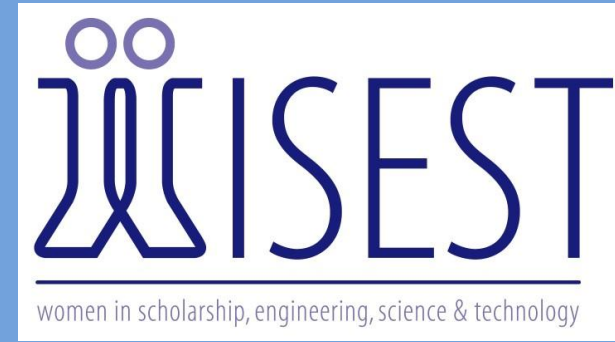


Evaluating the acquisition of antibodies against a VAR2CSA peptide in malarial-exposed pregnant populations



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1. Background

- Malaria occurs when *Plasmodium* parasites infect red blood cells.
- It's transmitted through the bites of infected female Anopheles mosquitos.
 - 619 000 deaths in 2021¹
- Infection with *Plasmodium falciparum* during pregnancy leads to severe health outcomes in mothers and infants².
 - Death, anemia, miscarriage, pre-term delivery and low-birth weight
- Placental malaria occurs when red blood cells infected with *P. falciparum* accumulate within the placenta.
 - VAR2CSA** is a protein on the surface of the infected red blood cells that allows them to attach to the placenta³.
 - Antibodies acquired against VAR2CSA are protective⁴.
 - Cross-reactive peptide 2 (CRP2)** maps to a region in VAR2CSA, and we hypothesize that antibodies to CRP2 contribute to protection against placental malaria

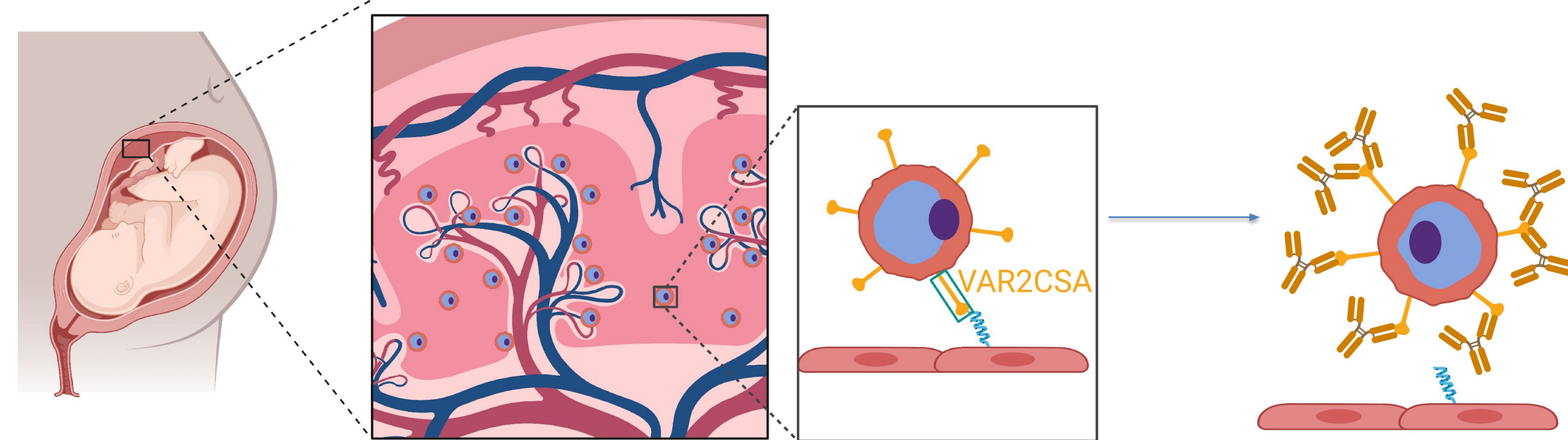


Figure 1. Placental malaria with and without the presence of antibodies

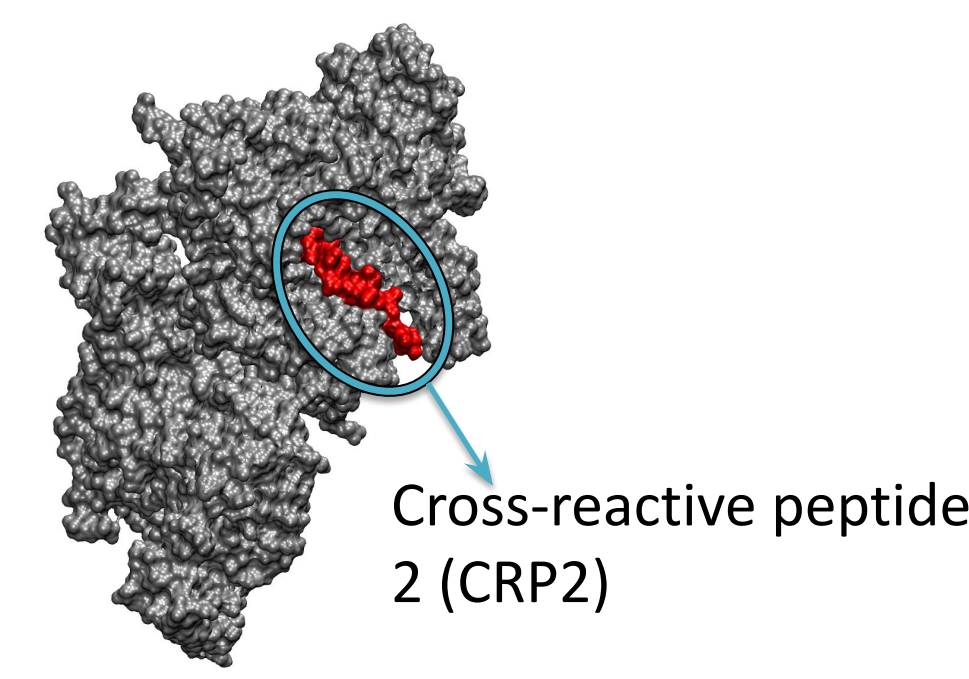


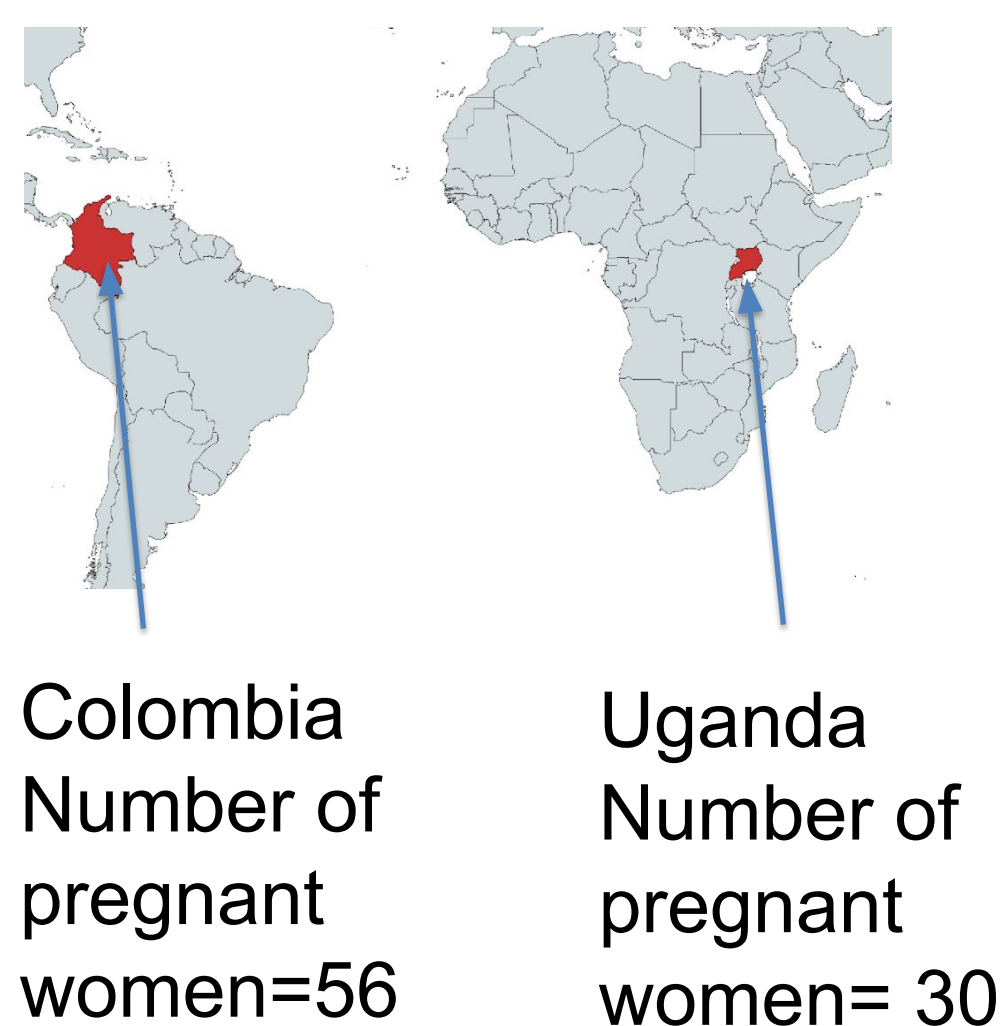
Figure 2. 3-dimensional structure of VAR2CSA showing CRP2 (red)

Research Question

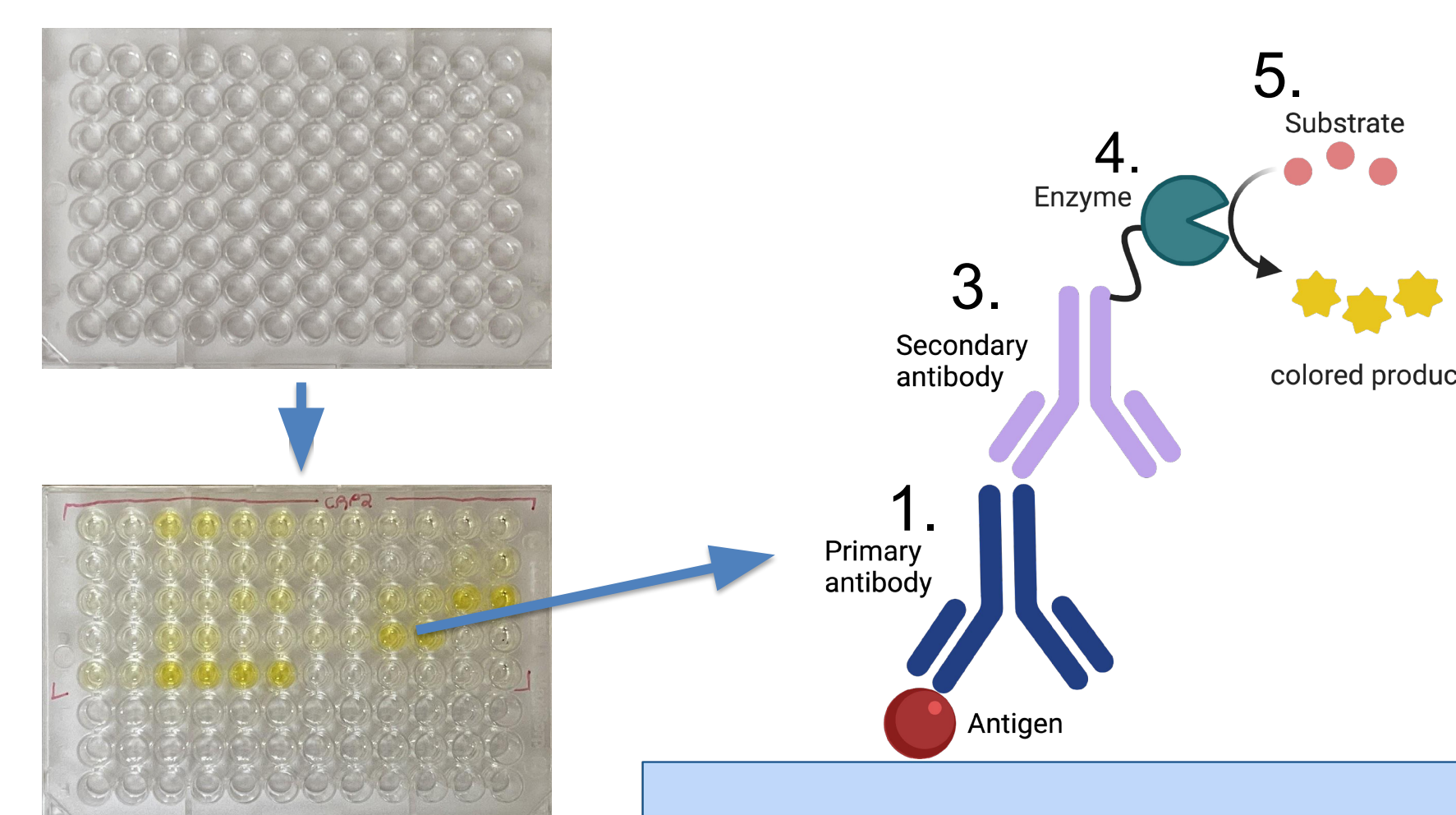
Do pregnant women living in malaria-exposed areas acquire antibodies against CRP2?

2. Methods

A. Sample collection



B. Screen samples by ELISA (enzyme-linked immunosorbent assay)

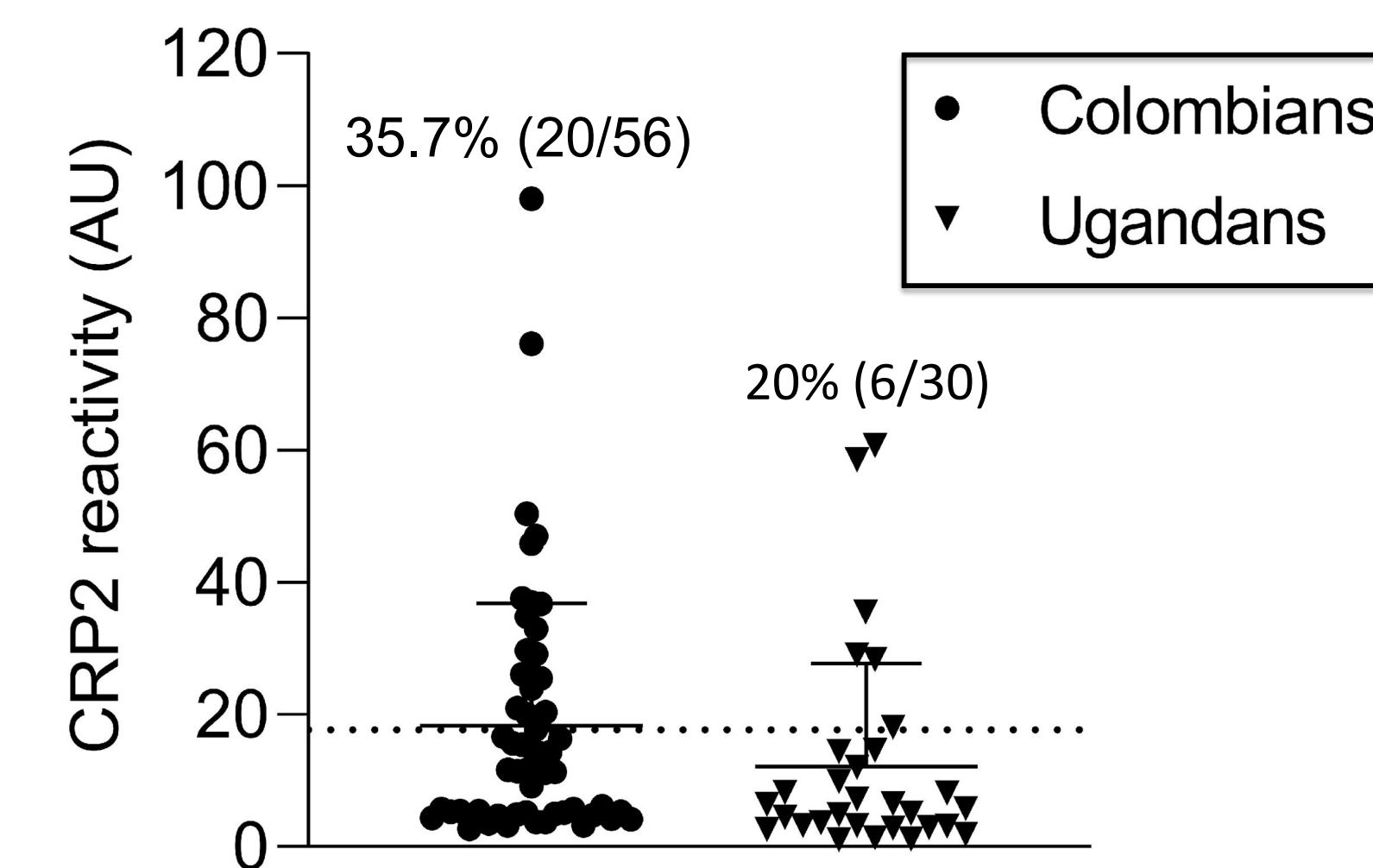


C. ELISA protocol

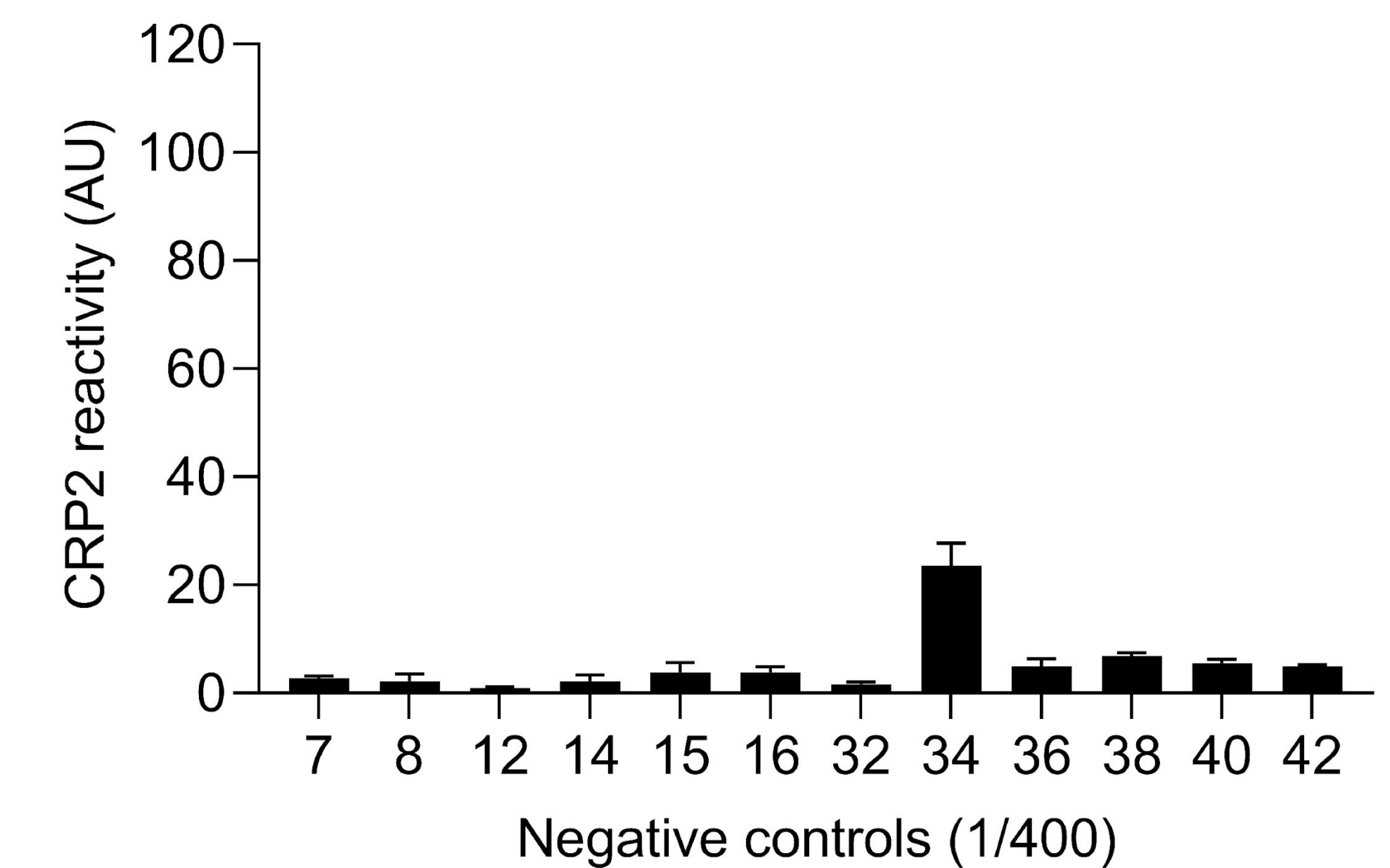
- Coating; add CRP2 antigens to plate wells
- Blocking; add a buffer to each well which prevents non-specific binding
- Add serum samples
- Add secondary antibody which is conjugated to an enzyme
- Add a substrate to form a coloured product

3. Results

A. Malaria exposed pregnant women acquire antibodies to CRP2



B. Limited reactivity of unexposed Colombians to CRP2



C. Amino acid residues in CRP2 are conserved



Logo plot showing the limited variability of the amino acid residues in CRP2. Plot was generated using 722 sequences from different regions in the world.

Figure 5. Reactivity of sera to cross reactive peptide 2. Samples collected from (A) Colombian (N=56) and Ugandan (N=30) pregnant women and (B) unexposed Colombians were screened for the presence of CRP2 antibodies at 1/400 dilution. The unexposed samples were screened twice to determine a cut off for seropositivity (dashed line in A). Data are represented as mean +/- SD. Logo plot in (C) was generated using WebLogo⁵. CRP2 – cross-reactive peptide 2.

4. Conclusions

- Pregnant women living in malaria exposed regions naturally acquire antibodies against CRP2, indicating that CRP2 is accessible to antibodies generated by the host immune system.
- CRP2 has a sequence with limited variability, suggesting its ability to generate antibodies that recognizes different VAR2CSA variants.
- Further studies are needed to examine the functionality of CRP2 antibodies. For example, studying the capability of CRP2 antibodies to block infected red blood cells binding to the placenta.

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