SIV AND LYMPHOMAGENESIS IN THE MACACA ANIMAL MODEL: CHRONIC NON-CYTOLITIC SIV INFECTION OF SIMIAN B CELL LINE UPREGULATES THE EXPRESSION OF CD23 AND CD40 CELL SURFACE MARKERS.

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SIV as well as HIV retroviruses induce in vivo polyclonal B cell activation and have been associated with the appearance of lymphomas, but their pathogenetic role in the development of the lymphoproliferative disease is not yet understood. We have already described the presence of SIV in tumor cells of oligoclonal B- and T-cell lymphomas in SIV-infected cynomolgus monkeys (*Maggiorella et al., Blood, 1998*). To elucidate the possible role of SIV in the development of lymphoproliferative disorders, two simian lymphoblastoid B cell lines (SL-691 and SL-P1) were established in vitro to investigate: 1) the genotypic and phenotypic profile of these cells, 2) their susceptibility to SIV infection, and 3) the phenotipic modifications possibly associated with SIV infection. Both cell lines had a detectable level of CD4 mRNA (RT-PCR); expressed typical B cell lineage markers, such as CD20; could be discriminated by the differential expression of CD23, CD40, CD28, κ- and λ-chains; were coinfected with the *Macaca fascicularis* Herpes virus (HVMF-1) and with a simian type D retrovirus (SRV-2). Of importance, SL-691 but not SL-P1 cells were susceptible to chronic non-cytolitic, highly productive SIV infection. The differential susceptibility to SIV infection might be not attributed to different expression of CXCR4 (present on both cell lines as determined by cytofluorimetric analysis) or of CCR5 (absent on both cell lines). Of note, similarly to EBV infection/transformation in human cells, SIV infection upregulated the expression of CD23 and CD40 cell surface markers whereas CD20 expression, that disappeared in SL-691 cells, was maintained in the SIV-infected counterpart (*Titti et al., submitted*). Our results, even if they do not prove the transforming properties of SIV because of the simultaneous presence of other coinfecting viruses with known transforming activity, nevertheless shows that SIV or its products (such as tat, nef or env) induce relevant phenotypic changes on a simian B cells, add new data on the role of SIV in the development of lymphoproliferative disease.

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