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1712. The CDC SHIELD Orange County Project – Baseline Multi Drug-Resistant Organism (MDRO) Prevalence in a Southern California Region

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Background. MDROs can spread between hospitals, nursing homes (NH), and long-term acute care facilities (LTACs) via shared patients. SHIELD OC is a regional decolonization collaborative involving 38 of 104 countywide adult facilities identified by their high degree of direct and indirect patient sharing with one another. We report baseline MDRO prevalence in these facilities.

Methods. Adult patients in 38 facilities (17 hospitals, 18 NHs, 3 LTACs) underwent point-prevalence screening between September 2016–April 2017 for MRSA, VRE, ESBL, and CRE using nares, skin (axilla/groin), and peri-rectal swabs. In NHs and LTACs, residents were randomly selected until 50 sets of swabs were obtained. Swabbing in hospitals involved all patients in contact precautions. An additional set of swabs were also performed for all LTAC admissions from November 2016–February 2017.

Results. The overall prevalence of any MDRO among patients was 64% (44%–88%) in NHs, 80% (range 72%–86%) in LTACs, and 64% (54–84%) in hospitals (contact precaution patients) (Table 1). Only 25%, 64%, and 81% of patients were already known to harbor an MDRO in NHs, LTACs, and hospitals, respectively. Known MDRO patients also harbored another MDRO 49%, 63%, and 34% of the time for NHs, LTACs, and hospitals, respectively. In LTACs, MDRO point prevalence was 38% higher than the usual admission prevalence (65% higher for MRSA, 34% higher for VRE, 95% higher for ESBL, and 50% higher for CRE).

Conclusion. MDRO carriage in highly inter-connected NHs and LTACs was widespread, rivaling that found in hospitalized patients on contact precautions. MRSA, VRE, and ESBL carriage far outnumbered CRE carriage. A history of MDRO was insensitive for identifying MDRO carriers, and many patients carried multiple MDROs. The extensive MDRO burden and transmission in long-term care settings suggests that regional MDRO prevention efforts must include MDRO control in long-term care facilities.

Table 1. SHIELD OC MDRO Point Prevalence in Acute and Long-Term Care Patients

	Patients Swabbed	Any MDRO	MRSA	VRE	ESBL	CRE
18 Nursing Homes – Random Sample of All Residents						
Nares	900	28%	28%	-	-	-
Axilla/Groin	900	47%	30%	10%	22%	1%
Peri-Rectal	900	52%	25%	15%	31%	1%
All Body Sites	**2700**	**64%**	**42%**	**16%**	**34%**	**2%**
3 Long Term Acute Care Hospitals (LTACs) – Random Sample of All Patients						
Nares	150	23%	23%	-	-	-
Axilla/Groin	150	61%	17%	37%	27%	7%
Peri-Rectal	150	73%	19%	52%	35%	7%
All Body Sites	**450**	**80%**	**33%**	**55%**	**39%**	**9%**
17 Hospitals – Patients on Contact Precautions						
Nares	713	30%	30%	-	-	-
Axilla/Groin	713	32%	13%	14%	14%	1%
Peri-Rectal	713	48%	13%	23%	24%	3%
All Body Sites	**2139**	**64%**	**37%**	**25%**	**27%**	**3%**

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1762. Complicated *Staphylococcus aureus* Bacteremia (SAB) Is Associated with Genetic Variation in *GLS2*

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Session: 214. Host–pathogen Integration
Saturday, October 7, 2017: 8:30 AM

Background. SAB is a serious, common infection. We used whole exome sequencing (WES) to examine the cumulative effect of coding variants in each gene on risk of complicated SAB in a discovery set of patients, and then evaluated the nominally significant genes in a replication set of patients using custom-capture sequencing.

Methods. The discovery set comprised 84 complicated SAB cases (endocarditis or bone/joint infection) frequency-matched by age (in deciles), sex, and bacterial clonal complex (CC5/30, CC8) to 84 uncomplicated SAB controls. All were white inpatients at Duke University. WES utilized Agilent SureSelect 72Mb capture kits, followed by sequencing on an Illumina HiSeq2000, alignment and base calling with a standard pipeline. The SKAT-O and EPACTS packages were used for gene-based association tests and logistic regression models with Firth bias correction, respectively. Both controlled for age, sex, and clonal complex as covariates. The replication set of 122 complicated SAB cases and 118 uncomplicated SAB controls was frequency matched by age, sex, and clonal complex. All were white Europeans collected by the Statens Serum Institute. An Agilent SureSelect 2Mb capture array captured genic sequence for 342 genes nominally associated with complicated SAB in discovery (SKAT-O $P < 0.035$). Sequencing and data analysis proceeded as for WES. A Bonferroni-corrected gene-based test P-value of $1.5 \times 10^{-}4$ determined significance in the replication set.

Results. One gene, *GLS2*, was significantly associated with complicated SAB in the replication set ($P = 1.2 \times 10^{-4}$). The strongest single-variant association in all 342 genes was rs2657878 in *GLS2* ($p = 5 \times 10^{-4}$). This variant is strongly correlated with a missense variant (rs2657879, $p = 4.4 \times 10^{-3}$) in which the minor allele (associated here with complicated SAB) has previously been shown to reduce circulating glutamine levels.

Conclusion. Comprehensive examination of the coding sequence for association with complicated SAB in a two-stage discovery/replication design identified a novel candidate gene. *GLS2* is an interesting candidate for complicated SAB due to its role in regulating glutamine production, a key factor in activation of T-cell production.

Disclosures. **V. Fowler Jr.**, Pfizer, Novartis, Galderma, Novadigm, Durata, Debiopharm, Genentech, Achaogen, Affinium, Medicines Co., Cerexa, Tetraphase, Trius, MedImmune, Bayer, Theravance, Cubist, Basilea, Affinergy, Janssen, xBiotech, Contrafect: Consultant, Consulting fee; NIH, Basilea, MedImmune, Cerexa/Forest/Actavis/Allergan, Pfizer, Advanced Liquid Logics, Theravance, Novartis, Cubist/Merck; Medical Biosurfaces; Locus; Affinergy; Contrafect; Karius: Grant Investigator, Research grant; Green Cross, Cubist, Cerexa, Durata, Theravance; Debiopharm: Consultant, Consulting fee; UpToDate: author on several chapters, Royalties

1763. Role of M Cells in Human Mucosal Immunity to *Mycobacterium tuberculosis*

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Session: 214. Host–pathogen Integration
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Background. Mycobacterium tuberculosis (Mtb), the causative agent of tuberculosis (TB), is a bacterial pathogen that infects roughly one-third of the worldÕs population and causes 1–2 million deaths per year. The current paradigm is that phagocytosis of Mtb by patrolling alveolar macrophages initiates Mtb infection. While this model can account for pulmonary TB, it does not adequately explain the occurrence of extrapulmonary forms of TB that manifest in the absence of obvious lung involvement, such as tuberculous cervical lymphadenitis, also known as scrofula. We hypothesized that specialized epithelial cells called microfold cells (M cells) may be an alternate portal of entry for Mtb. Previously we demonstrated that Mtb is able to transcytose across an epithelial barrier in an M cell dependent manner and that M cell mediated transcytosis is vital for Mtb pathogenesis in a mouse model of tuberculosis.

Methods. We used an in vitro M-cell mediated translocation assay and a Mtb mutant lacking a key virulence factor, ESAT6. We used biochemistry and genetics to identify a novel receptor for ESAT6. We also developed a novel explanted human adenoid Mtb infection model to study mucosal immunity.

Results. We now demonstrate that the Mtb virulence factor ESAT6 is necessary and sufficient to mediate binding and transcytosis by M cells in vitro and in vivo, and that uptake of Mtb by M cells requires a unique cell surface ESAT6 receptor. We developed a novel explanted human adenoid model of M cell biology and demonstrate rapid Mtb transcytosis by primary human tissue within 60–120 minutes. Using flow cytometry we find that Mtb is first ingested by M cells and then after transcytosis, by tissue resident antigen-presenting cells. Explanted adenoids from 10 independent donors display a wide range of Mtb uptake.

Conclusion. We conclude that Mtb ESAT6 is necessary for Mtb uptake by M-cells and that binding and transcytosis require a host receptor. Because explanted adenoids display a wide range of Mtb uptake, M cell mediated transcytosis may confer differential susceptibility to scrofula and disseminated disease. These findings are significant as M cells could potentially serve as the basis for novel therapeutic targets against primary Mtb infection.

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1764. Investigating Immune Correlates of Protection to Tuberculosis Using an Ultra-Low Dose Infection in a Mouse Model

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