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STEM CELL RESEARCH

Ballot Proposal 08-02 November 2008 General Election Placed on the ballot by initiative petition

Complete to 10-22-08

THE CONTENT OF THE BALLOT PROPOSAL:

The following is the official language as it will appear on the ballot.

MBRYO A	ND HUMAN EMBRYONIC STEM CELL RESEARCH IN MICHIGAN
The prop	osed constitutional amendment would:
	nd use of human embryos for any research permitted under federal law ct to the following limits:
The embro o o o	ryos: are created for fertility treatment purposes; are not suitable for implantation or are in excess of clinical needs; would be discarded unless used for research; were donated by the person seeking fertility treatment.
	de that stem cells cannot be taken from human embryos more than 14 days cell division begins.
• Prohi resear	bit any person from selling or purchasing human embryos for stem cell rch.
	ibit state and local laws that prevent, restrict or discourage stem cell rch, future therapies and cures.
	Should this proposal be adopted?

- **BRIEF SUMMARY:** A "YES" vote is a vote in favor of allowing research to be conducted on human embryos created for fertility treatments but which would otherwise be discarded if not donated for research and treatment purposes. Proposal 08-2 would place regulation of the research under federal laws and regulations—with some restrictions—and would prohibit any state or local laws or ordinances that prevented, restricted, obstructed, or discouraged any allowable research or therapies or that created a disincentive for any person to engage in or associate with allowable research, therapies, or cures. The proposal would not alter Michigan's current prohibition on human cloning.
 - A "NO" vote is a vote against allowing research to be conducted on donated human embryos created, but unused, for fertility treatments.
- **FISCAL IMPACT:** Ballot Proposal 08-2 does not appropriate any funds or establish any direct costs or revenue to the State of Michigan or to local units of government. If the proposal results in new stem cell research activity in Michigan, some economic benefit will be generated that may also have a positive fiscal impact on local and state government revenues.

BACKGROUND INFORMATION:

Referendum Process. The proposed law has been placed on the ballot as the result of a petition drive sponsored by the Stem Cell Ballot Question Committee. Under Section 2, Article XII of the State Constitution, "Amendments may be proposed to this constitution by petition of the registered electors of this state." The State Constitution requires that petitions for constitutional amendments contain at least 10 percent of the total vote cast for all candidates for governor at the most recent gubernatorial election.

Any amendment proposed by petition must be submitted to the voters at the next general election not less than 120 days after it was filed. An amendment approved by a majority of the electors voting on the question becomes part of the Constitution and takes effect 45 days after the election. It subsequently can only be amended or repealed the voters, after a proposed amendment has been placed on the ballot either by another petition drive or by two-thirds vote of each house of the legislature.

What Stem Cells Are. There are two types of stem cells – embryonic stem cells and adult stem cells. Stem cells taken from embryos have the potential to develop into every type of cell found in the human body. As a result, scientists and medical researchers around the globe have focused their research on human embryonic stem cells (hESC) as a potential source of therapies and cures for such debilitating illnesses as Parkinson's, diabetes, and Alzheimer's, and for spinal cord and other injuries. The cells are harvested from embryos during the blastocyst stage, about 3-7 days old, when the embryo has about 200 cells and the cells are still undifferentiated – meaning that they are all the same and have not yet begun to specialize in particular types of cells such as brain, heart, or bone.

In addition, some success has been reported in developing stem cells from a single cell taken from an embryo created for fertility treatments. Known as preimplantation genetic

diagnosis, a technique used to test some embryos for severe genetic disease prior to implantation, a single cell is taken from the embryo when it has about eight cells. Usually, the embryo is not harmed and is still suitable for implantation; scientists involved in this research believe the technique may be used to develop embryonic stem cell lines without destruction of the embryo.

Adult stem cells, thought to aid in the repair of diseased or damaged cells, are found in many tissues of the body but act differently from other cells. In general, a mature cell can only produce a cell exactly like it; that is, a skin cell begets a skin cell, a brain cell begets a brain cell. An adult stem (AS) cell, however, can give rise to several types of related cells. For example, therapies using AS cells derived from bone marrow have been used for almost 50 years to treat various cancers of the blood and lymphatic system; more recently, stem cells found in umbilical cord blood have been used in treatments for about 70 diseases including blood cancers, sickle cell anemia, brain cancer, multiple sclerosis, and Parkinson's. Uses for AS cells have been limited because they are rare, hard to isolate, and are limited in their ability to form different types of cells.

Recently, scientists have found a way to use genetically-altered viruses to trick an adult stem cell, like a skin cell, into behaving like an embryonic stem cell. Known as induced pluripotent stem (iPS) cells, researchers believe them to hold the promise of having the same ability to form every cell type as do embryonic stem cells. Early research used four genes inserted into retroviruses to trigger the reaction, but retroviruses are known to cause cancer, so the suitability of these induced iPS cells for therapies that could be transplanted into humans is limited. More recently, scientists have been able to trigger the same iPS cells from adult stem cells using harmless adenoviruses.

In addition, a new type of stem cell dubbed "endometrial regenerative cells" has recently been discovered in menstrual blood capable of developing into at least nine cell types including heart, liver, and lung. Already it has been used in animal models to stimulate blood-vessel growth in damaged limbs to prevent the limbs from withering. Human trials involving people facing amputations are expected to begin in 2009.

Cloning. Until discovery of the somatic cell nuclear transfer (SCNT) process, researchers relied on donated embryos left over from fertility treatments on which to conduct scientific studies. SCNT is a procedure used in transferring the nucleus of a human somatic cell (a cell that is not an egg or sperm cell, such as a skin cell) into an egg cell from which the nucleus has been removed or rendered inert. The resulting embryo is a genetic duplicate, or clone, of the person or animal donating the somatic cell. SCNT was the process used by scientists in Scotland to clone Dolly, the sheep, in the late 1990s. Human embryos created by SCNT have been used to create stem cell lines used in stem cell research.

Human Embryonic Stem Cell Research. According to information provided by the Michigan Legislative Service Bureau, the term "human embryonic stem cell research" can apply to a variety of activities. Depending on what is permitted under a state's law, hESC research can encompass the creation of a human embryo using the SCNT

procedure, the extraction of stem cells from an embryo, and/or the subsequent study or use of cells or tissues derived from embryos.

State Law. Michigan criminalizes research on live embryos, though research is allowed on a dead embryo or fetus with the mother's written consent. For decades, the Public Health Code has prohibited research on a live embryo, fetus, or neonate; performing or offering to perform an abortion whereby research could be conducted on the embryo or fetus as payment, in whole or part, for performance of the procedure; and selling, transferring, distributing, or giving away an embryo, fetus, or neonate for research purposes (this includes unused embryos from fertility treatments). A violation is a fiveyear felony. This prohibition effectively makes it illegal for researchers to harvest stem cells from an embryo and use those cells to derive stem cell lines.

Michigan law has, however, been interpreted as allowing research on hESC lines developed outside of Michigan. Several labs in the state, including one located at the University of Michigan, are currently conducting stem cell research programs; some are federally funded and some are privately funded.

Regarding cloning, legislation was enacted in Michigan in 1998 to prohibit human cloning and prohibit the use of state funds to support human cloning. "Human cloning" is defined as the use of SCNT (described above) to produce a human being. Penalties include a civil fine of \$10 million, a criminal penalty of up to 10 years imprisonment and/or a fine not to exceed \$10 million, and administrative sanctions for individuals and facilities licensed under the Public Health Code. This prohibition not only prevents scientists from cloning an individual, but also effectively prevents researchers in this state from using the SCNT process to create embryos from which embryonic stem cell lines could be derived.

Federal Law. Federal law does not prohibit either human embryonic stem cell research or human cloning, though federal policy does currently restrict the use of federal funds for embryonic stem cell research to hESC lines created prior to August 9, 2001. Federal policy also prohibits the use of federal funds for research involving cloning for the purpose of reproduction and research.

Other States. State laws regarding hESC research vary greatly. Some states ban research on human embryos. Some states restrict public funding of research or ban cloning for research purposes. Nine states specifically permit hESC research; eight of these allocate state funds for the research. Some states only fund adult stem cell research. Missouri amended its state constitution in 2006 to allow human embryonic stem cell research and to ban human reproductive cloning (therapeutic cloning using the SCNT is permitted). Because embryonic stem cell research is permitted under federal law, the research is also allowed in all states that do not specifically prohibit it, even if the state does not have a law on the books to allow the research.

The Debate. Since an embryo is destroyed when cells are harvested, embryonic research is controversial. Viewpoints differ on when life begins and range from the moment of

fertilization to viability outside the womb to actual delivery. Some feel that since the embryos would be discarded anyway, embryo research should be supported as a way for the embryos to be used for the greater good. Others, who feel that the sanctity of life attaches at conception or early development, raise ethical, moral, and religious concerns regarding science that benefits from the taking of human life, even if others benefit from the knowledge gained. Some people feel that if viable stem cell lines can be cultivated from iPS cells (from adult stem cells), the moral concerns that attach to embryonic stem cell research would be avoided. To date, however, the general consensus among the greater scientific community is that it is too soon to predict which path of research will yield the desirable outcome of providing relief for individuals suffering from yet untreatable diseases and injuries and that therefore both avenues of research should be supported. Banning human cloning for reproductive purposes has wide support globally by scientific and medical societies.

Proponents' Perception of the Problem. As some see it, requiring Michigan-based researchers to buy and transport hESC lines from labs in other states or countries is expensive and time-consuming. Even using the federally-approved hESC lines is not without problems; only 21 lines are currently available and all are contaminated with mouse cells, thereby limiting their usefulness in developing medicines or therapies that could be used in humans. Despite recent advances in using chemicals or genetically altered viruses to trick adult stem cells into developing embryos from which embryonic stem cells could one day be gleaned, the general consensus among scientists is that embryonic stem cell research still holds the greatest potential in finding needed cures and therapies. Therefore, much research is still concentrated on embryonic stem cells. Scientists feel that Michigan's prohibition on using live embryos for research is having a chilling effect on the state's ability to expand its life sciences programs at universities and in the private sector and on attempts to develop new enterprises in Michigan that could help diversify the state's economy and provide high paying jobs.

Further Reading. The proponents of the proposal, CureMichigan, have a website at: www.CureMichigan.com/.

An opposition group, Michigan Citizens Against Unrestricted Science & Experimentation (MiCause), has a website at: www.micause.com/.

The Citizens Research Council of Michigan has issued a report on the 2008 ballot proposals. It is available at: www.crcmich.org/.

A DESCRIPTION OF THE BALLOT PROPOSAL:

Proposal 08-2 would add Section 27 to Article 1 of the State Constitution. In general, the proposal would:

- Specify that it would not alter the state's current ban on human cloning.
- Allow any research permitted under federal law on human embryos, except that:

* Stem cells could only be taken up to the 14th day after cell division begins. (Time during which an embryo is frozen would not count against the limit.)

* Only embryos created for in vitro fertility (IVF) treatments could be used, and then only with the donor's voluntary and informed written consent <u>and</u> if either (1) the embryos were in excess of the clinical needs of the donor and would otherwise be discarded if not used for research <u>or</u> (2) were not suitable for implantation and would be discarded if not used for research.

- Describe the purpose of permitting this research as, "To ensure Michigan citizens have access to stem cell therapies and cures, and to ensure that physicians and researchers can conduct the most promising forms of medical research in this state and that all such research is conducted safely and ethically."
- Prohibit the purchase or sale of human embryos for stem cell research, therapies, or cures.
- Require all stem cell research, therapies, and cures be conducted and provided in accordance with state laws of general applicability (including laws on scientific and medical practices and on patient safety and privacy) to the extent the laws do not:

* Prevent, restrict, obstruct, or discourage any stem cell research or stem cell therapies and cures permitted by the proposed constitutional amendment; or,

* create disincentives for any person to engage in or otherwise associate with such research or therapies or cures.

• Provide that if any of the above provisions were held to be unconstitutional, the remaining provisions would still be enforceable.

ARGUMENTS MADE BY PROPONENTS OF THE BALLOT PROPOSAL:

For:

There are many misconceptions about what Proposal 2 would or wouldn't do. As written, the Proposal would:

* Allow research on live human embryos under certain conditions. Most importantly, research would be restricted to donated embryos no longer needed for fertility treatments or not suited for implantation that were willingly donated with informed consent, and that otherwise would be discarded.

* Allow persons to donate their own unused embryos for research, something which is currently prohibited.

* Place embryonic research under federal regulation. Many states have chosen to do likewise.

* Restrict harvesting of stem cells to embryos 14 days and younger.

* Keep the current ban on human cloning and the prohibition on using state funds for human cloning research.

Proposal 2 would not:

* Force any person to donate unused IVF embryos to research. A person or couple could still choose to discard the leftover embryos, continue to freeze them, or donate them to another couple seeking fertility treatments.

* Create embryo farms or encourage women to undergo fertility treatments just to sell the embryos to researchers for money. The proposal would prohibit the sale or purchase of embryos for stem cell research purposes. Current law already prohibits selling an embryo for any other research purpose.

* Invalidate the current ban on human cloning or using state funds to support the procedure, somatic cell nuclear transfer, used in human cloning research.

* Allow research to be conducted on fetuses. Proposal 2 states clearly only human embryos, not fetuses, could be used for research allowed under federal law.

* Raise taxes. Unlike measures enacted by other states, Proposal 2 does not earmark tax money or raise revenue through the sale of bonds for embryonic research or embryonic stem cell research.

* Prevent the legislature from seeking an amendment to the proposal if warranted in the future. The legislature can place an amendment to the Constitution on the ballot by a two-thirds vote of each chamber.

For:

Supporters of Proposal 2 say passage makes sense for several reasons. First, since it is now a criminal offense to remove stem cells from a live embryo (because doing so results in harm or destroys the embryo), Proposal 2 is needed to allow the derivation of new embryonic stem cell lines here in Michigan rather than requiring researchers to buy and transport stem cell lines from other states, a costly and time-consuming practice. That alone would stem the flight of scientists from Michigan to states more conducive to conducting life-saving and life-improving research and would encourage the growth of bio-sciences here. Passage of the proposal would bring and retain the type of high-paying scientific research jobs the state needs to become economically diversified.

<u>Under Proposal 2 only IVF embryos slated for destruction could be used for research</u> purposes. Instead of being destroyed, these embryos could be used to find life-saving or

<u>life-enhancing preventions, therapies, and cures for many diseases and injuries killing</u> <u>and crippling state residents</u>. Many couples left with extra embryos beyond their needs would like to know their embryos were serving a noble purpose rather than just going to the incinerator as medical waste. While they can currently choose to donate embryos to an infertile woman, some are not comfortable knowing that their biologic child would be raised by strangers. <u>Note that the current ban on embryo research does not preserve life</u> because it does not prevent the discarding of unused embryos.

In addition, despite recent advances in the field of induced pluripotent stem cells derived from adult stem cells, the general consensus among scientists is that the greatest potential for cures and meaningful therapies remains with embryonic stem cell research, and that both embryonic and adult stem should be allowed to be researched thoroughly. Human ESC research is only 10 years old – just the beginning by scientific standards. What if embryonic stem cell research was halted now on the premise that all the answers lay within adult stem cell research, only to find at a future date that adult stem cell research yielded nothing that could be safely injected, ingested, or transplanted into humans? Many years, decades even, of research will ultimately produce the best results, most agree that both lines of research should continue.

Opponents fear that the proposal would create a climate of unregulated experimentations on humans, but supporters counter that is unlikely to happen. <u>A host of federal rules</u>, regulations, and policies would be triggered to protect human subjects once the research progresses to human trials. Meanwhile, respectable scientific research doesn't happen in a vacuum. The U.S. National Academy of Sciences (NAS) and the International Society for Stem Cell Research (ISSCR) addresses stem cell research with guidelines incorporating accepted procedures for recombinant DNA (used, among other things, to develop insulin for diabetics), human subject protection, and animal research as well as institutional oversight provided by multidisciplinary committees comprising scientists, clinicians, community members, ethicists, and legal counsel. (Information derived from "Matching Best Research with Best Ethical Practice: The NAS and ISSCR Guidelines for Stem Cell Research" by Patrick Taylor, J.D., Stem Cell Lines – a publication of the Harvard Stem Cell Institute – Summer, 2008.)

For:

<u>Proposal 2 would not result in bizarre human-animal experimentation because it would</u> <u>not alter the state ban on human cloning</u>. Even though scientists at two English universities are currently licensed under that country's laws to conduct experiments using the SCNT process to insert human DNA from a skin cell into a stripped out cow's egg, it is not likely that similar research could be conducted under Proposal 2. Such research would most likely fall under the state ban because SCNT is not allowed to create a human embryo and the product of this type of research could be considered to be human since it would be an identical genetic match to the skin cell – in other words, a clone.

ARGUMENTS MADE BY OPPONENTS OF THE BALLOT PROPOSAL:

Against:

The proposal as drafted contains several weaknesses in language that could make it broader in scope than described by proponents and could lead to unintended consequences. For example:

* Proposal 2 is being marketed as pertaining only to stem cell research. However, as worded, <u>the actual language to be added to the State Constitution (which is different from the wording on the ballot) would allow any embryonic research permitted under federal law</u>. A court could interpret this passage to be broader in scope than just harvesting stem cells from leftover IVF embryos and therefore could include research such as using live embryos to test drug safety or the effect of toxic chemicals.

* <u>Generally accepted research guidelines restrict the harvesting of stem cells to the blastocyst stage (an embryo that is 3-5 days by some definitions, 5-7 days by others).</u> Yet, the proposal would allow stem cells to be taken up to 14 days after the beginning of <u>cell division</u>. This is almost twice as long as ethically recommended by the research community. The actual language also contradicts information posted on the Cure Michigan website which states that the proposal only allows "research using five-to-six-day old, microscopic embryos..."

* Most national and international medical and scientific societies agree that research should not be conducted on, nor should embryos be cultured, beyond 14 days – a point considered to be well before neural precursors could develop and before cells begin to differentiate. The proposal, however, if interpreted to allow research other than stem cell harvesting, does not restrict the time period that the research could be conducted and so the proposal could possibly allow research up to the point where the embryo can be considered a fetus, a time period well past the nationally and internationally recognized ethical guidelines.

* Even if the proposal does not alter the current ban on human cloning, since it does not place that ban within the Constitution, <u>it does nothing to strengthen or protect the cloning ban</u>. The ban on cloning is statutory, meaning that it can be amended or repealed by a simple majority of each legislative chamber and approval by the governor. Amending or repealing the Constitution, on the other hand, would take either another petition drive or a two-thirds majority of each chamber to place an amendment or repeal before the voters.

* The proposal overreaches by putting limits on state and local laws (laws of "general applicability"), including laws on patient safety and privacy and scientific and medical practice. Under the proposed constitutional amendment, state and local laws could not "obstruct, restrict, or discourage" research and therapies permitted under the Constitution or create "disincentives" for persons to engage in or associate with (presumably, fund) such research, therapies, or cures. These terms are highly subjective and could lead to years of expensive litigation, at taxpayers' expense. Meanwhile, it is not clear what impact such language would have on laws of general applicability. One concern is that a

lab could ignore state or local laws protecting a patient's privacy or safety, or generally accepted and regulated medical and scientific practices, just by claiming that the law "restricted" their operations. As stem cell research advances and human clinical trials and then treatments become available, these labs and researchers should not be free to opt out of regulations that other medical and research facilities must follow just because they decide a law "restricts" or "obstructs" or "discourages" them from doing what they want to do.

While the proposal does not specifically say that state or local governmental units can't regulate embryonic or embryonic stem cell research, if researchers can cry "foul" at state and local laws of general applicability, as discussed above, a law specific to embryonic or embryonic stem cell research may not be enforceable under the proposal

* The proposal would place embryonic research under federal regulation. Currently, the federal government only regulates funding for human embryonic research. Therefore, <u>it</u> could be argued that human embryonic research conducted in Michigan would have little governmental oversight.

Against:

Because promising alternatives exist, it is premature to resort to amending Michigan's Constitution to allow research that destroys living embryos. To date, there have been no embryonic stem cell-based treatments or cures. In comparison, adult stem cell-based treatments have been used for decades to treat numerous diseases. In recent years, scientists have made great progress with tricking adult stem cells into behaving like embryonic stem cells, thus making the need to harvest cells from living embryos unnecessary.

The use of embryonic stem cells has long been promoted over adult stem cells by scientists because of the flexibility of an embryonic stem cell to differentiate into any cell type made them preferable to the more limited adult stem cell. Embryonic stem cells are *pluripotent* – meaning that a cell can develop into any of the more than 200 cell types in a human body. Adult stem cells, on the other hand, are *multipotent* – they can only develop into a limited number of cell types; for instance, stem cells from blood can only be tweaked into becoming a blood-related cell. But new advances may overcome this advantage.

Among the new alternatives, induced pluripotent stem cells (iPS), preimplantation genetic diagnosis, and menstrual blood stem cells all have the potential to create viable stem cell lines from which long-sought-after cures and therapies could be developed. (These alternatives are described earlier in the <u>Background</u> section.) Further, iPS cells may prove more desirable than embryonic stem cells in the long run because they could be refined to use a patient's own cells, thus avoiding problems with immune rejection associated with treatments based on donor cells. Most compelling is that cell lines produced by any of these procedures render the debate on the morality and ethics of embryonic research moot as they do not sacrifice one human life for another.

Against:

It is inappropriate to lessen statutory restrictions on embryonic research by amending the State Constitution. It would be better to propose a statutory change; that is, to amend the Public Health Code through the normal legislative process, which would give opportunity for debate on the merits of the proposed language and for public input. Flawed or unworkable passages could be redrafted before a bill reached the governor's desk, and language resulting in untended consequences could be easily amended in a subsequent bill. If legislative action is not feasible, a ballot proposal could make the changes, but in statute rather than in the State Constitution.

Further, if developing technologies subsequently required the law be updated, it would be easier and quicker to do so through the normal legislative process. Should the proposal pass, amending or repealing the language would be very difficult – it would take a vote of the people, with language placed on the ballot either through another petition drive or a two-thirds majority of each chamber. Instead of passing this proposal, voters should encourage state lawmakers to consider measures drafted more precisely and less likely to result in unintended research practices being made legal in the state.

Legislative Analyst: Susan Stutzky Fiscal Analyst: Susan Frey

• This analysis was prepared by nonpartisan House staff for use by House members in their deliberations, and does not constitute an official statement of legislative intent.