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Ferdinand Roesch

PhD Supervisor: Pr. Dr. Olivier Schwartz

Institut Pasteur, 28 rue du Docteur Roux, 75015 Paris, France

Hyperthermia and HIV

HIV-infected individuals may experience fever episodes. Fever is an elevation of the body temperature accompanied by inflammation. It is usually beneficial for the host through enhancement of immunological defenses. In cultures, transient non-physiological heat shock (42–45°C) and Heat Shock Proteins (HSPs) modulate HIV-1 replication, through poorly defined mechanisms. The effect of physiological hyperthermia (38–40°C) on HIV-1 infection has not been extensively investigated. We have shown in our work that culturing primary CD4+ T lymphocytes and cell lines at a fever-like temperature (39.5°C) increased the efficiency of HIV-1 replication by 2 to 7 fold. Hyperthermia did not facilitate viral entry nor reverse transcription, but increased Tat transactivation of the LTR viral promoter. Hyperthermia also boosted HIV-1 reactivation in a model of latently-infected cells. By imaging HIV-1 transcription, we further showed that Hsp90 co-localized with actively transcribing provirus, and that this phenomenon was enhanced at 39.5°C. The Hsp90 inhibitor 17-AAG abrogated the increase of HIV-1 replication in hyperthermic cells. Altogether, our results indicated that fever may directly stimulate HIV-1 replication, in a process involving Hsp90 and facilitation of Tat-mediated LTR activity. This work was published in Roesch *et al.* Plos Path 2012.

We would like to continue this work by a more systematical study of the cell types affected by hyperthermia. Thus, it would be interesting to follow HIV-1 replication under conditions of hyperthermia in different types of T lymphocytes (CD4, CD8), but also in B lymphocytes (CD19, CD20), dendritic cells (CD11c), monocytes (CD14). The status of cell-activation under hyperthermia (CD25, CD69) is also a parameter we would like to monitor. Finally, we find it important to control that hyperthermia does not influence the levels of cell viability in all these cell types (Annexin V).