Vaccines 1

180
Generation of immunogenic EBV virus like particles devoid of viral DNA

S. P. Hundt[1], R. Feederle[1], K. Gärtner[1], W. Fuchs[2], H. Granzow[2], H.-J. Delecluse[1]

[1]DKFZ, Pathogenesis of Virus Associated Tumors, Heidelberg, Germany
[2]Friedrich-Loeffler-Institut, Institute of Molecular Biology, Greifswald-Insel Riems, Germany

The Epstein-Barr virus (EBV) is an oncogenic virus that has recently been gaining notoriety due to its increasing association with various cancers. It is estimated that EBV infection contributes to up to 2% of all tumours worldwide. Therefore, the generation of EBV prophylactic or therapeutic vaccine is a high priority. Recently, virus-like particles (VLPs) have emerged as attractive vaccine candidates. VLPs contain all structural proteins of the wild type viruses, but they lack the viral genome. Therefore, they cannot replicate and propagate, but they can elicit a specific immune response. In order to generate EBV VLPs, we attempted to block packaging of the virus DNA that takes place during virus replication. We have previously described an EBV mutant that lacks the DNA packaging signals, the terminal repeats (TR). This virus produces large amounts of defective particles, both VLPs and light particles (LPs). However, ΔTR particles exhibit minimal virus DNA contamination. To completely prevent DNA packaging, we constructed a series of mutants that lack proteins involved in virus maturation. We characterized the phenotype of those mutants in vitro and in particular their ability to produce DNA-free defective particles. Deletion of BBRF1 resulted in the production of restricted amounts of defective particles (VLPs/LPs), devoid of viral DNA. However, an EBV mutant that lacks BFLF1 and BFRF1A produced large amounts of DNA-free defective particles and elicited specific CD4+ T cell immune response, comparable in intensity to the one obtained with wild type controls. Therefore, defective particles produced by ΔBFLF1/BFRF1A fulfill the requirements for an effective and safe preventative vaccine.

Corresponding author:
Sophia Pavlova Hundt
sophia.hundt@dkfz.de