

Resident Activated T-Cells Persist During Periods of HSV-2 Quiescence

September 17, 2012

J Graham

Herpes simplex virus-2 (HSV-2) is the most common cause of genital herpes, and its lifelong infection of human hosts is characterized by dynamic cycles of replication and quiescence. HSV-2 reactivation occurs frequently, and while some episodes result in genital lesions, the majority of reactivations are subclinical and typically last less than 12 hours. Recent studies have suggested that HSV antigen might frequently be presented into the mucosa, stimulating host innate and adaptive immune cells that are present. Following this antigen presentation, T-cells can then be activated to control and clear the viral infection. However, it is unclear how frequently resident CD8+ T-cells might encounter HSV antigen, especially during times of asymptomatic viral infection. Therefore, Vaccine and Infectious Disease Division's Dr. Tao Peng and Dr. Jia Zhu, along with Khamson Phasouk, Dr. David Koelle, Dr. Anna Wald and Dr. Larry Corey, analyzed CD8+ T-cells present in HSV-2-affected skin areas during clinically asymptomatic reactivations in order to determine whether these T-cells exhibit effector function during quiescent time periods.

In this study, CD8+ T-cells were purified from healed lesion biopsies of nine HSV-2 seropositive patients and expression profiles were compared to control CD8+ T-cells. T-cells were isolated using cell type-specific immunofluorescent staining and laser capture microdissection. RNA was then isolated and expression profiles of control cells and CD8+ T-cells from previously healed lesions were compared. Control T-cells were from an identical anatomic site that was not associated with known HSV reactivation. From healed lesions, CD8+ T-cells were isolated from the junction between the dermal and epidermal layers of the skin. A set of 987 differentially expressed genes were selected from the 18,401 genes of the array for further analysis, and a heat-map of hierarchical clustering of these genes showed a pattern of up- and down-regulation that was uniform across all nine patients (see figure).

Further analysis of the genes differentially expressed between lesion-resident and control CD8+ T-cells showed that lesion-resident T-cells up-regulated a network of genes involved in immune response against infection. These included increased expression of antimicrobial and metabolism genes, which are indicative of T-cell activation. The resident T-cells also had increased expression of antiviral cytokine genes, which recruit and activate other immune cells to the site of infection.

Given the direct analysis of T-cell expression from the cell type specific sorting, coupled with matched control T-cell cells from the same patient, this study gives a unique look at gene expression profiles captured in the true physiological state. Resident CD8+ T-cells persisting at the site of previous herpes lesions were found to highly express genes linked to activation, proliferation, and antiviral activity, indicative of effector function. The results of this study give further insight into the complex relationship between the immune system and HSV-2 during frequent cycles of reactivation and quiescence.

[Peng T, Zhu J, Phasouk K, Koelle DM, Wald A, Corey L.](#) 2012. An effector phenotype of CD8+ T cells at the junction epithelium during clinical quiescence of HSV-2 infection. *J Virology*. 86:10587-10596

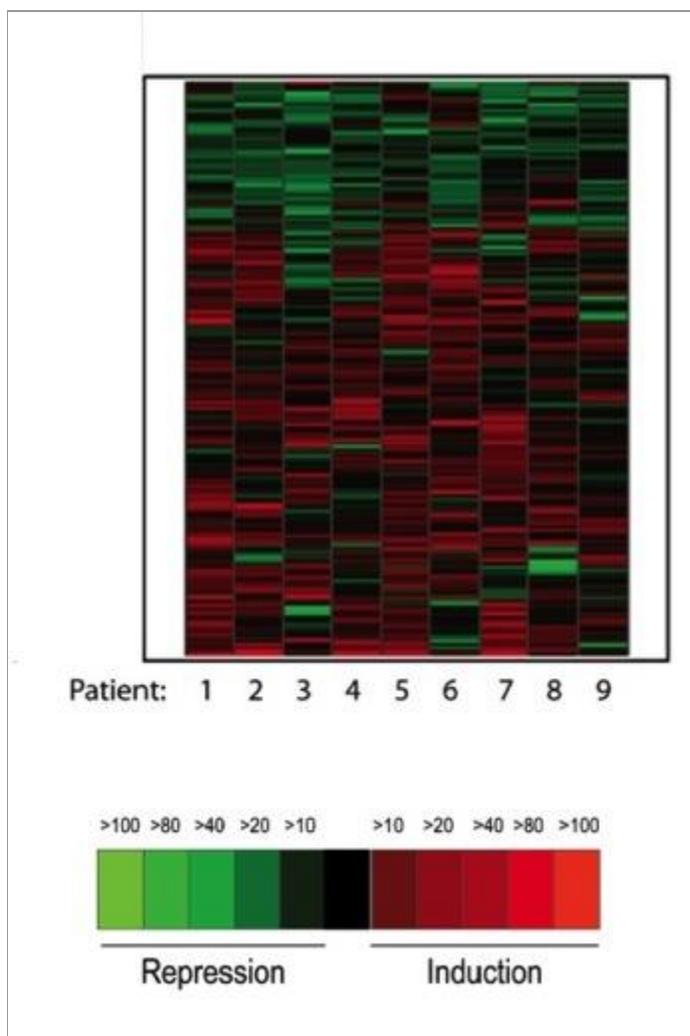


Image courtesy of authors

Transcriptional profiling of laser captured resident CD8+ T-cells from 8 week post-healed biopsies and contra-lateral control T-cells. Of the 987 differentially expressed genes, 737 are upregulated and 250 are down regulated including several genes linked to activation, proliferation, and antiviral activity.