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Adjuvants for the potentiation of the activity of β-lactam antibiotics against methicillin-resistant *Staphylococcus aureus**

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OBJECTIVES/GOALS: Methicillin-resistant *Staphylococcus aureus* (MRSA) is a human bacterial pathogen and is classified as a serious threat. MRSA has become resistant to most B-lactam antibiotics (penicillins and cephalosporins). The goal of this study is to identify an antibiotic adjuvant capable of resurrecting B-lactams for the treatment of MRSA infections. METHODS/STUDY POPULATION: A fluorescence-reporter assay was used to screen a compound library. Minimum-inhibitory concentrations were assessed for the compounds against various MSSA and MRSA strains. A common resistance mechanism to B-lactams by MRSA is by the function of the bla operon. One gene in this operon encodes for a B-lactam sensor/signal transducer protein BlaR, the primary target of this study. Inhibition of BlaR by compound 1 (best potentiator of oxacillin) was studied by nano-differential scanning fluorimetry (nanoDSF), surface plasmon resonance (SPR), scanning electron microscopy (SEM), and time-kill assays. RESULTS/ANTICIPATED RESULTS: We identified 80 compound hits from a 1,974-compound NCI library. Twenty-four compounds showed potentiating ability (2- to 4,096-fold decrease in MIC for oxacillin). Seven compounds exhibited melting temperature shifts by nanoDSF of BlaR, indicating binding. SPR determined compound 1 has a binding affinity of 31 micromolar to BlaR-SD. SEM images showed disruption in the *S. aureus* cell wall on exposure to compound 1 and oxacillin. *S. aureus* N315 showed 3-log reduction in bacterial count treated with a mixture of compound 1 and oxacillin. DISCUSSION/SIGNIFICANCE OF IMPACT: Compound 1 targets BlaR-SD, which restores S. aureus susceptibility to treatment by oxacillin. There are currently few antibiotics available in the clinic capable of treating MRSA infections. The combination hold promise of a treatment option for MRSA.

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Inclusion of cytomegalovirus viral Fc gamma receptors in a glycoprotein B protein subunit vaccine improves Fc-mediated effector responses

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OBJECTIVES/GOALS: We hypothesized that adding cytomegalovirus (CMV) viral Fc gamma receptors (vFcγRs) to a glycoprotein B (gB) protein subunit vaccine would improve vaccine-elicited Fc mediated effector functions such as antibody dependent cellular phagocytosis (ADCP) and cytotoxicity (ADCC), over gB subunit alone. METHODS/STUDY POPULATION: We immunized rabbits (n = 4 per group) at Weeks 0, 4, and 8 with 20μg gB alone or with one vFcgR (gp34, gp68, or gp95) at 20μg or 40μg, adjuvanted with squalene emusion, Addavax. Plasma from immunized rabbits was analyzed for antigen-specific IgG binding via enzyme-linked immunosorbent assays (ELISAs). ADCP was measured by conjugating whole virions to a fluorescent marker (AF647), incubating the fluorescent virus with rabbit plasma, and measuring uptake of virus by THP-1 monocytes via flow cytometry. ADCC was measured by natural killer cell degranulation via flow cytometric detection of CD107a expression following co-incubation with CMV-infected fibroblasts and rabbit plasma. RESULTS/ANTICIPATED RESULTS: Each vFcγR demonstrated immunogenicity, although average vFcγR-binding IgG titers were between 4- to 10-fold higher in animals receiving the 40μg dose of each vFcγR compared to the 20μg dose. We observed similar IgG binding responses against gB among all vaccine groups. Comparing groups at peak immunogenicity (Week 10), ADCP responses were improved over gB alone by approximately twofold in animals receiving 40ug of each vFcγR. This effect was maintained across several human CMV strains with variable vFcγR genes. ADCC responses were undetectable in all animals immunized with gB alone, yet those receiving 40μg gp34 or gp95 demonstrated detectable ADCC. DISCUSSION/SIGNIFICANCE OF IMPACT: HCMV-specific ADCP and ADCC are associated with protection against vertical CMV transmission, so a vaccine including vFcγRs which can improve vaccine-elicited Fc-effector responses is promising toward reducing the immense global impact of congenital CMV and associated neurologic birth defects.

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Music use for dementia care in urban elder care communities in Northeast Kansas

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OBJECTIVES/GOALS: Research supports the use of music to improve the care and well-being of adults living with dementia; however, the practice and implementation of music in elder care communities is not regulated. The goal of this qualitative study was to survey elder care communities in Northeast Kansas to determine the use of music with people living with dementia. METHODS/STUDY POPULATION: We interviewed staff (n = 10) at five elder care communities in the Kansas City Metro area and observed musical activities and artifacts in shared living spaces within each community. Interview questions included details of the frequency and purpose of using music, who determined which music to use, and any effects, positive or negative, the interviewee believed to be associated with the use of music. Musical events, visiting musicians or music therapists leading group sing-alongs were observed at two communities, and music-related activities led by staff were observed at two others. RESULTS/ANTICIPATED RESULTS: Music was used in some way at each of the five communities. Each location had recorded music available to residents in the shared living spaces, and most had a piano in the main lounge area. During the sing-along and music-related activities, residents were observed singing along to songs from memory, engaging with one another and the group leader and smiling. Staff employed by each community varied in their level of musical training and experience, from none to a full-time music therapist in residence. Staff interviewed said they believed music was helpful to aid memory recall, reduce anxiety, and to engage interest. Interestingly, a music therapist at one site also described how music

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