

Solving the 50-year-old riddle: the link between *Plasmodium falciparum* Malaria and Endemic Burkitt's Lymphoma



It has been a conundrum for a long time: the link between endemic Burkitt's lymphoma (eBL) with *Plasmodium falciparum* malaria infection. We know that eBL is caused by the oncogenic virus, Epstein-Barr virus (EBV), but why is the disease more associated with people who contract malaria?

In this month's PLoS Pathogens, David Thorley-Lawson and colleagues have published a mini-review of two studies that shed light on this seemingly unrelated association. EBV is found in nearly all cases of eBL and has been shown to be a potent transforming virus for human B cells. What is thought to happen, is that the c-myc gene is translocated into one of the immunoglobulin loci in B cells. These events occur specifically when B cells transit into the germinal centres (GC) of lymph nodes. In a healthy person, this would normally lead to B cell death. However, EBV is thought to rescue these cells and allow them to survive with the translocated c-myc gene.

The authors report on several studies and propose that all adults are persistently infected with EBV. As a consequence, newly infected B cells are continually being produced that transit the GC and become latently infected memory B cells. Because malaria is immunosuppressive, this results in an

elevated throughput of EBV-infected cells in the GC. As *P. falciparum* also induces deregulation of the enzyme Activation-Induced Cytidine Deaminase (AID), important for inducing and regulating antibody diversity, there is enhanced DNA damage, c-myc translocations and ensuing lymphoma. Therefore, the link between malaria and eBL is focused around the ability of the parasite to deregulate AID, and enhances c-myc translocation of EBV infected B cells resident in the GC of lymph nodes. EBV allows these cells to survive and propagate resulting in eBL.

[Thorley-Lawson, D. et al, 2016. The Link between Plasmodium falciparum Malaria and Endemic Burkitt's Lymphoma–New Insight into a 50-Year-Old Enigma. PLOS.](#)