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Poster presentation

Isolation of a human betaretrovirus resembling mouse mammary tumor virus (MMTV) from patients with primary biliary cirrhosis

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Background

A human betaretrovirus resembling the MMTV has been cloned from biliary epithelial cells and perihepatic lymph nodes of patients with primary biliary cirrhosis (PBC) [1]. The human betaretrovirus can trigger a PBC specific phenotype *in vitro* and antiviral therapy improves both biochemical and histological disease in patients with PBC. The human betaretrovirus can be detected in perihepatic lymph nodes in 75% of PBC patients by immunochemistry and RT-PCR [1]. Our goal was to provide proof that a human betaretrovirus infects patients by isolating the human betaretrovirus and detecting viral integration sites.

Methods

DNA from livers, biliary epithelium and lymph nodes was used to identify proviral integration sites using linker mediated PCR. PBC peri-hepatic lymph node homogenates were co-cultured with Hs578T cells and infected cells were subcloned, clonally expanded and tested for betaretrovirus infection.

Results

Betaretrovirus was detected by RT-PCR in 16 supernatants from 28 subcloned Hs578T co-cultured cells. Betaretrovirus particles were identified by electron microscopy and 17 Integration sites were identified in infected Hs578T cells.

47 integration sites were identified from patients' samples. In patients with PBC, 1 or 2 integration sites were detected in 4 of 5 PBC biliary epithelial samples, 1 of 3 liver samples and 1 to 14 integration sites (median 5) were found in 7 of 10 PBC lymph nodes. Of note, the human betaretrovirus preferentially integrated within genes in 61% samples. Clustering of 3 or more sites within 15,000 Kb was observed on chromosomes 4, 5, 6, 8 and 11.

Conclusion

The unequivocal detection of viral integration sites in the human genome and viral isolation studies provide proof that patients with PBC have infection with a transmissible betaretrovirus. Most PBC patients have evidence of betaretrovirus infection in biliary epithelial cells targeted by the disease process, whereas the perihepatic lymph nodes have the highest viral burden.

References

1. Xu L, Shen Z, Guo L, Fodera B, Keogh A, Joplin R, O'Donnell B, Aitken J, Carman W, Neuberger J, Mason A: **Does a betaretrovirus infection trigger primary biliary cirrhosis?** *Proc Natl Acad Sci of the USA* 2003, **100:**8454-8459.