

HTLV-1 Subtype C chronically infected cell line clones for the *in-vitro* study of viral transmission and pathogenesis.

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Background:

HTLV-1 subtype C is endemic at high prevalence in some first nations people residing in remote communities in Central Australia. The few available full provirus sequences show that this subtype has a relatively high sequence divergence from the more globally distributed HTLV-1a prototype strain. The most common clinical manifestation of infection with the HTLV-1c strain is the lung inflammatory disease, bronchiectasis. Knowledge about HTLV-1c subtype-specific virological properties is limited.

Methods:

Lethally gamma-irradiated peripheral blood mononuclear cells from an infected patient were used to initiate transfer of HTLV-1c into engrafted human immune cells in humanised (hu-NSG) mice producing rapid disease progression from a high proviral load. HTLV-1c infected Jurkat cells were made by co-culture with CD3/CD28 activated splenocytes from hu-NSG mice and clones prepared by endpoint dilution.

Results:

HTLV-1c infection of clones was confirmed by ddPCR of proviral DNA with Env, Tax, Gag and Hbz with specific primers. Clones had provirus ranging from 1 to 4 integration sites/cell and expressed diverse levels of viral proteins. Analysis of selected cellular genes found that Galectin-1, a glycan binding protein with immunoregulatory activity, was consistently overexpressed by HTLV-1c infected cell clones. Clones expressing Tax demonstrated diminished apoptosis induction after Vinblastine treatment and downregulated the pro-apoptotic factor Bax. We quantified HTLV-1c cell-to-cell virus transmission from Jurkat producer clones into BHK-21-HTLV-1c LTR-Luc reporter cells that produce Luciferase in response to the expression of HTLV-1c X-region genes including Tax.

Conclusion:

We report the first described chronically infected HTLV-1c Jurkat T-cell line clones and characterised some distinctive virus and host properties. This will allow further investigation of HTLV-1c viral pathogenesis and serve as infectious donor cells in a cell-cell transmission reporter system for vaccine and antiviral studies.

Disclosure of Interest Statement:

Nothing to disclose.