

## Editorial

# The Potentially Useful Varicella Zoster Virus

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Varicella Zoster Virus (VZV), a double-stranded DNA virus that belongs to the alpha group of herpes viruses, is a highly contagious human neurotropic virus [1-4]. Primary infection or chickenpox occurs in childhood then the virus becomes latent in the nerve ganglia [4,5]. Immunosuppression predisposes to reactivation of VZV to cause herpes zoster decades later [4-8].

VZV behaves differently from other herpes viruses as it has the following characteristic features: having the smallest viral genome; losing almost all the genes that are not essential for its survival; being cell-associated and highly fusogenic; lacking inhibitors of autophagy; being an exclusively human pathogen; having a species-specific cytokine profile; and having an inverse relationship with glioma [1-4,8-14]. Additionally, it has recently been reported to have: association with Graft Versus Host Disease (GVHD) in recipients of Hematopoietic Stem Cell Transplantation (HSCT); having Bone Marrow (BM) stimulatory effects in patients with cytopenias and BM failure; and having antitumor actions in patients with Hematologic Malignancies (HMs) and solid tumors [2,15-22].

Recently, there is growing evidence suggesting several beneficial effects of the virus in immunocompromised hosts and these effects are translated into prolongation of survival [15,16]. The reported beneficial effects of VZV include: (1) stimulation of BM activity in patients with HMs and BM failure syndromes, (2) antitumor effects in various HMs and solid tumors, and (3) association with GVHD which has anticancer effects [2,14-23]. In addition, there are several reports on the safety of the live-attenuated VZV vaccine even in immune suppressed individuals and on the emerging role of the virus in cancer immunotherapy [24-33]. The reported beneficial effects may occur through several direct or indirect immunological mechanisms including: (1) alterations in BM microenvironment due to stress-induced hematopoiesis; (2) cells that are involved in the immunobiology and pathogenesis of the virus such as: Mesenchymal Stem Cells (MSCs), dendritic cells, Natural Killer (NK) cells, T-cells and mononuclear cells; (3) cellular proteins such as open reading frames, glycoproteins, promyelocytic leukemia protein, chaperons, and small ubiquitin-like modifier proteins; (4) extracellular vesicles, exosomes, and micro-RNAs; and (5) signaling pathways, cytokines,

chemokines, and interferons [23,34-67].

The beneficial effects of VZV deserve further evaluation and should encourage scientists and researchers to give this potentially useful virus enough attention [2,23,67]. The antitumor effects as well as the stimulatory effect exerted by the virus on the 3 cell lines in the BM can be explained by one or more of the suggested mechanisms or may be due to a new mechanism that needs elucidation [2,15,23,67]. Ultimately, the virus itself; modified or engineered versions of the virus; or specific elements obtained from the serum of patients infected with VZV such as certain cytokines (e.g. interleukin-6 and tumor necrosis factor- $\alpha$ ) and cells (e.g. MSCs and NK cells) may become novel therapeutic modalities in the management of patients with BM failure syndromes, HMs and solid tumors.

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