



PREFACE

On February 28, 2001, Tommy G. Thompson, Secretary of Health and Human Services, requested that the National Institutes of Health prepare a summary report on the state of the science on stem cells. This report was developed in response to his request. It provides the current information about the biology of stem cells derived from all sources—embryo, fetal tissue, and adult.

Since 1998, when human pluripotent stem cells were first isolated, research on stem cells has received much public attention, both because of its extraordinary promise and because of relevant legal and ethical issues. Underlying this recent public scrutiny is decades of painstaking work by scientists in many fields, who have been deciphering some of the most fundamental questions about life with the goal of improving health.

In the last several decades, investments in basic research have yielded extensive knowledge about the many and complex processes involved in the development of an organism, including the control of cellular development. But many questions remain. How does a single cell—the fertilized egg—give rise to a complex, multi-cellular organism? The question represents a fundamental challenge in developmental biology. Researchers are now seeking to understand in greater detail the genetic factors that regulate cell differentiation in early development.

Put simply, stem cells are self-renewing, unspecialized cells that can give rise to multiple types all of specialized cells of the body. The process by which dividing, unspecialized cells are equipped to perform specific functions—muscle contraction or nerve cell communication, for example—is called differentiation, and is fundamental to the development of the mature organism. It is now known that stem cells, in various forms, can be obtained from the embryo, the fetus, and the adult.

How and whether stem cells derived from any of these sources can be manipulated to replace cells in diseased tissues, used to screen drugs and toxins, or studied to better understand normal development depends on knowing more about their basic properties. In this respect, stem cell research is in many ways no different than many other areas of modern biology; it is advancing because new tools and new knowledge are providing the opportunities for new insights. Like all fields of scientific inquiry, research on stem cells raises as many questions as it answers. This report describes the state of the science of stem cell biology and gives some clues as to the many and varied questions that remain to be answered.

WHAT IS THE SCOPE OF THE REPORT?

The report is a review of the state of the science of stem cell research as of June 17, 2001. Included in this report is subject matter addressing stem cells from adult, fetal tissue, and embryonic sources. Because so much of the progress made to date was dependent on animal models, a significant emphasis is placed on understandings gained from mouse models of development and mouse stem cell research. The report also devotes substantial attention to scientific publications on the characterization of specialized cells developed from embryonic stem cells and the plasticity of adult stem cells. A general overview of early development is provided in the Appendix to assist the reader in understanding the key events in formation of cells, tissues, and the whole organism.

Both scientific and lay publications use a variety of terms to describe stem cells and their properties. For this reason, this report adopts a lexicon of terms and it is used consistently throughout. To aid the reader, a glossary and terms section is provided. In several

places in the report, discovery timelines are provided. The various sources of stem cells are described, as are the techniques used to isolate and develop them. A comprehensive listing of various stem cell isolation and characterizations is also included.

In order to ensure the reader is provided information both about the basic biology of stem cells, and their therapeutic potential, the report contains several chapters focused on particular diseases which might benefit from stem cell research. These chapters on the use of hematopoietic stem cells, followed by focus features on specific nervous system diseases, diabetes, heart disease, and autoimmune diseases serve merely as examples of the many applications of stem cells that are being pursued. Also included are features that review aspects of stem cells as therapeutic delivery tools for gene therapy and, importantly, the safety considerations for developing stem cell-based therapies.

WHAT IS NOT IN THE SCOPE OF THE REPORT?

NIH recognizes the compelling ethical and legal issues surrounding human pluripotent stem cell research. Because extensive discussions regarding these issues have been presented in various forums elsewhere, they are not part of this review of the state of the science. Also, the report does not make recommendations pertaining to the policies governing Federal funding of such research.

HOW WAS THE REPORT DEVELOPED?

The report was prepared under the auspices of the Office of Science Policy, Office of the Director, NIH. Several approaches were taken to obtain relevant scientific information for the report. A thorough review of the extant literature, including more than 1200 scientific publications was conducted. Scientific experts (both domestic and international) from all areas of relevant biomedical research in stem cells were interviewed in depth. While the majority of the work presented in this report emanates from investigators in academic laboratories, extensive discussions were held with scientists in the private pharmaceutical and biotechnology sectors. Thus, the report makes every effort to encompass what is known and not known about stem cell biology and is, therefore, not limited to research that is or has been funded by the NIH.

In recent months, there have been many reports in the lay press regarding scientific discoveries on various types of stem cells. The science represented in this report focuses exclusively on scientific publications or public presentations. In cases where technical or logistical information key to the understanding of the details of science was needed, personal communications with the information sources were cited.