

**P010** Restriction of human polyomavirus BKV DNA replication in murine cells and extracts

**Irina Tikhanovich<sup>1</sup>, Cathal Mahon<sup>1</sup>, Heinz P. Nasheuer<sup>1</sup>**

*1. National University of Ireland, Galway,  
Dept. of Biochemistry, Galway, Ireland*

The human polyomavirus BKV causes persistent and asymptomatic infections in most humans and is the etiologic agent of polyomavirus associated nephropathy (PVAN) and other pathologies. Unfortunately, there are no animal models with which to study activation of BKV replication in the human kidney and the accompanying PVAN. A sensitive in vitro replication assay was developed with purified BKV TAg that supported robust BKV DNA replication in human cell extracts, but not murine cell extracts. In vitro assays revealed differences in replication specificity between BKV TAg and the TAg of simian virus 40 (SV40) and human polyomavirus JC (JCV) and their respective origins; and unlike SV40 TAg, addition of human replication proteins, DNA polymerase  $\alpha$ -primase, replication protein A, or topoisomerase I to BKV TAg did not rescue BKV DNA replication in murine extracts. Notably, addition of murine extracts to BKV TAg in human extracts inhibited BKV DNA replication at a step prior to or during unwinding of BKV DNA. These results implicate features of BKV TAg distinct from SV40 TAg and JCV TAg, that restrict replication in murine cells and that may modulate BKV replication in human cells.