IL-12p70, IL-8, IL-4 Cytokine responses but not antibody responses are associated with protection to clinical conversion of asymptomatic infections in highly exposed individuals in Cameroon

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Background
The asymptomatic carriage of malaria parasites, particularly for extended durations in areas with high transmission of P. falciparum represents a serious challenge to malaria elimination globally. Two keys immunological processes, including anti-parasite and anti-disease immunity have been implicated in establishment and maintenance of asymptomatic infections. However, the immunological factors that determine the conversion from asymptomatic infections to symptomatic malaria remain poorly understood.

Objective
We sought to this study to determine the association between antibody or cytokine responses and clinical conversion of asymptomatic infections in highly exposed persons in Cameroon.

Methods
Asymptomatic P. falciparum infected individuals (Infected + No fever (T°C< 37.5) were followed for 10 weeks, during which time some developed malaria-associated fever (ST-ASM) and others remained asymptomatic (LT-ASM).

Mass screening Sampling 1
Malaria diagnostic

Treatment

Sampling Follow-up

1 2 3 4 5 6 7 8 9 10
Weeks

• Non-infected
• Symptomatic
• Asymptomatic

Malaria diagnostic

Plasma (-80 °C)

Indirect Elisa

LumineX technology

Antiplasmodial antibody to:

- Total P. falciparum soluble protein extract (SE)
- Recombinant proteins: EBA-175, MSP-1c19, MSP-4p20

Multiplex-based 38 Cytokines measurement (MILLIPLEX KIT): IL-1α, IL-1β, IL-1RA, IL-2-IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-12p40, IL-12p70, IL-13, IL-15, IL-17A, IFN-α2, IFN-γ, TNF-α, TNF-β, IP-10, MCP-1, MCP-3, MIP-1α, MIP-1β, Eotaxin, FcαR1, Flt3L, GRO, GRO-CSF, G-CSF, G-CSFR, SCD40L, Flt-3L, EGF, FGF-2, TGF-α and VEGF

Results
High prevalence of asymptomatic malaria and low clinical conversion rate in this population

No association between plasma antiplasmodial antibody levels and clinical conversion from asymptomatic to symptomatic malaria

Low pro-inflammatory and Th2 regulatory cytokine responses are associated to clinical conversion from asymptomatic to symptomatic malaria

Biased in IL-10 to pro-inflammatory cytokine ratios is associated to clinical conversion from asymptomatic to symptomatic malaria

Conclusion
Taken together, the above findings implicate cytokine but not antibody responses in clinical conversion during asymptomatic infections in highly exposed Cameroonians.

References

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