



Decreased percentage of plasmacytoid dendritic cells and increased plasma levels of IFN- α in Fulani children undergoing *Plasmodium falciparum* infection in Mali.



Charles Arama^{1,2}, Pablo Giusti¹, Stefanie Boström¹, Victor Dara², Boubacar Traore², Amagana Dolo², Ogobara Doumbo², Stefania Varani¹ and Marita Troye-Blomberg¹.

1 Department of Immunology Wenner-Gren Institute Stockholm University.

2 Malaria Research and Training Centre FMPOS University of Bamako.



Background (1)



Plasmodium falciparum (Pf) infections are complex and immunity is acquired only after long time exposure.

Understanding the host's immune response involved in the protection of this disease may help to develop new strategies to control malaria

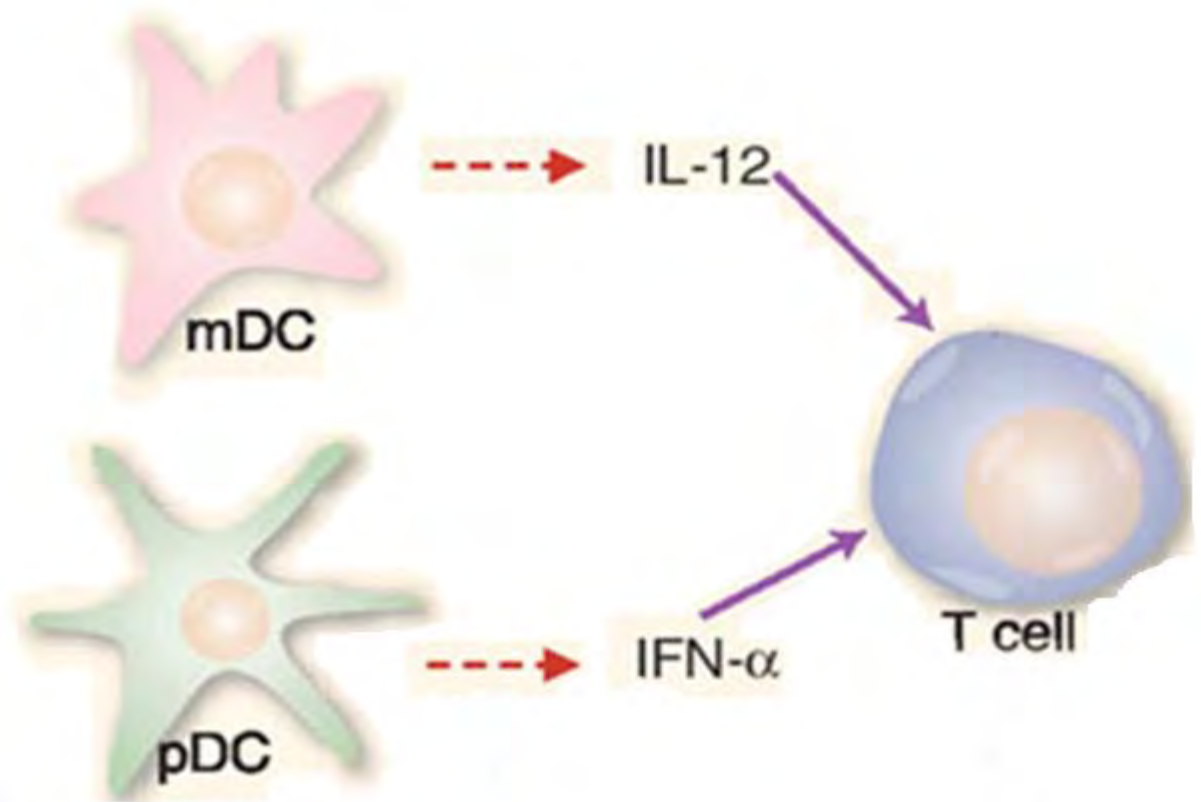
The Fulani are more protected against malaria as compared to the Dogon:

- Lower parasite rate
- Less affected by the disease
- Higher levels of anti-malaria-specific IgG and IgE antibodies
- Higher spleen enlargement rate

Background (2)

Dendritic cells (DC)

- **Myeloid DC**
 - Blood Dendritic Cell Antigen (BDCA) 1+
 - BDCA3+
- **Plasmacytoid DC**
 - BDCA2+





Background (3)



- Dendritic cells (DCs) are crucial for activating naïve T cells thereby bridging innate and acquired immunity.
- Increased numbers of BDCA3+ DCs have been associated with severe malaria
- BDCA2+ DCs (pDC) produce IFN- α and are important for viral immunity .
- The exact role of pDC remains unclear during malaria infection.
- However, increasing evidence suggest that they produced high level of IFN- α through TLR9 induced responses by Hemozoin or malaria parasites DNA *in vitro*.



Hypothesis & Aim



- We hypothesise that the relative protection of Fulani may be related to the properties of their antigen presenting cells
- The aim of this study was to investigate the role of plasmacytoid DC in Fulani children that are relatively protected against malaria, as compared to Dogon Children.



Methods (1)



The study was carried out in Manteourou village, District of Koro in north-eastern Mali during the malaria transmission season 2008.



37 Fulani and 40 Dogon children from 2 to 10 years of age were enrolled in the study.

Methods (2)

Written informed consent was obtained from parents of each child before enrolment in the study

Ethical approval was obtained from the Ethic committee of FMPOS Mali.



The children were divided in to 4 groups according to ethnicity and slide positivity:

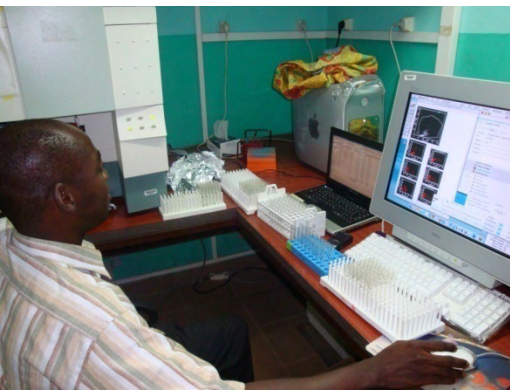
- infected Dogon (n=20),
- uninfected Dogon (n=20),
- infected Fulani (n=14)
- uninfected Fulani (n=23).

Methods (3)



Antibodies to malaria antigens and cytokines were measured in the plasma using indirect ELISA and CBA

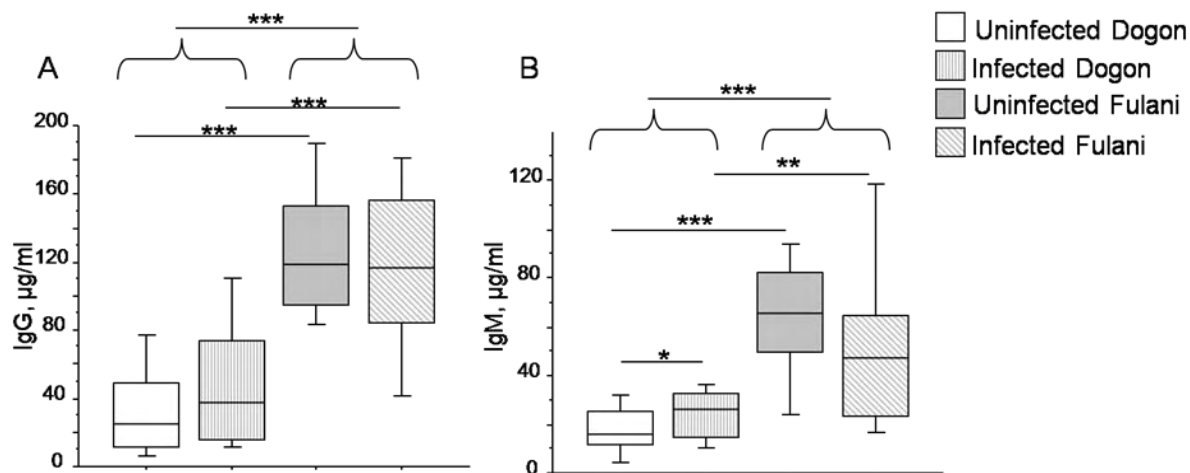
PBMCs were fixed and stained for phenotypic analysis of DCs FACS



Results (1)

Specific antibody responses to *Pf* antigen in Fulani and Dogon children

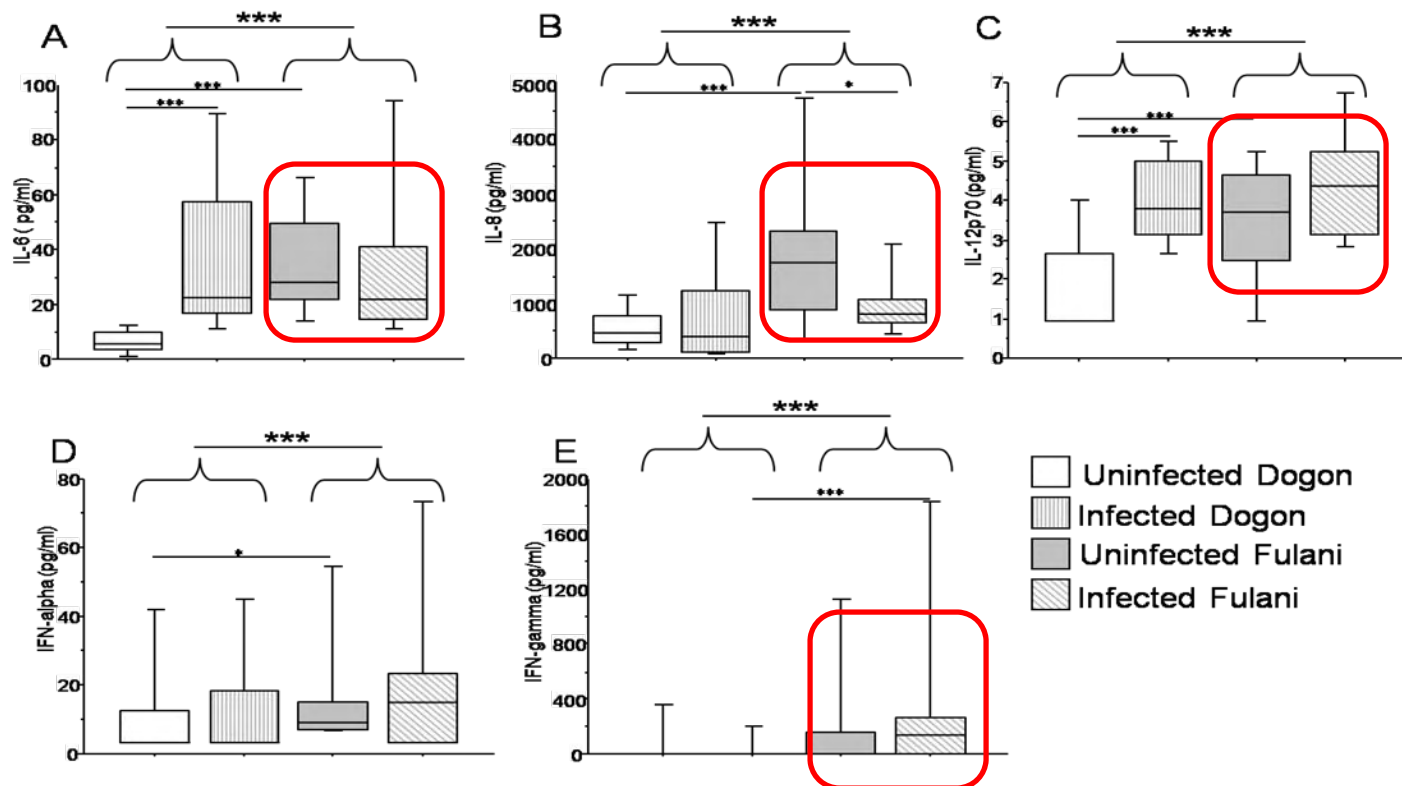
Fig 1



Results (2)

Intraethnic and interethnic difference in cytokine plasma levels.

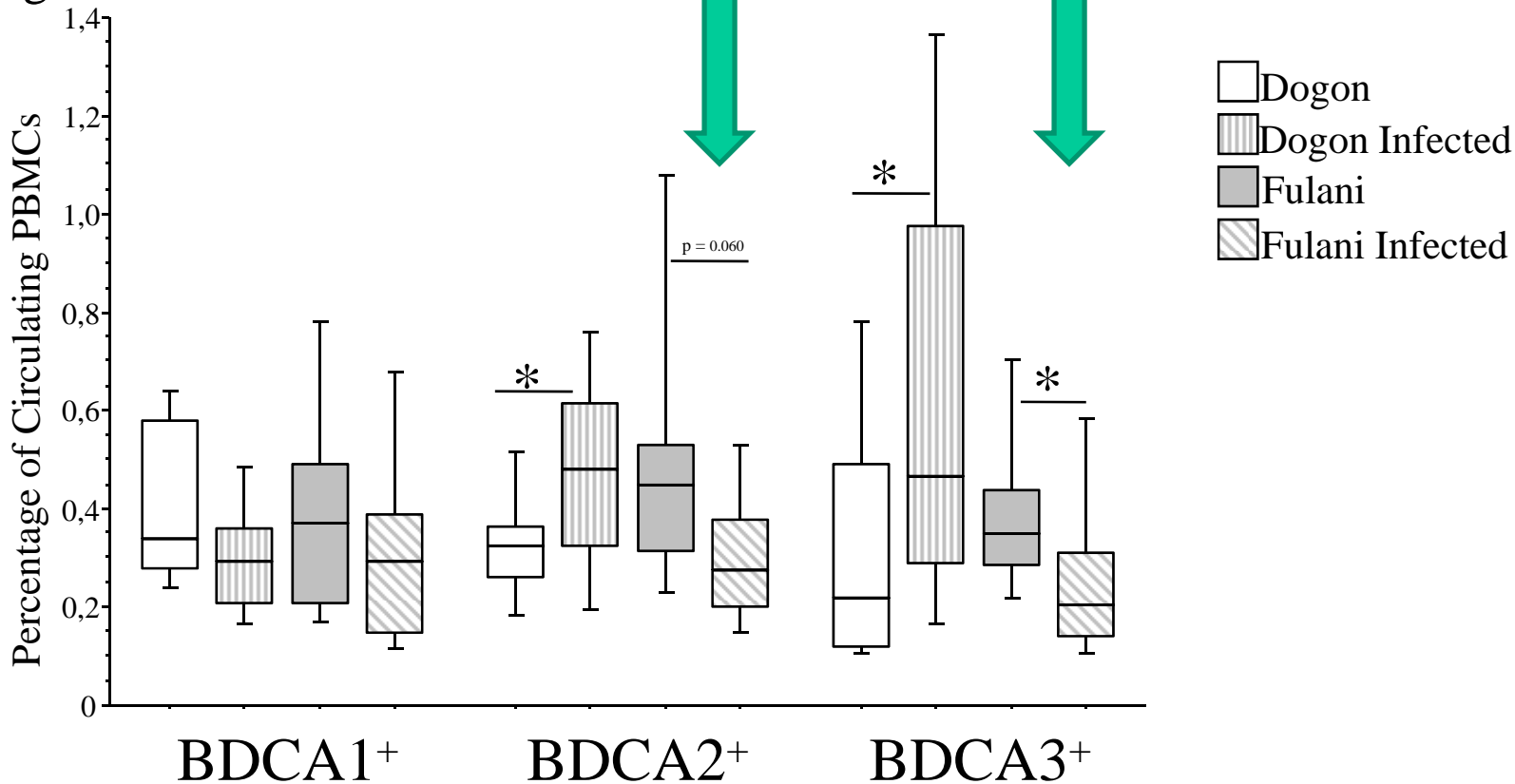
Fig 2



Results (3)

Interethnic and intraethnic differences in circulating dendritic cell frequency.

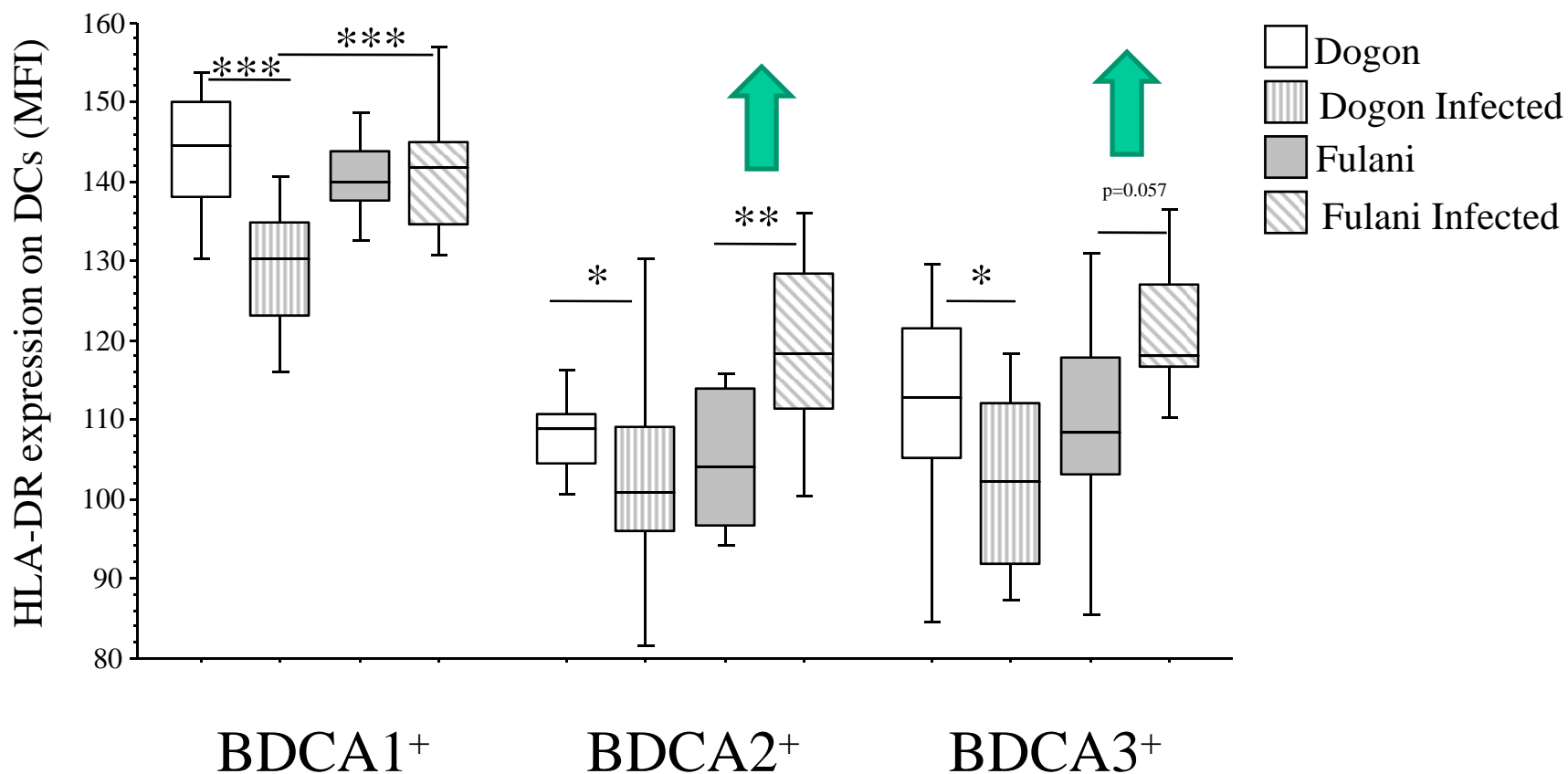
Fig 3



Results (4)

Interethnic and intraethnic differences in activation HLA-DR expression on circulating dendritic cells.

Fig 4





Conclusion



The Fulani children exhibited higher titers of malarial antibodies than the Dogon children.

The Fulani exhibited a stronger pro-inflammatory cytokine profile as reflected by higher serum levels of INF- α , γ , IL-6, IL-8 and IL-12p70 as compared to the sympatric ethnic tribe, the Dogon.

The pDC in the infected Fulani had higher HLA-DR expression.

The pDC of the infected Fulani could be more potent to activate acquired or innate immune responses as compared to the pDC of infected Dogon children.



Acknowledgements



All the villagers of Manteourou for their kind manners and willingness to participate in this study

EDCTP for the funding

