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NIH Releases Human Pluripotent Stem Cell Research Guidelines

On August 25th, 2000 the NIH published the final version of the guidelines governing NIH-funded research on human pluripotent stem cells (HPSC'S) in the *Federal Register*. These guidelines have been anticipated since 1998 when two scientific teams published their results on the successful isolation and propagation of these cells. Since these cells were derived from human fetal tissue in one instance and donated human embryos in the other, considerable controversy surrounded these accomplishments in light of the recent Department of Health and Human Services (DHHS) ban on fetal embryo research. The NIH and countless other scientists were quick to acknowledge the potential benefits of continued research in this area, but realized that significant ethical considerations were also involved. The major impetus by NIH to open this area to Federal funding resulted from both a desire to involve talented "non-corporate" investigators in this exciting field as well to provide a means of stringent regulation, guidance and oversight for those receiving federal funding in this area. While guidelines were being prepared, the NIH notified the scientific community that a moratorium on Federally funded pluripotent stem cell research would be in effect. The August 25 publication of the guidelines lifts that absolute restriction but adherence to this document must be verified even before application for funding can be sought. During this time period, scientists working in the field could not utilize DHHS funds. They had to either resort to private funding sources or curtail current studies. This ban had no effect on the corporate research sector. While the NIH realized the priority of research on HPSC's, they had to also consider public, federal and congressional opinion since this was closely related to the Federally-banned fetal embryo research field. The following is a chronology of events leading up to the final version of the HPSC research guidelines and concluding with a summary of the actual document.

December 2, 1998: Harold Varmus, MD, Director, NIH Appears before Senate Appropriations Subcommittee on Labor, Health and Human Services, Education and Related Agencies

Dr. Varmus appeared before the Senate subcommittee to discuss the recently published reports on the isolation and propagation of the first human HPSC's. He took this opportunity to summarize the important findings published by Drs. John Gearhart from Johns Hopkins University and James Thomson from the University of Wisconsin. He noted that "for the first time, scientists have obtained human stem cells that can give rise to many types of cells in our body". It was pointed out that the two scientists derived the HPSC's from different

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sources: Dr. Gearhart's group derived them from fetal gonadal tissue destined to form germ cells while Dr. Thomson and co-workers used human embryos, created by *in vitro* fertilization. Dr. Varmus took this opportunity to clarify many terms and definitions – including the definition of pluripotentiality and how this was different from totipotent cells (capable of forming a viable fetus) and the more committed counterparts such as hematopoietic stem cells which can only reconstitute a single tissue type. These definitions were crucial given the "scientific, ethical and societal issues raised by this research." Potential applications of HPSC's were then reviewed. This theme would appear repeatedly through subsequent hearings and NIH documents. HPSC research could help unravel events during human development such as those that turn genes on and off. This has obvious implications for diseases such as cancer. They could also contribute to the safety and efficacy of drug development since a human HPSC line could be used in pre-clinical testing. Also various human disease states could be mimicked with this approach, and candidate drugs evaluated *ex vivo*. Lastly, HPSC's may allow the generation of cells and tissues for transplantation - the newly evolving field of ***somatic cell therapy*** (see article on SCR_X meeting in this issue). This could lead to cures and the alleviation of suffering from an untold number of human maladies including Parkinson's and Alzheimer's disease, spinal cord injury, stroke, burns, hear disease, diabetes, osteoarthritis and rheumatoid arthritis. In the last portion of his talk, Dr. Varmus expounded on the role of the Federal government in HPSC research. He first emphasized that while Dr. Thomson's work used cells derived from embryos created by *in vitro* fertilization but not used for infertility treatment, the NIH could not, and did not support this work which falls within the Congressional ban on human embryo research. On the other hand, Dr. Gearhart's work derived HPSC's from fetal tissue from terminated pregnancies for which the Public Health Service Act does authorize Federal funding of human fetal tissue research and provides safeguards for its conduct. It was noted, however, that in this case, neither scientific group utilized NIH funding for their HPSC research. Dr. Varmus also stressed that since HPSC's were produced from embryos and fetal tissue, it did raise a number of ethical concerns. Examples given included concern that HPSC research would encourage the creation of human embryos for research purposes; this would also violate the 1994 Presidential directive banning NIH funding of such work. He also noted that the President had asked the National Bioethics Advisory Commission to undertake a thorough review of the issues associated with HPSC research.

January 26, 1999: NIH Director's (Dr. Varmus) Statement on Research Using HPSC's made before the Senate Appropriations Subcomittee…

Dr. Varmus again briefed the Senate Subcommittee. This time he reviewed discussions between The NIH and DHHS, the end result of which was that HPSC research can be supported with Federal funds. He again reviewed the science and the promise of HPSC research. He then discussed the DHHS ruling of January 15th, 1999 which concluded that DHHS funds can be used to support research using HPSC's that are derived from human embryos: the statutory prohibition on human embryo research does not apply to research utilizing human HPSC because HPSC's are not embryos (note that the DHHS did not state that derivation of the HPSC's from embryos was supported). This decision relied heavily on the science-based definition of organism: an individual constituted to carry out all life functions. HPSC's do not fit this definition. In addition, Dr. Varmus stated that DHHS funds can be used for HPSC's derived from human fetal tissue if the existing laws and regulations governing fetal tissue research are obeyed. It was now up to the NIH to enact guidelines for such research. The first step was to notify all researchers *via* the NIH website that they cannot use DHHS funds to begin research using human HPSC's until further notice. This essentially shut down all public funded HPSC research until NIH could establish and finalize the guidelines.

December 2, 1999: NIH Publishes Draft Guidelines for Stem Cell Research

The NIH released a draft of the proposed guidelines for human HPSC research in the Federal Register. The NIH web site noted that the guidelines recommend procedures to help ensure that NIH-funded human HPSC research is conducted in an ethical and legal manner. The draft guidelines were originally opened for public comment for 60 days. This was later extended an additional four weeks. The NIH issued a national press release announcing the Federal Register notice and many of the Nation's newspapers carried articles on this area of research and on the draft guidelines. The NIH later noted that patient groups, scientific societies and religious organizations convened meetings and discussion groups and disseminated materials about HPSC research and the Guidelines. In addition the NIH held a public meeting of their oversight HPSC working group on April 8th, 1999 where the public again had an opportunity for oral testimony.

May 2000: Stem Cells: A Primer

The NIH released an excellent review on stem cells on their website http://www.nih.gov/news/stemcell/primer.htm In addition to definitions and description of the various stem

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cell types, there is an excellent discussion as to why adult stem cells may not be an adequate replacement for embryo or fetal-derived HPSC's.

August 25, 2000: NIH Releases Final Guidelines on HPSC Research and also Releases the Moratorium on Human HPSC Research

Prior to release, NIH announced the final guidelines on their website. Following this 8/23 announcement, a statement appeared on 8/24 discussing the scope of the guidelines and also reviewed the most frequently received comments and questions regarding the draft documents. The various changes to the final document as well as arguments for not changing some sections targeted by opponents were reviewed. While all those involved in this field should review the entire final document published in the Federal Register on 08/25/2000 (also found at http://www.nih.gov/news/stemcell/index.htm), the 08/23/00 website summary is also quite useful. The specifics of the guidelines follow from this document:

- NIH funds can be used to study cells derived from human embryos **only** if they were derived from frozen embryos that were created for the purposes of fertility treatment and were in excess of clinical need.
- The guidelines prohibit the use of inducements, monetary or otherwise for the donation of the embryo.
- All prospective or funded investigators must follow both the guidelines and all laws and regulations governing human fetal tissue and its transplantation.
- The donation of human embryos or fetal tissue must be made without any restriction regarding the individual(s) who may be the recipient of the cells derived from the human HPSC's for transplantation.
- The HPSC derivation protocol must be reviewed and approved by an Institutional Review Board.
- Informed consent will discuss HPSC research/ transplantation, long term storage of cells and that the research is not intended to provide direct benefit to the donor. It will also not involve the transfer of donor embryos to another woman's uterus (derivation of HPSC's prevents this). The possibility that the results of the research may have commercial potential and that the donor will not receive any benefits from such future commercial development must also be included in the informed consent process.
- Research ineligible for funding included the actual derivation of HPSC's from human embryos (subsequent research can be funded if there was adherence to the final guidelines), research using HPSC's to create/contribute to a human embryo, HPSC's derived from human embryos created for research purposes, research involving HPSC's derived using somatic cell nuclear transfer, research involving the combination of human HPSC's with an animal embryo and reproductive human cloning using HPSC's derived from somatic cell nuclear transfer.

Oversight of the HPSC field is also detailed including a discussion of the NIH HPSC Review Group (HPSCRG) which will document compliance with the guidelines. The working group will also hold public meetings when new discoveries or cell lines must be considered for funding.

The NIH and its advisors must be complimented for a thorough, but quite reasonable investigation of this exciting new field and for having the foresight to implement guidelines at the outset for future study by NIH-funded scientists. Realizing the importance of HPSC research, they communicated almost immediately with the DHHS to determine the impact of the fetal embryo research ban for this area. They also sought the opinions of numerous scientific and societal groups prior to drafting and finalizing the guidelines. No doubt, this served as an excellent training exercise for many similar future scientific discoveries that will be just as controversial as HPSC research.

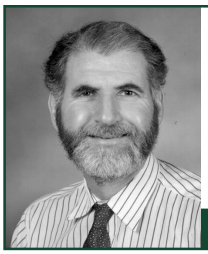
Steve Noga

{ For related articles, see pages 6 and 7 }

ISHAGE at ASH

Aside from the GMP Workshop being held November 30, 2000 in San Francisco, ISHAGE will also have a booth at the ASH conference. Please drop by.

The ISHAGE Advisory Board will be meeting Friday, December 1, 2000 from 4:00 - 5:30pm in the San Francisco Marriott (55 - 4th Street) in the Pacific Suite 1 room. The ISHAGE Executive Committee is meeting immediately thereafter.



From the President's Desk

Robert Negrin, MD

This has been an active and exciting time for ISHAGE. Our society continues to sit at the forefront of the emerging field of cellular therapeutics. The expanded focus of the society towards a variety of different cellular therapeutics creates new and exciting initiatives for further growth. Continuing on the lead of Malcolm Brenner and the outstanding San Diego meeting, we are actively planning for the upcoming meeting in Quebec City in June 2001. This too will be an outstanding meeting with a broad array of presentations on the state-of-the-art in transplantation biology, gene therapy, stem cell biology, immunotherapy, as well as evaluation of minimal residual disease. In addition, we will continue on the format of oral presentations from selected abstracts, workshop presentations, as well as technical breakfasts which proved to be so valuable. In addition, the society will continue in our efforts to support practical meetings such as the GMP meeting prior to the ASH in San Francisco, as well as meetings on minimal residual disease in Germany and flow cytometry prior to the Quebec Annual meeting. Cytotherapy continues to be a major voice from our society in the field of hematopoietic and cellular therapies. Under the excellent leadership of Nancy Collins and Adrian Gee, the new format of Cytotherapy continues to present novel ideas and concepts. We encourage our membership to support this journal and to send in papers for review. The telegraph has expanded under the leadership of Iain Webb and continues the excellent model that Steve Noga developed. Please click on to the ISHAGE web-site which is expanded and has a host of interesting sources of information, chat room ahd library.

Like all things, there are some dark clouds on the horizon. In collaboration with the International Society of Gene Therapy, we hope to help mold the discussion with regulatory agencies on the appropriate guidelines which will help govern our field. I encourage you all to get involved in this process. In our society, the Legal and Regulatory Committee has taken this lead under the direction of Donna Przepiorka. I encourage you to voice your concerns and ideas so that we can articulate our positions in a coherent way. In addition, we are hopeful that our legal difficulties may be drawing to a conclusion.

After leaving San Diego, I was more convinced than ever that our society plays an important role in the field of cellular therapeutics and hematopoietic cell transplantation. I encourage your involvement to strengthen the society and voice your concerns and suggestions on how we can better meet your needs. As our society goes through the inevitable ebb and flow that all young societies must endure, we appreciate your continued support and hope to find ways to communicate more effectively.

On a more personal note, it is a great honor for me to be involved with such a dedicated group of individuals who have worked long and hard to develop the society and point it in the right direction.

ISHAGE Announcements

It is time to renew your membership for 2001! You may do so online (www.ishage.org) or respond to the membership renewal fax you will be receiving soon.

ISHAGE is considering adding a Laboratory Membership for 2001 whereby a laboratory or research facility may apply for a membership on behalf of a number of staff members. Three levels are being considered for different sized centers: (a) under 10, (b) 10-19, and (c) 20 or over. For further information, watch the ISHAGE website (www.ishage.org) or contact the ISHAGE Head Office by phone at 604.874.4366 or email at headoffice@ishage.org.

Currently underway are plans for three different events for June 14, 2001, before ISHAGE 2001 officially commences:

1. FAHCT Training Workshops
2. The Third Bi-Annual Conference on Applications of Flow Cytometry in Blood and Marrow Stem Cell Transplantation
3. Corporate Symposia

An ISHAGE Membership Directory is now available online (www.ishage.org) to members only.

From the Editor's Desk

Iain Webb, MD

Time for Strategic Planning

In this issue, several reports are included that present the recently released NIH guidelines governing NIH-funded research involving human pluripotent stem cells. This document is the result of several years of work and provides a framework for the future use of these cells in the United States. The question we must now address is how and where will our institutions provide the results of this exciting research to our patients?

Advances have recently been made in the understanding of the biology as well as potential clinical applications of pluripotent and non-hematopoietic stem cells that will in the foreseeable future translate into novel therapies for patients. At present, much of the work performed in our facilities focuses on the production of cellular components used to support the therapy of malignancies or, increasingly, function as therapeutic agents in themselves. However, with the proliferation of reports identifying the ability of stem cells to differentiate into musculoskeletal, neural and hepatic tissue, the use of stem cell based cellular products to treat benign diseases is assured. We should all hope that these advances will lead to strategies to heal severed spinal cords, cure Parkinson's disease and muscular dystrophy as well as restore hepatic and other organ function.

As noted above, non-hematopoietic stem cell products are currently being produced by clinical cell processing facilities. In many cases, the same laboratory which provides peripheral blood, bone marrow and umbilical cord blood derived stem cells provides these components. In others, separate facilities have been constructed to culture and/or genetically modify dendritic cells, antigen-specific T cells and tumor vaccines.

As new cell-based treatments for benign conditions are introduced, the production of these therapeutic agents could be performed in existing facilities or additional facilities could be constructed. One could conceive of multiple laboratories in the major centers run by rheumatologists, neurosurgeons, hepatologists, etc. etc., few of whom will be entering the field with the expertise that our members have accumulated over the years. Proactive involvement by our membership will not only facilitate the production of quality products, it will eliminate much of the startup time involved in learning GTPs from scratch, thereby getting the therapies to the patients faster.

Our staff also need to make sure that we will have a laboratory facility that will be able to produce a wide variety of novel cellular products. Several institutions have recently built or are planning to build new cell processing facilities. These facilities represent a significant academic investment and therefore will need to be able to function for many years. If they are to be able to serve the full spectrum of patients, academic facilities will need to have flexible multiuse designs that can be modified as needed. In addition, they will need staff from diverse backgrounds who can adapt the facility's functions as well as communicate in a common language with the users.

This is an exciting time. It is unclear where we are headed, but with some foresight and maintenance of open channels of communication with the various individuals and societies working in the field, I think we will go far.

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NIH Announcement of Publication of Final Guidelines for Stem Cell Research

The National Institutes of Health (NIH) today put on display at the *Federal Register* its final *Guidelines* for research involving human pluripotent stem cells. The *Guidelines* detail the procedures to help ensure that NIH-funded human pluripotent stem cell research is conducted in an ethical and legal manner.

Such research promises new treatments and possible cures for many debilitating diseases and injuries, including Parkinson's disease, diabetes, heart disease, multiple sclerosis, burns and spinal cord injuries. The NIH believes the potential medical benefits of human pluripotent stem cell technology are compelling and worthy of pursuit in accordance with appropriate ethical standards. The NIH has developed the *Guidelines* for stem cell research in a careful and deliberate way to assure that the ethical, legal, and social issues relevant to human pluripotent stem cell research are addressed prior to NIH funding of that research.

Human pluripotent stem cells hold great promise for advances in health care because they can give rise to many different types of cells, such as muscle cells, nerve cells, heart cells, blood cells, and others. Further research using human pluripotent stem cells may help scientists generate cells and tissue that could be used for transplantation to treat many diseases; improve understanding of the complex events that occur during normal human development and of what goes wrong to cause diseases and conditions such as birth defects and cancer; and change the way drugs are developed and tested for safety and potential efficacy.

The *Guidelines* prescribe the documentation and assurances that must accompany requests for NIH funding for research using human pluripotent stem cells from human embryos or fetal tissue. The *Guidelines* state specific criteria for informed consent and establish a Human Pluripotent Stem Cell Review Group to review documentation of compliance with the NIH *Guidelines*. In addition, the *Guidelines* delineate areas of research involving human pluripotent stem cells that are ineligible for NIH funding.

In an effort to help ensure that any research utilizing human pluripotent stem cells is appropriately and carefully conducted, the NIH sought the advice of scientists, patients and patient advocates, ethicists, clinicians, lawyers, the National Bioethics Advisory Commission (NBAC), members of Congress, among others in drafting these *Guidelines*. The draft *Guidelines* were published for public comment in the *Federal Register* and after reviewing and considering all comments, the NIH will publish the final NIH *Guidelines* in the *Federal Register* on August 25, 2000.

Members of the Human Pluripotent Stem Cell Review Group will be named shortly, after which NIH will begin accepting requests for funding. Additional information about stem cells can be found on the NIH website at http://www.nih.gov/news/stemcell/index.htm.

NIH News Release - Wednesday, August 23, 2000

NOTICE TO ALL ISHAGE MEMBERS - ELECTIONS 2001

The Executive Committee is seeking your input for the upcoming ISHAGE elections. In 2001, the following **five** positions are open for election (all positions commence June 2001):

President-Elect: The President-Elect serves a two-year term after which succession to President for a further two-year term is automatic. The President-Elect is a member of the Executive Committee and performs the duties of the President in his/her absence or incapacity.

Treasurer: The Treasurer serves a three-year term and may be re-elected once for an additional three-year term. The Treasurer is a member of the Executive Committee and is responsible for reporting to the Executive Committee on financial matters and monitoring the Society's financial transactions, budgeting and accounting.

Europe Regional Treasurer: The Europe Regional Treasurer serves a three-year term on the ISHAGE-Europe Regional Executive Committee and may be re-elected once for an additional three-year term. A Regional Treasurer is responsible for reporting to the Regional Executive Committee on financial matters and monitoring the Regional Section's financial transactions, budgeting and accounting.

Two Advisory Board Representatives: The Advisory Board provides advice and input to the President and Executive Committee on the long range development and policies of ISHAGE. Currently, the Advisory Board meets twice a year, at the ASH Conference and the ISHAGE Annual General Meeting. Each year, one M.D. or Ph.D. member and one Technical member are elected to serve two-year terms on the Advisory Board.

If you are interested in or would like to nominate another ISHAGE member for any of the positions listed above, please fill in fax the form inserted into this issue of the Telegraft or from the ISHAGE website (www.ishage.com) to the ISHAGE Head Office at **604.874.4378.**

PLEASE NOTE THE **DEADLINE** FOR RECEIPT OF NOMINATIONS IS **FEBRUARY 28, 2001.**

NIH Published Fact Sheet on Human Pluripotent Stem Cell Research Guidelines

The Promise of Stem Cell Research

Human pluripotent stem cells are a unique scientific and medical resource. They can develop into most of the specialized cells and tissues of the body, such as muscle cells, nerve cells, liver cells, and blood cells and they can divide for indefinite periods in the laboratory, making them readily available for research, and potentially, treatment purposes. Scientists derived these unique cells from human embryos and from non-living fetuses.

The establishment of human pluripotent stem cell lines represents a major step forward in the understanding of human biology. These unique cells have captured the interest of scientists and the public, particularly patients and their advocates. Although such research promises new treatments and, possibly even cures for many debilitating diseases and injuries, including Parkinson's disease, diabetes, heart disease, multiple sclerosis, burns and spinal cord injuries, the NIH acknowledges that the ethical issues related to this research need due consideration.

The Need for *Guidelines* to Govern Research Using Pluripotent Stem Cells

Federal law currently restricts the use of Department of Health and Human Services (DHHS) funds for human embryo research. DHHS funds cannot be used for the derivation of stem cells from human embryos. The Congressional restriction, however, does not prohibit funding for research utilizing human pluripotent stem cells because such cells are not embryos.

The purpose of the NIH *Guidelines* is to prescribe procedures to help ensure that NIH-funded research in this area is conducted in an ethical and legal manner. By issuing these *Guidelines*, the NIH aims to enhance both the scientific and ethical oversight of this important arena of research and the pace at which scientists can explore its many promises. These *Guidelines* will encourage openness, help make certain that researchers can make use of these critical research tools, and help assure public access to the practical medical benefits of research using these cells.

In an effort to help ensure that any research utilizing human pluripotent stem cells is appropriately and carefully conducted, the NIH sought the advice of scientists, patients and patient advocates, ethicists, clinicians, lawyers, the National Bioethics Advisory Commission (NBAC), members of Congress, among others in drafting these *Guidelines*. The draft *Guidelines* were published for public comment in the Federal Register and after reviewing and considering all comments, the NIH will publish the final NIH *Guidelines* in the *Federal Register* on August 25, 2000.

Specifics of the *Guidelines*

The *Guidelines* prescribe the documentation and assurances that must accompany requests for NIH funding for research using human pluripotent stem cells derived from human embryos or fetal tissue.

- For studies using cells derived from human embryos, NIH funds may be used only if the cells were derived from frozen embryos that were created for the purposes of fertility treatment and were in excess of clinical need.
- The *Guidelines* prohibit the use of inducements, monetary or otherwise, for the donation of the embryo. There must also have been a clear separation between the fertility treatment and the decision to donate embryos for this research.
- Investigators who propose to use human pluripotent stem cells from fetal tissue will be expected to follow both the *Guidelines* and all laws and regulations governing human fetal tissue and human fetal tissue transplantation research.
- The *Guidelines* require that the informed consent specify whether or not information that could identify the donor(s) will be retained.
- They require that the donation of human embryos or fetal tissue be made without any restriction regarding the individual(s) who may be the recipient of the cells derived from the human pluripotent stem cells for transplantation.
- They also require review and approval of the derivation protocol by an Institutional Review Board.
- The informed consent should include statements that the embryos or fetal tissue will be used to derive human pluripotent stem cells for research, that may include human transplantation research; that derived cells may be kept for many years; that the research is not intended to provide direct medical benefit to the donor; and, for cells derived from embryos, that embryos donated will not be transferred to a woman's uterus and will not survive the stem cell derivation process.

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- The informed consent must also state the possibility that the results of the research may have commercial potential, and that the donor will not receive any benefits from any such future commercial development.

Areas of Research Ineligible for NIH Funding

As required by law, NIH funds cannot be used for the derivation of pluripotent stem cells from human embryos. The *Guidelines* also set forth several other areas of research that are ineligible for NIH funding, including: 1) research in which human pluripotent stem cells are utilized to create or contribute to a human embryo; 2) research utilizing pluripotent stem cells that were derived from human embryos created for research purposes; 3) research in which human pluripotent stem cells are derived using somatic cell nuclear transfer; 4) research utilizing human pluripotent stem cells that were derived using somatic cell nuclear transfer; 5) research in which human pluripotent stem cells are combined with an animal embryo; and 6) research in which human pluripotent stem cells are derived using somatic cell nuclear transfer for the purposes of reproductive cloning of a human.

Requirements for Investigators Applying for Funds

A request for NIH funds for research using these cells must include a signed assurance that the cells were derived from human embryos in accordance with the *Guidelines* and that the institution will maintain documentation in support of the assurance.

This assurance must also affirm that:

- The human pluripotent stem cells to be used in the research were, or will be, obtained through a donation or through a payment that does not exceed the reasonable costs associated with the quality control, processing, transportation, preservation, and storage of the stem cells.
- The proposed research is not a class of research that is ineligible for NIH funding.

Investigators must also submit:

- A sample informed consent document, with patient identifier information removed, and a description of the informed consent process along with documentation of IRB approval of the derivation protocol.
- An abstract of the scientific protocol used to derive human pluripotent stem cells along with a title of the research proposal that proposes the use of human pluripotent stem cells.

Ensuring Compliance with the *Guidelines*

Investigators requesting NIH funds for research using pluripotent stem cells will need to provide documentation that they are in compliance with the *Guidelines* prior to receiving NIH funds for this class of research. Submitted documentation will be reviewed by a newly-created NIH working group called the Human Pluripotent Stem Cell Review Group (HPSCRG).

Members of the working group will:

- Review documentation of compliance with the *Guidelines* for funding requests that propose the use of human pluripotent stem cells
- Advise the NIH Center for Scientific Review Advisory Committee (CSRAC) of the outcome of their review, which, if appropriate, will be approved by the CSRAC. This decision will be forwarded to the funding Institute or Center.
- Hold public meetings when a request proposes the use of a line of human pluripotent stem cells that has not been previously reviewed by the HPSCRG.

In no event will NIH fund research or allow existing funds to be used for research using human pluripotent stem cells derived from human embryos or human fetal tissue until the derivation protocol has received HPSCRG review and CSRAC approval. Continued compliance with the *Guidelines* is a term and condition of the NIH award.

Additional information about stem cells can be found on the NIH website at http://www.nih.gov/news/stemcell/index.htm (the final guidelines will be available on this site as soon as they are released).

NIH News Release - Wednesday, August 23, 2000

ISHAGE Fast Facts

ISHAGE currently has approximately 1100 member from 39 countries.

ISHAGE was founded in 1992.

ISHAGE 2001 will be the Seventh Annual Meeting of the Society.

ISHAGE is one of the two founding organizations for FAHCT - the Foundation for the Accreditation of Hematopoietic Cell Therapy.

Somatic Cell Therapy (SCR_X) Meeting Scheduled for May 2001

The Johns Hopkins University, ISHAGE and AABB will sponsor the 1st Annual Somatic Cell Therapy (SCR_X) Symposium on May 3-6, 2001, at South Seas Plantation, Captiva Island, Florida. What is SCR_X? In guidance documents updated by FDA in 1998, somatic cell therapy is defined as "the administration to humans of autologous, allogeneic or xenogeneic living cells which have been manipulated or processed *ex vivo*." Examples of somatic cell therapies include (but are not limited to) gene therapy/ engineering, implantation of cells to replace defective proteins, infusion of activated lymphoid cells, implantation of hepatocytes, pancreatic islet cells, myocytes, neural elements, hematopoietic stem cells, bone, cartilage and *ex vivo* expansion of various cellular components. Why SCR_X? With the derivation of pluripotent stem cells and their varied progeny - a whole new field is emerging. There are many similarities to the hematopoietic field and many institutions will no doubt integrate SCR_X research into existing or expanded stem cell GLP/GMP processing facilities. At present, the proposed regulations are broad and open to considerable interpretation. It is anticipated that more directed standards will be enacted by FDA in the next few years. This is an excellent opportunity for those working in the field of somatic cell therapy, including scientific, regulatory, societal and legal experts to come together, and discuss how best to structure and implement these guidelines. While this symposium will necessarily review many of the accomplishments in this field (derivation/culture of pluripotent stem cells, pancreatic islet cell culture, dermal grafts, etc.), there will be an emphasis on the scientific, regulatory, ethical and legal ramifications resulting from work in this field. This meeting will use two formats: didactic sessions run by leaders in the field of somatic cell therapy and workshops which will compare and contrast corporate vs investigator driven SCR_X approaches; one afternoon will be devoted to the technology while the other will deal with regulatory and legal issues. It is hoped that the workshop syllabus will aid the meeting participants in formulating guidelines and regulations in their specific areas. The organizing committee includes Steve Noga (chair), Janice Davis, Scott Burger, Scott Rowley, Andrew Pecora and Liana Harvath.

The major areas to be covered in the 1st meeting will be:

Somatic Cell Sources
- hematopoietic stem cells
- lymphoid cells
- stromal/mesenchymal cells
- bone/cartilage
- neural tissue
- pancreas/myocytes/hepatocytes

Genetic Engineering
- DNA recombinant materials
- Packaging/vector/cytokine production
- Various therapeutic approaches

***Ex Vivo* Expansion**
- Hematopoietic/pluripotent stem cells
- Lymphoid/dendritic cells
- Stromal/mesenchymal cells
- Other tissues

CME accreditation will be issued by The Johns Hopkins University (JHU). The first program mailing will be sent to ISHAGE and AABB members in November 2000. The announcement will also be found on the JHU CME website. I hope to see you in Captiva!

Stephen J. Noga

Ex Vivo Expansion - Current Issues

For the past decade or longer a number of investigators have explored the use of growth factors to expand various subsets of hematopoietic cells *in vitro*. The initial focus of preclinical studies was to attempt to expand the true pluripotent hematopoietic stem cell population, however, to date this has not been achieved. Therefore, studies have focussed on expanding committed progenitor cells and/or mature hematopoietic cell populations. At this stage it is important to consider the clinical need for expanded cell populations to understand what cell populations may be required to provide clinical benefit. The major clinical application for *ex vivo* expanded cells explored to date has been for cellular support of cancer patients receiving myeloablative high dose chemotherapy (HDC). There are three cellular sources routinely used to support patients receiving HDC including bone marrow (BM), mobilized peripheral blood progenitor cell products (PBPC) and cord blood (CB) cells.

Peripheral Blood Progenitor Cells

PBPCs are by far the most commonly used cellular graft and in the autologous and allogeneic setting these cells provide rapid recovery of neutrophils and platelets in approximately 9 and 14 days respectively. Patients receiving PBPC grafts have durable long-term engraftment. Therefore, investigators have evaluated the potential of *ex vivo* expanded cells to further shorten or potentially eliminate neutropenia and thrombocytopenia. A second potential advantage of ex vivo expanded autologous PBPC would be to provide a tumor free graft as some tumor cells (e.g. breast cancer cells) do not routinely survive well *in vitro* and therefore expansion cultures may provide a purging effect. Initial studies using ex vivo expanded autologous PBPC cells demonstrated that the cells could be safely infused but did not result in shortened time to neutrophil or platelet engraftment. However, recent studies by three groups have demonstrated a significant decrease in neutropenia when expanded PBPCs were transplanted. Paquette and colleagues from UCLA published in a recent issue of Blood that PBPC mononuclear cells expanded in a static 10-day culture in teflon bags with defined media supplemented with the combination of stem cell factor (SCF), granulocyte colony stimulating factor (G-CSF) and megakaryocyte growth and development factor (MGDF) reduced post-transplant neutropenia. Using the same static culture conditions and combination of growth factors to expand CD34-selected cells from PBPC, Reiffers and colleagues in Bordeaux and our own studies in Denver, have demonstrated a significant decrease in the period of neutropenia.

Bone Marrow

Ex vivo expansion of BM has been investigated as a method to eliminate the harvesting of BM under general anaethesia and to purge BM grafts of tumor cells. Starting with small aliquots of BM, studies by Stiff and colleagues from Chicago using the Aastrom expansion device, have demonstrated that 11 of 12 breast cancer patients (92%) transplanted with *ex vivo* expanded BM, remained progression-free at a median of 27 months post-transplant. The median time to neutrophil engraftment was 17 (range 13-24) days, and platelet engraftment was 26 (range 18-61) days. Three patients received their unmanipulated back-up product for platelet non-engraftment.

Umbilical Cord Blood

Cord blood (CB) cells are the third source of a cellular graft and provide an additional option for patients who are allogeneic transplant candidates and do not have a suitable BM or PBPC donor for allogeneic transplant. The periods of neutropenia and thrombocytopenia are longer in patients receiving CB compared to BM or PBPC and this has been shown to be related to the total number of nucleated cell per kg of the recipients body weight. This has limited the use of CB somewhat to smaller pediatric patients. Several groups have evaluated the *ex vivo* expansion of CB as a means of increasing the number of cells in a CB graft. Kurtzberg and colleagues from Duke University and Stiff and colleagues from Loyolla University have expanded CB using the Aastrom device. We have expanded CD34-selected CB cells at the University of Colorado using teflon bags and the same growth factors and culture conditions described above for PBPC. All of the studies to date have demonstrated expansion of total nucleated cells and progenitor cells but infusion of these cells has not resulted in any improvement of the time to recovery of neutrophils or platelets. However, the patients transplanted with expanded CB cells have engrafted neutrophils and platelets in the same time frame as smaller pediatric patients who received substantially larger cell doses of unexpanded CB cells. Further studies are needed to define the optimal conditions for expansion of CB.

Limitations of Clinical Studies of *Ex Vivo* Expanded Cells

Despite the encouraging data being published on clinical applications of *ex vivo* expanded PBPC there are still major

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barriers to be overcome in moving this technology forward. Access to clinical grade growth factors for use in the *ex vivo* culture has been one of the major issues. The need for combinations of growth factors has been limited by the requirement for supply by two or more pharmaceutical companies that are unable to reach agreements between each other. This has limited the combinations of growth factors that have been used clinically. Some studies in Europe have use research grade growth factors however, to date no studies have been approved by the FDA in the United States, using research grade growth factors. In addition the cost of research grade growth factors may be prohibitive, particularly for expansion of PBPC that require 10 liters or more of culture media due to the high numbers of cells. Therefore to date the combinations of growth factors available for clinical use has been limited and the optimal combination of growth factors still needs to be defined.

In protocols utilizing $CD34^+$ cells as the starting population, cost of the separation devices and reagents becomes a major issue. A single CD34-selection costs approximately $5,000 to $6,000. For PBPC expansion protocols, several selections may be required. In our experience the higher the purity of $CD34^+$ cells in the starting population the better the expansion. Higher purities also result in more consistent expansion from product to product. Using the Isolex 300i for selection of $CD34^+$ cells from CB products we have had a number of separations with only 10 to 30% purity and these products have performed poorly in expansion culture. Approaches such as the protocol of Paquette and colleagues, using mononuclear cells from PBPC, may overcome this problem for PBPC however, no data has been published for expansion of mononuclear cells from CB.

As a closed culture system is optimal for clinical expansion protocols, bags have been widely used. This enables the use of transfer couplings which eliminate any "open" processing of the cells and minimize the possibility of contamination. The American Fluoroceal teflon bags have been used by a number of groups, but Nexell Therapeutics also manufacture bags suitable for clinical applications. An alternative approach is the use of continuous media exchange such as the device developed by Aastrom. However, to date access to this device has been limited to a few investigators and no comparison has been performed between this system and the cultures in bags.

Other variables in expansion cultures include media and sera, with some protocols using defined serum free media while some protocols utilize media supplemented with fetal calf serum (FCS). Comparison of results to date with different media plus or minus FCS is difficult due to the use of different combinations of growth factors in the different studies. A number of companies are working on formulations of defined serum free media and controlled clinical studies will bee needed to compare these media in the future.

Finally a major issue to be considered is the requirement for good manufacturing procedures (GMP) cell processing facilities. What will the FDA require for generation of expanded cell products? *Ex vivo* expanded cells are considered as more than minimally manipulated products and currently, and will continue to, require IND applications and licensing approval. As the expanded cells are considered a manufactured product, release criteria and product specifications need to be considered carefully.

In summary, there is emerging data demonstrating clinical applications of *ex vivo* expanded cells. It is clear that the optimal culture conditions, including growth factor combinations, have not been defined and future clinical studies are needed. Access to reagents and the costs of performing the clinical studies remains a major problem that is currently limiting the studies being undertaken.

Ian McNiece and Elizabeth J. Shpall

Report on the HSANZ/WAA Meeting

The annual scientific meeting of the Haematology Society for Australia and New Zealand (HSANZ) and the Australasian Society for Blood Transfusion (ASBT) was combined this year with the 8th Congress of the World Apheresis Society (WAA). The meeting was held in Perth, Western Australia and also attracted other satellite meetings such as the annual meeting of the Bone Marrow Transplant Scientist's Association of Australasia (BMTSAA) and a meeting sponsored by the Therapeutic Goods Administration (Australia's FDA equivalent) on Blood Safety and Supply; the latter two meetings unfortunately coinciding on the same day. There was much to interest those with an abiding love of blood cells. Because of obvious space limitations I will focus on laboratory and pre-clinical information presented at the meetings.

The BMTSAA meeting began with a presentation on the development and operation of the NIH's laboratory facilities for cell processing by Dr. Elizabeth Read. Dr. Read was able to elicit information from the audience as to how many similar centres were available in Australia, whilst the audience asked detailed questions about the frequency of positive microbiology in long term cultures, surface and environmental microbiology of the critical areas in the facilities and questions about the environments for gene transfer as opposed to cell culture. Professor Derek Hart (Mater Hospital, Queensland) discussed the identity, function and opportunities for use of dendritic cells (DC) in immunotherapy, whilst co-workers in Sydney discussed the search for predictable days for high potency DC collections from patients with myeloma using G-CSF, GM-CSF or IL3/G-CSF. Using standard assays (based upon CMRF44) sequential days of testing could not reveal an optimum time for collections however flt3-L was flagged as an obvious candidate for mobilisation. Other highlights were the studies of by Dr. Rice using factorial analysis to uncover optimal cytokine combinations to expand viable, antigen-receiving DC from cryopreserved cord blood $CD34^+$ cells.

The focus upon DC progressed through to the HSANZ meeting with similar presentations reporting the benefits of isolation of DC by selection (rather than expansion), overviews on the clinical use of DC preparations, posters on late rebounds in DC numbers (day 18+) post GCSF mobilisation and again post transplant. The Papers presented at the Presidential Symposium included evidence that various subsets of fresh and cryopreserved cells, separated by number of divisions using CFSE, could be expanded from cord blood and maintained engraftment potential when tested in the NOD-SCID mouse model (Dr. Julia Wood, et al).

There were also some presentations which weren't about DC. Scott Ragg reported at the BMTSAA meeting that there was life in the bottom of our freezers: products stored over an average of 10 years not only demonstrated adequacy for transplantation, but in some cases cells previously claimed to be unsuitable for transplantation could be shown to be suitable using modern criteria. Dr. Annabella Chang reported that whilst $CD34^+$ quality assurance suggested that single-platform methods were optimal, only a minority of centres were doing this routinely. Dr. Chang also canvassed the need to routinely incorporate viability into CD34 testing, especially with overnight stored collections of blood stem cells. Dr. Julie Campbell (HSANZ meeting) reported how she made 2 cm lengths of blood vessel in rabbit peritoneum using polyethylene 'seeds' and demonstrated that these everted living tubes could operate as blood vessels, and the source of the tube-forming myofibroblasts was bone marrow.

The WAA meeting brought a wider perspective onto the scene, with many presentations highlighting the range of available novel apheresis technologies as well as advancements with the existing technologies in providing efficient blood stem cell collections with reduced contamination with platelets. Dr. Jeane Hester spoke of both the origins and history of apheresis as well as the prospects of new or re-appraised cellular therapies. Presenters at the WAA meeting highlighted the role of apheresis in cellular therapies, and Dr. Harvey Klein discussed the benefits of performing virus-mediated gene therapy in an ex-vivo setting as well as reviewing recent successes in gene therapy.

The ASBT meeting closed with a session on the TGA's new interests in regulation of fresh cells (as opposed to their prior interest being limited to plasma and certain banked tissues). Dr. Read spoke of the evolution of hematopoietic stem cell standards arising from the AABB and FAHCT which obviously had implications on how Australia may approach self-regulation in this area. Discussion arose about the costs of compliance, and about the difficult issues of processing and banking virally seropositive collections. The TGA's own sponsored meeting provided much controversy, little of which was directly applicable to cellular therapeutics, however there was much about risk-management in public health, advances and retreats in blood safety testing as well as models for cost effectiveness for these technologies.

Overall, these interlocked (and sometimes competing) meetings covered an unexpectedly broad scope of cell therapies, including basic science, as well as device and technology specific developments (CliniMACS, Isolex studies) as well as all aspects of processing from collection through to clinical outcomes.

Dominic Wall

Tech Talk…Discarding Old Products

What to do with all of those products! If you are like us, many of the products in your liquid nitrogen tanks have been stored for years, and are unlikely ever to be used. Without a consent to discard products, or a receiving facility to which to send products, what can we do? In this issue of Telegraft, we will try to address some of these dilemmas, or at least share our woes, though we by no means pretend to have the answers.

Various Product Categories

Products to be discarded may be allogeneic or autologous, and seem to fall into four categories: 1) back-up products, 2) products containing inadequate cell dose, 3) products intended for infusion but not used, and 4) products collected for patients who have since died. Undoubtedly there are many other reasons why the cell engineering laboratory acquires products that would be better discarded.

Back-ups generally are collected as part of investigational treatment protocols, when there is risk of non-engraftment. Happily, however, these patients do engraft, but paradoxically this creates a problem for the laboratory. Without physician or patient consent for eventual product discard, the laboratory continues to store these back-up products. Other products will have been collected for a specific process, such as CD34 selection, but after collection failed some process continuation criterion. These products, despite containing an inadequate dose, or or some other limitation, will have been cryopreserved to buy time while a new plan was developed. Our third category includes products that were collected with full intent to infuse, but for which the procedure was cancelled for some reason. The patient may have failed protocol criteria at the last minute, or may have relapsed before the transplant. Products stored for patients who have died may be discarded after the laboratory obtains a certificate of death, and the physician involved signs off. The cell engineering laboratory may offer the product to the physician's research laboratory, provided the physician has IRB approval.

Consent Forms and SOPs

Certainly, hindsight is a helpful thing. Our consent forms and SOPs now specify that back-up products will be stored for one year. At the end of this time, the patient or physician may choose to have the product sent to another storage facility or discarded by the laboratory. This does not simplify life completely, of course. One can spend numerous hours locating wandering physicians to follow up on patients, or to obtain permission to ship the back-up product. We have sent patients certified letters requesting permission to discard products. This is emotionally not a simple situation for the patient, however, some of whom are reluctant to see the product discarded out of the hope that storing it somehow wards off the possibility that it will be needed. The next task is to arrange for the receiving facility to accept the product. Here at least one is dealing with another laboratory, so communication and mutual understanding is more likely. Even so, not many laboratories welcome products that will sit forever in their storage tanks.

The most difficult problem is what to do with those products collected under the old consent forms and SOPs, when there was no provision for discarding the product. Does the laboratory have the right to discard these products simply because they have changed their SOP? Attorneys at several hospitals were no help at all, either declining to give an opinion, or else voicing the unhelpful but very legal view that it would really be best never to discard anything, and please don't bring this up in the future, thank you.

One possibility that may work for very old products is to thaw a sample bag or cryovial, and measure cell viability, number, $CD34^+$ cells, and CFU-GM. If the dose or number of viable cells, $CD34^+$ cells, or CFU-GM is below a predetermined, fairly low threshold, it is not too difficult to obtain the patient's and physician's permission to discard the product. If above, then one must obtain permission to discard or ship the product, or to retain it in storage for a fee. Clearly, though, no one has a simple solution to this vexing problem. We welcome suggestions!

Scott Burger and Kathy Loper

ISHAGE Year 2000 Corporate Members

ISHAGE wishes to thank its year 2000 Corporate Members for their support. They are:

- Amgen Inc.
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- Systemix Inc.

ISHAGE Corporate Memberships for 2001 are now being sold. For further information contact the ISHAGE Head Office by phone at 604.874.4366 or email at headoffice@ishage.org .

Accreditation Renewals

The first transplant programs to earn FAHCT-accreditation are approaching their renewal dates for certification. FAHCT-accreditation is valid for three years. Programs required to renew their accreditation will receive a renewal registration form, an inspection checklist and a list of required documentation six months prior to their expiration date.

Cord Blood Inspections

The NETCORD-FAHCT "International Standards for Cord Blood Collection, Processing, Testing, Banking, Selection and Release" were published in June 2000. The first training of cord blood inspectors was held in San Diego, California at the annual ISHAGE meeting. Currently, a cord blood bank mock inspection will be conducted in November. At that time inspectors will complete a checklist and develop the guidance manual to accompany the standards. Inspections of cord blood banks will begin in January 2001.

Inspector Training

The next inspector training course will be held on February 14, 2001 in Keystone, Colorado at the Tandem BMT Meetings of ASBMT and IBMTR/ABMTR. Individuals interested in participating should contact the FAHCT Office for registration materials.

Accredited Facilities

Forty-seven BMT centers have earned voluntary FAHCT accreditation in the following categories:

Autologous peripheral blood progenitor cell transplantation, including collection and laboratory processing:
- Baptist Cancer Center/Response Oncology, Memphis, TN
- Baystate Medical Center, Springfield, MA
- Cancer & Hematology Centers of Western Michigan, Grand Rapids, MI
- Cancer Institute of New Jersey/Robert Wood Johnson University Hospital, New Brunswick, NJ
- Fox Chase Cancer Center, Philadelphia, PA
- Holy Cross Hospital, Silver Spring, MD
- IMPACT Center of Middle Tennessee, Nashville, TN
- Marshfield Cancer Center, Marshfield, WI
- Northwest Ohio Stem Cell Transplant Program, Toledo, OH
- Our Lady of the Lake Regional Medical Center, Baton Rouge, LA
- Providence Portland Medical Center, Portland, OR
- University Medical Center, Lubbock, TX
- Via Christi Regional Medical Center, Wichita, KS

Autologous marrow & peripheral blood progenitor cell transplantation, including collection and laboratory processing:
- Memorial Medical Center, New Orleans, LA
- SUNY Upstate Medical University, Syracuse, NY

Just the FAHCTs

Autologous peripheral blood progenitor cell collection, marrow and peripheral blood progenitor cell transportation, processing and storage:
- Pacific Northwest Regional Blood Services, Portland, OR

Allogeneic & autologous peripheral blood progenitor cell transplantation, including collection and laboratory processing:
- University of Chicago, Chicago, IL

Allogeneic & autologous peripheral blood progenitor cell collection, marrow and peripheral blood progenitor cell transportation, processing and storage:
- The Canadian Blood Services, Ottawa, Ontario, CAN

Allogeneic & autologous peripheral blood progenitor cell collection, progenitor cell processing, cryopreservation, transport and storage:
- New York Blood Center, Valhalla, NY

Allogeneic & autologous marrow and autologous peripheral blood progenitor cell transplantation, including collection and laboratory processing:
- Children's Hospital of Philadelphia, Philadelphia, PA

Allogeneic & autologous marrow, peripheral blood progenitor cell transplantation, including collection and laboratory processing:
- Baylor University Medical Center, Dallas, TX
- Cardinal Glennon Children's Hospital, St. Louis, MO
- Children's Hospital/Dana-Farber Cancer Institute Pediatrics Hematopoietic Stem Cell Transplantation Program, Boston, MA
- Children's Memorial Hospital, Chicago, IL
- Christiana Care Health Services, Newark, DE
- Dana-Farber Cancer Institute/Brigham and Women's Adult Hematopoietic Stem Cell Transplant Program, Boston, MA
- Fox Chase-Temple Bone Marrow Transplant Program, Philadelphia, PA
- H. Lee Moffitt Cancer Center, Tampa, FL
- Hackensack University Medical Center, Hackensack, NJ
- Indiana Blood and Marrow Transplantation, Indianapolis, IN
- Rush Presbyterian - St. Luke's Medical Center, Chicago, IL
- Stanford University Medical Center, Stanford, CA
- Texas Transplant Institute, San Antonio, TX
- Tulane University Medical Center, New Orleans, LA
- University of Alabama at Birmingham, AL

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- University of California, San Diego, CA
- University Medical Center, Tucson, AZ
- University of Minnesota Hospital, Minneapolis, MN
- University of Pittsburgh Cancer Institute, Pittsburgh, PA
- University of Texas, MD Anderson Cancer Center, Houston, TX
- University of Utah Health Sciences, Salt Lake City, UT
- Wayne State University/Karmanos Cancer Institute, Detroit, MI

Allogeneic & autologous marrow, peripheral blood progenitor cell and cord blood cell collection, processing and transplantation:

- UCLA Hematopoietic Stem Cell Transplant Program, Los Angeles, CA
- University of Louisville Blood and Marrow Transplant Program, Louisville, KY

Allogeneic & autologous marrow and peripheral blood progenitor cell transplantation, including cell collection and processing, and allogeneic human cord blood collection, transportation and storage in association with the Civitan Regional Blood Center:

- Shands Hospital - University of Florida, Gainesville, FL

Allogeneic & autologous marrow and peripheral blood progenitor cell transplantation, including bone marrow collection, and also the PBPC collection and laboratory processing services provided by contract with the Canadian Blood Services:

- Ottawa General Hospital, Ottawa, Ontario, CAN

Progenitor cell transportation, processing and storage of products for more than one clinical program:

- Progenitor Cell Therapy, Cellular Therapy Laboratory, Hackensack, NJ

Linda Miller

Foundation for the Accreditation of Hematopoietic Cell Therapy

FAHCT Accreditation Office: (402) 595-1111
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Facilities Registered	183
Facilities Inspected	117
Accredited	47
Inspected/Pending Accreditation	70
Inspections in Process	17
Facilities Completing Checklists	49
Inspectors Trained	306

Upcoming Meetings

ISHAGE GMP 2000 Workshop. November 30, 2000. San Francisco, California. Contact:ISHAGE Head Office, 777 West Broadway, Suite 401, Vancouver, BC, Canada, V5Z 4J7. Tel: 604-874-4366; Fax: 604-874-4378. E-mail: ishage@malachite-mgmt.com; Website: www.ishage.org

42nd ASH Annual Meeting. December 1-5, 2000. San Francisco, California. Contact: The American Society of Hematology, 1900 M Street NW, Suite 200, Washington, DC, USA, 20036. Tel: 202-776-0544; Fax: 202-776-0545; E-mail: ASH@hematology.org; Website: www.hematology.org

3rd International Symposium on Minimal Residual Cancer. February 16-18, 2001. Hamburg, Germany. Contact: CPO Hanser Service, PO Box 1221, D-22882 Basbuttel. Tel: +49.40.670.88.20; Fax: +49.40.670.32.83. E-mail: hamburg@spo-hanser.de; Website: www.mrc-symposium.de.

Mesenchymal and Nonhematopoietic Stem Cells Meeting. March 22-24, 2001. Hyatt Regency Hotel, New Orleans, Louisiana. Meeting information, registration and abstract forms available soon at www.ishage.org. For further information, contact: Edwin Horwitz, MD, PhD, St. Jue Children's Research Hospital, 332 North Lauderdale, Memphis, TN, USA, 38015. Tel: 901-495-2746; Fax: 901-495-2176; E-mail: edwin.horwitz@stjude.org.

The 9th Annual International Symposium on Recent Advances in Hematopoietic Stem Cell Transplantation. March 29-31, 2001. San Diego, California.

Somatic Cell Therapy Meeting & Workshop. May 3-6 2001. Captiva Island, Floria. Contact: Office of Continuing Medical Education, Johns Hopkins University School of Medicine, Turner 20, 720 Rutland Avenue, Baltimore, MD, USA, 21205-2195. Tel: 410-955-2959; Fax: 410-955-0807. Email: cmenet@jhmi.edu; Website: www.med.jhu.edu/cme.

7th International ISHAGE Annual Meeting. June 14-17, 2001. Quebec City, Quebec, Canada. Contact: ISHAGE Head Office, 777 West Broadway, Suite 401, Vancouver, BC, Canada, V5Z 4J7. Tel: 604-874-4366; Fax: 604-874-4378. E-mail: ishage@malachite-mgmt.com; Website: www.ishage.org

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Telegraft Editorial Board

Mesenchymal and Nonhematopoietic Stem Cells

Recent Progress and Current Controversies

March 22-24, 2001
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New Orleans, Louisiana, USA

ISHAGE

CHAIRS: Edwin Horwitz, MD, PhD; Brian Butcher, PhD; Darwin Prockop, MD, PhD; Armand Keating, MD, FRCP(C); Malcolm Brenner, MB, PhD, FRCP, FRCPath

KEYNOTE SPEAKER: John Gearhart, MD, The Johns Hopkins University Medical Center, Baltimore, Maryland

SESSION I

Characterization of Mesenchymal Stem Cells/Marrow Stromal Cells (MSCs)
Paul Simmons, PhD - Peter MacCallum Cancer Institute, Melbourne, Australia
James Triffitt, PhD - University of Oxford, Oxford, United Kingdom
Don Phinney, PhD - Tulane University Health Sciences Center, New Orleans, LA
Gary Stein, PhD - University of Massachusetts, Worcester, MA
Catherine Verfaillie, MD, PhD - University of Minnesota, Minneapolis, MN
Pamela Robey, PhD - National Institutes of Health, Bethesda, MD
Alan Flake, MD, PhD - Children's Hospital of Philadelphia, Philadelphia, PA
Paul Schwarzenberger, MD - Louisiana State University Health Sciences Center, New Orleans, LA

SESSION II

Clinical Trials
Edwin Horwitz, MD, PhD - St. Jude Children's Research Hospital, Memphis, TN
Armand Keating, MD, FRCP(C) - Princess Margaret Hospital and the University of Toronto, Toronto, ON, Canada
Stanton Gerson, MD - Case Western Reserve University, Cleveland, OH

WORKSHOP I

Effects of Systemic Infusion
Chair: Malcolm Brenner, MB, PhD, FRCP, FRCPath

WORKSHOP II

Characterization of MSCs
Chair: Armand Keating, MD, FRCP(C)

SESSION III

Therapy of the Central Nervous System
Evan Snyder, MD - Children's Hospital of Boston, Boston, MA
David Panchision, PhD, National Institutes of Health, Bethesda, MD
Darwin Prockop, MD, PhD - Tulane University Health Sciences Center, New Orleans, LA

SESSION IV

Therapy of Skeletal and Cardiac Muscles
Kathy Jackson, PhD - Baylor University Medical Center, Houston, TX
Emanuela Gussoni, PhD - Division of Genetics, Children's Hospital, Boston, MA

SESSION V

Clinical Use of the Cells
Adrian Gee, PhD - Baylor University Medical Center, Houston, TX
Malcolm Brenner, MD, PhD - Baylor University Medical Center, Houston, TX

Sponsored by: Tulane University Health Sciences Center, St. Jude Children's Research Hospital and the International Society for Hematotherapy and Graft Engineering (ISHAGE)

Meeting information, registration,hotel and abstract forms may be downloaded from the ISHAGE website at www.ishage.org. For further information contact Edwin Horwitz, MD, PhD, St. Jude Children's Research Hospital, 332 North Lauderdale, Memphis, TN, USA, 38105. Tel: 901-495-2746; Fax: 901-495-2176; Email: edwin.horwitz@stjude.org.

ISHAGE.ORG REPORT

Over the past several months there have been significant changes to the ISHAGE website (www.ishage.org) that warrant a moment of surfing to explore. To give you a taste, here are a couple of the changes:

1. An online membership directory available for members only.

   Members are listed alphabetically and alphabetically by country. Included is contact information for each member that would otherwise exist in a printed directory. A search engine is also provided. For username or password information use the email link provided.

2. Improved ISHAGE committee sites.

   Each ISHAGE committee has a sub-site. The Legal & Regulatory Affairs and Gene Therapy committees have had very informative sites for some time. Recently, the Tumor Evaluation committee and particularly the Graft Evaluation committee have put up information that is definitely worthy of viewing.

   Enhanced online membership services include the following:

   - Members may now renew their membership as well as provide change of address notification by using the membership form on the site.
   - Information on ISHAGE meetings, ISHAGE-affiliated meetings, and other upcoming meetings is now available on the site.
   - The Call for Nominations Form for the ISHAGE 2001 elections is available on the site for members to print, fill-in and submit by fax.
   - Employment advertisements (typically posted for two-month periods).

Watch for the ISHAGE 2001 site, complete with program, meeting registration, and abstract information to appear in the upcoming months.

ISHAGE considers its website to be an important tool for communication both with and between its members. We encourage you to use the Discussion Lounge, visit the site regularly, and forward your suggestions for the site to the Head Office (headoffice@ishage.org).

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BMT Technologists

The BMT Technologists will be responsible for performing various cell processing procedures including, but not limited to, cell counting, buffy coat and MNC preparation, purging, cryopreservation and infusion. The exact level of the open positions will be dependent upon the applicants previous experience. Medical Technologist or a bachelor's degree in a scientific related field and at least 1 year experience in hematopoietic cell processing is required. Knowledge of flow cytometry, apheresis or blood banking would be beneficial.

Flow Cytometry Supervisor

The Flow Laboratory performs cell analysis for the BMT clinical protocols and research studies. The supervisor will be responsible for general work flow of the lab, maintaining our CAP accreditation, and interacting with investigators to develop appropriate antibody panels for the clinical studies. Ideal candidate will possess a bachelor's degree in a scientific related field with at least 5 years of experience in Flow Cytometry.

In return for your expertise, we offer a competitive salary and a comprehensive benefits package. Interested candidates should send resumes by e-mail: ***rortiz@notes.mdacc.tmc.edu*** *(no attachments please) or mail to:* ***Attn: R. Ortiz, Human Resources, 1515 Holcombe Blvd., Box 205, Houston, TX 77030.*** *Reference code* ***ISHAGE1100*** *when applying. EEOE/Smoke-free environment.*

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Stem Cell Technologist

The Hematopoietic Stem Cell Laboratory at the University of Utah is accepting applications for an individual to work in a stimulating, FACHT-approved, laboratory performing innovative cellular therapies. Our laboratory supports a Pediatric and Adult Stem Cell Transplant Program and the Huntsman Cancer Institute. We specialize in apheresis, cryopreservation, T cell depletion, positive and negative selection and other novel cellular therapies.

We offer flexible hours and excellent educational opportunities. The successful candidate must possess an MT(ASCP) or Bachelors Degree in science or a related field. Previous experience in hematopoietic progenitor cell processing preferred. Experience with cell culture, gene therapy, GMP quality control and flow cytometry highly desirable.

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