Walter Doerfler, J Antivir Antiretrovir 2014, 6:2
http://dx.doi.org/10.4172/1948-5964.S1.022

OMICS Group Conferences
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4th World Congress on
Virology

October 06-08, 2014 Hilton San Antonio Airport, TX, USA

Epigenetic effects upon the insertion of foreign DNA into Mammalian genomes: Consequences for oncology and evolution

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Studies on mammalian cells with integrated viral (adenovirus type 12, Ad12) genomes (1-3) led to the unexpected finding that cellular genomes as foreign DNA recipients exhibited genome-wide alterations of DNA methylation patterns (4). Similar changes were documented in cells carrying bacteriophage lambda DNA as foreign inserts (4, 5). As a corollary, transcriptional profiles in Ad12 DNA or lambda DNA transgenomic hamster cell genomes were significantly altered (6). We have also investigated this problem in human cells transgenomic for a 5.6 kbp bacterial plasmid. We first established that the transcriptional activities in 28,829 genome segments of five non-transgenomic human cell clones were very similar to identical. Thus, it became feasible to compare transcriptional activities in these genome segments between transgenomic and non-transgenomic clones. Transcriptional activities were increased in 144 genome segments in plasmid-transgenomic HCT116 clones, and decreased in 198 regions when compared to non-transgenomic cells. (S. Weber and W. Doerfler, unpublished). The possible significance of these observations for the mechanism of viral oncogenesis will be discussed (7, 8). The hypothesis has been put forward that the frequent insertion of foreign DNA in evolving cell systems over evolutionary time periods might have played a role in generating genomes with altered transcriptional, hence altered functional, characteristics. The ensuing selection of cells or organisms could have helped evolve the optimally adapted genome activities (9).

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