

Human CD1c+ dendritic cells are refractory to BK polyomavirus but transmit it to human primary renal tubular epithelial cells and protect it from neutralization

The BK polyomavirus (BKPv) is a ubiquitous virus infecting approximately 80% of the worldwide population. It infects cells by binding to b-series gangliosides on target cells. Mainly asymptomatic, the primary infection occurs during childhood and leads to a low-level replication state in the reno-urinary epithelium. In immunocompromised individuals, especially kidney transplant (KTx) patients, BKPv reactivates in the grafted kidney. To date, the absence of marketed treatment often leads to a polyomavirus-associated nephropathy (PVAN), ultimately leading to graft loss at late stages. An increase in the CD1c+ myeloid DC infiltrate has already been documented in BKPv reactivating kidneys although no role for this DC subset was suggested. Here we investigated the interplays between the BKPv and monocyte-derived DC (moDC) or CD1c+ DC from the blood and kidney of healthy donors.

We demonstrated that BKPv particles from the most frequent circulating genotypes were internalized into moDC in a sialic acid-dependent manner. Particles were endocytosed in pleiomorphous tubules resembling CLIC/GEEC endocytic vesicles and to a lesser extent into macropinosome-like vesicles. Interestingly, BKPv was also efficiently captured by CD1c+ DC from the blood and kidney but not by pDC. We showed that moDC and CD1c+ DC were not activated by either virions or virus-like particles. Interestingly, they failed to acquire infection. However, BKPv-loaded DC were capable of efficiently transferring virions to permissive cells. We finally demonstrated that endocytosed BKPv particles were protected from the neutralization by the serum of BKPv-reactivating KTx patients.

Altogether, these results suggest an unprecedented direct role for CD1c+ DC and potentially for inflammatory DC in the spreading of reactivating BKPv in the kidney of KTx patients.

Keywords : myeloid dendritic cells, BK polyomavirus, renal transplantation, trans-infection

Authors :

References : , , ,

Authors

Franck Halary 1,

1. CRTI/UMR1064, Nantes, FRANCE