HIV-mediated up-regulation of invariant chain (CD74) correlates with generalized immune activation in HIV+ subjects.

Abstract:
HIV Nef-mediated up-regulation of invariant chain (li chain, also CD74) is presumed to play an active role in HIV immunopathogenesis. However, this has not been definitely ascertained. In order to help elucidate this hypothesis, li chain, CD4, HLA-DR and HLA-ABC expression was analyzed ex vivo in monocyte-derived macrophages (MDMs) from HIV(+) subjects. Viral load, CD4(+) T cell count and immune activation were also determined in enrolled subjects. Correlations between these parameters and the modulation of cell surface molecules in infected cells were studied. li chain expression was found to be up-regulated in infected MDMs derived from all patients but one (median fold up-regulation 2.47±1.82 (range 0.87-7.36)). Moreover, the magnitude of li chain up-regulation significantly correlated with higher activation of B and CD4(+) T cells (studied by HLA-DR and CD38 expression). On the other hand, lower HLA-ABC (i.e. stronger down-regulation) in infected MDMs was associated with higher CD4 counts. No correlation was observed between the magnitude of li chain up-regulation and the other Nef functions studied here. This is the first study reporting that li chain up-regulation occurs on naturally infected antigen presenting cells obtained directly from HIV(+)+ subjects. Moreover, it is also shown that the magnitude of this up-regulation...
correlates with immune activation. This allows postulating an alternative hypothesis regarding the contribution of Ii chain up-regulation to HIV-mediated immune damage.