BK Virus Diversity And Its Association With Hemorrhagic Cystitis

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Introduction: BK Polyomavirus (BKPyV) is a non-enveloped, circular, double-stranded DNA virus with a seroprevalence of more than 80% in adults. In immunocompetent hosts, it rarely causes clinical disease; however, in immunocompromised individuals, it may cause BKPyV-associated nephropathy, ureteral stenosis, and hemorrhagic cystitis (HC). HC can affect up to 25% of children undergoing bone marrow transplantation, and results in prolonged hospitalizations, increased blood transfusion requirements, and a higher risk of death. No vaccine or antiviral treatments have been approved for BKPyV infection; thus, the most effective therapy involves reducing the use of immunosuppressive drugs.

Hypothesis: This study evaluated the hypothesis that the risk of HC after hematopoietic stem cell transplant (HSCT) is a function of both BKPyV diversity and the host response to the virus. To that end, BKPyV diversity at the population and within-host levels were evaluated in patients with and without HC.

Methods: We used an existing cohort of 193 children and young adults undergoing HSCT at the Children's Hospital of Philadelphia and the Cincinnati Children's Hospital Medical Center. DNA was extracted from 5 samples from patients suffering from HC using a 1 mL urine elution. The resulting DNA was linearized and later amplified via PCR. The amplified NCCR product was evaluated by next generation sequencing (NGS). Consensus sequences were generated for each sample and compared to reference sequences in a phylogenetic tree to visualize viral diversity.

Results: BKPyV subtyping is frequently based on evaluation of a small portion of the viral genome – often the VP1 region. Analysis of the NCCR in the 5 samples found that all NCCR sequences were unique and clustered with BKPyV subtype I references.

Conclusions: There are currently four distinct BKPyV subtypes (I-IV), with subtype I being the most common in the US. Preliminary analysis suggests these samples belong to this same subtype, although other BKPyV subtypes may be identified when the larger study population is examined fully. Future analysis should be focused in the VP1 region of the genome, where considerably variation is expected. As such, further work is necessary to establish a more robust association between BKPyV subtypes and HC.

Acknowledgements: This study was supported in part by NIH grant T35DK060444 and R01 NIDDK 125418 07/01/2020 – 06/30/2025