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Opinion

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Dualism of Viruses in Oncology

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ABSTRACT

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Opinion

In the last months all over the world we have been crying, talking, and writing a lot of viruses, given the pandemic that has hit our planet. It is not the first time that mankind has been overwhelmed not only by wars and natural disasters but also by as unexpected as trembling infectious events. On more than one occasion there have been many deaths ascribable to serious viral infections. Nowadays, the deadest virus of all can be Human Immunodeficiency Virus since Global Health Observatory (GHO) data indicated that more than 30 million of persons perished after it was identified in the early 1980s. In 1967 experts identified Marburg virus, its mortality in the first outbreak was 25%, but it was more than 80% in the 1998-2000 outbreak in the Democratic Republic of Congo, as well as in the 2005 outbreak in Angola [1]. Ebola infection caused by Ebola virus (EBOV) is another severe disease with a high case–fatality rate [2]. Rabies is a fatal viral infection of mammals and domestic dogs cause around 95% of all estimated yearly 59,000 rabies deaths among human [3].

Smallpox is caused by the variola virus (VARV) and although a successful vaccination program led to its eradication, about 400 million of fatalities have been estimated in the 20th century [4]. Also, Dengue, rotavirus, and coronaviruses as SARS-CoV, MERS-CoV daily infect and, in the worst cases, kill many people in different parts of the globe [5-7]. In this opinion letter we would like to highlight the dualism of the physiopathology of these simple but powerful infective agents. The notion of duality can be found in many areas but here we would like to highlight this concept in virology since viruses, like two sides of the same coin, can in particular cases exert an oncogenic or an oncolytic action (Figure 1).In several cases viruses, aside from causing infections immediately identified as such, in a much more sneaky way, can be the cause of the onset of a whole series of tumors [8] or, in a much more unexpected and surprising way, they can counteract the onset or spread of some forms of cancer [9,10].

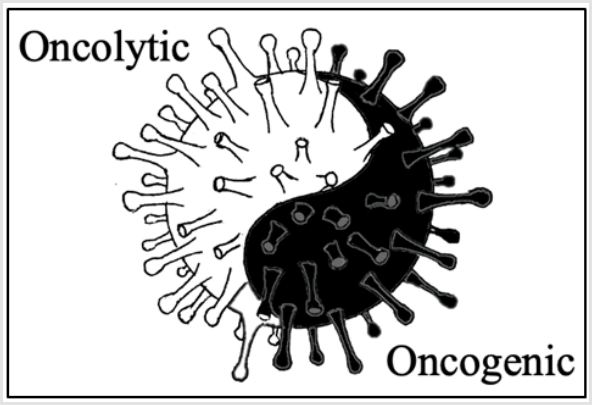

Figure 1: The dualism of the physiopathology of viruses: oncolytic and oncogenic capability.

Viruses as human papillomaviruses (HPVs), Epstein–Barr virus (EBV), hepatitis B virus (HBV), hepatitis C virus (HCV), human T-lymphotropic virus 1 (HTLV-1), Kaposi sarcoma-associated herpesvirus (KSHV) and Merkel cell polyomavirus (MCPyV) can manipulate the host cellular signaling and transcriptional systems inducing several different cancer establishment and progression phenomena as summarized in the oncogenic virus section of Table 1.On the other hand, as listed in the oncolytic section of the Table1, oncolytic virotherapy (OVT), recently emerged as promising alternative solution in cancer treatment since, after contagion,

oncolityc viruses, by interfering with the protein synthesis of tumor cells, can end cells by virus self-replication. Furthermore, oncolytic viruses can induce effective antitumor immunity reactions by engage and activate cytotoxic T-lymphocytes, mast and natural killer cells promoting the release of tumor antigens and cytokines [11-13]. To conclude, this opinion letter aims to highlight aspects that, although they are still under study, are already showing a great potential in the treatment of several bad prognosis oncological diseases. OVT approach requires more attention than that based on the use of chemotherapy and monoclonal antibodies because viruses remain pathogens that must be handled and engineered with great care. Furthermore, which is certainly no less important, while the side effects of chemotherapy can occur from their first administrations, a complex bioengineering process like the integration of a viral nucleic acid into a host cell, is never fully controllable on a short and long time scale.

Table 1: List of oncogenic or oncolytic viruses with related pathologies and bibliographic references.

ONCOGENIC		ONCOLITYC	
VIRUS	**PATHOLOGY**	**VIRUS**	**PATHOLOGY**
Papillomaviruses (HPVs)	Cervical, anal, oropharyngeal cancers[14-16].	Herpes simplex virus	Angiosarcoma, epithelioid sarcoma, Kaposi's sarcoma, gastrointestinal stromal tumor, Leiomyosarcoma, melanoma, soft tissue sarcoma [17], cutaneous squamous cell carcinoma (cscc) of the head and neck [18], brain tumors [19,20].
Hepatitis B virus (HBV)	Hepatocellular carcinoma[21-24], biliary cancer[25], non-Hodgkin's lymphoma, especially diffuse large B-cell lymphoma[25,26], intrahepatic cholangiocarcinoma[27-29], pancreatic cancer[30], colorectal cancer[31,32].	Adenovirus	Retinoblastoma[33], lung cancer[34].
Hepatitis C virus	Hepatocellular carcinoma[21,35-37], non-Hodgkin's lymphoma, especially diffuse large B-cell lymphoma[26,38,39], intrahepatic cholangiocarcinoma[27,29,40], pancreatic cancer[41].	Pox virus	Lung cancer[42-44], ovarian cancer[45], brain[46].
Epstein-Barr virus	Malignant lymphomas [47-50], Hodgkin lymphoma[51-53], Burkitt's lymphoma[54-56], gastric cancer[57-59], nasopharyngeal carcinoma[60-62], breast cancer[63,64], thyroid[65,66].	Newcastle disease virus	Melanoma[67], breast carcinoma[68], ovarian carcinoma[69], Digestive tract tumors[70], colorectal carcinoma[71], pancreatic carcinoma[72-74], renal cell carcinoma[75], glioblastoma multiforme[76].
Kaposi sarcoma-associated herpesvirus	Kaposi sarcoma, primary effusion lymphoma[77-82].	Reovirus	Liver cancers[83], astrocytoma[84,85], gliomas[86], ependymoma, lymphoma, ovarian, tubal, or peritoneal cancer[87].
Human T-lymphotropic virus 1	T-cell leukemia/lymphoma[88-91].	Vesicular stomatitis virus	Colorectal cancer[92], multiple myeloma[93].
Merkel cell polyomavirus	Merkel cell carcinoma[94-98].	Retrovirus	Hematological malignancies[99], hepatocellular carcinoma[100,101], gastric cancer[102], liver cancer[103].

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