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New vectors for gene delivery: Human and mouse artificial chromosomes

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Abstract

Our human artificial chromosomes (HACs) have been generated mainly by a "top-down approach" (engineered creation). HACs with acceptor sites exhibit several characteristics required by an ideal gene delivery vector, including stable episomal maintenance and capacity to carry large genomic loci plus their regulatory elements, thus allowing the physiological regulation of the introduced gene in a manner similar to that of native chromosomes. Mouse artificial chromosomes (MACs) with acceptor sites were also created from a native mouse chromosome. The lessons learned and prospects identified from studies on the construction of HACs and MACs, their ability to drive exogenous gene expression in cultured cells, and transgenic animals. Multiple integration sites were also loaded in HAC/MAC. The recent emergence of stem cell-based tissue engineering has opened up new avenues for gene-and cell-therapies. Possible applications for medical and pharmaceutical use of HACs and MACs are also proposed, e.g., evaluation of function and safety for during and foods, toxicity for chemicals, mechanistic studies of genetic disorders, navigation and monitoring-system for cell differentiation, and model animals for genetic disorders.

Biography

Mitsuo Oshimura studied in RPMI, USA (1974-1977); Tokyo Medical and Dental University (1977-1982), NIEHS/NIH, USA (1982-1986), Kanagawa Cancer Center (1986-1990), and currently is the Director of Chromosome Engineering Research Center (CERC), Tottori University. He has developed human artificial chromosomes for use as gene delivery vectors to overcome various problems in existing conventional vector systems. He is also involved in developing various new and ideal HACs that will be useful for designing HAC-based gene and cell therapies, as well for humanized animal models. He was felicitated with the following Awards: 1993: Princess Takamatsu Foundation Cancer Research Award 1998:Biomedical Research Award from Japan Economy News paper 2002: The 2002 Award from Japanese Human Genetic Society.