

## Toward safe and effective gene and cell therapies using human artificial chromosomes and stem cells

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Random integration of conventional gene delivery vectors can be associated with transgene-silencing. Furthermore, integrated sequences can activate oncogenes adjacent to the insertion site, resulting in the activation or silencing of transgenes. Human artificial chromosome (HAC) is exogenous mini-chromosome artificially created by chromosome engineering. Various HACs exhibit several potential characteristics desired for an ideal gene delivery vector, including stable episomal maintenance and the capacity to carry large genomic loci with their regulatory elements, thus allowing the physiological regulation of the introduced gene in a manner similar to that of native chromosomes.

For ideal gene – and cell - therapy using iPS cells, following are crucial: efficient generation and differentiation of iPS cells; no integration of transgene into the host genome. Most importantly, it is necessary to evade a problem of teratoma formation and malignant transformation when using the iPS cells to cell transplantation therapy.

Currently, we have constructed HAC-based cell-reprogramming vectors. Then, mouse and human iPS cells were generated using the HAC vectors. These iPS cells have no integration of transgene, and showed normal karyotype. To show their pluripotency, these iPS cells differentiated to three germ layer cells by generation of teratoma. We also aim to develop a safeguard system to eliminate undifferentiated cells and malignant transformation of transplanted cells using HAC.

### Biography

Narumi Uno has completed his master's degree at the age of 22 years from Tottori University, and is currently a graduate student studying for his doctoral thesis. He has published 3 papers in reputed journals.

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