Reconstructing chromosomes: Functional studies using genomic engineering

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The microcell-mediated chromosome transfer is an important method for mapping genes to specific human chromosomes when the gene has a specific cellular function. In this symposium, several examples of mapping and cloning of important genes, using various genomic engineering techniques and functional assays, are introduced. Thus, putative cellular senescence genes including a telomerase repressor gene were mapped to several loci by deletion mapping of revertants that were escaped from senescence of tumor cell lines with the transferred chromosome and by transfer of sub-chromosomal fragments of chromosome into tumor cells. For further detailed mapping and cloning, human genomic sequences on the transferred chromosomes could be targeted at a high frequency in the chicken pre-B cell line DT40 that is proficient for homologous recombination, thereby allowing for the subsequent modification of human genes and chromosomes. In addition, our most recent advance for functional studies is introduced, in that human chromosomes or chromosome fragments were introduced into mouse embryonic stem (ES) cells and viable chimeric mice were produced, and human genes were expressed in a proper tissue-specific manner in adult chimeric tissues.

Following topics are introduced and discussed, based on our chromosome engineering technology:

1) Mapping cellular senescence genes
2) Identification of novel imprinting genes and mechanistic studies of genomic imprinting
3) Production of mice with a human chromosome and their application, i.e., mice producing human antibodies and Down's syndrome model mice.