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Lab resource: Stem cell line

Generation of an induced pluripotent stem cell line from chorionic villi of a Turner syndrome spontaneous abortion

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ABSTRACT

A major cause of spontaneous abortions is chromosomal abnormality of foetal cells. We report the generation of an induced pluripotent stem cell line from the fibroblasts isolated from chorionic villi of an early spontaneously aborted foetus with Turner syndrome. The Turner syndrome villus induced pluripotent stem cell line is transgene free, retains the original XO karyotype, expresses pluripotency markers and undergoes trilineage differentiation. This pluripotent stem cell model of Turner syndrome should serve as a tool to study the developmental abnormalities of foetus and placenta that lead to early embryo lethality and profound symptoms like infertility in 45 XO survivors.

Resource table.

Name of Stem Cell Line	TS ViPSC Line
Institution	School of Regenerative Medicine, Manipal University
Person who created the line	Shagufta Parveen
Contact person and Email.	Shagufta Parveen; shagufta.parveen@manipal.edu
Date Archived/Stock date	June 2014
Origin	Chorionic villus fraction of Turner syndrome spontaneously aborted foetus
Type of Resource	45 XO Induced pluripotent stem cells
Subtype	Pluripotent stem cell line
Key transcription factors	OCT4, LIN28, SOX2, KLF4, LMYC and shRNA for TP53
Authentication	Identity and purity of the stem cell line confirmed by karyotyping, STR analysis, *Ori P & EBNA 1* PCR, analysis of pluripotency markers and ability to differentiate into cells of 3 germ layers
Link to related literature	NA
Information in data bases	NA
Ethics	Manipal Hospital Ethics Review Board approval obtained

1. Resource details

Turner syndrome (TS) is one of the most common monosomy syndromes. 99% of these 45 XO embryos die at early stages of gestation. The survivors who are phenotypically females suffer from a broad spectrum of abnormalities including short stature, abnormal organs and infertility. These abnormalities have been hypothesised to be caused by haplo insufficiency of genes that escape X chromosome inactivation as in the case of normal females. However not enough data is available regarding abnormal development of tissues and organs in affected individuals. Mice models with XO syndrome are typically fertile and do not represent the human symptoms *in toto*. Human TS pluripotent stem cell lines can serve as excellent models to improve the understanding of the human syndrome at a molecular and cellular developmental level.

We reprogrammed chorionic villus cells (CVCs) to pluripotency by nucleofecting them with episomal plasmids expressing the 6 reprogramming factors OCT4, LIN28, SOX2, KLF4, LMYC and shRNA for *TP53* (Okita et al., 2011). To define the pluripotent and genetic state of the line we conducted pluripotency tests, differentiation tests, karyotype analysis and determined cell identity by DNA profiling (Martí et al., 2013).

Embryonic stem cell like colonies appeared 12 days post nucleofection. These colonies were picked and a stable Turner syndrome villus induced pluripotent stem cell line (TS ViPSC) line was established on mouse embryonic feeders. The TS ViPSC colonies were flat and compact with smooth bright edges typical of pluripotent stem cell colonies (Fig. 1). Although slow growth rates of other TS iPSC lines

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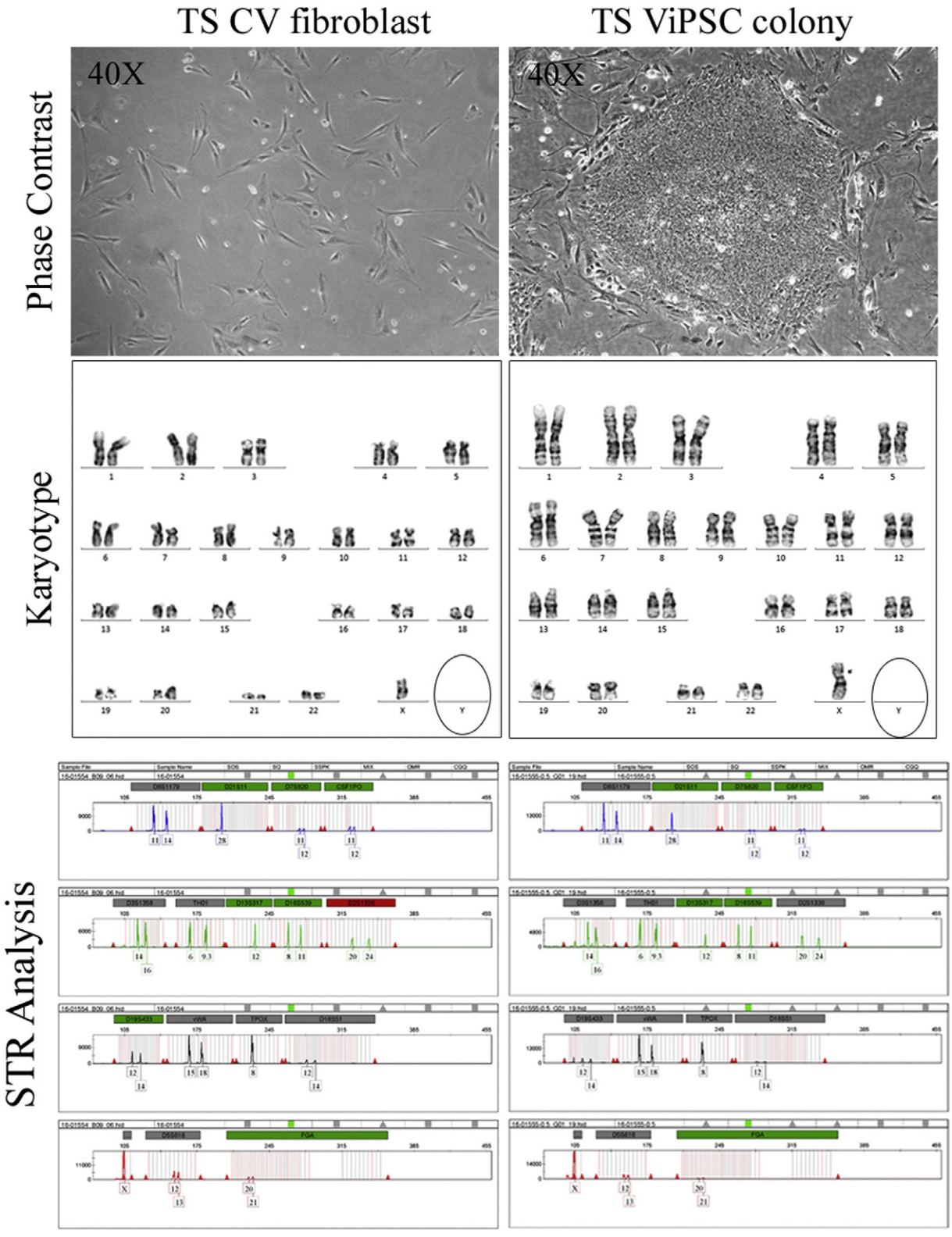

Fig. 1. Morphology and Genetic analysis of TS CVCs and TS ViPSCs. Phase contrast images of TS CVCs and TS ViPSCs with their respective karyotypes and STR profiles below.

has been reported earlier (Luo et al., 2015), our TS ViPSC line had a growth rate similar to other normal pluripotent stem cell lines maintained alongside in the laboratory. This distinction may be of practical use and could be relevant in understanding the processes involved in the syndrome.

The original 45 XO karyotype (Fig. 1) of the donor CVCs was maintained in TS ViPSCs even after prolonged maintenance (passage 25) indicating that the process of reprogramming with episomal vectors and *in vitro* culture conditions did not alter this iPSC line chromosomally. The iPSC line established in this study was confirmed to be identical