

Pluripotent Stem Cells, identical except for different Sex Chromosomes (XX vs. XY), and designed for drug development (Hadasit)

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Need

Gender differences arise from the influence of sex chromosomes or hormones. There is no suitable preclinical model that focuses on the chromosome-based gender difference and its role in health and disease. The same medical condition may have markedly different incidence and symptoms in a sex-dependent manner – for example, prognosis and outcome of myocardial infarction, different incidence of autoimmune diseases, and the prevalence, pathophysiology and symptoms of mental disorders such as autism, depression and schizophrenia. Moreover, drugs may cause different rates of adverse effects in men and women. The FDA withdrew ten prescription drugs during 1997-2001, eight of which were more dangerous to women than to men. Nevertheless, women remain under-represented in clinical studies, and cell and animal research studies are often biased, with female animals and cell-lines being a minority.

Innovation

Induced pluripotent stem cells (iPSCs) can be generated from a human adult cell. The invention is a matched pair of human iPSCs that bear identical chromosomes except for XX and XY. This was accomplished by reprogramming adult EBV-immortalized B cells of a mosaic Klinefelter Syndrome patient, cloning iPSCs, and screening. The paired iPSC lines were confirmed by HLA and karyotype as originating from the same donor.

Indications/Applications

The autosomal-identical iPSCs (AI-iPSCs), the first human model for sex-dependent differences, will enable studies of sex-dependent differences in all human cells and tissues, including for the following applications:

- 1) Cell function and metabolism
- 2) Research and preclinical studies
- 3) Regenerative medicine
- 4) Drug development – adverse effects, pharmacokinetics, pharmacodynamics
- 5) Ex-vivo modeling
- 6) Disease modelling – phenotypes and pathogenesis
- 7) Effects of sex chromosomes versus hormones
- 8) X-inactivation studies

Competitive Advantage

This technology addresses a clear unmet need in the field of gender-based research, drug development, and safety-monitoring by providing an in-vitro human model to address gender differences.

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