Investigating the effect of HIV-1 infection on cytoskeleton dynamics

HIV type 1 (HIV-1), the most common and pathogenic strain of the AIDS-causing virus, predominantly replicates in T-cell areas of secondary lymphoid organs. HIV-1 hijacks cytoskeleton dynamics to ensure viral entry, transport within, and exit from, target cells. In particular, the viral protein Nef induces actin cytoskeleton changes and impairs cell migration toward chemokines.

In this study, researchers have investigated the effect of HIV-1 infection on cytoskeleton dynamics by using innovative analysis techniques to characterize the morphology, adhesion and motility of HIV-1-infected lymphocytes. In HIV-1-infected lymphocytes, Nef was shown to promote filopodium-like formation and inhibit membrane ruffling. Lymphocyte migration toward various chemokines was also shown to be inhibited by Nef.

Researchers also showed that Nef impairs cell adhesion on the extracellular matrix (ECM), by studying the ability of T cells +/- Nef to adhere to fibronectin-coated surfaces. Adhesion assays were performed using an Opera® high content screening system to acquire confocal images of entire wells, and Acapella® image analysis software to quantify the total number of adhered cells per well. The adhesion to fibronectin was shown to be reduced by 50% in Nef-positive cells (figure 1A).

The effect of Nef on the motility of living T cells was also analyzed, using time-lapse confocal microscopy. T cells were transduced with either Nef or a control vector, and live cell data imaging was performed using an UltraVIEW® spinning-disk system, with images acquired every 10 sec for up to 15 min (figure 1B). Control cells were generally mobile, and dynamically extended/retracted large ruffles, whereas Nef-positive cells were less mobile.

In conclusion, the complex effects of Nef on the lymphocyte actin cytoskeleton and cellular morphology likely impact the capacity of infected cells to recirculate and communicate with antigen presenting cells (APCs) and other cells and to disseminate infection. The researchers suggest that Nef may facilitate viral spread and contribute to AIDS pathogenesis by manipulating the migration of lymphocytes.

Figure 1: Nef impairs T-cell adhesion. (A) Quantification of cell adhesion. Jurkat cells, either non-transduced (NT) or transduced with either wild type Nef or GFP (control) were left to adhere to a fibronectin-coated surface. The number of bound cells was calculated using Opera with Acapella software and the percentages of adherent cells are shown (data shown are the means and SD of 4 independent experiments). (B) Visualization of Jurkat control cells (i) and Nef-expressing cells (ii) by time-lapse microscopy using an Ultra VIEW system. The images shown are snapshots from two movies.