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Epstein-Barr virus particles induce centrosome amplification and chromosomal instability

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Infections with Epstein-Barr virus (EBV) are associated with cancer development, and EBV lytic replication, the process that generates virus progeny, is a strong risk factor for some cancer types. During this thesis project, we could demonstrate that the EBV infection of B-lymphocytes, both *in vitro* and in a mouse model, leads to an increased rate of centrosome amplification, associated with chromosomal instability. We found that EBV infection increases the rate of aneuploidy and to a certain extent of translocation. These effects could be reproduced with EBV virus-like particles devoid of EBV DNA, but not with defective EBV virus-like particles that cannot infect host cells because they lack the gp110 fusion protein. Screening of a large panel of EBV proteins showed that the viral tegument protein BNRF1 induces centrosome amplification, via overduplication, and that BNRF1-deficient viruses largely lose this property. These findings identify a new mechanism by which EBV particles can induce chromosomal instability without establishing a chronic infection, thereby conferring a risk for development of tumors that do not necessarily carry the viral genome. Therefore, the frequency of tumors induced by the EBV infection might be underestimated. Moreover, the production of EBV particles that takes place in the majority of the world population might be associated with an increased risk of cancer development. Altogether, this work underscores the need for the development of an effective preventative vaccine against EBV infection.