Cellular mechanisms of HIV-1 transmission through macrophage-T cell interactions

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Antiretroviral therapy (ART) prolongs the life span of HIV infected individuals and reduces AIDS-related mortality. However, ART is not curative, as evidenced by the rapid rebound in HIV-1 viremia seen in patients after treatment interruption[1,2]. One possible explanation is the presence of viral reservoirs in various tissue compartments, serving as depots for latently infected cells that can spontaneously reinitiate virus production[3]. Recent findings show that ART is less effective at suppressing HIV-1 infection when the virus is transmitted through direct cell-to-cell contact between infected and uninfected cells[4]. Given the densely packed nature of mucosal and lymphoid tissues, where high levels of viral replication is observed, it is conceivable that cell-to-cell HIV-1 transmission plays a critical role in viral dissemination *in vivo*.

The roles of $CD4^+$ T cells and monocytes/macrophages in viral transmission, spread and pathogenesis are not clearly defined[5]. Unlike T cells, infected macrophages produce lower amounts of virus and can persist for months because of their ability to resist virus-induced cytotoxicity[6]. Since macrophages and T cells are found in high numbers within lymphoid organs[7] and frequently interact with each other *in vivo*, it is possible that macrophage-derived HIV-1 is readily transmitted to T cells through specialized cell-to-cell contacts[8,9]. The objective of this pilot project is to characterize the cellular dynamics of macrophage:T cell interactions using live cell imaging approaches, and to dissect the role of viral and host adhesion molecules that regulate this process. Using a number of fluorescent reporter HIV-1 strains and imaging techniques in 3D collagen matrix, Drs. Fowke and Murooka will examine the kinetics and dynamics of HIV-1 spread through direct macrophage:T cell interactions.

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