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Discoveries with the adenovirus type-12 system: Integration of viral DNA and epigenetic consequences

The human adenovirus type-12 (Ad12) system has been used to investigate basic mechanisms in molecular biology and viral oncology. Ad12 replicates in human cells, but undergoes a completely abortive cycle in Syrian hamster cells. Ad12 induces neuro ectodermal tumors in newborn hamsters (*Mesocricetus auratus*). Each tumor cell or Ad12-transformed hamster cell carries multiple copies of integrated Ad12 DNA. Ad12 DNA usually integrates at one chromosomal site which is not specific; Ad12 DNA can integrate at many different locations. Virion or free intracellular Ad12 DNA remains unmethylated at CpG sites, whereas the integrated viral genomes become de novo methylated. Inverse correlations between Ad12 promoter methylation and activity were described for the first time in this system and initiated active research in the field of DNA methylation and epigenetics. Promoter methylation is an important factor in long-term gene silencing. We have also discovered that the insertion of foreign (Ad12, bacteriophage lambda, plasmid) DNA into mammalian genomes can lead to genome-wide alterations in methylation and transcription patterns in the recipient genomes. This concept has been verified recently in a pilot study with human cells which had been rendered transgenomic for a 5.6 kbp bacterial plasmid. Currently, we study epigenetic effects in Ad12 infected cells and in Ad12 induced hamster tumor cells. These genome-wide epigenetic alterations are considered crucial elements in (viral) oncogenesis.

Biography

Walter Doerfler has completed Munich Medical School (LMU), Doctor of Medicine thesis in Anatomy and Internships in Munich and Trenton, NJ, USA. He did his Postdoctoral studies in Molecular Genetics at the Max-Planck-Institute for Biochemistry in Munich and in the Department of Biochemistry, Stanford University Medical School.

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