# Oral Session III

# Herpesvirus Infections II

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Antisense Oligonucleotides Against BZLF-1 Inhibit Induction of the Productive Replication of EBV.

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Productive replication of Epstein-Barr Virus (EBV) can be induced efficiently in the latently EBV infected Burkitt's Lymphoma (BL) derived cell line Akata by crosslinking the surface with anti-immunoglobulin gamma (αIgG) antibodies. Within 24 hrs, the number of early antigen (EA) and viral capsid antigen positive cells increases from 0.5% to 40-70% (Takada *et al.*). The first event in this induction is the activation of the immediate early EBV gene BZLF-1. Activation of BZLF-1 by itself is sufficient to induce the productive cycle of EBV in BL cells (Miller *et al.*). We have shown before, that this induction is effectuated by signal transduction pathways acting on the BZLF-1 promoter (Daibata *et al.*). Incubation of these cells with unmodified or phosphorothioate derivatives of antisense oligonucleotides to the BZLF-1 gene inhibits this induction by 50 to 75%. Inhibition was measured by the numbers of EA-positive cells or by the amounts of linear EBV DNA produced as measured in Gardella gels. Random or unrelated oligonucleotides have no significant effect on this induction; random phosphorothioate oligonucleotides effect this only moderately and at higher concentrations.