

## Application for drug discovery using mammalian artificial chromosomes

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The conventional vector system for expression of desired genes in mammalian cells has problems such as insertion of the vector into the host and restriction of the introduced DNA size. To solve the problems, we constructed a human artificial chromosome (HAC) vector and a mouse artificial chromosome (MAC) vector that do not contain any endogenous genes using our unique chromosome engineering technology. The HAC/MAC as gene delivery vectors can deliver Mb-sized gene cluster and multiple genes, and are stably and independently maintained with defined copy numbers in host cells, as well as being transferrable to any other cell line via microcell-mediated chromosome transfer (MMCT). We have demonstrated several applications for drug discovery using the HAC/MAC, including 1) Humanized mice/rats and multifunctional model cells for predicting human drug metabolism, 2) Novel Down syndrome model animals and cells for identifying the responsible genes and the preclinical study, 3) Basic study for gene and cell therapy of Duchenne muscular dystrophy, and 4) Fully human antibody-producing animals for antibody drug. Thus, HAC/MAC technology can be expected to be used not only for basic research but also for applied research such as drug discovery and medical applications.