Non-viral *ex vivo* therapeutic strategy in chemically derived hepatic progenitor with adenine base editor and prime editor

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Background: The adenine base editor (ABE) and prime editing converts nucleotide in living cells without double strand DNA breaks. Chemically derived stem/progenitor cells are attracting attention as the most applicable cell sources for clinical trials. Combining these attracting techniques, we show an *ex vivo* therapeutic strategy to treat hereditary disease.

Methods: We generate chemically derived hepatic progenitors (CdHs) from a tyrosinemia mouse model caused by a mutation in base pair A into G, correcting it via ABE and prime editing, and then transplanting it into the model mouse to cure it.

Results: Corrected CdHs with ABE repopulated the liver with fumarylacetoacetate hydrolase-positive cells after transplantation and increased survival rate. In addition, the substitution of non-target A in ABE editing window of the CdHs is reduced after transplantation.

Conclusions: This strategy offers a safer and specific way to apply a base editor to clinical applications.

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