



## Review Article

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# An overview on human polyomaviruses developing cancer in humans

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## Abstract

The family Polyomaviridae included about a dozen of human polyomaviruses (HPyVs), of which MCPyV, SV-40, JCV and BKV viruses have been reported to cause cancer in human. Merkel cell carcinoma is a very aggressive type of skin cancer caused by the MCPyV5. Similarly, while SV-40 and JCV viruses developed brain tumor cancer, the BK virus has been linked to renal transplantations and nephropathy producing urinary bladder tumor and prostate cancer in human. In this paper we have tried to summarize the recent information gained in the field of human polyomaviruses causing cancer in human.

**Keywords:** Human polyomaviruses, Cancer, Virus.

## INTRODUCTION

Viruses are among the few causes of cancer contributing to a variety of malignancies. In 1966, when Peyton Rous was awarded a Nobel prize in physiology and medicine for his discovery of Rous chicken sarcoma virus as a cause of cancer, a renewed interest came in the field of microbial origin of cancer. Viral origin of cancer has been the second most important risk factor for cancer development in human[1]. And, the possible role of viruses in the development of cancer has been the subject of much intensive studies during the past several decades. The present paper deals with the study of different human polyomaviruses causing skin, bone and brain tumor cancers. Several other cancers like urinary bladder and prostate cancer have also been reported. The present paper is prepared and discussed on the basis of researches done so far in the field of viral origin of cancer. The authors have gone through several original research papers in order to explore the facts regarding the human polyomaviruses causing cancer in human.

Human polyomaviruses are DNA tumor viruses whose infections are widespread but largely asymptomatic causing non-neoplastic diseases in immunocompromised patients. Today, the human polyomavirus (HPyV) family consists of Merkel cell polyomavirus (MCV or MCPyV5) HPyV5, Simian virus-40 (SV-40), Trichodysplasia spinulosa virus (TSV) HPyV8, JC Virus (JCV) HPyV2, BK Virus (BKV) HPyV1, KI Virus (KIPyV) HPyV3, WU Virus (WUPyV) HPyV4, MW Virus (MWPyV) HPyV10, HPyV6, HPyV7, HPyV9, HPyV12 and HPyV13. These human polyomaviruses (HPyVs) have been linked to develop a variety of diseases and cancer in human[2,3]. There are at least four human polyomaviruses found in nature causing cancer in human. They are Merkel cell polyomavirus, SV-40, Jc virus and BK virus.

Merkel cells are found in the skin where they function mainly as touch receptors and were originally described in the late 1800 by Friedrich Merkel, a German anatomist [4]. Merkel cell carcinoma (MCC) is a type of skin cancer, that was first described by Cyril Toker in 1972 as a trabecular tumor of skin [5]. And, their causal organism was named and described as Merkel cell polyomavirus (MCV or MCPyV) by Feng, 2008 in Pittsburg [6]. It causes a very aggressive type of skin cancer. This is mostly seen in older people who are generally immunocompromised with higher frequency of transplantations [7,8]. Further, not very much is known that how people become infected with this virus, might be transmitted with the help of saliva, respiratory droplets, shedding from healthy skin and the gastrointestinal tissues. Usually, the peoples are infected with this virus even before the age of 20, but the infection doesn't cause any symptom; being only the carrier of virus it rarely leads to MCC. While on the other hand, this is also true that nearly 80 % of all MCC tumors have been found to be infected with the MCV. However, there are little evidences in the oncogenesis of tumors [9]. At present, there is no vaccine or proper medications available to prevent or treat the Merkel cell carcinoma [10,11]. Lastly, Merkel cell polyomavirus was the first to be established as the cause of human cancer whose DNA fragments have been isolated from

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Merkel cell carcinoma with the help of Digital Transcriptome Subtraction (DTS) [6,12].

Simian virus 40 (SV-40) is a small DNA tumor virus of monkey origin. SV-40 was discovered by Maurice Hilleman in 1960 as a contaminant of polio vaccine [13]. Shortly, after its discovery, this is shown to be a potent oncogenic DNA tumor monkey virus causing primary brain and bone cancers, malignant mesothelioma and non-Hodgkin lymphoma [13-26]. The production of contaminated polio vaccine during the period of 1955 to 1963 with SV-40 was, in fact, led to the discovery of this vacuolating oncovirus as a pathogen. Infectious SV-40 survived the vaccine inactivation treatments and millions of people worldwide exposed accidentally as a part of vaccination programme. Since, the studies on the consequences of this accidental exposure to people are not available, there link to the development of cancer in these people could be derived as incidental [27,28]. However, strong biological evidences suggest that SV-40 exposure could lead to cancer in human [26,29].

A type of human polyomavirus which was formerly known to us as papovavirus is polyomavirus 2 or JC virus. This is John Cunningham virus which was named using the two initials of the same progressive multifocal leukoencephalopathy (PML) patients from which the virus was isolated [30]. The virus was identified by ZuRhein and Chou and by Silverman and Rubinstein in 1965 [30,31]. JC virus is transmitted via infecting the tonsils and possibly by the gastrointestinal tract. It spreads in other body parts as well and may cross the blood brain barrier [32,33]. More than 80% of human populations are usually living in coexistence of JC virus worldwide exhibiting JCV- specific antibodies [34]. Infections with this virus occur in the stage of early childhood and the virus remains in a latent form throughout life, reactivating when the immune system of the body is impaired [28]. The virus having tremendous oncogenic potential develops a fatal demyelinating disease producing tumors in human brains and experimental animals. It produces progressive multifocal leukoencephalopathy mostly in immunocompromised patients [32,35-39]. JC virus also produces lung cancer in human [40].

BK virus was first isolated in 1971 from the urine of a renal transplant patient, initials B. K. [41]. This virus has been linked to hemorrhagic cystitis after allogenic hematopoietic stem cell transplantation and nephropathy after kidney transplantation [28,42,43]. BK virus is similar to JC virus, innocuous in immunocompetent individuals, often latent in renal and another cells [42]. But, when immunocompromised as in case of renal transplant it may result in graft-dysfunction known as BK virus associated nephropathy (BKVAN) [43]. It may produce tumors malignancy and bladder cancer [43-50]. Still, it is not known that how this virus is transmitted [41]. BK virus may also produce prostate cancer and Kaposi sarcoma in human [44,46].

Last but not the least, in the same family Polyomaviridae, there are some other members of polyomaviruses which do not cause cancer in human. For instance, Trichodysplasia spinulosa is a rare skin disease characterized by the papules, spines and alopecia on the face of immunocompromised patients [51]. TSV has been reported to be the cause of *Trichodysplasia spinulosa*. TSV particles have been demonstrated in patients suffering from Trichodysplasia spinulosa [52,53]. Whether TSV is involved in other diseases or tumors remains to be investigated. Similarly, the KI and WU polyomaviruses were both reported in 2007 [54,55]. Several studies have investigated whether these polyomaviruses are involved in tumor development and so far the results have been found negative [56-58].

## CONCLUSION

In general, while most of these HPyVs infections are benign only four of them have caused cancer in human. They are Merkel cell polyomavirus, SV-40, JC virus and BK virus. Merkel cell polyomavirus is a very aggressive type of skin cancer mostly found in older people with high

frequency of transplantations. The next human polyomavirus is a monkey virus isolated as a contaminant from polio vaccine. It causes brain tumor in human. Similarly, a kind of human polyomavirus isolated from a PML patient also produces brain tumor in human. Lastly, the BK virus isolated from the urine of a renal transplant patient have sometimes, developed renal bladder or prostate cancer in those who have undergone kidney transplant or prostactomy respectively. Currently, there is no vaccine or medications available to prevent these infections however, the researches are underway to treat the HPyVs infections causing cancer in human.

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## Conflict of Interest

The authors have declared no conflict of interest. They have approved the final version of the manuscript contributing equally.

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