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Intrinsic bactericidal activity to assess breadth of immunity following a University-based meningococcal vaccination campaign

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Background

Between 2009 and 2015, seven outbreaks of meningococcal disease due to Neisseria meningitidis serogroup B occurred at universities in the United States. A seroprevalence study was conducted among students to analyze immune responses following a university based 4CMenB vaccination campaign [1]. Vaccine effectiveness is inferred from the measurement of antibody-mediated, complement-dependent serum bactericidal activity (SBA). Externally derived human complement SBA (hSBA), is an established measure of responses to specific meningococcal vaccine antigens. Intrinsic complement SBA (iSBA) provides an

opportunity to assess vaccine-induced antibody responses against a diverse spectrum of meningococcal stains without identifying an external complement source for each strain.

Aim/Methods
We selected a panel of 30 different N. meningitidis serogroup B strains and tested 120 sera collected from university students processed to preserve complement activity using an iSBA assay we developed. The strain panel includes outbreak, breakthrough, vaccine antigen, and invasive disease clinical isolates. iSBA of sera diluted 1:4 and 1:8 was determined and merged with hSBA results for two antigen test strains and a university outbreak strain. We assessed the breadth of response to the 30 strains and the relationship between iSBA and hSBA results using conditional inference trees and LASSO regression methods.

Results
iSBA at 1:4 and 1:8 was determined against all 30 strains for sera from 118 participants. By individual strain, the proportion of sera that killed at 1:4 ranged from 11% to 97.5%. Vaccinated individuals were more likely to have positive iSBA (≥1:4) against meningococcal strains than unvaccinated individuals, although there was great variability in responses by strain. The strength of the association between the iSBA assay positivity and hSBA seropositivity (>=4) for a given strain varied by strain, with vaccination status increasing the prediction ability for one strain well-matched to the NadA component of the vaccine.

Conclusions
iSBA may provide insight into meningococcal vaccine responses, breadth of vaccine coverage, and strain variability. Correlations in iSBA responses were identified between strain pairs. The associations between iSBA and hSBA seropositivity suggested complex relationships that should be explored further. iSBA is a feasible method for assessing antibody responses against antigenically diverse invasive disease isolates.