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In Vivo Analysis of the Replication Capacity and Pathogenic Potential of HIV Primary Isolates from an Elite Suppressor

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Background: HIV-infected elite suppressors (ES) have viremia below clinical limits of detection in the absence of anti-retroviral therapy. Host genetics play an important factor in determining viremic control. This control is thought to be mediated by improved recognition of the virus by the immune system and increased genetic pressure. This may yield mutations in the viral genome and have an increased fitness cost and thus lower replication capability. Although isolates from ES have been shown to replicate in vitro studies, their ability to replicate and cause disease in vivo is unknown. Therefore, we sought to evaluate ES-derived isolates in vivo using the BLT humanized mouse model for HIV infection.

Methods: HIV isolates ES38-5 and ES38-9 were cultured from the $CD4^+$ T cells of a previously described ES. BLT humanized mice were generated as previously described. Mice received an intra-venous injection of ES38-5 or ES38-9. HIV viral RNA in the plasma was monitored by real-time PCR. Cell populations were phenotyped using polychromatic flow cytometry.

Results: Both isolates were able to establish sustained HIV replication in vivo. Interestingly, there was an apparent difference between the maximum viral loads seen with the two viruses. This difference cannot be attributed to issues related to the PCR-based detection method or to different donor tissue used for the generation of the humanized mice. In addition, we observed declines of the $CD4^+$ T cells in the blood of the mice infected with ES isolates.

Conclusion: These results demonstrate that the viral isolates from some ES are replication competent and pathogenic as they induce T cell depletion in vivo. Our results support the hypothesis that the low levels of viremia in ES are mediated by the host's genetics and immune response rather than due to a defect in viral replication.