INFECTIOUS DISEASE

A deadly partnership

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URLs

Plasmodium falciparum
http://www.ncbi.nlm.nih.gov/sites/entrez?Db=genomeprj&cmd=ShowDetailView&TermToSearch=9538

PfEMP1
http://www.ncbi.nlm.nih.gov/entrez/viewer.fcgi?db=protein&id=124015261

Endemic Burkitt's lymphoma (eBL), an aggressive B-cell lymphoma, is the most prevalent childhood cancer in equatorial Africa. Malaria and Epstein-Barr virus (EBV) infections are co-factors in the aetiology of this disease, but how do these pathogens interact to cause eBL? Reporting in *PLoS Pathogens*, Chêne and co-workers have identified a protein that is produced by the malaria parasite *Plasmodium falciparum* and that can induce reactivation of EBV from latently infected B cells. Virus reactivation, in turn, might increase the risk of developing eBL.

Infection with EBV during infancy results in a lifelong latent infection of memory B cells, although not all EBV infections result in B-cell tumorigenesis. eBL is restricted to malaria-endemic regions of Africa, and acute malaria infection dramatically increases the levels of circulating EBV. According to earlier research published by the authors, the cysteine-rich inter-domain region 1-α (CIDR1α) of the highly expressed protein *P. falciparum* erythrocyte membrane protein 1 (PfEMP1) induces proliferation and activation of memory B cells. The latest report details the effects of CIDR1α on the reactivation of latent EBV in B cells.

Chêne *et al.* showed that red blood cells infected with *P. falciparum*, which express huge amounts of PfEMP1, and purified CIDR1α both bind to EBV-carrying B cells. Importantly, the binding of CIDR1α to EBV-carrying B cells resulted in a large increase in virus titre that could not be attributed to either increased apoptosis (leading to virus release) or B-cell proliferation. To directly show that CIDR1α stimulates reactivation of EBV from latency to a lytic replication cycle, the authors used a B-cell line that is a reporter for induction of the lytic replication EBV cycle through a fusion of green fluorescent protein (GFP) to an EBV lytic gene. They showed that the addition of CIDR1α results in the upregulation of GFP expression, with a concomitant increase in released EBV genomes that is consistent with reactivation of the EBV lytic replication cycle. CIDR1α had the same effect on EBV-carrying B cells from the tonsils of both healthy donors and those suffering from eBL.

The detection of high antibody titres to EBV lytic proteins is usually a prelude to the onset of eBL. Elucidating the mechanisms underlying the link between exposure to malaria and increased EBV replication represents an important advance in the understanding of eBL carcinogenesis.

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ORIGINAL RESEARCH PAPER Chêne, A. *et al.* A molecular link between malaria and Epstein-Barr virus reactivation. *PloS Pathogens* **3**, e80 (2007)