# region-specific LOH-inducing applied to HLA region and the sensitive region extracted by GWAS

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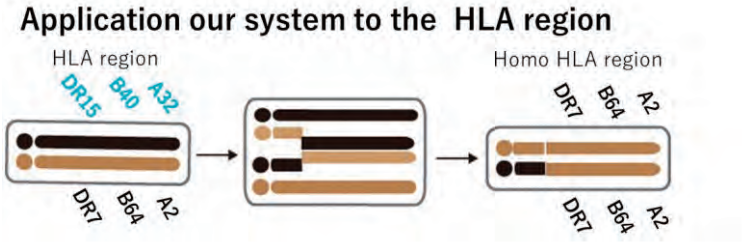
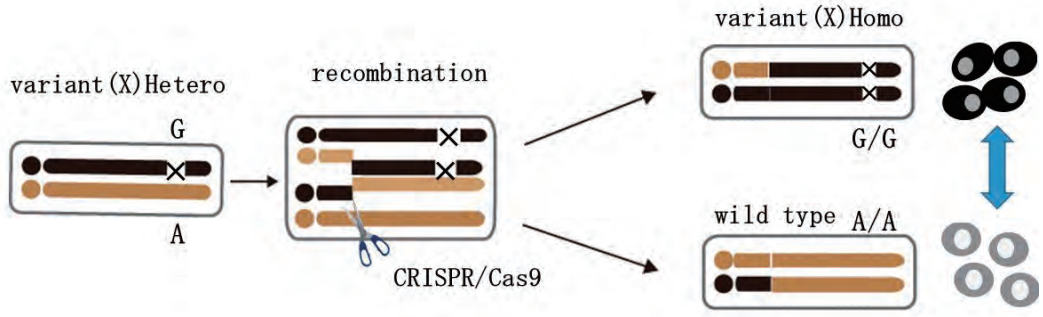
## Project Outline

= Background and Purpose =
When loss of heterozygosity (LOH) is correlated with loss or gain of a disease phenotype, it is often necessary to identify which gene or genes are involved. Here, we developed a region-specific LOH-inducing system based on mitotic crossover in human induced pluripotent stem cells (hiPSCs).




We applied this system to the short arm of chromosome 6, where human leukocyte antigen (HLA) loci are located. Genotyping and flow cytometric analysis demonstrated that LOHs associated with chromosomal crossover occurred at the expected positions. Although careful examination of HLA-homozygous hiPSCs generated from parental cells is needed for cancer predisposition and effectiveness of differentiation, they may help to mitigate the current shortcoming of hiPSC-based transplantation related to the immunological differences between the donor and host.




Assuming that parental hiPSCs bear a heterozygous mutation on the target chromo-some and an allele-specific DSB is introduced on that chromosome during the 4N stage of the cell cycle, the genomic region from the site of the DSB to the telomere would contain either a homozygous mutation or no mutation after crossover and chromosome segregation. This phenomenon can then be used to identify genes responsible for certain diseases. When X is a recessive mutation (parental hiPSCs do not have the disease phenotype), some of the clones have the disease phenotype after crossover .

Application: Muscle atrophic lateral sclerosis, Alzheimer's disease
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