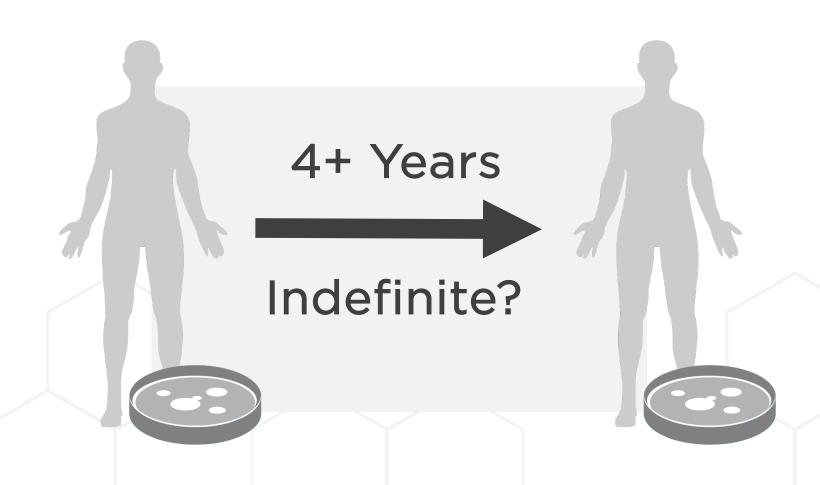
Body Site

Microbiome relevance?



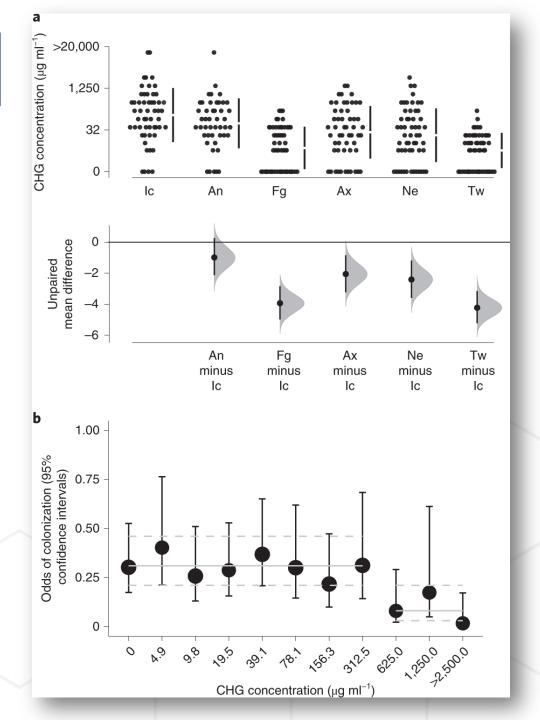
C. auris colonization last years, may be indefinite

- Colonization can last very long times, perhaps indefinitely
- Colonization status can fluctuate between sampling
- Some individuals do not become colonized despite high exposure



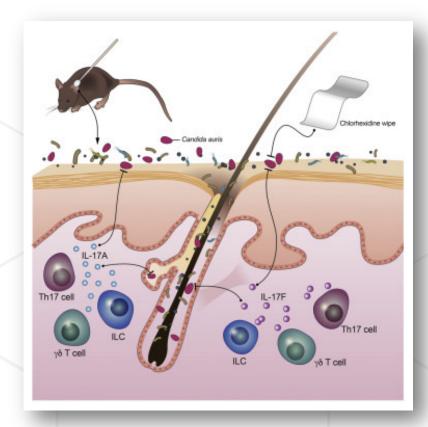
What we know about *C. auris & CHG*

- Looking at cohort in vSNF unit
- Measured CHG concentrations achieved on skin
- Reduction in colonization observed if CHG > 625 µg/mL
- Much higher than required in vitro (16 32 µg/mL)
- Take away May be difficult to achieve CHG concentrations necessary in practice



Mouse-model work

 C. auris colonized to base of hair follicles, may provide safe harbor



- Clades differed in ability to colonize
- Chlorhexidine was evaluated for decolonization, may be protective
 Huang et al, Cell Host Microbe. 2021.

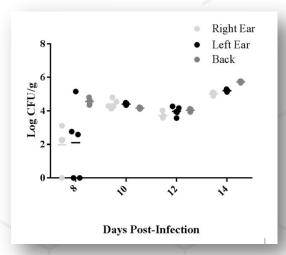
- Achieved stable C. auris colonization
- Terbinafine and Clomitrazole based products evaluated for suppressing colonization



1% CLOTRIMAZOLE

 Colonization burden reduced, not eliminated

UNTREATED

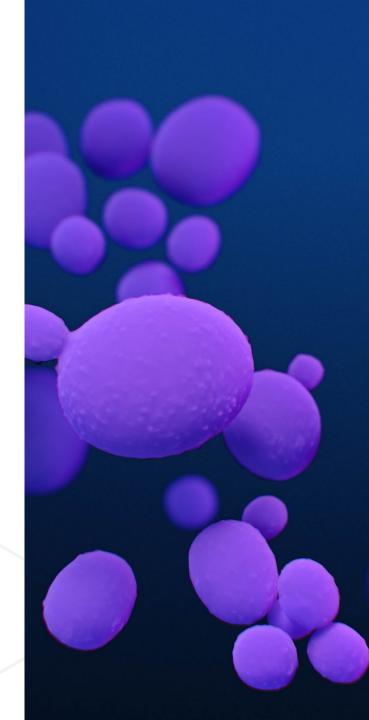


Ghannoum et al, Antimicrobial Agents Chemotherapy. 2021.

WHAT WE NEED

C. auris colonization summary

- C. auris can asymptomatically colonize patients' skin, which increases their risk of developing infection and contributes to environmental contamination and transmission
- Healthcare facilities often ask about decolonization treatments, but no options available
- Patients colonized with C. auris are increasingly stuck at the wrong level of care because other facilities refuse to accept them.
- Public health need for decolonization or pathogen reduction strategies to address *C. auris* colonization
- Need standardized laboratory models to help evaluate the efficacy of decolonization and pathogen reduction strategies



Special thanks



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- Julie Segre and NIH
- Susan Huang and UCI

Thank you.



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