

# Human pluripotent stem cell research: Past, present and future

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Pluripotent stem cells, with their ability to form all cell types present in the body, are a unique resource for studies of human cell biology and have caught the public interest as providing treatments for diseases and injuries. Mammalian pluripotent stem cells were first discovered in studies of mouse teratocarcinomas, tumors of germ cell origin composed of mixtures of cell types and tissues. The tumors were found to contain a unique type of stem cell, called embryonal carcinoma (EC), that could grow indefinitely and could also produce all cell types found in the tumor. The fact that EC cells could also be derived from early embryos grafted to ectopic sites led to attempts to obtain these cells from growing early staged embryos in culture. This led to the derivation of embryonic stem (ES) cells that have proved to be superior to EC cells as research tools. With the recognition that EC and ES cells shared properties with cells of the early embryo and germ cells, attempts were made to obtain pluripotent stem cells directly from primordial germ cells, resulting in the derivation of embryonic germ (EG) cells. EC, ES and EG cells were subsequently derived from human tumors, human embryos, and human primordial germ cells, respectively.

Studies utilizing pluripotent stem cells, most notably ES cells, have now provided us with molecular insights into the basis of pluripotency (or stemness) and into the mechanisms involved in cell differentiation. They have also enabled the isolation of various cell types that have been grafted into animal models of human diseases and injuries to demonstrate proof of principle studies in cell-based therapies. The successes of proof of principle experiments must be received with circumspection as it will take great effort to develop cell-based therapies that are effective and safe.

Recent experiments inducing pluripotent cells from cells of the adult via transgenesis of a small number of transcription factors (selected from studies of embryonic stem cells) have surprised and excited investigators in the stem cell biology. These results portend the future. Through the study of stem cells, we will learn how to instruct our cells, both in the dish and in the body, to generate stem cells and appropriate specialized cells to effect therapies.

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development. Dr Gearhart is a leader in the development and use of human reproductive technologies, embryo and germ cell manipulations and in the genetic engineering of cells. In 1998, Dr Gearhart's group at Johns Hopkins published the first report on the derivation of pluripotent stem cells from germ cells of the human embryo. His research is focused on the basic science of stem cells, stem cell specialization, and the generation cell-based therapies for a number of diseases and injuries. Dr Gearhart was a founding member of ISSCR.