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## Conversion of human fibroblasts into neuro sphere-like cells using a single polycistronic vector

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The unique capability of neural progenitor cells to induce regeneration in several animal models of neurological disorders, make them the best potential cell source for regenerative medicine. To date, direct lineage conversion has shown many distinct advantages in the field of cellular reprogramming to capture the patient specific neuronal progenitor cells on a dish to enhance the knowledge of basic processes of human disease, development and drug discovery. A number of studies have demonstrated that transient expression of Yamanaka factors with appropriate supporting signals can efficiently convert fibroblasts into NPCs–called iPSC-factor–based reprogramming. Here, we used a minimalist approach combining a single polycistronic doxycycline (dox)-inducible lentiviral vector containing SOX2, OCT4, cMYC and KLF4 with small molecule inhibitors to convert human fibroblasts into NPC-like cells. We limited the exogenous expression of Yamanaka factors for 14 days. The treated human fibroblast cells exhibit neurosphere- like morphology within 28 days post transduction. The immunostaining of the resulted cells showed that they were positive for neural markers: Sox2, PAX6 and NESTIN. However, under the same defined condition, no colonies formed from transduced human fibroblasts when weexpunged these small molecules from our induction regime. This finding showed the important power of developmental signals which could enable partially converted human fibroblast cells morphed into neural progenitor-like cells. The present study is the first demonstration that the presence of neural inducer chemical dual SMAD inhibitors can mediate human fibroblasts reprogramming to NPC-like cells via a single polycistronic vector of Yamanaka factors.

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## Comparative assessment of the effects of prenatal exposures to bisphenol A (BPA) and di (2-ethylhexyl) phthalate on testicular development in male rats

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The industrial chemicals bisphenol A (BPA) and di (ethyl hexyl) phthalate (DEHP) are widely used in the manufacture of polycarbonate plastics and other consumer products. BPA and DEHP are known to possess hormonal activity, thereby raising concerns that exposure of the population to them may lead to adverse effects on reproductive health. The present study was designed to investigate the effects of prenatal exposures to BPA and DEHP on testicular development. Timed pregnant Long-Evans dams were gavaged with BPA at 2.5 or 5 and DEHP at 5 or 50 µg/kg body weight from gestational day 12 to parturition at day 21. Male weanling rats were assessed at 21, 35 and 90 days post-partum. Therefore, expression of estrogen receptors 1 and 2, androgen receptor and the aromatase enzyme were analyzed using Western blotting procedures and Densitometry. Differences between groups were determined by one-way ANOVA and post-hoc analysis using the Dunnett's test or the student's T-test for two groups. Results showed that expression of ESR1 in testes of pre-pubertal rats at 21 days of age was not affected by exposure to test chemicals in utero ($P>0.05$) but the levels were decreased at 35 days of age ($P<0.05$). In contrast, expression of ESR1, ESR2, AR and aromatase were increased in testes of adult rats at 90 days of age ($P<0.05$). Inhibition and increased expression of cognate receptors for steroid hormones and the enzyme aromatase at all stages of development have the potential to alter the developmental trajectory for testicular development and affect the capacity for steroid hormone production and germ cell development. These observations support our previous observations and other reports demonstrating that the testis is a major target for endocrine disrupting chemicals such as BPA and DEHP.

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