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WU and KI polyomaviruses

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ABSTRACT

Background: In 2007, two novel human polyomaviruses were reported, the Karolinska Institute polyomavirus (KI) and the Washington University polyomavirus (WU), both were discovered in respiratory tract samples from individuals with acute respiratory tract infections, and they were categorized among Polyomaviridae family. Both viruses were detected in specimens from patients with respiratory tract disease on all continents suggesting a worldwide distribution. Serological studies have shown that similarly to BK and JC, infection with the new polyomaviruses KI, WU is common in the general population.

Primary infection probably occurs early in childhood, as suggested by the seroprevalence in young people (<21 years of age), which is similar to that of adults. KI and WU polyomaviruses have been detected in respiratory samples from children and adult patients with acute respiratory symptoms from around the world. And some studies also found that there is a relationship between these two viruses and some other diseases.

Introduction

Polyomaviruses are non-enveloped DNA viruses with an icosahedral capsid that is 45 nm in diameter and a circular, double-stranded genome that is about 5 Kb in length. Polyomaviruses belong to the Polyomaviridae family. Previously, International Committee on Taxonomy of Viruses (ICTV) commended dividing the family of Polyomaviridae into three genera: Genus Orthopolyomavirus, Genus Wukipolyomavirus and Genus Avipolyomavirus [1]. The current ICTV classification system recognizes six genera and 117 species, of which nine could not be assigned a genus, the six genera are: Genus Alphapolyomavirus, Genus Betapolyomavirus, Genus Deltapolyomavirus, Genus Epsilonpolyomavirus, Genus Gammapolyomavirus and Genus Zetapolyomavirus [2]. According to human polyomaviruses, there are 14 viruses distributed between alpha, beta and delta polyomaviruses **(Table 1)** [3]. This review focused on the Karolinska Institute polyomavirus (KI) and Washington University polyomavirus (WU) polyomaviruses, as information was mentioned about them, including the history of their discovery and their structure, as well as the diseases that were associated with their infection, and finally the diagnostic methods that were used.

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Table 1. Human polyomaviruses.

Virus name	Genus	discovery	Ref.
BK polyomavirus	Beta	1971	[4]
JC polyomavirus	Beta	1971	[5]
KI polyomavirus	Beta	2007	[6]
WU polyomavirus	Beta	2007	[7]
Merkel cell polyomavirus	Alpha	2008	[8]
Human polyomavirus 6	Delta	2010	[9]
Human polyomavirus 7	Delta	2010	[9]
Trichodysplasia spinulosa polyomavirus	Alpha	2010	[10]
Human polyomavirus 9	Alpha	2011	[11]
MW polyomavirus	Delta	2012	[12]
STL polyomavirus	Delta	2013	[13]
Human polyomavirus 12	Alpha	2013	[14]
New Jersey polyomavirus	Alpha	2014	[15]
Lyon IARC polyomavirus	Alpha	2017	[16]

History

Until 2007, only two human polyomaviruses were known to infect human, beings: BK and JC. In 2007 almost coincidentally, two novel HPyV were reported, the KI identified in Stockholm, Sweden and the WU identified in St Louis, USA. Both were discovered in respiratory tract samples from individuals with acute respiratory tract infections [6,7].

Classification, structure and genome

Typical members of the family Polyomaviridae form small, non-enveloped, icosahedral particles with 40-45 nm in diameter containing a supercoiled dsDNA genome. The virion is made up by 72 pentamers of the structural protein VP1, each pentamer binds to a single copy of VP2 or VP3. The genome is attached to cellular histones. There is no evidence hinting at a virus structure for KI and WU differing from other polyomaviruses, also both of them belong to beta-polyomaviruses [3,17]. The classification of KI viruses as polyomaviruses was made first through sequence homology, and thus it was not surprising that their genomic organization and size was consistent with previously known viruses of this family. Each has coding regions for a small and large T (tumor) antigen (T-ag) protein, and three capsid proteins VP1, VP2, and VP3, with VP3 representing the product of an internally initiated reading frame of VP2. The large T-ag proteins have apparent domain homologies as found in other PyVs. Neither a middle T-ag nor an agnoprotein open reading frame has been identified in any of these PyVs. Other PyVs such as simian virus 40 SV40, BKV, JCV, and murine polyomavirus MPyV also encode a microRNA (miRNA) made during lytic infection, presumably to autoregulate early gene expression at late times during infection, but none has yet been characterized for WU and KI [3]. The DNA length of KI 5,040 bp while the DNA length of WU 5,229 bp, the two viruses differ substantially from each other as shown by the percentage of amino acid identity and phylogenetic analysis. Yet they are phylogenetically more closely related to each other than to SV40, BK [18].

Epidemiology

Both viruses were detected in specimens from patients with respiratory tract disease on all continents suggesting a worldwide distribution [19–21]. Serological studies have shown that similarly to BK and JC, infection with the new polyomaviruses KI, WU is common in the general population.

Primary infection probably occurs early in childhood, as suggested by the seroprevalence in young people (<21 years of age), which is similar to that of adults, followed by lifelong persistence in the body [22]. Primary acquisition of WU, KI, occurred most commonly when children were approximately 12 months of age [23]. Using ELISA testing with VP1 recombinant proteins, the prevalence in the adult population was found to be 55% for KI, 69% for WU [24].

Diseases associated with KI and WU

KI and WU have been detected in respiratory samples from children and adult patients with acute respiratory symptoms from around the world [18].

The pathogenic role of WU and KI in respiratory disease is a subject of dispute. There are two opinions regarding the pathogenicity of these two viruses to the respiratory system, one of them states that these two viruses are pathogenic and this based on the detection of higher viral loads among patients with more severe illness, and found higher rates of convulsions and higher viral loads, or observation that those viruses as the only detectable pathogens with respiratory symptoms [25,26]. The other opinion suggests there is no association between infections with the two viruses and respiratory disease [27,28].

There are several studies that looked for the relationship between these two viruses and different types of tumors: breast cancer, glioma, urinary bladder tumor, acute lymphoblastic leukemia, lung adenocarcinoma, Primary Malignant Melanomas of Mucous Membranes and Neuroblastomas; The two viruses were not detect in all these types of tumors [29–33]. Also there were some studies reveals on the detection WU and KI in transplantation recipients, these studies have found that immunocompromised patients are more susceptible for infection and may there is a background for reactivation of these viruses or the viruses could trigger the development of organ damage [34,35].

WU and KI were detected in stool samples, they may act as an opportunistic pathogen in the gastrointestinal (GI) tract, colonize the GI tract without causing any disease, or be a part of the endogenous gut virome that are reactivated by other viral infections. However, although positive samples were obtained from patients who had acute gastroenteritis without any apparent clinical respiratory symptoms, we cannot exclude the possibility that the detection of these two viruses in fecal specimens might result from its transient presence in patients who have swallowed virus containing sputum or nasal secretions. It is also possible that WU and KI persists in the respiratory tract without inducing symptoms or KI and WU reactivated and were excreted in the gastrointestinal tract. Because of frequent co-infections, a clear correlation between novel polyomaviruses and clinical symptoms could not be established [27,36,37]. Also both viruses were detected in urban sewage [38].

WU and KI can infect the human tonsils which may represent the initial site of infection, or presence of these two viruses in tonsil tissue assess the possibility that the virus can establish latent and/or persistent infection and/or virus replication at this site [39] WU may invade into the middle ear and cause otitis media [40], also both viruses do not establish neuropersistence and the neurotropic potential of these viruses is very limited [40].

The DNA detection of WU and KI in saliva samples of both HIV-positive and healthy control children, although the frequency of infection was significantly higher among the HIV-infected children. These findings suggest that saliva may be a route of transmission and that the oral cavity could be a site of virus replication and persistence [41]. The DNA of both viruses are frequently detectable in brains of HIV positive individuals but that their presence does not seem to be associated with Progressive multifocal leukoencephalopathy PML or other signs of brain injury [42]. Both KIP and WU are not shed in urine suggesting that the two viruses do not persist in the urinary tract unlike BK and JC [43]. Also there no evidence of mother-to-fetus transmission [44]. Recently both viruses were detected in COVID-19 patients [45].

Diagnosis

KI and WU were first detected in the respiratory tract samples of patients with respiratory symptoms [6,7]. Following this finding, other body compartments and specimen types have been screened: stool, whole blood, plasma, serum, cerebrospinal fluid, lymphoid tissue, urine and lung tissue [36,37,39,43,46–49]. Several conventional PCR formats as well as real-time PCR protocols were developed reporting sensitivities up to 100% and specificities up to 97% for detection of KI and WU infections [7,50,51].

Detection of virus-specific antibodies or antigens by enzyme linked immunosorbent assays (ELISA), or immunofluorescence assays (IFA) are useful for retrospective or epidemiological studies [22,52]. Immunohistochemistry was also used to study viral tissue tropism, and no specific histopathological lesions were found associated with the presence of KI and WU [42,53,54]. In 2020, Wang et al success in culture WU on human airway epithelial (HAE) cells [55]. According to KI, there is no culture system is known at this time.

Conclusion

There is in dispute about whether these two viruses are pathogenic or not, despite their presence with many diseases. KI and WU have been detected in respiratory samples from children and adult patients with acute respiratory symptoms from around the world. The two viruses were not detecting in tumor samples and immunocompromised patients are more susceptible for infection with these viruses.

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