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Letter

HIV-1 gp120 does not induce Quinolinic acid production by macrophages

Several studies have implicated Quinolinic acid (QUIN), an endogenous neurotoxin and a macrophage product in the pathogenesis of the AIDS dementia complex (ADC) (Heyes, 1991). Previous studies from our laboratory have shown that HIV-1 infected macrophages may produce potentially neurotoxic concentrations of QUIN (Brew, 1995). We therefore sought to determine whether a component of HIV-1 rather than the whole virus might be able to induce QUIN production by macrophges. We chose to use the HIV-1 envelope glycoprotein gp120 because of its known neurotoxic potential which appears to be mediated by the macrophage. In addition, several investigators have demonstrated that stimulation of macrophages with gp120 results in the production of potentially neurotoxic metabolites (Wahl, 1989). Moreover, gp120 is known to cause neuronal cell death in hippocampal cultures from foetal mice (Brenneman, 1988).

Initially, an unglycosylated recombinant form of gp120 which was expressed in *Baculo* virus was examined (American Bio-Technologies Inc, Cambridge, MA, USA). In addition, as glycosylation of gp120 is essential for binding to CD4, we also examined two glycosylated forms which were raised in Chinese hamster ovary (CHO) cells (MRC AIDS Reagent Project, Herts EN6 3QG UK). gp120 derived from SF2 was chosen as we have shown that this laboratory strain induces QUIN production even at very low levels of productive infection (Brew 1995). W61D gp120 was also investigated as it is derived from a field isolate ACH320.3.1 which is known to replicate in a range of cells including monocyte/macrophages. Primary human macrophages were obtained from peripheral blood mononuclear cells by the plastic adherence technique as described previously (Brew, 1995).

No significant QUIN production was observed in any of the three treatment groups (see Table 1). QUIN production with each form of gp120 was comparable to the negative control (untreated macrophages). The data from these experiments show that these forms of gp120 alone are not sufficient to induce QUIN production in an *in vitro* system of cultured macrophages. It is possible however, that gp120 derived from these other HIV-1 isolated may lead to QUIN production by macrophages but this seems unlikely in view of the fact that we have previously shown that SF2 can lead to macrophage related QUIN production (Brew, 1995). Moreover, as Giulian *et al* have shown that gp120 is capable of stimulating the production of heat-stable, protease-resistant toxins from macrophages (Giulian, 1993) these molecules are probably not involved in macrophage related QUIN production. These data and our previous results suggest that other HIV-1 proteins maybe important i.e. gp41, Tat, nef in the induction of QUIN production by macrophages.

Table 1

	QUIN concentration nM/L 24 h	*QUIN concentration nM/L 36 h*	*QUIN concentration nM/L 48 h*
SF2 gp120 1 μg/ml	129.5	151.8	224.3
W61D gp120 1 μg/ml	137.8	154.6	55.8
HIV-1gp120 (Baculovirus) 1 μg/ml	69.3	99.6	216.6
γ-IFN 100 IU/ml (postive control)	763.8	1905.7	6207.5
Macrophage media (negative control)	132.5	99.6	204.3

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