Mammalian Mammary Tumor Virus (MMTV) and breast cancer: Integration sites of MMTV in breast cancer patients and their role in cancer progression

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**Aim/Background:** Detection of mouse mammary tumor virus (MMTV) in human breast cancer samples from all over the world has led to the acknowledgement of MMTV as a probable cause of breast cancer. Although its role is still debatable in humans, it is accepted as a cause for mammary tumors in mice. Reporting the presence of MMTV-like sequences in human breast cancer samples from Pakistani breast cancer patients, we also present a supposition that integration of MMTV might be, in part, responsible for breast cancer development.

**Methods:** After establishing presence in study samples, blood and tumor tissues, samples were processed for detection of probable integration sites of MMTV genome by employing linker-mediated polymerase chain reaction (LM-PCR) followed by sequence analysis of all possible clones.

**Results:** The study identified multiple (16) distinct, non-random integration sites of MMTV in human breast cancer tissues. MMTV-like sequence integrations have been found to be in or near transcription start sites, growth, DNA repair proteins and tumor suppressor genes, thus giving cells a distinct advantage for transformation and sustained survival.

**Conclusions:** Our data suggests that integration in the genome might give cells a distinct advantage for survival of transformed cells. Although the link is still not clear, further studies on these integration sites might reveal a link between MMTV-like sequences and human breast cancer. The resulting data lends support to the idea of a viral etiology of breast cancer. Furthermore, it also indicates anomalous behavior of MMTV-like sequences. Previous data suggests a totally random integration of MMTV in both mouse and human genome in cell lines. However, some sites were found to be repeating in different samples, thus, also supporting sequence specific bias in integration.

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