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HJR 588: Medical, Ethical, and Scientific Issues Relating to Stem Cell Research Conducted in the Commonwealth

November 15, 2005

HIGHLIGHTS

- **The final meeting of the Study included the last presentation on stem cell research in Virginia and a vote on proposed recommendations to the 2006 Session of the General Assembly.**

The final meeting of the joint subcommittee completed review of stem cell research activities in Virginia and included a public hearing, information on cord blood banking, and a work session.

REVIVICOR, INC.

Dr. David L. Ayares is the chief executive officer of Revivicor, Inc., based in Blacksburg. Revivicor, a recent spin-off company of PPL Therapeutics, is a biopharmaceutical company that has produced products used in treatment, for example, alpha-1-antitrypsin (AAT), which was awarded "orphan drug" status by the federal Food and Drug Administration in 1999 has been used in clinical trials for treatment of hereditary emphysema and cystic fibrosis. Revivicor is a world leader in animal cloning technology, being a subsidiary of the company in Scotland that produced Dolly, the Sheep, the first cloned animal. Revivicor concentrates on advancement of biomedical products and regenerative medicine, with a diverse product development pipeline focused on creating genetically modified pig organs and cells for xenotransplantation applications (between species, such as from pigs to humans), stem cell therapies for diabetes, and development of human polyclonal antibodies from genetically modified livestock for biological warfare countermeasures.

Dr. Ayares' research at Revivicor has primarily focused on pigs in order to develop a solution to the donor organ shortage for patients needing transplants. Revivicor is responsible for the first successful cloning of pigs as well as the first successfully cloned knockout pigs—pigs that are lacking the gene associated with hyper acute rejection of xenografts (use of tissue from one species to treat another species). The goal of this animal cloning technology is to produce pig tissue that can be used in humans without being rejected. The gene that was "knocked out" or removed from the pigs is responsible for production of a sugar on pig cell surfaces that is foreign to the humans and will, therefore, trigger an immune response leading to hyper acute rejection by humans within minutes of the transplant.

HIGHLIGHTS

- **Three states, Florida, Massachusetts, and New Jersey, have different models of public cord blood banks, which were reviewed and discussed.**

Bearing in mind that even human to human transplants require the use of immunosuppressants, drugs that inhibit the body's immune system to control graft versus host disease, the goal of this research is to produce organs and cells that are tolerized, i.e., modified so as to be histocompatible with the human recipient. In other words, Revivicor's mission is to produce pig tissue and cells that can be used to treat humans without requiring lifelong treatment with immunosuppressants, e.g., pancreatic islet cells for the treatment of diabetes.

Revivicor has been awarded four grants from the Advanced Technology Program (ATP) of the National Institute of Standards and Technology within the United States Department of Commerce, a federal grant initiative to promote the technology development in private industry. Dr. Ayares explained that the federal ATP is very important to private research efforts, as venture capital is difficult to obtain for the basic research that is necessary to develop pre-clinical biotechnology. Because basic research is time consuming and the outcomes are unpredictable, investors are difficult to attract.

In 2000, PPL Therapeutics (Revivicor's parent company) was awarded a $1.9 million ATP grant to fund research relating to the production and differentiation of pluripotent stem cells without using embryos. This research was exclusively conducted on nonhuman species, i.e., pigs, and involved changing or transdifferentiating pig skin fibroblast cells into pig embryonic-like stem cells. The concept was considered a viable option for deriving large numbers of pluripotent stem cell lines without the supply constraints acknowledged to exist with the embryonic-derived lines. Somatic cell nuclear transfer, an expertise of Revivicor, was used on the readily available skin cells to transdifferentiate the pig skin fibroblasts to stem cells. However, the development of the stem cells was limited and the cultures did not continue to divide indefinitely. Although the research goal was not reached before the grant expired, much was learned, and the goal of transdifferentiating skin cells into stem cells may still be successful as some recent research appears to indicate.

CORD BLOOD BANKING

Dr. Curtis Thorpe, technical advisor to the joint subcommittee from the Virginia Department of Health, presented information on cord blood banking that had been researched by staff. The joint subcommittee had asked whether other states or countries supported cord blood banking systems and the feasibility and cost of establishing a statewide umbilical cord blood banking system in Virginia.

Other States' Cord Blood Banking Initiatives

Three states, Florida, Massachusetts, and New Jersey, have different models of public cord blood banks.

Florida's program is a consortium between the University of Florida, University of Southern Florida, the University of Miami, and the Mayo Clinic in Jacksonville and provides for the collection, screening for infectious and genetic diseases, tissue typing, and cryopreservation of cord blood as a public resource. The Florida program offers the opportunity to donate to the pregnant woman at the time of hospital or birthing facility admission, requires written disclosure from providers who financially benefit from cord blood, and authorizes the consortium to charge reasonable fees to recipients.

Massachusetts' program is a partnership with the University of Massachusetts Medical School at Worchester, established as a public cord blood bank for umbilical cord blood and placental tissue donated by maternity patients at certain participating hospitals. Licensed hospitals must inform pregnant women of the opportunity to donate cord blood and educate maternity patients about cord blood banking. Research institutions may agree to pay the estimated expenses of the collection and

storage of the donated umbilical cord blood and placental tissues. Massachusetts also established a 15-member Biomedical Research Advisory Council to make recommendations to the governor about biomedical research relating to cord blood and placental tissue.

New Jersey's program provided for a $ 5 million loan to establish the New Jersey Cord Blood Bank to the Coriell Institute for Medical Research, an internationally known, not-for-profit biomedical research institution with a long history of cell banking, cryogenic storage, and retrieval of human cell cultures. Strong relationships between the cord blood bank and the collecting hospital are established, and written informed consent must be obtained from any woman choosing to donate cord blood. The Coriell Institute for Medical Research is required to repay the state loan as reimbursement is received for cord blood released for therapy.

In some states, such as Maryland, cord blood banking is regulated by requiring hospitals to allow pregnant patients to donate umbilical cord blood to certified cord blood banks and prohibiting charges for the donation. Further, Maryland law notes that employees who have bona fide religious objections cannot be required to collect cord blood and hospitals are not required to make patients' arrangements for cord blood donations.

Other Countries' Cord Blood Banking Initiatives

In a growing number of countries across the world, cord blood banking initiatives have been established. Brazil, for example, has a public cord blood bank at one maternity hospital in Rio de Janeiro. Colombia recently established a cord blood banking program through the University of Antioquia.

India also recently announced a government cord blood banking initiatives in four locations through a contract with a private firm. In Korea, the Seoul Cord Blood Bank is not a government program and is run by the same private firm that operates in India. Singapore has a established in 2004, that provides free cells to any child whose cord blood has been donated; others are charged for the units. Australia has a national network of cord blood banks in Melbourne, Sydney, and Brisbane and registers cord blood in the Australian Bone Marrow Registry.

The European Union forbids profit-making from the sale of body material; however, operating expenses may be recovered. France prohibits private cord blood banking, considering cord blood a national resource and having only three hospitals that collect it. In the United Kingdom, the National Health Service collects cord blood for the public good, with 80 or more units having been released for transplantation. Italy prohibits private cord blood banking and has a network of public cord blood banks maintained by its national health system.

National Marrow Donor Program

The United States' National Marrow Donor Program is part of a world-wide network of 500 medical facilities that searches for a donor or cord blood match when a patient needs a transplant and facilitates an average of 200 bone marrow or blood cell transplants each month. The National Marrow Donor Program has a registry of more than 45,000 cord blood units in cord blood banks across a number of states.

Cord Blood Banking in Virginia

In Virginia only approximately 5 percent of umbilical cord blood is not being banked in the medical schools, primarily for the use of pediatric oncologists for children cancers. Most stored cord blood in Virginia is being deposited at parents' expense in private storage facilities.

Process for a Virginia Cord Blood Banking Initiative

The first step for developing a public cord blood banking initiative in Virginia would be to develop a database of existing cord blood supplies and perhaps legal authority to access any privately banked cord blood during an emergency. In order to store umbilical cord blood to meet a

JOINT SUBCOMMITTEE STUDYING MEDICAL, ETHICAL, AND SCIENTIFIC ISSUES RELATING TO STEM CELL RESEARCH IN THE COMMONWEALTH

HIGHLIGHTS

- **The United States' National Marrow Donor Program is part of a world-wide network of 500 medical facilities that searches for a donor or cord blood match.**
- **Most stored cord blood in Virginia is being deposited at a patient or parent's expense in private storage facilities.**

JOINT SUBCOMMITTEE STUDYING MEDICAL, ETHICAL, AND SCIENTIFIC ISSUES RELATING TO STEM CELL RESEARCH IN THE COMMONWEALTH

HIGHLIGHTS

- **Start up costs for the initial year of a cord blood banking program in Virginia would be $1.5 to $2 million, with maintenance costs estimated at $1 million per year, and monitoring costs unestimated.**

statewide emergency, a capacity of at least 40,000 doses would be needed, with the cells stored for up to five years to ensure recycling to maintain cell integrity.

Drawing from other states' programs as examples, a cord blood banking program could be integrated into an existing cell storage infrastructure or started as a new cord blood initiative under state supervision, or contracted with a private sector provider. Integration into an existing system would probably be the least expensive option, involving coordination with existing facilities at Virginia Commonwealth University's School of Medicine, the University of Virginia's School of Medicine, and the Eastern Virginia Medical School and its contracting hospitals, as well as the private hospital systems in Western and Northern Virginia—for a total of five sites covering all regions of the Commonwealth.

Site requirements would be approximately 400 to 500 feet of space, at least 2 liquid nitrogen freezers, at least 2 vent hoods, and access to fluorescent cell sorting and tissue typing. Costs at each of the five sites are estimated as $200,000 for equipment, two laboratory technicians per site at approximately $50,000 each plus benefits; and supplemental salary for an existing supervisor to manage an additional program. The approximate start up costs for the initial year would be $1.5 to $2 million, with maintenance costs estimated at $1 million per year, and monitoring costs unestimated. If implemented, a collaborative arrangement of this kind would make cord blood accessible to all parts of the state.

Establishing a new system would be more expensive and may require a new building or a renovated structure specifically designed for the cord blood bank. The new system would also require equipping and would probably have to be a GMP facility with a level V laboratory that is strictly regulated. The costs of such a facility and system could be as high as $20 million to initiate.

A third operation would be to contract with a private stem cell storage company, which would require a bid process and could present issues relating to control of the cord blood and access in any statewide or regional emergency.

With any of these options, various issues relating to patient privacy, recycling of cells over five years old as new cells enter the system, and perhaps sale of exiting cells to research programs or others to offset costs.

PUBLIC HEARING

Three speakers registered and spoke during the public hearing and two statements were submitted and read for the record. The submitted statements were from Dr. John T. Bruchalski, an obstetrician/gynecologist practicing in Fairfax, in support of cord blood banking and adult stem cell research and Ms. Moira Hall, a 20 year old diagnosed with Hodgkin's Lymphoma. She was treated with high-dose chemotherapy with stem cell support using cells donated by a twin sister; when this treatment was not successful, she received a second transplant of cells donated by a younger brother, which resulted in successful remission.

Representing the Virginia Society for Human Life, Dorothy Tims expressed strong opposition for human embryonic stem cell research and support for the use of adult stem cells. She stated that "[t]he weakest and most vulnerable member of the human family—the embryo—should not be the subject of scientific experimentation" and that "[i]t is never morally or ethically justified to destroy one human being in order to possibly save another." Ms. Tims described the advances that have been and are being made in adult stem cell research, using alternatives to embryonic stem cells such as cord blood, bone marrow, and neural stem cells. She called for the use of research money and efforts to be directed to the adult stem cell therapies that are "free of the ethical dilemmas associated with destructive human embryo research." Ms. Tims closed by stating that the VSHL

encourages continued efforts in the scientific community to develop treatment for life threatening and life limiting diseases in a manner free from ethical issues.

Mr. Richard M. Doerflinger, Deputy Director of the Secretariat for Pro-Life Activities, United States Conference of Catholic Bishops, presented a notebook of supplemental materials to the joint subcommittee. Mr. Doerflinger, while noting that the Catholic Church does not oppose stem cell research, stated that destruction of human life at any stage was opposed, thus, human embryonic stem cell research is opposed. He noted that adult stem cells and stem cells from cord blood provide viable alternatives and cited the many advances in the research and therapies using adult stem cells. He also mentioned the drawbacks to embryonic stem cell research, such as the development of teratomas. Mr. Doerflinger said that even the embryonic stem cell researchers now have reduced expectations from their studies. He also reflected that excess embryos are not available in the numbers required to produce the number of cell lines desired, which would take the destruction of millions of embryos. Dr. Doerflinger described the potential for exploitation of women in the creation of the embryos, including the current controversy involving Korean research, including reports that one laboratory technician donated oocytes for the creation of the embryos used for the research. Mr. Doerflinger described human reproductive cloning, which almost all groups oppose, as potential fetus farming.

Dr. Michael Valente, a physician practicing neurology in the Commonwealth, who came as a taxpaying citizen who objects to the possibility of using state tax money to fund human embryonic stem cell research. He stated that embryonic stem cell research using mice has not produced any cure for diseased mice. He also said that adult stem cells from bone marrow, pancreas tissues, and discarded placentas, even nasal epithelium, are being used to treat diabetes, heart disease, leukemia, and other diseases. Dr. Valente stated that he sees value in taxes when used for necessary services, but he is opposed to using public money for unproven research. He said that his medical background provided him special insight in this regard, and that scientists are moving away from embryonic stem cell research to the use of adult and umbilical cord blood stem cells

RECOMMENDATIONS

Having received an issues analyses prior to the meeting that also set out six broad topics for discussion, the joint subcommittee decided on motion and a unanimous vote that the only recommendation for the 2006 Session would be the establishment of a Virginia Cord Blood Banking initiative. Included in the motion was that the joint subcommittee would seek continuation of the study for another year.

HJR 588: Joint Subcommittee Studying the Medical, Ethical, and Scientific Issues Relating to Stem Cell Research Conducted in the Commonwealth

The Hon. R. G. Marshall, *Chairman*

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HIGHLIGHTS

- **The joint subcommittee unanimously agreed to only recommend the establishment of a Virginia Cord Blood Banking initiative, and included in the motion was that the joint subcommittee would seek continuation of the study for another year.**