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## Human Mammary Tumor Virus (HMTV) and cancer

Melana Stella .M, Marin .T, Nartey .T, Jaffer .S, Holland J.F and Pogo B.T.G Mount Sinai School of Medicine, USA

Eleven percent or more of cancers worldwide are linked to viral causes. In many cases individuals are infected with a virus but Donly a certain percentage develop cancer (19). Similar to other individuals who carry a high risk for developing cancer due to viral infections such as HPV, EBV, HBV, HCV, SV40 and McPyV results from our laboratory and that of others suggest that individuals who are infected with HMTV carry a risk of developing breast cancer.

Retroviral sequences homologous to the  $\beta$ -retrovirus mouse mammary tumor virus (MMTV), the etiological agent of mammary tumor in mice, are present in 40% of American women's breast cancers. A 660 bp sequence, homologous to MMTV env gene with no significant homology to any other viral or human sequence reported in the GenBank, is found in breast cancer and in the breast milk of 7.6% of healthy American women.

A complete provirus structure with 95% homology to MMTV has been isolated from two human breast tumors and named human mammary tumor virus (HMTV).  $\beta$ -retroviral particles from primary cultures of metastatic breast cancer cells (MSSM) have been isolated and characterized HMTV. Virion RNA is more than 90% homologous to MMTV RNA and to the HMTV proviral DNA. HMTV is able to infect a variety of cells bringing about striking molecular changes, as seen by co-culture experiments between MSSM cells and normal human epithelial breast cells, B and T human lymphocytes and human dendritic cells. Protein expression was only observed in 10-20% of the infected cells by FACS analysis suggesting the presence of innate resistance in human cells after HMTV infection, as well as in breast cancer cells. The human retroviral restriction factors APOBEC F and G, the TRIM proteins such as TRIM 1, TRIM 21 and TRIM 25 and Tetherin are all highly expressed in HMTV cells as measured by quantitative RT-PCR. Disruption of the cytoskeleton and evidence for epithelial-mesenchymal transition (EMT) are additional molecular changes seen in infected cells.

In conclusion, HMTV is able to infect a variety of cells bringing about striking molecular changes. Whether these changes play a role in tumorigenesis remains to be shown.

Stella.Melana@mssm.edu