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A broadly-protective vaccine against meningococcal disease in sub-Saharan Africa based on Generalized Modules for Membrane Antigens (GMMA)

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Neisseria meningitidis causes epidemics of meningitis in sub-Saharan Africa. These have mainly been caused by capsular group A strains, but W and X strains are increasingly contributing to the burden of disease. Therefore, an affordable vaccine that provides broad protection against meningococcal disease in sub-Saharan Africa is required.; We prepared Generalized Modules for Membrane Antigens (GMMA) from a recombinant serogroup W strain expressing PorA P1.5,2, which is predominant among African W isolates. The strain was engineered with deleted capsule locus genes, lpxL1 and gna33 genes and over-expressed fHbp variant 1, which is expressed by the majority of serogroup A and X isolates.; We screened nine W strains with deleted capsule locus and gna33 for high-level GMMA release. A mutant with five-fold increased GMMA release compared with the wild type was further engineered with a lpxL1 deletion and over-expression of fHbp. GMMA from the production strain had 50-fold lower ability to stimulate IL-6 release from human PBMC and caused 1000-fold lower TLR-4 activation in Human Embryonic Kidney cells than non-detoxified GMMA. In mice, the GMMA vaccine induced bactericidal antibody responses against African W strains expressing homologous PorA and fHbp v.1 or v.2 (geometric mean titres [GMT]=80,000-200,000), and invasive African A and X strains expressing a heterologous PorA and fHbp variant 1 (GMT=20-2500 and 18-5500, respectively). Sera from mice immunised with GMMA without over-expressed fHbp v.1 were unable to kill the A and X strains, indicating that bactericidal antibodies against these strains are directed against fHbp.; A GMMA vaccine produced from a recombinant African N. meningitidis W strain with deleted capsule locus, lpxL1, gna33 and overexpressed fHbp v.1 has potential as an affordable vaccine with broad coverage against strains from all main serogroups currently causing meningococcal meningitis in sub-Saharan Africa.

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