Exogenous DNA at the service of evolution: remodeling of the human genome over time, insertional mutagenesis, HERV's and cancer.

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Key words: Retrovirus, HERV's, cancer, HMTV, and evolution

Introduction.

Various studies have identified viruses involved in the biogenesis of cancer, when viruses pass between species become aggressive. Mouse mammary tumor virus (MMTV) has been extensively studied in mice and is known to contribute to mammary tumors by insertional mutagenesis, due the integration of the viral genome into the host DNA that leads to gene expression and cell cycle alterations. Breast cancer reports from different countries indicate the presence of short sequences integrated in DNA with high similarity to (MMTV) and low similarity with Endogenous Human Retroviruses (HERVs). Also transcripts and viral particles with β-retrovirus structure have been detected in culture media, providing evidence of possible mechanisms of infection in humans involving nasal mucosa, saliva and zoonoses.

Methods.

From breast tumors and healthy tissue DNA from 458 Mexican women, we evaluated the presence of a fragment of the HMTV (MMTV-like) Env gene by nested PCR. We performed a high-throughput retroviral insertional mutagenesis screen in 50 samples, we determined HMTV insertion sites as well as HERV's in the human genome through NGS; adapted to the method of splinkerette, taking advantage of Long Terminal Repetitions (LTR's) flanking their genomes

Results.

The prevalence of HMTV in the tumor tissues was 12.4%, and that in the non-affected breast tissues was 15.7%. In addition, the prevalence of HMTV in both the tumor and adjacent tissues from the same patient was 8.3%. An increased frequency of the virus was observed in patients aged 46–55 years. In relation to the sequences found Short Intermediate Nuclear Elements (SINE), with Alu elements as more numerous members corresponding to 10.6%. The Long Interspersed Nuclear Elements (LINEs), with L1 elements are its most numerous members, covering 16.9% and Human Endogenous Retroviruses (HERV's) occupying 8%. We found genes adjacent to viral insertion related to breast cancer such as *WNT4, MAD1L1, MEF2D, NCOR2, PRKCZ, SKI, SNX9, TNS1, ALK, CACNA1E, ELAVL1, PRDM16, RASA3, RGS12, RPS6KA2, SCUBE1, SLC39A2, THRSP*, among others.

Conclusions.

Results coincide with works on MMTV in mice, breast cancer in humans and other cancers such as lung, prostate and leukemia. We identified common insertion sites, found genes not previously to be associated with mammary cancer or previously been linked to cancer in general. Currently, the genome HMTV is not reported, therefore the complete sequence, proviral gene structure and its biogenesis in breast cancer are unknown.

Acknowledgements.

The funding sources CONACyT grants and the FIS IMSS grant.

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