The antibody response of pregnant Cameroonian women to VAR2CSA ID1-ID2a, a small recombinant protein containing the CSA-binding site.

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Public Summary:
In pregnant women, Plasmodium falciparum-infected erythrocytes expressing the VAR2CSA antigen bind to chondroitin sulfate A in the placenta causing placental malaria. The binding site of VAR2CSA is present in the ID1-ID2a region. This study sought to determine if pregnant Cameroonian women naturally acquire antibodies to ID1-ID2a and if antibodies to ID1-ID2a correlate with absence of placental malaria at delivery. Antibody levels to full-length VAR2CSA and ID1-ID2a were measured in plasma samples from 745 pregnant Cameroonian women, 144 Cameroonian men, and 66 US subjects. IgM levels and IgG avidity to ID1-ID2a were also determined. As expected, antibodies to ID1-ID2a were absent in US controls. Although pregnant Cameroonian women developed increasing levels of antibodies to full-length VAR2CSA during pregnancy, no increase in either IgM or IgG to ID1-ID2a was observed. Surprisingly, no differences in antibody levels to ID1-ID2a were detected between Cameroonian men and pregnant women. For example, in rural settings only 8-9% of males had antibodies to full-length VAR2CSA, but 90-96% had antibodies to ID1-ID2a. In addition, no significant difference in the avidity of IgG to ID1-ID2a was found between pregnant women and Cameroonian men, and no correlation between antibody levels at delivery and absence of placental malaria was found. Thus, the response to ID1-ID2a was not pregnancy specific, but predominantly against cross-reactivity epitopes, which may have been induced by other PfEMP1 antigens, malarial antigens, or microbes. Currently, ID1-ID2a is a leading vaccine candidate, since it binds to the CSA with the same affinity as the full-length molecule and elicits binding-inhibitory antibodies in animals. Further studies are needed to determine if the presence of naturally acquired cross-reactive antibodies in women living in malaria endemic countries will alter the response to ID1-ID2a following vaccination with ID1-ID2a.

Scientific Abstract:
In pregnant women, Plasmodium falciparum-infected erythrocytes expressing the VAR2CSA antigen bind to chondroitin sulfate A in the placenta causing placental malaria. The binding site of VAR2CSA is present in the ID1-ID2a region. This study sought to determine if pregnant Cameroonian women naturally acquire antibodies to ID1-ID2a and if antibodies to ID1-ID2a correlate with absence of placental malaria at delivery. Antibody levels to full-length VAR2CSA and ID1-ID2a were measured in plasma samples from 745 pregnant Cameroonian women, 144 Cameroonian men, and 66 US subjects. IgM levels and IgG avidity to ID1-ID2a were also determined. As expected, antibodies to ID1-ID2a were absent in US controls. Although pregnant Cameroonian women developed increasing levels of antibodies to full-length VAR2CSA during pregnancy, no increase in either IgM or IgG to ID1-ID2a was observed. Surprisingly, no differences in antibody levels to ID1-ID2a were detected between Cameroonian men and pregnant women. For example, in rural settings only 8-9% of males had antibodies to full-length VAR2CSA, but 90-96% had antibodies to ID1-ID2a. In addition, no significant difference in the avidity of IgG to ID1-ID2a was found between pregnant women and Cameroonian men, and no correlation between antibody levels at delivery and absence of placental malaria was found. Thus, the response to ID1-ID2a was not pregnancy specific, but predominantly against cross-reactivity epitopes, which may have been induced by other PfEMP1 antigens, malarial antigens, or microbes. Currently, ID1-ID2a is a leading vaccine candidate, since it binds to the CSA with the same affinity as the full-length molecule and elicits binding-inhibitory antibodies in animals. Further studies are needed to determine if the presence of naturally acquired cross-reactive antibodies in women living in malaria endemic countries will alter the response to ID1-ID2a following vaccination with ID1-ID2a.