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Session: **BS3**: Saturday May 2 – 15:00:17:00 – Cure, Vaccines and immunology

Track:	Basic Sciences
Subject:	Eradication Strategies Towards an HIV Cure
Presentation Type:	Oral
Title of Abstract:	**Latency Reversing Agents: impact on Human Macrophages Susceptibility to HIV-1 Infection and Viral Production**
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Abstract

Background: Long term persistence of HIV-1 is thought to be the consequence of viral latency in some T CD4+ cell populations. It is postulated that viral reactivation combined with antiretroviral treatment would allow clearance of these latently infected cells. This so-called "shock and kill" strategy relies on the use of latency reversing agents (LRAs). These non-discriminant agents were reported to reverse latency of T cells *in vivo*. However, knowledge regarding their effect on other latently infected populations such as macrophages is scarce. Therefore we aimed to monitor the impact of 3 different classes of LRA agents on macrophage's susceptibility to HIV-1 infection and viral production.
Methods: Primary human monocyte-derived macrophages (MDMs) were exposed for 24h with optimal doses of LRAs either used alone or in dual combinations. Studied LRAs were bryostatin-1 (protein kinase C agonist), JQ-1 (Bromodomain inhibitor) and romidepsin (histone deacetylase inhibitor). Susceptibility to infection and viral production were assessed using a reporter gene detected by flow cytometry, or via an ELISA of the viral capsid. Viability was determined by fluorescent dye exclusion.
Results: Treatment of MDMs with LRAs did not alter cell viability. Bryostatin-1 or romidepsin stimulation prior to HIV-1 inoculation was associated with a 90% and a 50% decrease of infection rate, respectively. This could be linked to the downregulation of CD4 and CCR5 expression induced by bryostatin-1 and romidepsin, respectively. Furthermore, treatment with bryostatin-1 after HIV-1 infection induced a strong decrease in viral and cell-associated CAp24 production without modulating HIV-1 transcription.
Conclusions: None of the LRA tested was able to increase HIV-1 production *in vitro*. Actually, our data indicate that bryostatin-1 stimulation of infected macrophages dramatically decreases HIV-1 production. Thus, our data suggest that LRAs treatments have distinct outcomes in macrophages and T cells, which need to be better deciphered to achieve an HIV-1 cure.