Testicular germline stem cells

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Abstract | Stem cells have the ability to both differentiate into other mature cell types and maintain an undifferentiated state by self-renewal. These unique properties form the basis for stem cell use in organ replacement and tissue regeneration in clinical medicine. Currently, embryonic stem cells are the best-studied stem cell type. However alternative stem cells such as induced pluripotent stem cells and other adult stem cells are also being actively investigated for their potential for cell-based therapy. Among adult stem cells, emerging research has focused on evaluating the pluripotency potential of testis stem cells. To date, stem cells with embryonic-like potential have been created from adult testis germ cells. These cells could provide patient-specific, non-embryo-derived stem cells for men in the future.

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Introduction

Stem cells are cells that have the ability to both differentiate into other, more mature cell types, and to maintain an undifferentiated state by self-renewal. These properties confer potential for stem cells to be used for tissue regeneration and organ transplantation in medicine. Given that germ cell allocation is an early event in embryo development, testis germline stem cells may be more easily 'reprogrammed' to develop embryonic-like stem cell potential than other types of adult cells. In this Review, we provide an overview of the current scientific understanding of the creation, assessment and clinical potential of testis-derived stem cells.

Stem cells

The potential of stem cells to commit and differentiate into other cell types is termed stem cell potency. Depending on their origin, stem cells range from totipotent (potential to generate a whole organism), through pluripotent (differentiates into most cell types, including all three somatic germ layers [endoderm, mesoderm, and ectoderm] and germ cells), multipotent (differentiates into multiple cell types, including many somatic germ layers or germ cells) and oligopotent (differentiates into only a few somatic or germ cell types), to unipotent (differentiates into one somatic or germ cell type). Potency is usually restricted by the developmental stage of the stem cell. Stem cells from early embryogenesis are generally able to differentiate into more cell types than are those from late fetal life or adulthood. Stem cells from fertilized oocytes and early embryos are totipotent and can give rise to a complete organism, whereas stem cells from the inner cell mass of slightly older blastocysts, termed embryonic stem cells, are pluripotent. Stem cells from neonatal tissues, amniotic fluid, cord blood, and adult tissues are categorized as adult stem cells and are usually multipotent, oligopotent or unipotent. Embryonic stem cells (Figure 1a) have been the subject of much research and discussion because of their potential to differentiate into almost all body cell types and the ease with which they are propagated in cell culture. In comparison, the potency of adult stem cells is more limited. Adult stem cell populations are also difficult to expand in culture, which limits their practical application in cell-based, regenerative medicine.

An alternative source of pluripotent stem cells for human applications, other than embryos, has become a highly prized research goal for several reasons. First, a need exists to expand sources of stem cells to improve the clinical utility of cell-based therapy. Second, immunological matching of stem cells to recipients might be necessary to avoid rejection in stem-cell-based therapy. Finally, moral, ethical and political controversies surround the source and manipulation of embryonic stem cells, especially those from human embryos, which restricts their use for research and clinical applications.

The discovery that differentiated, nonembryonic cells can be reprogrammed into pluripotent stem cells using just four factors[1] has removed many of the ethical issues associated with embryo manipulation, and has also circumvented potential problems associated with immune rejection that might affect stem cells when they are transplanted into patients. These created pluripotent stem cells are termed induced pluripotent stem cells (iPSCs) and were first described by Takahashi and Yamanaka[1] in mice in 2006. The same researchers also demonstrated iPSC derivation from human cells (Figure 1b)[2] in work that has since been confirmed by others.[3,4] One concern with iPSCs is the level of genomic disruption that occurs with viral delivery of the reprogramming factors using retroviral or lentiviral vectors. Theoretically, these viral

Competing interests
P. J. Turek and R. A. Reijo Pera declare that they hold, or have applied for, patents related to testicular germline stem cells, on behalf of The Turek Clinic, San Francisco and Stanford University, CA, USA. K. Kee declares no competing interests.

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