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Introduction:

Unlocking the mysteries of life, advancements in genetics give us hope that we may someday use them to cure diseases and save lives. The nobility of the field cannot be argued. With new biotechnology, doctors and researchers hope to improve the quality of our food, enhance the efficacy of medication, cure illness by harvesting organs; essentially improve the quality of life. They want to end disease and make medicine perfect, flawless.

But certainly it is not that easy. Perfection is imperfection all on its own. It is much more complicated than simply finding the code to a lock. To understand the essence of life, scientists need to experiment, some would argue, with life itself. Others question our desire to know so much in the first place.

This controversy has drawn attention from all areas, including the nation’s highest offices in Congress and the White House. However, these parties have been unable to state the facts about stem cells and advancements in genetics, making the public largely unaware of many details on the subject. This article hopes to answer questions and correct misconceptions about two major topics in biotechnology: stem cells and personalized medicine (pharmacogenomics).

Stem Cells: What are they?

Stem cells have been a major topic in the media and were recently a primary issue in the latest presidential election. Stem cells are important because they differ from other kinds of cells in the body. All stem cells—regardless of their source—have three general properties: they are capable of dividing and renewing themselves for long periods; they are unspecialized; and they can give rise to specialized cell types. There are two types of stem cells, embryonic and adult.

Embryonic Stem Cells:

Embryonic stem cells, as their name suggests, are derived from embryos. Specifically, embryonic stem cells are derived from embryos that develop from eggs that have been fertilized in vitro—in an in vitro fertilization clinic—and then donated for research purposes with informed consent of the donors. They are not derived from eggs...
fertilized in a woman’s body. The embryos from which human embryonic stem cells are derived are typically four or five days old and are a hollow microscopic ball of cells called the blastocyst. Most of the political controversy regarding the usage of embryonic stem cells revolves around the question, “is an \textit{in vitro} egg a life?” This question challenges the age-old abortion issue with a new angle on procreation involving scientific manipulation.

**Adult Stem Cells:**

Adult stem cells are undifferentiated cells found among differentiated cells in a tissue or organ. They can renew themselves, and can differentiate to yield the major specialized cell types of the tissue or organ. The primary roles of adult stem cells in a living organism are to maintain and repair the tissue in which they are found. Some scientists now use the term somatic stem cell instead of adult stem cell. Unlike embryonic stem cells, which are defined by their origin, the origin of adult stem cells in mature tissues is unknown. Adult stem cells are thought to reside in a specific area of each tissue where they may remain quiescent (non-dividing) for many years until they are activated by disease or tissue injury. The adult tissues reported to contain stem cells include brain tissue, bone marrow, peripheral blood, blood vessels, skeletal muscle, skin, and liver tissue. Scientists in many laboratories are trying to find ways to grow adult stem cells in cell culture and manipulate them to generate specific cell types so they can be used to treat injury or disease. Some examples of potential treatments include replacing the dopamine-producing cells in the brains of Parkinson’s patients, developing insulin-producing cells for type I diabetes and repairing damaged heart muscle following a heart attack with cardiac muscle cells.

Scientists are still trying to answer the following questions about adult stem cells. Until these questions are answered, an applicable clinical stem cell therapy will be difficult to implement.

- How many kinds of adult stem cells exist, and in which tissues?
- What are the sources of adult stem cells in the body? Are they “leftover” embryonic stem cells, or do they arise in some other way? Why do they remain in an undifferentiated state when all the cells around them have differentiated?
- Do adult stem cells normally exhibit plasticity, or do they only transdifferentiate when scientists manipulate them experimentally?
- Does a single type of stem cell exist—possibly in the bone marrow or circulating in the blood—that can generate the cells of any organ or tissue?
- What are the factors that stimulate stem cells to relocate to sites of injury or damage?

**What is the Difference between Embryonic and Adult Stem Cells?**

Human embryonic and adult stem cells each have advantages and disadvantages regarding potential use for cell-based regenerative therapies. Adult and embryonic stem cells differ in the number and type of differentiated cell types they can become. Embryonic stem cells can become all cell types in the body. Adult stem cells are generally limited to differentiating into different cell types of their tissue of origin. However, some evidence suggests that adult stem cell plasticity may exist, increasing the number of cell types a given adult stem cell can become.

A potential advantage of using stem cells from an adult is that the patient’s own cells could be expanded in culture and then reintroduced into the patient’s body. The use of the patient’s own adult stem cells would mean that the cells would not be rejected by the immune system. This represents a significant advantage, as immune rejection is a difficult problem that can only be circumvented with immunosuppressive drugs. Embryonic stem cells from a donor introduced into a patient could cause transplant rejection. However, whether the recipient would reject donor embryonic stem cells has not been determined in human experiments.

**Controversy:**

In the case of embryonic stem cell research, the end that scientists hope to achieve is the relief of human suffering. That this is a humanitarian and worthy end is not in dispute. The controversy is about the means: namely, the consumption of donated embryos. More particularly, embryonic stem cell research and therapy would use donated embryos that, by virtue of donor instructions, will never enter a uterus. Is it moral to use this means to try to relieve human suffering? Ancient religious texts provide little guidance. The ancients did not understand embryology, did not imagine that scientists might create and nurture what we now understand as embryos in the laboratory. Nor can we get an answer from laboratory experiments. There is no test for whether an embryo is a person. Instead, we are left to our own devices, to our own moral reasoning.

**Current Policy:**

On August 9, 2001, President George W. Bush
announced that federal funds may be awarded for research using human embryonic stem cells if the following criteria are met:

- The derivation process (which begins with the destruction of the embryo) was initiated prior to 9:00 P.M. EDT on August 9, 2001.
- The stem cells must have been derived from an embryo that was created for reproductive purposes and was no longer needed.
- Informed consent must have been obtained for the donation of the embryo and that donation must not have involved financial inducements.

This policy was considered a compromise between parties for and against embryonic stem cell research. However, it placed serious constraints on the feasibility of such research within the United States; most researchers rely heavily on federal funding. This legislation is not an end-all for stem cell research, as the NIH's official interpretation of Bush's policy (August 2002) stated that there were 78 eligible lines. However, this policy only involved government funding and embryonic stem cell research continues unregulated among privately funded laboratories.

**Legal Situation:**

*Human Cloning Prohibition Act of 2001 and 2003:* The bill seeks to prohibit both therapeutic and reproductive cloning by making it illegal to perform or attempt to perform human cloning, to participate in an attempt to perform human cloning, and to ship or receive an embryo produced by human cloning. The Senate did not act on the bill, and therefore no legislation has resulted from the passage of this bill. Opposing bills were introduced before the 2001 and 2003 votes that would ban reproductive cloning, but legalize therapeutic cloning.

*State Regulation:* Seven states (California, Michigan, Louisiana, Rhode Island, Virginia, Missouri, and Iowa) have laws against cloning, which range from restriction of state funding of research to restriction of the conduct of therapeutic and reproductive cloning research.

*UN Cloning Ban:* In 2004, the United Nations attempted to impose a worldwide ban on human cloning research and practices. This proposition, however, reached stiff opposition from the Bush administration because the United States was seeking a broader resolution banning embryonic stem cell research entirely. The UN has since dropped the resolution and has left the issue unresolved.

**Pharmacogenomics (Personalized Medicine):**

Pharmacogenomics examines how a person’s genetic makeup affects his or her response to drugs. Researchers in the field are working on applying human genome knowledge to pharmaceuticals by identifying genes that account for varying drug reactions in different people. Eventually, they hope to be able to customize drug therapies for specific patient populations or even individuals. Currently, much of the research in the field of pharmacogenomics is focused on genes encoding either metabolic enzymes that can alter a drug’s activity or defective structural proteins that result in increased susceptibility to disease.

**How Pharmacogenomics Could Change the Way Medicine is Practiced Today:**

Currently, physicians prescribe medication through a trial-and-error method of matching patients with the right drugs. If the prescribed medication does not work for the patient the first time, the physician will try a different drug or dosage, repeating the process until the patient improves. As pharmacogenomics becomes more advanced, physicians eventually will be able to prescribe medication based on an individual patient’s genotype, maximizing effectiveness while minimizing side effects.

**Anticipated Benefits of Pharmacogenomics:**

Eventually, pharmacogenomics will provide tailored drug therapy based on genetically determined variation in effectiveness and side effects. This will mean:

**More powerful medicines:**

- Pharmaceutical companies will be able to produce therapies more targeted to specific diseases, maximizing therapeutic effects while decreasing damage to nearby healthy cells.

**Better, safer drugs the first time:**

- Recovery time will go down and safety will go up as the likelihood of adverse reactions goes down or is eliminated altogether.
More accurate methods of determining appropriate drug dosages:

- Current methods of basing dosages on weight and age will be replaced with dosages based on a person’s genetics - how well the body processes the medicine and the time it takes to metabolize it.

Better vaccines:

- Vaccines made of genetic material, either DNA or RNA, could provide the benefits of existing vaccines without all the risks. Theoretically, they would be able to activate the immune system but would be unable to cause infections.

Economic benefits:

Pharmacogenomics eventually can lead to an overall decrease in the cost of healthcare because of decreases in the:

- number of adverse drug reactions,
- number of failed drug trials,
- time it takes to get a drug approved,
- length of time patients are on medication,
- number of medications patients must take to find an effective therapy, and
- effects of a disease on the body (through early detection).

Some Ethical Issues:

Ethical Issue #1: “Good” or “Bad” Allocation of Scarce Resources?

- Many believe that pharmacogenomics, like other new fields spawned by the Human Genome Project, represents a misallocation of resources. Global efforts should be directed towards solving more urgent problems facing humanity, such as global famine and accessibility to potable water.
- However, opposing forces arguing in favor of pharmacogenomics state that:
  - In the U.S. alone, adverse drug reactions are thought to kill about 100,000 hospitalized patients annually. Another 2.2 million incur serious, but non-fatal, reactions. Physicians, in view of their Hippocratic Oath, are obligated to do no harm. Can physicians fulfill this obligation when the information available regarding the effectiveness of particular medicines is so meager?
  - This situation is further compounded by the fact that most adverse drug reactions result from the fact that medicines are a “one-size-fits-all.” In other words, although medicines are taken in different dosages depending on symptoms, patient age, weight and other clinical factors, these criteria may not be adequate in ensuring that a particular medicine will be safe and effective for a particular individual. Until recently, there has been no alternative to either developing or prescribing medicines.

Ethical Issue #2: Are Genes Really the Answer?

- Genes are not the only key to cures. Environment plays a role, too. Dietary and lifestyle behaviors are still likely to affect the safety and efficacy of medicines for particular individuals. Additionally, variation in drug response is not limited to micro polymorphisms. Environmental factors also play a role (such as sun exposure, drug/drug interaction, drug/food interaction). Additionally, scientists are poised to uncover why the metabolism of particular individuals absorbs and dispels pharmaceuticals in a particular manner.

Ethical Issue #3: Whose Right Predominates?

- The father of a tested subject opened a letter addressed to his child and learned that his child was susceptible to an x-linked genetic disease, thereby stating that the child’s father was also susceptible. The father feels his privacy has been invaded, since he was not the one who consented to being tested.

Legal Situation:

The State of Michigan has employed a relatively cautious approach to genetics legislation as compared to other state legislatures. It has defined genetic testing as: “information about a gene, gene product or inherited characteristics derived from a genetic test, including family history” and has banned discrimination in health insurance and employment based on genetic testing.

References

2. Barash, Carol Isaacson. Ethical Issues in Pharmacogenetics (2001)