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RESEARCH WATCH

The tale of autologous iPSCs: A monkey perspective

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The breakthrough invention of induced pluripotent stem cells (iPSCs) ignited huge excitement with the promise of unlimited autologous cell sources for future regenerative medicine.[1,2] However, before this expectation turns into reality the safety and efficacy of these autologous cell products have to be meticulously evaluated and validated. Towards this end much research effort has been concentrated on three clinically relevant aspects: tumorigenesis, immunogenesis, and efficacy. So far almost all of the in vivo studies are carried out through syngeneic mouse or human to immunocompromised mouse transplantations. While these small animal models are important in the initial proof-of-concept stages, the phylogenetic difference prevents a reliable extrapolation of the findings to the human species. On the other hand the ethical consideration renders it impossible to test iPSC products directly in human body, especially in early pre-clinical stage. The only ideal alternative model comes down to nonhuman primate due to its closeness to the human in terms of phylogenetics, physiology, and immune functions. One recent report published in the journal of ***Cell Reports*** described in detail the autologous transplantation studies using rhesus monkey iPSCs and their differentiated mesenchymal stromal cells.[3] The major findings from this study are: 1) undifferentiated rhesus iPSCs formed teratomas in the recipient animals as predicted, but with a higher input cell threshold when compared to the test using immunocompromised mouse. The formed teratomas elicited immune response, characterized as infiltrations by lymphocytes. 2) In contrast the differentiated iPSC product in the form of mesodermal stromal-like cells did not form teratomas after transplantation. As expected these cells differentiated further and formed nascent bone tissue in the implants. The differentiated engraftments and thus-derived bone tissues showed minimal signs of lymphocyte infiltrations. The significance of these findings is, for the first time, iPSCs as well as their differentiated derivatives are put to test in an autologous and immunocompetent nonhuman primate model closely related to human biology. Thus generated information will be extremely valuable in optimizing human iPSC culture and differentiation protocols to bring safe and effective cell products to the clinic trial.

Disclosure

The author declares no conflict of interest.

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