FLC-treated or untreated infected flies ($P < 0.0001$). As POSA is a cell-associated drug, we are conducting *C. auris* phagocytosis assays with Drosophila hemocytes that are co-incubated or not with POSA.

Conclusion. *Drosophila* is a promising, fast, and inexpensive *in-vivo* model to study pathogenesis and drug activity in *C. auris* candidiasis.

Disclosures. **N. Beyda**, Astellas: Scientific Advisor, Grant recipient. **D. P. Kontoyiannis**, Merck: Consultant, Research support and Speaker honorarium. Pfizer: Consultant, Research support. Astellas: Consultant, Research support and Speaker honorarium. Gilead: Speaker's Bureau, Speaker honorarium. F2G Inc.: Speaker's Bureau, Speaker honorarium. Cidara Inc.: Speaker's Bureau, Speaker honorarium. Jazz Pharmaceuticals: Speaker's Bureau, Speaker honorarium.

381. Morphologic Changes Associated With Echinocandin Tolerance Enhance Immunoevasion of *Candida glabrata*

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Background. Activation of the cell wall integrity pathway and enhanced cell wall chitin synthesis are compensatory mechanisms associated with the incomplete killing of *Candida glabrata* by echinocandins. Echinocandin-induced morphologic changes in *C. glabrata* have also been described, yet their correlation with cell wall composition and macrophage responses to echinocandin treated *C. glabrata* are not well characterized. Elucidating these relationships is needed to understand how *C. glabrata* is capable of resisting both echinocandin killing and host immune responses.

Methods. Three echinocandin-susceptible bloodstream isolates of *C. glabrata* were grown in liquid RPMI with or without inhibitory concentrations of micafungin (MFG; 0.004 μg/mL) or caspofungin (CAS; 0.008 μg/mL). Cells were stained with fluorescent markers specific for cell wall chitin, mannan, and viability, then imaged utilizing high-content single-cell techniques. Phenotypic characteristics of *C. glabrata* cells that survive echinocandin exposure were determined by comparing the morphology and abundance cell wall components among the viable and nonviable cell subpopulations. To identify cellular characteristics associated with reduced macrophage phagocytosis, CAS or MFG treated cells were co-incubated RAW 264.7 macrophage and imaged as above. Phenotypic characteristics of the nonphagocytized yeast cells before and after co-incubation with macrophage was compared.

Results. Compared with untreated controls, growth in MFG and CAS significantly increased the proportion of cells with multiple-buds (50% ± 10% and 40% ± 18% vs. 12% ± 6%; $P < 0.001$) and induced cellular enlargement (biovolume; 35 ± 9 μm^3 and 80 ± 58 μm^3 vs. 26 ± 5 μm^3; $P < 0.001$). Cell enlargement, reduced cell wall mannan, and increased chitin were highly correlated with survival to MFG and CAS exposure ($P < 0.001$). Comparison of the drug-exposed yeast cell population before and after co-incubation with macrophage found an increased proportion of viable cells and cells with a large diameter (≥7 μM) remained un-phagocytized, indicating strong phagocytic preference for small, nonviable yeast cells.

Conclusion. *C. glabrata* cells that survive echinocandins have distinct cell wall changes and are large in size. These cells tend to evade phagocytosis by macrophages, suggesting a potential mechanism by which *C. glabrata* may persist despite echinocandin treatment.

Disclosures. **N. D. Beyda**, Astellas: Grant Investigator and Scientific Advisor, Consulting fee and Research grant.

382. Virulence in *Candida glabrata* Is Not Attenuated by FKS Mutations but Associated With the Frequency of Cells With Distinct Morphology

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Background. Echinocandins are the first-line treatment for *C.* glabrata; however, echinocandin resistance is increasingly reported. Acquired *FKS*-mediated echinocandin resistance has been associated with the upregulation of chitin synthesis and attenuated fitness and virulence in *C. albicans*; however, conflicting data are reported in *C. glabrata*. Here, the influence of FKS mutations on fitness, virulence, morphology, and cell wall chitin was assessed among clinical strains of *C. glabrata*.

Methods. Three sets of isogenic paired strains consisting of an index-WT and persistent-*FKS* mutant (S663P), two un-paired *FKS* mutant strains (S663F and S629P), and a WT reference strain (CBS138) were included. Growth kinetics were measured over 24 hours in 96-well microplate containing liquid RPMI. After overnight growth in RPMI and staining with a chitin-specific fluorescent marker, morphology, and chitin were assessed at the single-cell level utilizing high-content imaging technique. Virulence was evaluated in *Galleria mellonella* larvae by injecting 10^7 cells/larvae. Mortality was assessed daily for 5 days.

Results. Significant differences in growth kinetics, frequency of morphologic phenotypes within the cell populations (nonbudding, single-bud, multiple-buds), and virulence were observed between strains obtained from different patients ($P < 0.05$ for each). However, no difference was observed between paired index-WT and persistent-*FKS* S663P mutants. Compared with index-WT and the CBS138 reference strain, *FKS* mutant isolates (S663P, S629P, and S663F) had significantly elevated cell wall chitin content ($P < 0.05$). Neither chitin content, the presence of an *FKS* mutation, nor *in vitro* growth characteristics were found to be associated with virulence. Virulence was strongly correlated with the frequency of multi-bud cells within the population however, with 5-day post-injection survival rates of 4% vs. 28% for high-frequency (>12% multi-bud cells) and low-frequency strains, respectively ($P < 0.001$).

Conclusion. Acquired *FKS*-mediated echinocandin resistance induced significant alterations in cell wall chitin content but was not observed to attenuate fitness or virulence. Virulence was highly associated with the frequency of cells with distinct morphology.

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383. An Increased Rate of *Candida parapsilosis* Infective Endocarditis Is Associated With Injection Drug Use

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Background. *Candida parapsilosis* fungemia typically occurs in patients with intravascular catheters or prosthetic devices. In 2017, we noted an increase in *C. parapsilosis* infective endocarditis (IE).

Methods. We retrospectively reviewed *C. parapsilosis* fungemia and IE from January 2015 to February 2018. Species were identified using MALDI-TOF, and confirmed by ITS sequencing.

Results. Between 2010 and 2017, there was no increase in cases of *C. parapsilosis* fungemia (mean: 13/year), but there was a significant increase in *C. parapsilosis* IE ($P = 0.048$) (Figure 1). From January 2015 to February 2018, 22% (12/54) of *C. parapsilosis* fungemia was complicated by IE. Demographics of *C. parapsilosis* fungemia included: community-acquired infection (87%), presence of vascular catheters (80%), opiate noninjection drug use (non-IDU, 44%), IDU (20%), and presence of cardiac devices (18%). Ninety-one percent (49/54) of *C. parapsilosis* fungemia was caused by *C. parapsilosis sensu strictu* (Cpss); *C. orthopsilosis* and *C. metapsilosis* accounted for 4% (2/54) each (1 isolate could not be subtyped). Cpss, *C. orthopsilosis*, and *C. metapsilosis* accounted for 83% (10/12), 8% (1/12), and 8% (1/12) of IE, respectively. Ninety-two% (11/12) of *C. parapsilosis* IE was left-sided, and 33% (4/12) involved multiple valves. Risk factors for *C. parapsilosis* IE were past or active IDU ($P < 0.001$), community-acquired fungemia ($P = 0.02$), prosthetic heart valve ($P = 0.01$) or implanted cardiac device ($P = 0.03$). Receipt of an antibiotic within 30 days was a risk for *C. parapsilosis* fungemia without IE ($P = 0.001$). Median age for IE vs. fungemia was 38 vs. 57 years ($P = 0.09$). By multivariate logistic regression, IDU ($P < 0.0001$), prosthetic valve ($P = 0.006$) or implanted cardiac device ($P = 0.04$) were independent risks for *C. parapsilosis* IE. 70% (7/10), 20% (2/10), and 10% (1/10) of patients with IDU and *C. parapsilosis* IE primarily used heroin, buprenorphine/naltrexone, and cocaine, respectively. 50% (6/12) of patients with *C. parapsilosis* IE underwent surgery; most common initial AF regimens were caspofungin and amphotericin B. Nonsurgical patients were suppressed with long-term azole; one relapsed requiring surgery. Thirty-day and in-hospital mortality for patients with fungemia vs. IE were 32% vs. 17% and 26% vs. 17%, respectively.

Conclusion. *C. parapsilosis* IE has emerged at our center. Unique aspects of *C. parapsilosis* pathogenesis that may account for emergence are a propensity to colonize skin, adhere to prosthetic material and form biofilm. *C. parapsilosis* IE may be an under-appreciated consequence of IDU and opioid abuse.

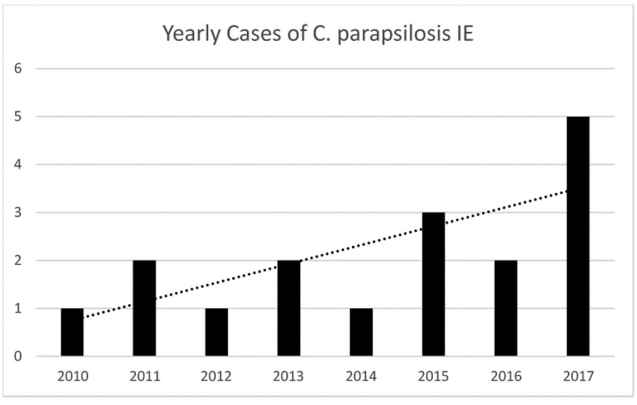

Figure 1. Cases of *C. parapsilosis* infective endocarditis

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