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A *Plasmodium falciparum* antigen increases HIV-1 replication in a human placenta-derived cell line

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Background

Malaria is endemic in countries of sub-Saharan Africa where there is also a high prevalence of HIV-1 infection, with pregnant women being the population most at risk to both infections. Epidemiological data and indirect evidence have established a link between placental malaria and an increased risk for HIV-1 mother-to-child transmission (MTCT), by unknown mechanisms.

Material and methods

The placenta-derived choriocarcinoma cell line BeWo and monocyte-derived macrophages (MDM) were infected with varying doses of luciferase reporter HIV-1 pseudotyped with the vesicular stomatitis virus protein G. A recombinant DBL3γ domain, derived from a placental *Plasmodium falciparum* Erythrocyte Membrane Protein 1 (PfEMP1) adhesin domain (DBL3γ-732), that binds to chondroitin sulfate A (CSA) and a non-CSA-binding PfEMP1 adhesin domain, DBL1α-varO domain were used to stimulate infected cells. In some experiments, DBL3γ-732 was preincubated with the Fab fragment of a specific or an irrelevant monoclonal antibodies (mAb) that inhibits, or not, binding to CSA. TNF-α was measured in the culture supernatants and luciferase activity was quantified at different time points in cell lysates to evaluate viral replication.

Results

Addition of DBL3γ-732 to BeWo cells, led to a dose-dependent increase of HIV-1 replication of up to 400 times the control level in the absence of DBL3γ-732. This enhancement was specific since it was inhibited by Fab fragment of an anti- DBL3γ-732 monoclonal antibody but not by the Fab of an irrelevant mAb. In contrast, the addition of DBL1α-varO domain does not increase viral replication. In MDM which presents surface CSA, both DBL domains strongly inhibit viral replication. The effect of DBL3γ-732 on HIV-1 replication is most likely mediated by TNF-α as this cytokine is significantly increased by DBL3γ-732 binding to BeWo cells and MDM.

Conclusions

This study shows, for the first time, a direct link between a *P. falciparum* antigen and an increase of HIV-1 replication in placental cells *in vitro*. If this is occuring *in vivo*, the presence of both infections could lead to a higher risk of HIV-1 *in utero* transmission. These data underline the importance of efficient malaria prophylaxis and antiretroviral interventions for pregnant women in areas where HIV-1 and malaria co-circulate.