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$^{\triangle}$*pce* and D39$^{\triangle}$*pce*), 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

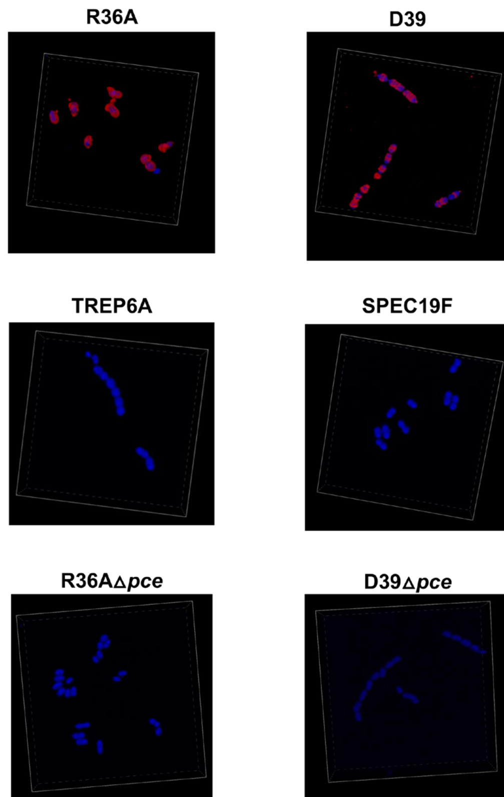

Figure 1. DBA binding results with confocal fluorescence microscopy. R36A and D39 are positive for DBA binding; TREP6A and SPEC19F strains are negative for DBA binding (negative controls); R36A Δ*pce* and D39 Δ*pce* each have an inactivated *pce* gene and are negative for DBA binding. Red: DBA staining; blue: DNA counter-staining.

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2598. Macrophage Migration Inhibitory Factor May Contribute to Disseminated Coccidioidomycosis Susceptibility

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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* polymorphisms have been associated with granulomatosis with polyangitis (GPA), sarcoidosis and tuberculosis. Despite the overlap between *MIF* and *Coccidioides* immunity, *MIF* has never been studied in coccidioidomycosis.

Methods: A549 cells transfected with *MIF* promoter/luciferase plasmids of 0 or 8 CATT repeats were stimulated with 50 µg/mL of inactivated *C. posadasii* 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 794 $CATT_{5-8}$ microsatellite and the -173 G/C 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 cells (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 -794 $CATT_7$ containing genotype was present in 40% of patients vs. 27% of controls (p = 0.240). Plasma MIF levels were higher in coccidoidomycosis patients with high- vs. low-expression alleles (P = 0.008), but lower in patients vs. controls (P < 0.0001).

Conclusion: *Coccoidioides* 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 expression *MIF* 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

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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* (Af).

Methods: Genes whose products were likely involved in histone modification were deleted in strain Af293 using CRISPR-Cas9. Virulence was assessed in a triamcinolone-treated mouse model of invasive pulmonary aspergillosis. The extent of Af-induced damage to the A549 pulmonary epithelial cell line was determined by Cr^{51} release assay.

Results: Af genes were selected for investigation based on their homology to genes encoding known histone modifying proteins and their high expression level in vivo. The genes were predicted to encode members of the COMPASS histone methyltransferase complex (*cclA/bre2*, *set2*/Afu5g06000), the SAGA histone acetyltransferase complex (*spt3*, *spt8*), and the RPDL histone deacetylase complex (*hosA*). The Δ*cclA* and Δ*set2* mutants had significant growth defects on rich media and were not tested further. The Δ*spt3* and Δ*spt8* mutants grew normally and had mild conidiation defects. The Δ*hosA* 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 the Δ*spt3,* Δ*spt8,* and Δ*hosA* mutants had only 40% mortality by 21 days. The Δ*hosA* mutant also had impaired capacity to damage pulmonary epithelial cells in vitro.

Conclusion: Ccla and Set2, components of the COMPASS complex, are required for normal growth in vitro. Spt3 and Spt8, members of the SAGA complex, are required for normal conidiation and virulence. HosA, part of the RPD3L 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.

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