Bovine herpesvirus 1 can replicate in human immortalized and transformed cells

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Cancer is one of leading causes of human death, especially in developed countries. Many treatment options for cancer are available, but each of them has its limitations and usually severe side effects. Therefore, there is a continuous search for new forms of cancer therapies. One promising area of research is the use of viruses. Oncolytic viruses can be genetically engineered, moreover, some naturally occurring viruses can selectively infect and damage cancerous tissues.

Bovine herpesvirus 1 (BoHV-1) is a dsDNA virus which belongs to the subfamily *Alphaherpesvirinae.* It has strictly restricted host range compared to other herpesviruses: BoHV-1 infects only cattle and cells of bovine origin. However, previous studies showed that it was possible to obtain productive BoHV-1 infection in a human cell line, MelJuSo (Koppers –Lalic, 2003). Recently it has been also suggested that BoHV-1 can be used as a human oncolytic vector due to its capability of replication in some human transformed cell lines (Cuddington, 2015).

The aim of my research is to study the oncolytic properties of BoHV-1: which human cells can be infected, how the infection is progressing and what affects the susceptibility of host cells.

I analyzed the replication and spread of BoHV-1 in human cells: HB2, MDA-MB-231, T47D, BT 474. This results were compared to the infection of bovine cells - epithelial MDBK cells, bovine macrophage cell line (BoMac) and primary bovine fibroblasts. I calculated virus titer both in medium and in lysed infected cells during 0 – 96 h.p.i. and analyzed viral growth curves. To characterize selected aspects of BoHV-1 infection in human cells, I compared intracellular localization of glycoprotein gE/gI complex (maturation of viral envelope glycoproteins requires their accumulation in Golgi apparatus before final assembly of a viral particle) and the impact of US3 multifunctional kinase on virus replication in human cell lines.

I have shown that human transformed or immortalized cells are susceptible to BoHV-1 infection. The infection, although much less efficient than infection of bovine cells, is productive and persistent. Example of BoHV-1 gE/gI complex analysis shows that intracellular localization of viral proteins is the same in bovine and human cells. HB2 cells (SV40 immortalized human cells) were the most susceptible to BoHV-1 infection. The oncolytic potential of BoHV-1 and the effect SV40-mediated immortalization on herpesvirus infection require further studies.