ASSESSMENT OF THE IMPACT OF MYCOTOXINS ON THE EPIGENOME AND THEIR SYNERGISTIC ROLE WITH EPSTEIN BARR VIRUS (EBV) IN ENDEMIC BURKITT LYMPHOMA (EBL) IN AFRICAN CHILDREN

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Epstein Barr Virus (EBV) infects more than 90% of population worldwide, however Burkitt's lymphoma that is associated with EBV is mostly endemic in African regions which are faced with unavoidable dietary mycotoxin exposure. Chronic exposure to mycotoxins and infection with oncogenic viruses have been shown to increase a person's risk of developing cancer. Therefore we hypothesized that both EBV and mycotoxins play a role in endemic Burkitt's Lymphoma (eBL) carcinogenesis. Our present study aims to determine the epigenetic alterations linking exposure to mycotoxins and/or EBV resulting in an increased risk of carcinogenesis of eBL. The overall study has three approaches; *in vitro* (using human B lymphocyte cells), *in vivo* (using humanized mice) and a cohort-based study (MISAME III; Burkina Faso).

Specific target genes (CCL22 and TGBI), previously identified after genome wide DNA methylation profiling shown to be differentially methylated in EBV negative- vs EBV positive-Burkitt's Lymphoma cases [1] were further investigated *in vitro* by exposing or infecting B lymphocyte cells with mycotoxins and/or with EBV followed by investigating epigenetic alterations such as methylation then expression analysis. Our findings revealed expressional and epigenetic deregulations of the genes TGFBI and CCL22. Investigating the mechanisms underpinning those deregulations, showed a DNA-methylation-dependent transcriptional silencing of TGFBI [2] that was attributed to the recruitment of DNMT1 methyltransferase which is linked with activation of the NF-KB pathway. As for CCL22, upregulation was observed in cells exposed to mycotoxins with effect increasing upon EBV infection suggesting a putative synergy between mycotoxins exposure and EBV infection in inducing CCL22 expression. Further investigation using mice models is ongoing involving determining the role of EBV and/or aflatoxin induced CCL22 overexpression in carcinogenesis. Also, blood from mothers and infants/children from Burkina Faso are being collected for evaluation of mycotoxin exposure, EBV infection, epigenetic alterations, and cytokine levels (including CCL22). BL tissue samples will be analyzed to further establish the link between mycotoxins and EBV in eBL.

These findings will provide validation as well as expand knowledge on epigenetic modifications that occur following mycotoxins' exposure and oncogenic virus infection leading to carcinogenesis. Our results will set the basis for future studies leading to a better understanding of eBL.

1.Hernandez-Vargas, H. et al, 2015 & 2017, Journal of Epidemiology 44, 1238-1248, (2015).
2.Manara F. & Jay A et al., 2022, Cancers, 14(5):1284. doi: 10.3390/cancers14051284