**Methods:** Fifteen pneumococcus strains expressing 14 different serotypes, including one non-encapsulated strain (R36A), were studied with flow cytometry (FC) and confocal fluorescence microscopy (CFM) for DBA binding. Pce enzyme activity was detected with a colorimetric assay using p-nitrophenyl-phosphorylcholine as the substrate. Mutant strains with pce knocked-out were constructed in R36A and D39 by replacing pce with Janus cassette. Both licD genes were sequenced for some of the strains.

**Results:** Ten of the 15 strains had Pce activity and all of them bound DBA (Table 1). When the pce gene was inactivated in two normally Pce-positive strains (R36A and D39), the strains did not show DBA binding by CFM (Figure 1). Thus, expression of Pce appears to be sufficient for expressing the DBA antigen. Of the five strains that had no Pce activity, two bound DBA. Sequencing of the licD genes in these two strains with positive DBA binding and negative Pce activity revealed one SNP in licD1 and four SNPs in licD2, resulting in a single amino acid difference each for LicD1 and LicD2, compared with R36A and D39.

**Conclusion:** DBA can bind to the terminal α-GalNAc-(1→3)β-GalNAc of pneumococcal TA and LTA, which is created by Pce. DBA binding is independent of capsule type. The unexpected binding of DBA to the two Pce-negative strains suggests that there is a Pce-independent mechanism for generating the target for DBA binding. Since LicD1 and LicD2 are involved in attaching PC to α-GalNAc-(1→3)β-GalNAc, we are now investigating their role in creating DBA targets independent of Pce.

### Table 1. Summary of DBA binding (DBA +/-) by FC and CFM, and associated Pce enzyme activity (Pce +/-)

|          | DBA (+) | DBA (-) | Total |
|----------|---------|---------|-------|
| Pce (+)  | 10      | 0       | 10    |
| Pce (-)  | 2       | 3       | 5     |
| Total    | 12      | 3       | 15    |

![Figure 1: DBA binding results with confocal fluorescence microscopy. R36A and D39 are positive for DBA binding. TREP6A and SPEC19F strains are negative for DBA binding (negative controls). R36A Δpce and D39 Δpce each have an inactivated pce gene and are negative for DBA binding. Red: DBA staining, blue: DNA counter-staining.](image.png)

**Disclosures. All authors:** No reported disclosures.

**2598. Macrophase Migration Inhibitory Factor May Contribute to Disseminated Coccidioidomycosis Susceptibility**

Camila D. Odio, MD; Lin Leng, PhD; Edwin Su, MS; Marta Pieczyhna, MS; John N. Galgiani, MD; Steven M. Holland, MD; Richard Bucala, MD, PhD; Yale Department of Internal Medicine, New Haven, Connecticut; University of Arizona College of Medicine, Tucson, Arizona; Laboratory of Clinical Immunology and Microbiology, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland

**Session:** 269. Pathogenesis and Host-Response Interactions

**Saturday, October 5, 2019: 12:15 PM**

**Background:** Disseminated coccidioidomycosis occurs in <1% of cases, and genetic polymorphisms may account for some of the variability in infection severity. Macrophage migration inhibitory factor (MIF) is an inflammatory cytokine with two promoter polymorphisms linked to variability in expression. High expression MIF promoter polymorphisms have been associated with granulomatous with polyangiitis (GPA), sarcoidosis and tuberculosis. Despite the overlap between MIF and Coccidioides immumity, MIF has never been studied in coccidioidomycosis.

**Methods:** A549 cells transfected with MIF promoter/luciferase plasmids of 0 or 8 CAATT were stimulated with 50 μg/mL of inactivated C. posadasi spherule lysate, and luciferase expression was measured as relative units (RU) of luminescence. Genomic DNA from patients with disseminated coccidioidomycosis (n = 37) and healthy controls (n = 371) was analyzed for the −749 CATT, −173 CATT, and −173 CATT microsatellite and the −173 CATT SNP. Cohorts were divided into self-identified African Americans and Caucasians, and allele frequencies were compared using Fisher exact test. Plasma MIF levels were analyzed by enzyme-linked immunosorbant assay using specific antibodies, and levels were compared by T-test.

**Results:** Human lung epithelial cells exposed to Coccidioides spherules had significantly higher MIF expression than unexposed controls (3.94 ± 0.44 vs. 3.02 ± 0.24 RU, P = 0.0162). Among Caucasians (n = 26), the high MIF expression −173C containing genotype was present in 50% of the coccidioidomycosis patients vs. 40% of healthy controls (P = 0.396). The −749CATT containing genotype was present in 40% of patients vs. 27% of controls (P = 0.240). Plasma MIF levels were higher in coccidioidomycosis patients with high- vs. low-expression alleles (P = 0.0088), but lower in patients vs. controls (P < 0.0001).

**Conclusion:** Coccidioides spherules stimulated MIF expression in human lung epithelial cells supporting the hypothesis that MIF is involved in immunity against this pathogen. In Caucasian subjects, the higher MIF expression genotypes were more common in patients with disseminated coccidioidomycosis when compared with healthy controls, although significance was limited by sample size. This is consistent with high MIF expression alleles associated with other granulomatous diseases, and may reflect destruction of the granuloma with pathogen dissemination.

**Disclosures. All authors:** No reported disclosures.

**2599. Studying the Effects of Altering Histone Modification on Aspergillus fumigatus Virulence**

Pam Lee, MD; Hong Liu, PhD; Scott Filler, MD; Harbor UCLA, Los Angeles, California

**Session:** 269. Pathogenesis and Host-Response Interactions

**Saturday, October 5, 2019: 12:15 PM**

**Background:** As there are few drugs for treating invasive aspergillosis, there is an urgent need for new antifungal agents. Enzymes involved in histone modification are possible antifungal drug targets. We set out to investigate whether genes whose products are involved in histone modifications influence the virulence of Aspergillus fumigatus (A).

**Methods:** Genes whose products were likely involved in histone modification were deleted in strain A293 using CRISPR-Cas9. Virulence was assessed in a tri-parental mating strain Af293 and ΔAf293 mutant had wild-type (WT) growth and conidiation in vitro. Mice infected with the WT strain had 100% mortality within 9 days whereas mice infected with the ΔAf293 mutant had only 40% mortality by 21 days. The ΔAf293 mutant also had impaired capacity to damage pulmonary epithelial cells in vitro.

**Conclusion:** Cds and Set2, components of the COMPASS complex, are required for normal growth in vitro. Sp3 and Sp8, members of the SAGA complex, are required for normal condensation and virulence. Hosa, A, of the RPDL3 complex, is necessary for maximal virulence and induction of host cell damage. Our results suggest that the Hosa histone deacetylase may be a promising drug target for treating invasive aspergillosis.

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**2600. Mannose-Binding Lectin Polymorphisms Are Important Modulating Factors in Community- and Hospital-Acquired Pneumonia Caused by Legionella spp.**

Porvias Kavalalkaras, MS; Ruta Prakashas, BS; Frederic Saab, BS; Ruta Petraitis, MD; Sophie Jarraud, PhD; Rasa Baneviciene, BS; Rita Planciunene, PhD; Thomas J. Walsh, MD, PhD (hon); Vidmantas Petraitis, MD; Well Cornell Medicine of Cornell University, New York, New York; Institute of Infectious Diseases and Pathogenic Microbiology, Prague, slide, and Lithuania; Poster Abstracts • OFID 2019:6 (Suppl 2) • S903