

## Role of Polyomavirus (BK) in Urinary Tract Pathology

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Polyomavirus hominis 1, better known as BK virus (BKV), infects up to 90% of the general population [1]. Following a typically subclinical primary infection, BKV establishes a lifelong persistent infection in the kidney and urinary tract. The introduction during the past two decades of new more potent immunosuppressive regimens has led to a significant increase in BKV associated pathology, including but not limited to BKV allograft nephropathy (BKAN), ureteral stenosis, and hemorrhagic cystitis [2,3]. Approximately 40 years ago, Koss described polyomavirus inclusion bearing cells for the first time in urine specimens [4]. He coined the term “decoy cells” to alert pathologists not to misdiagnose viral inclusion bearing cells as malignant cancer cells [3]. The name decoy cell is a descriptive term for epithelial cells with intranuclear viral inclusion bodies that can have different phenotypes (types 1-4) depending upon the state of viral replication and maturation as well as the state of cellular preservation [3]. The shedding of decoy cells generally indicates the (re)activation of polyomavirus (BK) in the urothelium [3]. Although productive infections with cytomegalovirus, herpes simplex virus or human papillomavirus can show nuclear abnormalities including viral inclusion bodies, typical decoy cells are generally not found in the urine in these infections [3].

Infection of BKV in rodent animal models or cells in culture often results in tumor formation or transformation, respectively [5]. An etiological role of BKV in human cancer, however, remains controversial. Multiple reports have demonstrated conflicting results in regards to the presence of BKV sequences and/or proteins in various tumor types [5]. Due to the lack of conclusive causality data from these studies, there does not appear to be a definitive association between BKV and human malignancies. On the other hand, several lines of evidence have suggested that BKV may play a significant role in the pathogenesis of bladder cancer in immunosuppressed patients [6,7]. Using immunohistochemistry and PCR technology, polyomavirus large T-Ag and/or BKV sequences have been reported in urothelial carcinomas in transplant recipients. Furthermore, a statistically significant association between urine cytological evidence of polyomavirus infection (decoy cells) and bladder cancer was demonstrated in immunocompetent patients [8].

The possible causative role of BKV in oncogenesis rests on the ability of BKV large T-Ag to inactivate the functions of tumor suppressor proteins of the pRB family, p103 and p107, thereby shifting the host cell cycle into a proliferative G2/S state, as well as on its ability to induce chromosomal aberrations in human cells. Binding of large T-Ag to p53 is thought to counteract apoptosis which would normally be triggered by the DNA changes and metabolic exhaustion [9].

Due to the still low number of reported cases, one cannot rule out entirely that BKV is not the main or the only cause of urinary tract carcinoma in the cases where its presence is documented. Further work will be needed in order to prove the exact molecular steps of oncogenesis. In the meantime clinical vigilance for early diagnosis of urinary tract malignancies in BKV positive immunosuppressed patients is warranted.

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