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Two types of human artificial chromosome vectors

Yuichi Iida
Institute of Regenerative Medicine and Bio-function, (CERC), Tottori University, Japan

Abstract

Conventional gene delivery vectors such as viral vectors, plasmid, bacterial artificial chromosome (BAC) might be associated with transgene-silencing because of position effect.

Human artificial chromosome (HAC) vector is considered as a promising system for gene delivery and express. The HAC is produced by 'top-down' and 'bottom-up' approaches. Both HAC can be episomally maintained in their nuclei and segregate normally. The 'top-down' approach can generate linear HAC ranging in approximately3~4Mb that retain natural centromeres and are mitotically stable in human and mouse cells. Moreover, we have succeeded in making trans-chromosomic-mice containing a HAC. It can be maintained *in vivo* and can produce mouse model. The bottom-up approach of HAC generation, initially developed in human fibrosarcoma HT1080 cells by introducing synthetic alphoid DNA cloned into a circular BAC vector. The tetO-HAC, generated by 'bottom-up' approach, can be eliminated from mammalian cells such as CHO and HT1080 cells. The tetO-HAC contains human chromosome 17 alphoid DNA and tet-operater sequences in its centromeric regions resulted in controlling the centromere function. We have demonstrated that the tetO-HAC can be eliminated from nuclei in human HT1080 remarkably. The combination of using two types of HAC would be powerful tool for cell reprogramming and gene collection of genetic disorders.

Biography

Yuichi Iida has completed his master's degree at the age of 23 years from Tottori University, and is currently a graduate student studying for his doctoral thesis. He has published 5 papers in reputed journals