

# Human evasion by virus essay sample

[Science](#), [Genetics](#)



The immune system has an immune arsenal that help in the combat of infections including the challenging viral infections (Iannello 2006). Upon infection by a virus, the host invariably reacts by activating its line of defenses. These immune defenses can fall into two main groups: the innate immune system (first line of defense) and adaptive immune response. The innate immune system is non-specific in nature, but the adaptive immune system is acquired following previous infections or vaccinations (Iannello 2006). However, viruses continue to undergo an evolution and have engineered strategies that evade the hosts' immune antiviral responses. This paper examines the strategies that viruses employ in the evasion of human immune responses. If such mechanisms are well-understood, they could be an eye-opener in the manufacture of novel therapies that counter viral infections especially at the evasion level.

Viruses tend to repress the transcription of MHC genes (Ploegh 1998). In this evasion strategy, viruses can suppress the genes that are required for the induction of an immune response. For instance, the Tat protein (a transcriptional protein) of the HIV-1 virus can repress a number of cellular gene promoters. The C-terminus of Tat protein carries the repressive capability and it associates with the transcriptional factor IID complex (Ploegh 1998). Consequently, it inhibits the histone acetyl transferase activity inherent in TFII250-factor (Ploegh 1998). This inhibition causes the repression of vital genes that mount immune responses such as  $\beta$ 2m and MHC class I. Other examples include the E7 and E5 of the human papilloma and bovine viruses; these proteins are oncogenic and are expressed in the early stages of the viral life cycle (Siegel et al. 1999). These oncogenes can

suppress the MHC class I mRNA to a certain level. Additionally, the E1A is also expressed early in the life cycle of the oncogenic adenovirus, Ad12. Most transcription components of the MHC class I pathway are inhibited by Ad12 (Siegel et al. 1999).

Secondly, viruses have engineered a strategy that limits the expression of MHC class I molecule particularly on the surface of antigen-presenting cells (APC) (Pasare and Medzhitov 2005). Under normal circumstances, APCs, in combination with MHC class I antigens present viral antigens prime antiviral CTL. CTL targets and kills viral-derived peptides. In essence, viruses prevent their recognition by CTL thus, enhancing their survival rate in the host (Pasare and Medzhitov 2005). These activities have been summarized in figure 1 and table 1.

Figure 1: Repression activity of viruses. Source: (Iannello 2006).

Thirdly, viruses tend to inhibit proteasome-mediated degradation, as well as the generation of peptides (Del Prete 1998; Charaborty, Veerogowda and Naik 2013). In the normal circumstances, peptides in the ER are required for the expression of MHC class I on cell surfaces. The production of these peptides occurs in the cytosol following the proteosomal degradation of viral proteins. In order to avoid their removal, viruses have engineered strategies of preventing the degradation of peptides thus limiting their overall pool (Del Prete 1998; Charaborty, Veerogowda and Naik 2013). For instance, EBV encodes EBNA-1, a nuclear protein that is needed for the replication of the viral episome in viral infected cells. EBNA-1 has a glycine-alanine rich domain, the GAr domain. This domain is responsible for the inhibition of degradation by 26S proteasome. Consequently, this reduces the pool of

EBNA-1-derived peptides that have to be presented to the of MHC class I on the cell surface (Del Prete 1998).

Figure 2: inhibition of antigen presentation to T-cells via MHC class I and II molecules.

Fourthly, viruses evade the immune system's counter-action through the blockage of TAP functions (Gatti and Pierre 2003). TAP is responsible for the translocation of viral peptides from the cytosol following proteosomal degradation to the ER. Thereafter, they are loaded in the MHC class molecules. In effect, viral evasion mechanisms prevent the loading of antigenic peptides onto the HMC class one molecules (Gatti and Pierre 2003). The absence of those peptides means that MHC class I molecules cannot be expressed on the cell surface. TAP is a heterodimer complex that is made up of TAP 1 and TAP 2; it is a vital component of PLC. UL49. 5 protein of bovine herpes virus is an example of viral proteins that distort the functions of TAP heterodimer and consequently the translocation of peptides to the MHC class I molecules (Gatti and Pierre 2003).

Fifthly, viruses may evade immune responses by degrading the PLC (Gulza and Copeland 2004). This strategy again limits the viral antigen presentation onto the MHC class I molecules. The Human Cytomegalovirus has unique genes that include US11, US6, US3 and US1; these genes can limit the expression of MHC class antigens on the surface virus-infected cells (Gulza and Copeland 2004). US11 and US2 have potent degradation capabilities. They cause a rapid degradation of nascent HLA class I molecules at the synthetic stage (Gulza and Copeland 2004). US2 showcases its activity by binding to the MHC class I molecules during the glycosylation stage (Liu

2005). This limits the transportation of MHC class I molecules and their associated degradation.  $\Upsilon$ -herpes viruses and poxviruses have immunoevasins that have an A-terminus rich in cysteine and histidine residues (K3 protein family) (Liu 2005). These proteins have ubiquitin ligase activity; it inhibits the expression of glycoproteins on the surface of MHC class I heavy chains.

In addition, viruses have engineered strategies that limit the intracellular trafficking of MHC class I antigens. MHC class I antigens are forced to be retained in the ER (Kurt-Jones et al. 2006). Human Cytomegalovirus US3 protein binds to MHC class I heavy chains causing their retention in the ER. Consequently, US3 interferes with the maturation of MHC class I heavy chains and their movement through the Golgi apparatus (Kurt-Jones et al. 2006).

If antiviral therapies have to succeed, they must target the evasive techniques of viruses. Pharmaceutical firms that manufacture these drugs must conduct concrete studies that identify molecular and cellular levels at which viruses evade the immune system. In this case, the therapy can target to undo the evasive technique of the virus or prevent the virus from initiating its evasive techniques.

## References

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