# Epstein Barr Virus (EBV) and Complement ($C_3$) Interactions With Human Lymphoid Cells

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EBV is a herpesvirus associated with several lymphoproliferative diseases in man [1]. It is the causative agent for infectious mononucleosis (IM), [2], and is associated with African Burkitt's lymphoma (BL) and carcinoma of the nasopharynx [3]. In addition, EBV has the ability to transform normal human (and some simian) lymphocytes in vitro, into continuously growing cell-lines [4]. Permanent lines can also be established directly from BL biopsies or IM lymphocytes [5]. Cell-lines established in either way were shown to be of the B lineage [6], and trials to infect non-B cells by EBV were unsuccessful [7]. Thus, EBV has a very restricted tropism in that it is able to infect and/or transform human (and certain simian) B lymphocytes, possibly due to specific viral receptors expressed on such cells only.

While scoring different human lymphoma cell-lines for presence of EBV-receptors, an interesting correlation was noticed between the expression of $C_3$-receptors and EBV-receptors [8]. These were simultanuesly present or absent, and in no case, was only one of them expressed. When receptor positive cells were incubated with EBV preparations, binding of EAC (indicator for $C_3$-receptors) was partially blocked. Incomplete inhibition of EBV binding to cells could be acheived by preincubating them with $C_3$ and two layers of antibodies. These results indicated that the EBV-receptor and the $C_3$-receptor were not identical but closely related structures on the membrane. EBV-receptors and $C_3$-receptors co-capped on the cell-membrane [9]. Neither of these receptors co-capped with other independent membrane markers such as IgM, Fc-receptors and $beta_2$ microglobulin indicating that the association observed was highly exclusive and specific.

In another experiment we have employed an EBV absorption bioassay [10] in which the binding of an infectious virus to EBV-receptors is measured quantitatively by testing the residual supernatant capacity to superinfect Raji cells, as manifested by the induction of Early Antigen (EA) synthesis. Incubation of cells with appropriate ligands for 4–6 hours at 37° led to a selective stripping of different membrane components including EBV-receptors and $C_3$-receptors [11].

It was shown that stripping of $C_3$-receptors drastically reduced the EBV absorbing capacity of the cells with similar efficiency to EBV-receptor stripping, while stripping of $beta_2$ microglobulin, IgM or Fc-receptors had no effect on the EBV absorptive capacity whatsoever.

Using the quantitative virus absorption bioassay it was also possible to compare the extent of EBV-receptor and $C_3$-receptor expression on different cell-lines. A very good correlation was found between the ability of the cells to absorb EBV and to bind $C_3$ [12].

A positive correlation between EBV receptors and $C_3$-receptors expression was also found among different subpopulations of normal human lymphocytes from peripheral blood [7]. Using a combined cell separation procedure [13] fractions enriched for B, T and non T non B (0) cells were obtained. The B cell enriched fraction had the highest virus absorptive capacity with the strongest expression of $C_3$-receptors. About 30% of the 0 cells expressed $C_3$-receptors and also exhibited a significant EBV binding capacity. A minor fraction of T cells had also $C_3$-receptors (about 10%) but did not show EBV binding activity. This is in line with the fact that many other non-B cells expressing $C_3$-receptors (e.g. erythrocytes, granulocytes, and monocytes) do not show any EBV binding activity, and association of $C_3$-receptors with EBV-receptors is found exclusively on B (and some 0) lymphocytes.

Taken together, the above results suggest that EBV has adapted the $C_3$-receptor on human B lymphocytes, to serve as its own receptor. It seems that the binding site of $C_3$ is not identical with that of EBV and the receptor association reflects adaptation to a structure associated with the $C_3$-receptor of the human B lymphocyte, which is missing from other $C_3$-receptor bearing cells.

## References

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