87

ANTI-RETROVIRAL ACTIVITIES OF BAICALIN IN VITRO AND IN VIVO. Hongshan Chen, Xing-quan Zhang, Li Teng, Xiao-xian Wu, Yao-zeng Lu, Xiao-shan Tang, Xian-shu Yang, xu- guang Yan, Institute of Medicinal Biotechnology, Institute of Experimental, Chinese Academy of Medical Sciences, Beijing, 100050, China.

Baicalin is a flavonoid isolated from Chinese traditional herb S. baicalensis. It competatively inhibited HIV-1 recombinant P66 reverse transcriptase with IC50 of 22uM in vitro, inhibited HIV-1 CPE, IFA and P24 in H9 cell cultures with IC50 of 1.6, 3.3 and 4.74 ug/ml, the selective indexes were 81.61, 39.58 and 27.55 respectively. Murine leukemia virus ip infected Balb/C mice resulted significant spleenomegaly, leukocytosis and slight anemia. Baicalin 3 g/kg per oral were given to 6 MULVrav infected mice, treatment was started 2 hrs. after infection bid for 20 days significantly inhibited the spleen index. white blood count and increased red blood count and hemoglobulin %. SIVmac strain iv infected Rhesus monkey developed viramia and lymphopathy effect. Baicalin 100 and 300 mg/kg, 2 monkeys in each dose group, were given by oral QD, 2 times before SIV infection and continously QD up to 60 days after infection. Blood samples were taken before; 10, 14, 17, 21, 30 days during and 2 and 30 days after treatment for SIV cultivation and PCR detection. The experimental monkeys were sacrifized 30 days after cessation of treatment, the lympho-nodes were taken for pathological study. The results showed that SIV were found in BCL treated monkey sera, but the pathological findings of the SIV infected monkey's lymph- nodes in treated group were less than that of the control group.

88

Sequences within the HIV-1 LTR Required for Strand Transfer By Integrase In Vitro

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Integration of the human immunodeficiency virus (HIV-1) provirus into the genome of the host cell is required for productive infection of cultured T-lymphoid cells. The endonucleolytic and strand transfer processes which are necessary for integration are mediated by a unique viral enzyme, integrase, presenting potential opportunities for the development of selective HIV therapeutics. It is therefore essential to evolve a detailed understanding of the functional interactions between this enzyme and its specific viral DNA substrate. We have used a plate based assay (Hazuda et al., 1994, NAR 22, pp. 1121-1122) which uncouples the requirement for donor and target substrates to analyze donor substrate sequences for their potential influence on the HIV-1 integrase-mediated strand transfer reaction. Using different retroviral LTR's as donor substrates, the MuLv LTR was shown to be inactive, and the HTLV LTR partially active relative to the analogous HIV sequence. Careful mutational analysis of the terminal 6 bases within the LTR known to be important for cleavage and strand transfer confirmed previous studies, but also demonstrated that sequence differences between the three LTR's within this region are insufficient to account for their disparate activities. To address this discrepancy, a series of chimeric LTR's were constructed switching defined sequences between HIV and MuLv. The results of these studies suggest that HIV integrase requires two additional upstream sequences within the LTR for efficient donor activity. In HIV, substituting either of these regions with sequences from the MuLv LTR reduced activity. In contrast, the activity of the MuLv LTR was enhanced when the HIV motifs were introduced. In either case, substituting the intervening sequences had no measurable effect. Further characterization of the contribution made by specific base pairs within the two regions identified by these chimera analyses is currently underway.