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Lab Resource: Stem Cell Line

Generation of a human induced pluripotent stem cell (iPSC) line from a patient with family history of diabetes carrying a C18R mutation in the *PDX1* gene

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ABSTRACT

Homozygous loss-of-function mutations in the gene coding for the homeobox transcription factor *PDX1* leads to pancreatic agenesis, whereas certain heterozygous point mutations are associated with Maturity-Onset Diabetes of the Young 4 (MODY4) and Type 2 Diabetes Mellitus (T2DM). To understand the pathomechanism of MODY4 and T2DM, we have generated iPSCs from a woman with a C18R heterozygous mutation in the transactivation domain of PDX1. The resulting *PDX1* C18R iPSCs generated by episomal reprogramming are integration-free, have a normal karyotype and are pluripotent *in vitro* and *in vivo*. Taken together, this iPSC line will be useful to study diabetes pathomechanisms.

Resource table

Name of stem cell line	*PDX1* C18R iPSC1
Institution	*Institute of Diabetes and Regeneration Research*
Person who created resource	Xianming Wang
Contact person and email	Heiko Lickert heiko.lickert@helmholtz-muenchen.de
Date archived/stock date	April 2014
Origin	Human dermal fibroblasts
Type of resource	Induced pluripotent stem cells from a woman carrying a *PDX1* C18R mutation
Sub-type	Cell line
Key transcription factors	OCT4, SOX2, NANOG, LIN28, KLF4, and L-MYC
Authentication	Identity and purity of cell line confirmed
Link to related literature	Not available
Information in public databases	Not available
Ethics	Informed written consent obtained

Resource details

The Tübingen Family Study for T2DM (TÜF study, $N = 2500$) was screened for known rare mutations in the MODY4 gene *PDX1*. By mass spectrometry-based genotyping, one heterozygous *PDX1* C18R carrier could be identified and recruited for full-thickness skin biopsy. From the biopsy material, the epidermal layer was separated from the dermis by dispase digestion and fibroblasts were isolated from the dermis by trypsin digestion using an established protocol (see the Materials and

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methods section). The *PDX1* C18R fibroblasts were expanded using commercially available growth media and deep-frozen in liquid nitrogen. From this collection of dermal fibroblasts, samples were tested for the presence of viruses pathogenic to humans (HBV, HCV, HIV) as well as for the presence of mycoplasma. All cultures were found to be negative for all of these potential contaminants. *PDX1* C18R primary fibroblasts were reprogrammed into iPSCs using nucleofection with three episomal plasmids encoding human *OCT4*, *SOX2*, *NANOG*, *LIN28*,

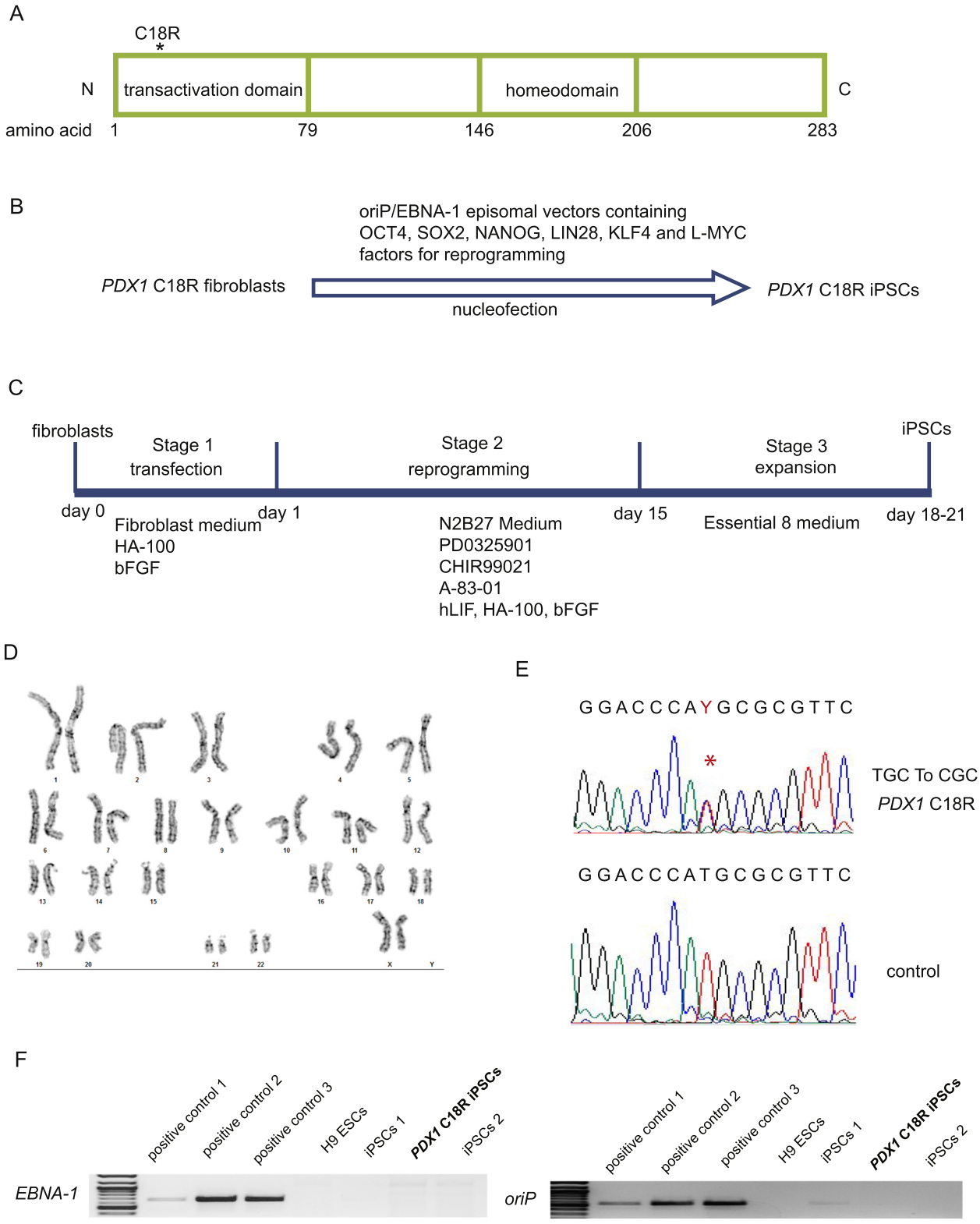

Fig. 1. Generation of *PDX1* C18R iPSCs. (A) An overview of the PDX1 protein structure. (B) Scheme shows the reprogramming factors for the generation of the *PDX1* C18R iPSC line. (C) Reprogramming protocol of skin fibroblasts into integration-free iPSCs using episomal vectors. (D) Normal karyotype (46, XX) of one *PDX1* C18R iPSC clone. (E) Sequencing result shows heterozygous T > C mutation in *PDX1*. (F) Semi-quantitative PCR confirms that episomal vectors did not integrate into the genomic DNA of the selected *PDX1* C18R iPSC clone. H9 ESCs and two independent iPSC clones (#1 and #2) were used as negative controls, whereas transfected fibroblast at day 6 were used as positive controls.