Establishment and characterization of immortalized porcine 11β HSD1-hepatocytes

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EP1: Adrenal cortex

Introduction

Glucocorticoid, known as cortisol, is a steroid hormone essential to the maintenance of homeostasis, and is released in response to stress and low blood glucose concentration. It is converted from cortisone by 11β hydroxysteroid dehydrogenase type 1 (11β HSD1). The liver plays a major organ in metabolism, has numerous functions, mostly consists of hepatocytes, and is a principal target of cortisol. In murine model, it was observed that too much cortisol or overexpression of 11β HSD1 induced obesity and the insulin resistance that accompanies metabolic syndrome.

Materials & Methods

In our previous study, 11β-HSD1-transgenic (TG) fibroblasts were established, and then the porcine model was generated by SCNT using those fibroblasts. Hepatocytes overexpressing 11β-HSD1 obtained from liver of this porcine model, and *in vitro* cultured. However, primary hepatocytes show short life span or low proliferation rate. To overcome these problems, SV40 large T antigen, oncogene, was transduced into primary 11β-HSD1-TG hepatocytes and those cells were immortalized.

Results

Immortalized 11β-HSD1-TG hepatocytes shows restored morphology, more rapid proliferation rate, and more expression of 11β-HSD1 than primary ones. Immortalized 11β-HSD1-TG hepatocytes increase the expression of gluconeogenic genes including G6Pase and PEPCK by cortisone treatment.

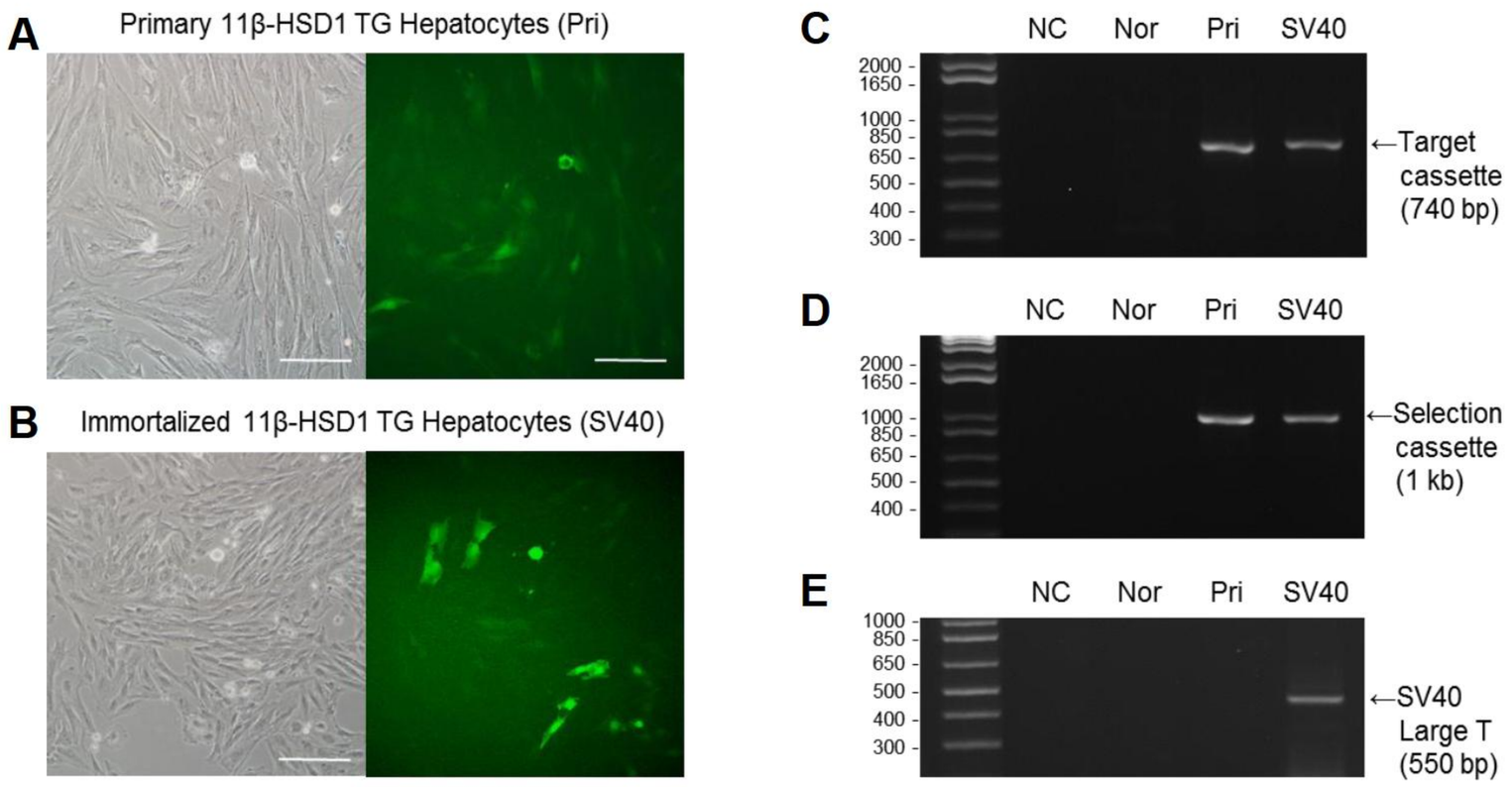
Conclusions

These immortalized cells maybe be useful for studying traits and potential pharmarcotherapeutic drugs for metabolic disorders induced by overexpression of 11β-HSD1 in hepatocytes.

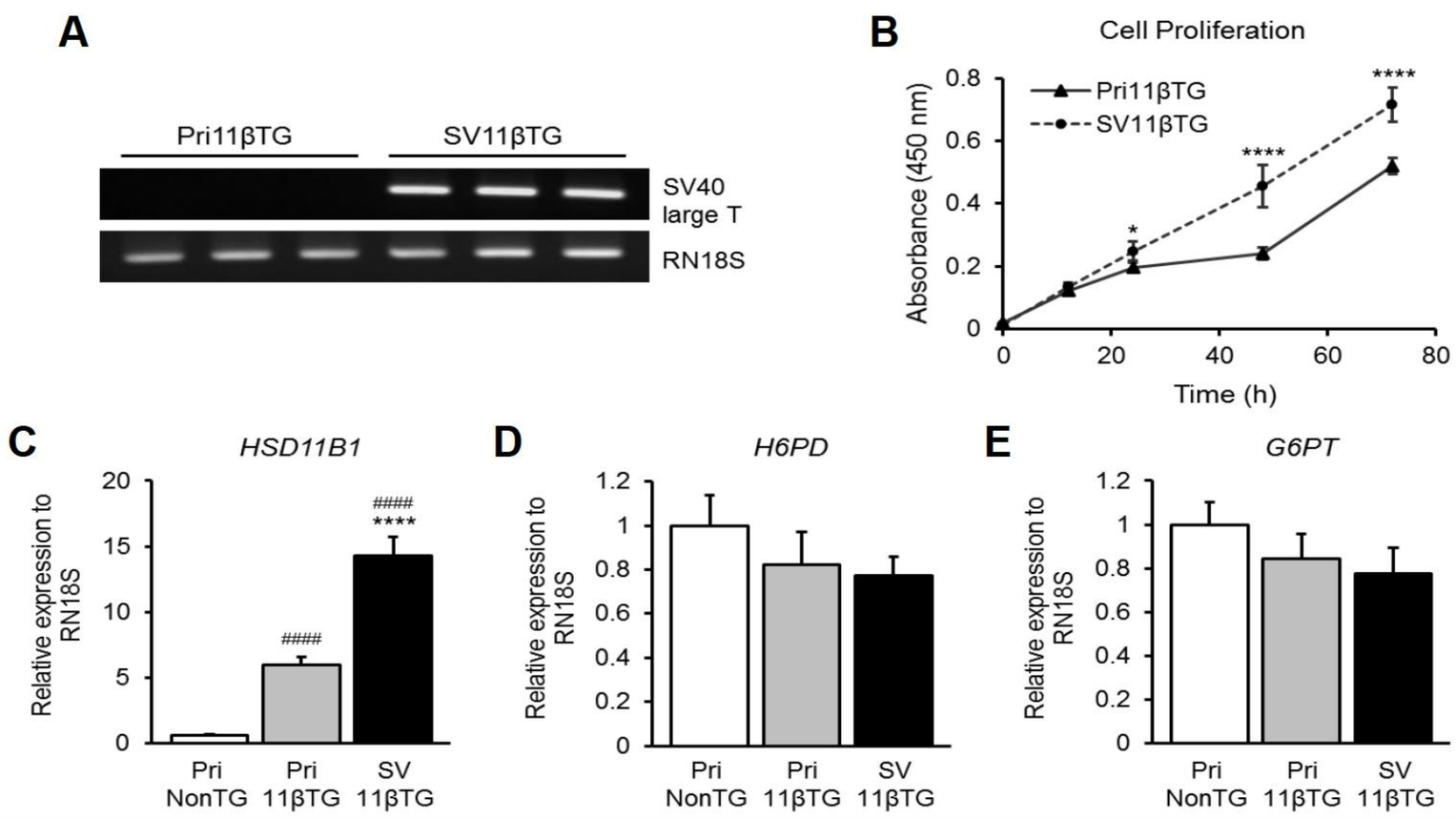
Reference

Morton NM1, Paterson JM, Masuzaki H, et al., 2004. Novel adipose tissue-mediated resistance to diet-induced visceral obesity in 11 beta-hydroxysteroid dehydrogenase type 1-deficient mice. Diabetes. 53(4):931-8

Result 1. Establishment of primary porcine 11β-HSD1-TG hepatocytes



Result 2. Expressions of SV40LT and triad G6PT-H6PD-HSD11B1



Result 3. Verification of functional hepatocytes after immortalization