

# Impact of early-life exposure to Epstein-Barr virus and mycotoxins on the epigenome of African children and endemic Burkitt lymphomagenesis

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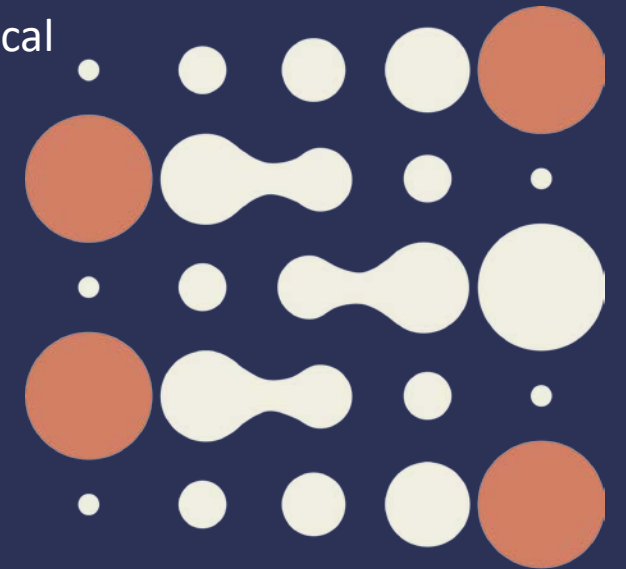
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# Introduction/Background/Motivation

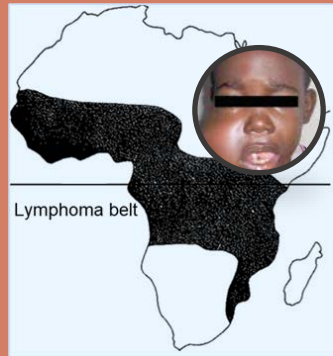
INTERPLAY EXPOSOME - EPIGENOME → BURKITT LYMPHOMA

MYCOTOXINS

INFECTIOUS AGENTS

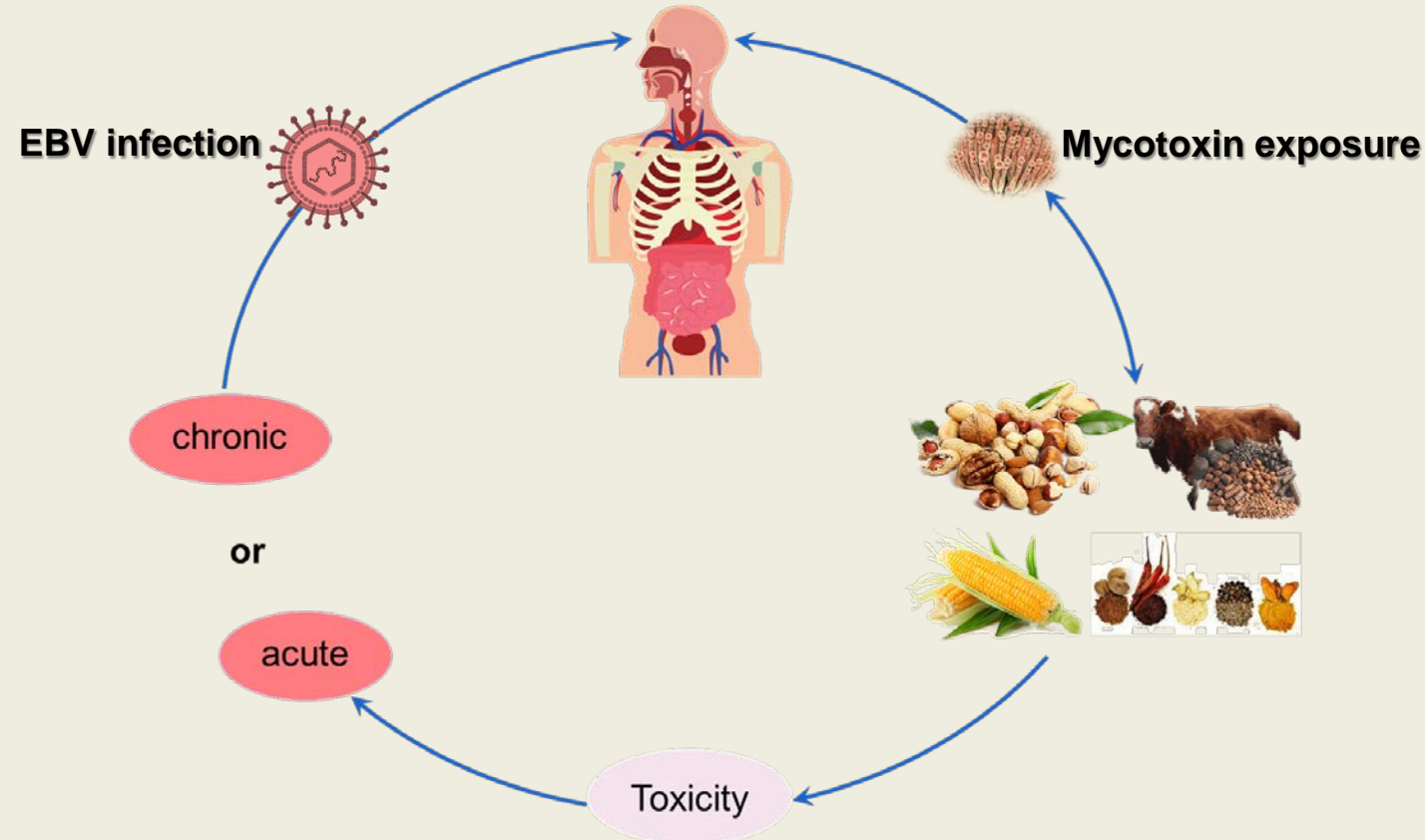
EPIGENETICS

BURKITT LYMPHOMA



SUBSAHARAN AFRICA

Epigenome deregulation → Carcinogenesis



# Design: Molecular Epidemiology Approach

## COHORT STUDY



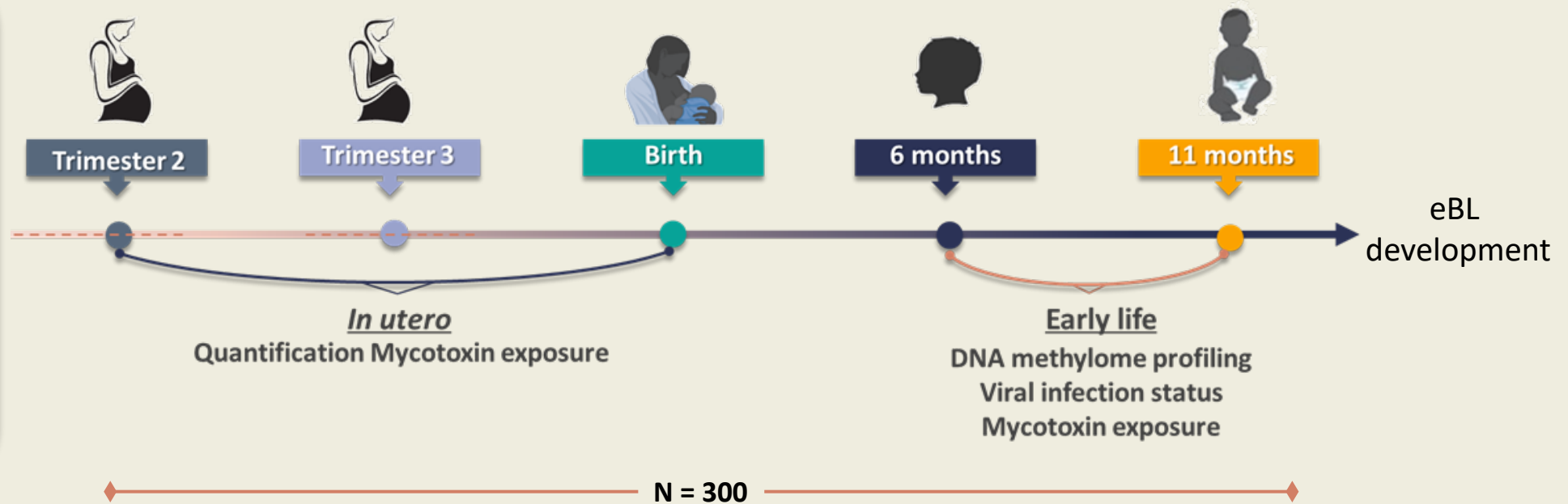
### Sample collection



Volumetric Absorptive Microsampling (VAMS)

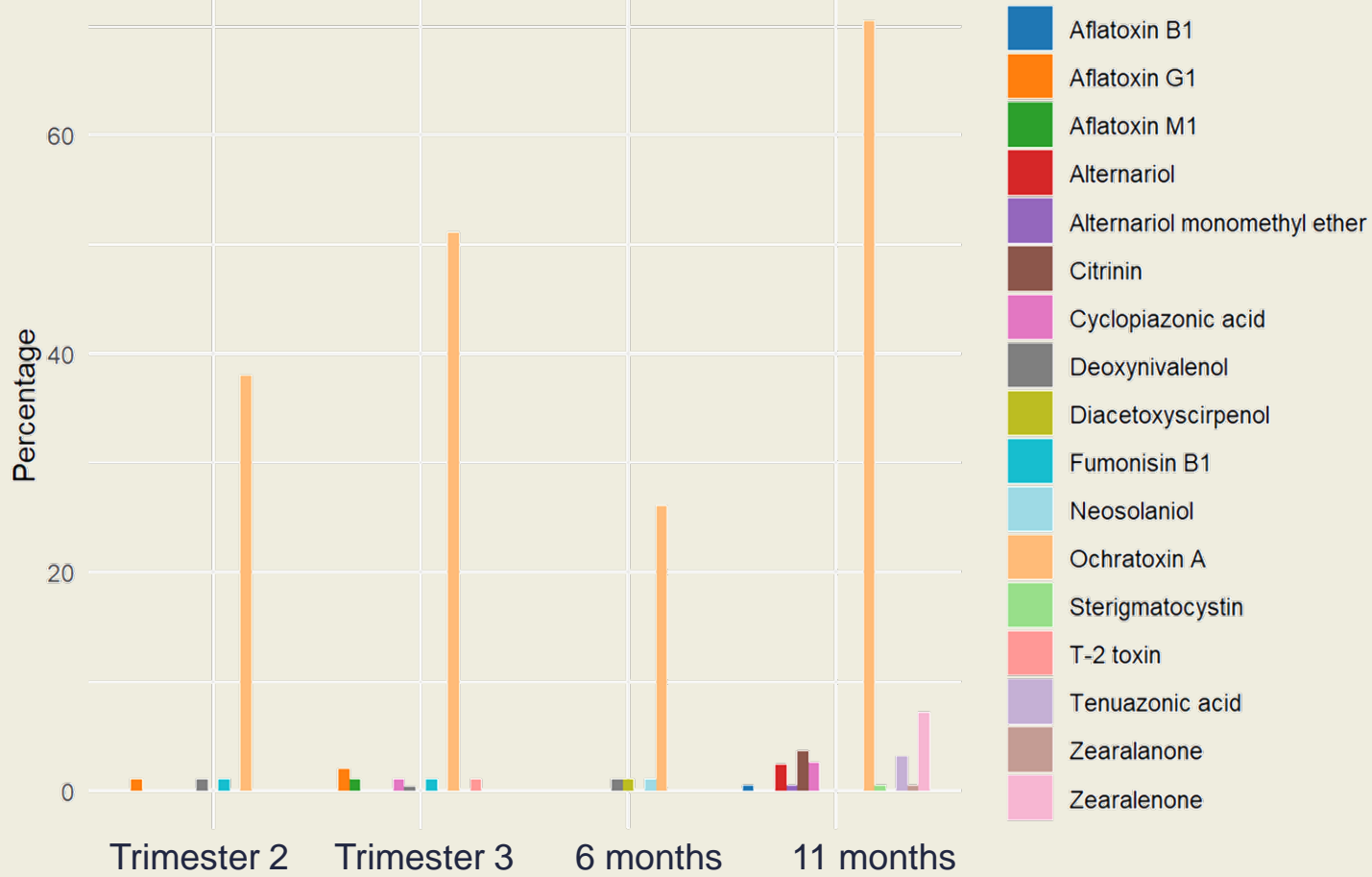


Dried Blood Spots (DBS)

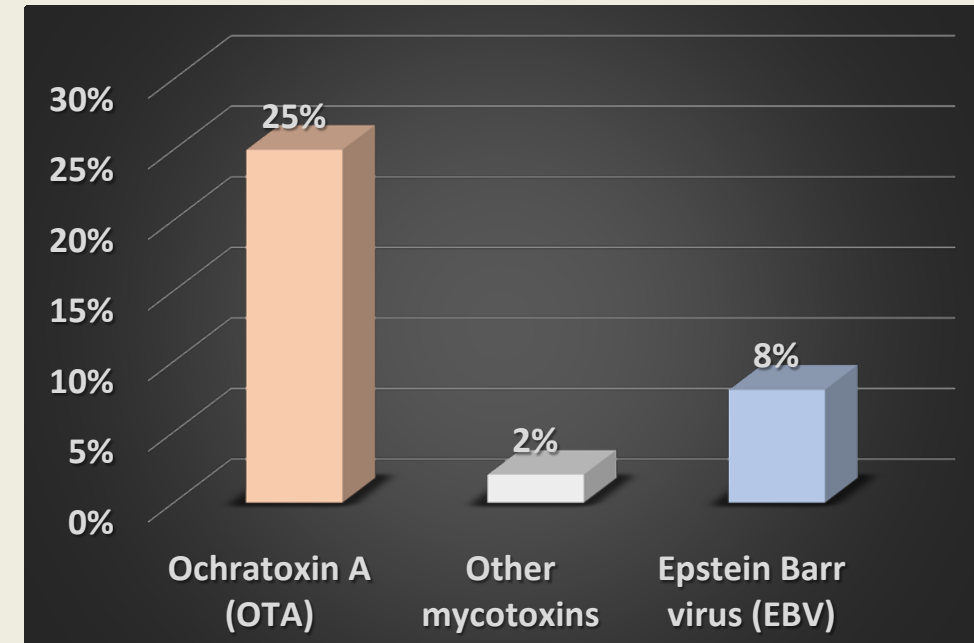


# Results

Prevalence of mycotoxins in mothers and children revealed by LC/MS



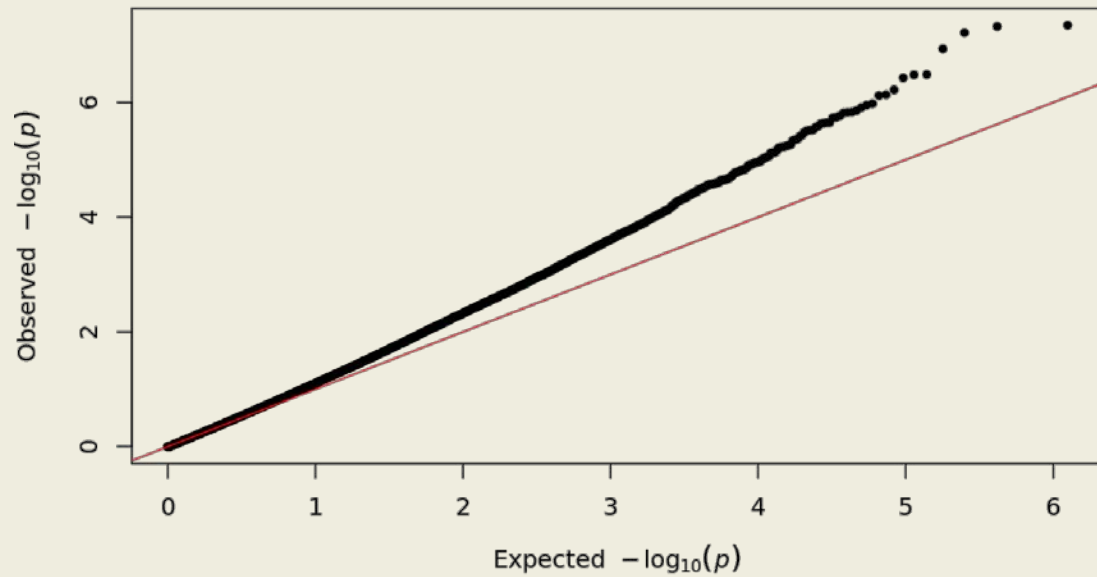
Mycotoxins and EBV prevalence in 6 month-infants from Burkina Faso



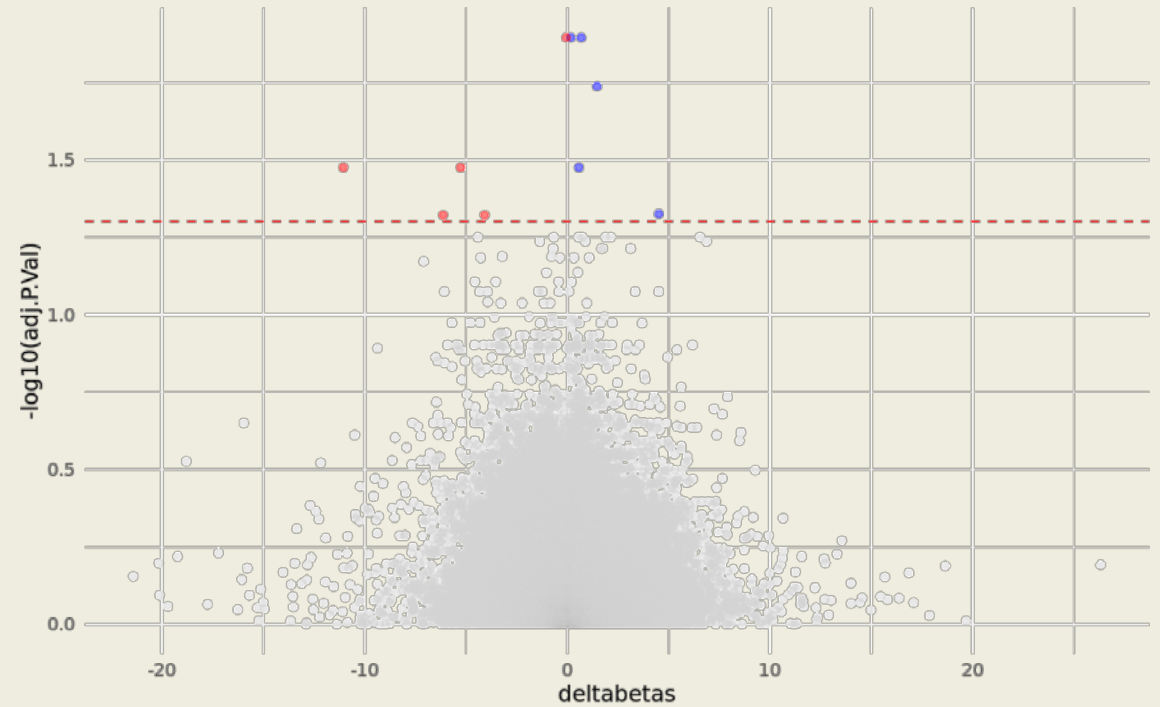
# Results: Methylome analyses of blood spots from children at 6 months.



QQ plot:  $\lambda=1.08057448190648$



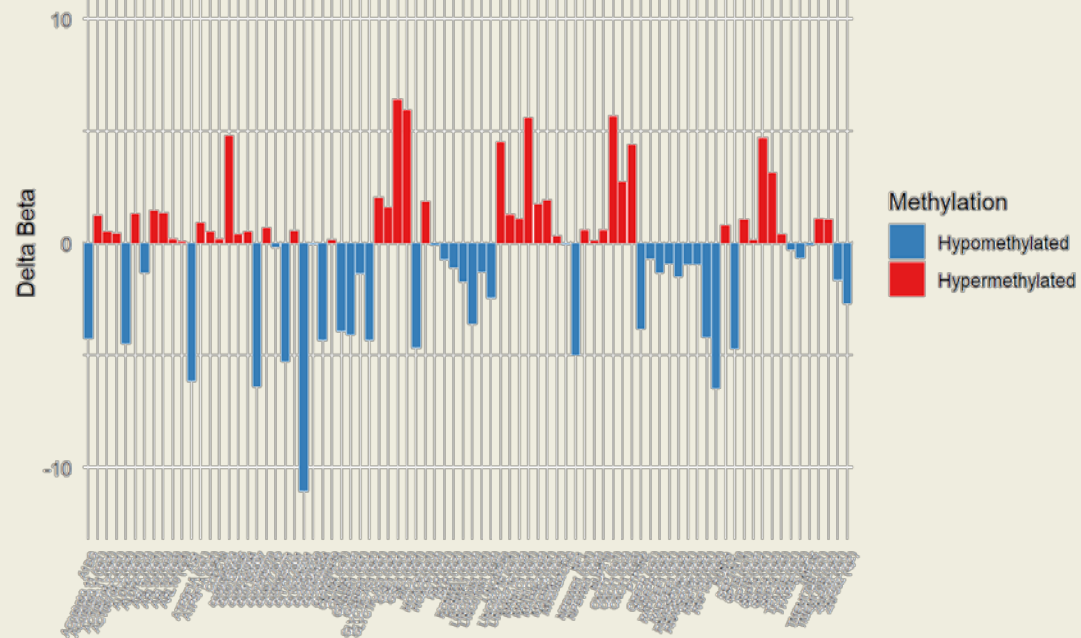
Volcano plot of differentially methylated positions (DMPs)



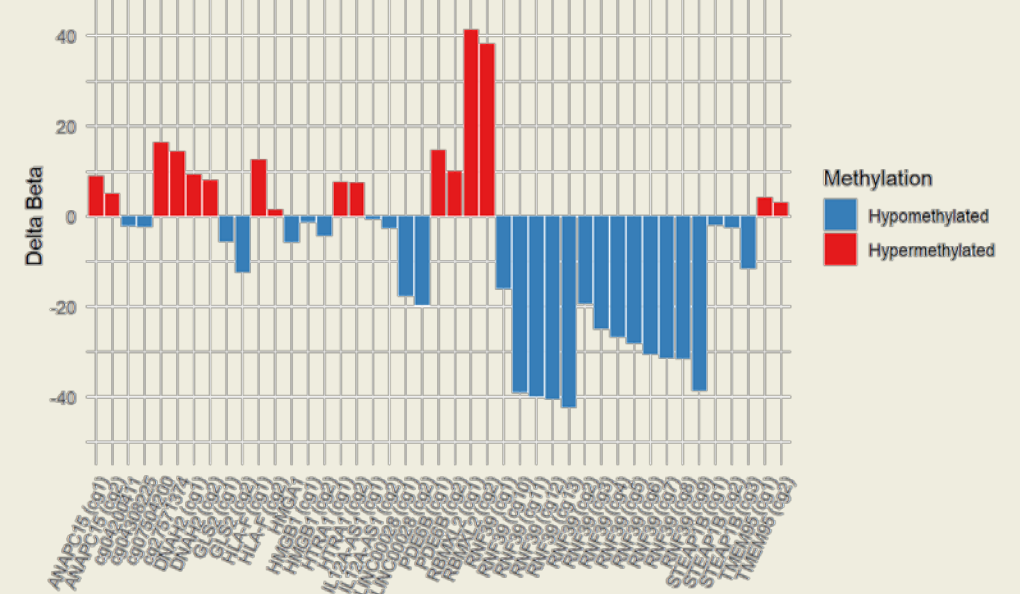
# Results: Methylome analyses of blood spots from children at 6 months.



Differentially methylated regions (and their related genes) associated with **EBV infection**

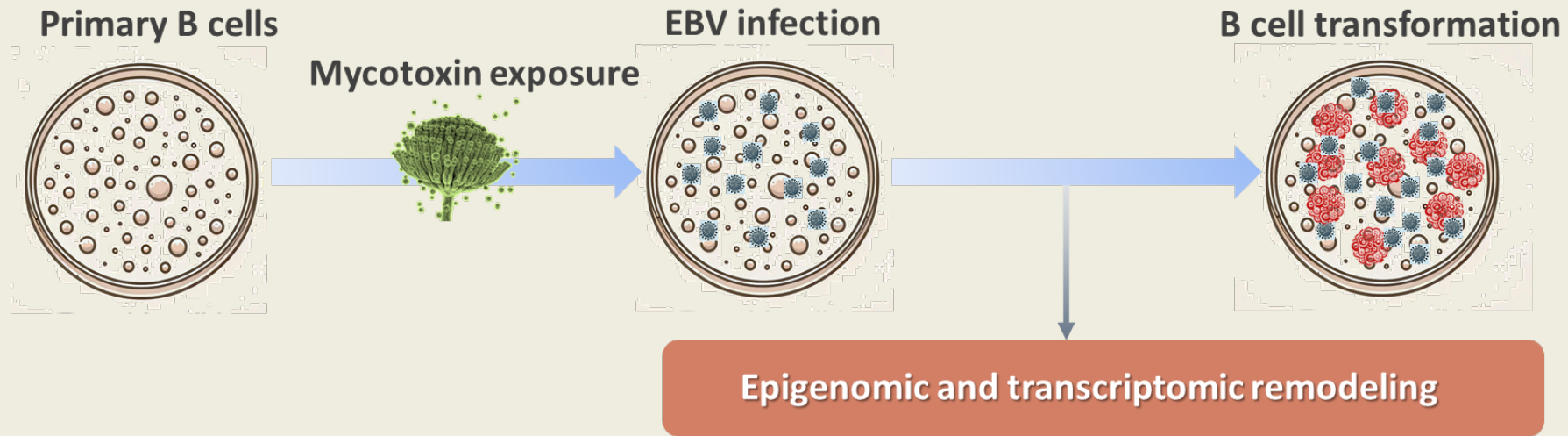


Differentially methylated regions (and their related genes) associated with both **EBV infection and OTA exposure**



**IDENTIFICATION OF DIFFERENTIALLY METHYLATED REGIONS AND GENES ASSOCIATED WITH EBV INFECTION ALONE OR IN COMBINATION WITH OTA**

# Design: In vitro Approach for validation and mechanistic analyses



↓ *Transforming growth factor TGFBI*, Manara *et al.* Cancers 2022

↑ *CCL22* cytokine, Odongo *et al.* PNAS 2023. Manuscript under revision.

**A SYNERGISTIC IMPACT OF THE MYCOTOXIN AFLATOXIN B1 AND EBV ON CANCER AND IMMUNE RELATED PATHWAYS.**

# Discussion and Conclusions

## Summary of findings:

- OTA is probably the most prevalent mycotoxin in Burkina Faso
- EBV infection and OTA exposure impacts DNA methylation profile of children at 6 months  
=> Biomarkers of exposure.

## Future plans:

- Methylome profiling of dried blood spots from children at 11 months
- Impact of *in-utero* and early life exposure to OTA on DNA methylation (longitudinal analysis).
- Methylome profiling of eBL tumours from Burkina Faso => identification of biomarkers of cancer risks.
- Using in-vitro approaches to reveal early mechanisms of eBL development induced by EBV and co-factors.



# Key take-home messages

- *In-utero* and early-life exposure to mycotoxins is a risk factor for EBV-associated Burkitt Lymphoma in children from Africa
- Basis for the development of biomarkers and direct rigorous actions for cancer prevention in LMICs



## Acknowledgments

International Agency for Research on Cancer

