Establishment, maintenance and reactivation from latency of the Herpes Simplex Virus type 1 (HSV-1)

Alba Sáez Fernández
1Autonomous University of Barcelona

INTRODUCTION

Herpes Simplex Virus 1 (HSV-1) is able to perform latency in the nucleus of sensory neurons (where replication and gene expression take place) after primary infection in skin or mucosa, from where it travels through its free nerve endings to the bilateral Trigeminal Ganglia (TG) of the Peripheral Nervous System (PNS) by retrograde microtubule-associated axonal transport. The objective of the current study is to review the existing knowledge about the elements that take part in establishment, maintenance and reactivation from latency in HSV-1 [1] [2].

ESTABLISHMENT.

Selective site of entry. VP16 is a structural tegument protein and a transcriptional activator of Intermediate Early (IE) genes. However, the virus is unable to initiate lytic infection when entering by distal axons (using animal models) (Figure 1), because VP16 is transported independently from capsids after the uncoating and it does not reach the cell nucleus, thus avoiding IE gene expression [1]. Latency-Associated Transcript. Major LATS are part of HSV-1 genome, and are highly expressed in latently infected neurons. They encode microRNAs, which repress IE gene expression by an antisense mechanism [3].

Reactivation.

HSV-1 antigen (Ag)-specific leukocytes, which inhibit reactivation, are found in association with neurons during HSV-1 infection [4] [5]. Major Histocompatibility Complex class 1 (MHC-1) is upregulated by major LATS in the infected cells of C57BL/6 mice, which attracts CD8 T cells (Figure 3). CD8 T cells, in turn, express a marker of exhaustion, PD-1 (induced by its ligand in infected neurons, PD-L1, upregulated by major LATS), leading to functional exhaustion of CD8 T cells. Human models, in contrast, show immunocompetent TG with no exhaustion phenotype. [5]

CONCLUSION

Data show a complex but regulated network of interactions between HSV-1 and its host. Mouse models are the most used but display low efficiency of reactivation of HSV-1, different epitope recognition by CD8 T cells and functional and phenotypic exhaustion of these cells. Those features are not found in human models. Therefore, mouse is not representative of human HSV-1 infection, and how each element affects latency cannot be fully elucidated, because of the differences in HSV-1 cycle observed when different human, animal or in vitro models are examined.

BIBLIOGRAPHY