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ISCT TELEGRAFT

International Society for Cellular Therapy
ISCT

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CONTENTS

New Australian legislation for accessing embryos and regulating the formation of embryonic stem cells for research and cell therapies

THE COMMONWEALTH OF AUSTRALIA HAS PASSED LEGISLATION that directly affects the formation of embryonic stem (ES) cells after a long and at times, bitter, debate in December 2002. The debate was free of political party directions and members of both Houses of Parliament were allowed a conscience vote. The eventual voting pattern of members of Parliament generally reflected the Australian community's views as reflected in recent Gallup polls of attitudes towards research involving ES cells.

The legislation was split into two Bills – the "Prohibition of Human Cloning Bill 2002" and the "Research Involving Embryos Bill 2002". The former addressed the formation of human embryos by procedures other than fertilization by sperm and effectively bans the deliberate initiation of embryogenesis by any other method. This would include parthenogenetic activation (chemical or electrical activation of eggs to form embryos), nuclear transfer (used for embryonic or somatic cell cloning) and embryo splitting (mechanical division of an embryo to produce twins).

More specific items of the "Prohibition of Human Cloning Bill 2002" specifies that it is a criminal offence to produce an embryo that is genomically identical to an already formed person. This prevents any research on exploring the merit of "therapeutic cloning" for producing ES cells for a person with a severe pathology or injury. The intention would be to produce cells or tissues that are completely compatible for transplantation to the patient. This would require the injection of the nuclei of the patient's cells (eg. skin cells) into donated human enucleated oocytes (eggs) to form an embryo for a brief period of time (~5-6 days). The Bill goes further to ban the genetic alteration of a human cell that could result in the inheritance of the alteration in the germ line. Other aspects of this Bill reinforce the objective to prevent either "reproductive" or "therapeutic cloning" and any commerce in trading of human gametes or embryos.

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New Australian legislation for accessing embryos **continued**

How would this affect the application of cell therapies involving derivatives of ES cells? The technique termed therapeutic cloning or Nuclear Transfer of Somatic Cells (NTSC) has been shown in proof of concept studies to generate stem cells capable of colonising all tissues of the body and reverse genetic disease. Hence this technique is potentially important for cell therapies and is strongly supported by many scientists and patients seeking therapies (eg. Christopher Reeve is a strong advocate for "therapeutic cloning"). The problem for this strategy is the large number of human oocytes required to produce an ES cell line (presently 30-100 or more are needed for each ES cell line). It is difficult to see the sustainability of this strategy. There are other options that are being actively explored and these include: somatic cell fusion with ES cells; ES cell cytoplasmic transfer; and the induction of immunological tolerance to foreign histocompatibility types. This Bill also bans the production of ES cells from donors with specific genetic and pathological disorders that may be useful for drug discovery to treat these conditions – a concern raised by some scientists.

The other Bill – "Research Involving Embryos Bill 2002" allows research on human embryos subject to a number of conditions. Embryos excess to the needs of couples treated by artificial reproductive technologies (ART) that includes in vitro fertilization (IVF), may be used for research under the terms of a license obtained from the National Health and Medical Research Council's Licensing Committee. The license is subject to a number of conditions including that use for research is authorised only in respect of an embryo created before 5 April 2002, if the research may damage or destroy the embryo. Embryos cannot be created for research and may only be formed for the intentions of achieving a pregnancy.

Under this Bill, excess embryos – perhaps 10% of those stored frozen prior to 5 April 2002 (around 70,000) may qualify. The couple must consent to such research. This may allow 2,000-4,000 excess embryos for all license submissions for embryo research. In reality, there may only be a few hundred available for forming ES cells in any year. While it is not possible to be certain how many of these frozen embryos are chromosomally normal (~ 50%) and capable of developing to blastocysts (~ 30%) – in reality it is likely that there will be few embryos that will form ES cells from those available under the license conditions. Perhaps up to 10 ES cell lines could be formed annually. This is a very small resource for a very major endeavour in research towards cell therapies. New methods are urgently needed to expand the ES cells formed to provide researchers with a reasonable quantity of cells for their work.

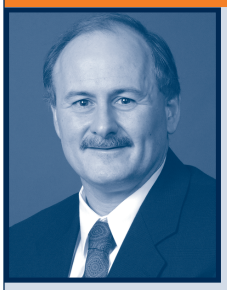
Nevertheless, the Bill on Research Involving Embryos provides the opportunity to derive new ES cell lines without animal cell contamination and under GMP conditions. This is an important step in the direction of providing pluripotent stem cells for research and will raise the hopes that severe conditions of tissue failure and damage may eventually be treated by cell therapies.

It is recognised by the scientific and medical community that the use of human embryos for therapeutic purposes raises ethical concerns for some members of the community. The onus is now on the researchers to show that the donation by couples of their excess IVF embryos will improve the quality of life, or save the lives of sick people. The merits of the humane donation of embryonic cells from embryos that would otherwise be disposed of should be recognised as equivalent to the value of conventional tissue donation under circumstances where needs are clearly demonstrated. The Parliamentary debates on these matters were focused for the large part, on this issue.

Mirror image legislation is proposed for all States of the Commonwealth of Australia with a review of the legislation after three years. If it can be shown that "therapeutic cloning" is essential for the application of stem cell therapies and/or larger numbers of ES cell lines are needed for specific differentiation pathways and compatibility for transplantation, the issues will need to be debated again. Given the legislation now passed, it may be difficult to amend this. However, it is unlikely that all State and Federal Parliaments would block forever any successful treatments by cell therapies that may involve NTSC methods or importations of cells derived from such methods.

Professor Alan Trounson
CEO, National Stem Cell Centre, Australia

from the President's Desk



It seems that all I talk about lately in this column is regulations, standards and their respective agencies. Quite frankly, these are the major issues confronting the ISCT leadership over the next few years. While ISCT, itself, is searching for its unique identity among the various closely allied societies, we see similar happenings elsewhere – even within the FDA. While we were just acquainting ourselves with the new office of Cellular, Tissue and Gene Therapies within CBER, FDA announced that CBER Director, Dr. Kathyrn Zoon was transferring to a new position at NIH and that Dr. Jesse Goodman was assuming the Directorship. This was on the heels of major changes within the CBER and CDER structure with a resultant transfer of $33 million from the CBER budget over to CDER. Products (and a resultant 213 FTE's) transferred over to CDER included therapeutic monoclonal antibodies, cytokines, growth factors, enzymes, etc. Efforts are currently underway to reintroduce ISCT to the FDA leadership. Not everything has changed in this regard. Long term contact, Dr. Phillip Noguchi is Director of the Office of Cellular, Tissue and Gene Therapies and together with Dr. Joyce Frey, have helped us understand the current regulatory environment. In fact, we are pleased that Joyce has agreed to head up a regular column in the ISCT Telegraft. Her insight and knowledge are invaluable to our organization. Also of interest, the FDA has delayed the Human Cells, Tissues, and Cellular and Tissue-Based Products registration by 1 year (January 21, 2004). FDA states this was necessary because the numerous comments received prevented finalization of the rule by January 21, 2003. This rule will not go away so hopefully those who have procrastinated up to the present time will heed the warning and register.

As already mentioned, we are not the only society whose members are feeling the affects of regulation. Certainly our colleagues in AABB and ASBMT have both similar and disparate issues to contend with. In fact, ASBMT was instrumental in starting a Task Force on Regulatory and Legislative Relations to represent the common interests of those in the field of hematopoietic cellular therapy. In addition to ASBMT, the IBMTR, NMDP, FACT and ISCT were represented. The purpose is to represent common interests of all groups working in this area with regards to legislation, reimbursement, etc at the Federal level. While ISCT and several of the other societies' missions do not fully encompass the Task Force mandates, it is important that we be represented and included in issues important to our membership. A liaison position has been created to represent ISCT to this Task Force. In a similar manner, ISCT has appointed a liaison to both the AABB Cellular Therapy and Cellular Therapy Standard Committees. This nurtures the mutual ground these committees share with ISCT.

Lastly, as ISCT forms these liaisons and committees with other closely related societies, it becomes very apparent that ISCT must better define its mission, goals and ráison d'étre'. After all, how can we offer our position on various issues if our platform is not clear to our ISCT leaders – or members for that matter? It is becoming more apparent that what makes ISCT (and ISHAGE before it) most unique is that its members truly span the fields of translational research! At first, we were concerned with the new science of bone marrow transplantation. Our members participated in pioneering science and technological advances. The FDA had to grapple with devices for isolating a heretofore unrecognized cell population that was to be the only source of cells for hematopoietic reconstitution. No standards, measurements or long term outcome parameters existed at this time. ISHAGE members played key roles in helping define many of the standards and guidelines used by FDA in reviewing such IND's and IDE's. Hematopoietic graft engineering and manipulation became buzz words and ISHAGE members remodeled the playing field. Now, several societies have taken up this banner as a subset of their mission statements, thus the common interests leading to liaisons, etc. However, as we now move forward into the new frontiers of embryonic stem cell research, cellular engineering and clinical gene therapy trials, we again see our (ISCT) members playing pivotal roles in the translational research components of these studies. A retreat is planned among the ISCT leadership to more closely define our mission in this new century, so look for more on this around the time of the annual meeting.

As always, it will be a pleasure to see my colleagues in Phoenix. Don't be a stranger, come up and say "hello"!

Stephen J. Nogo

ISCT President

from the Editor's Desk

The field of cell therapy is flourishing as never before, with a dazzling array of novel therapies in development and clinical trials. With growing scientific sophistication and power, of course, have come increasingly stringent regulations and controls. Cell therapy laboratories have risen to these challenges admirably. Validation, documentation, and other fundamentals of GMPs and GTPs are growing more ingrained, improving control and consistency of cell therapy products, and accuracy and precision of our analytical methods.

The outlook is not all rosy, of course – witness the jarring news that our most widely used cryopreservation vessel will no longer be manufactured, or the immediate human impact of recent events in retroviral gene therapy. We have no shortage of challenges, but the cell therapy community is practiced at rising to the occasion.

Inevitably, progress brings a growing awareness of how far we have still to go. One example, much on my mind of late, is staff training. As increasing numbers of GMP/GTP cell therapy laboratories are planned or constructed, we face a growing need for staff trained both in clinical cell engineering techniques and in GMPs and GTPs. Currently, training is conducted in-house, with laboratories investing months in training new staff members. Informal training has given way to more carefully developed programs, as reflected in the development of a certification program for cell therapy laboratory staff. Even so, each laboratory bears a considerable burden in administering its training program. Further, an active GMP clinical laboratory is not the best classroom, nor is it an ideal practice environment. Then there is always the nightmare possibility that a newly trained staff member, in whom 6 or perhaps 12 precious months have been invested, will go elsewhere, leaving the laboratory to begin anew.

Training for residents and fellows, our future laboratory directors, also needs attention. One often hears from residents seeking advice about making a career in this exciting, intriguing field. How do they obtain subspecialty training? What fellowship programs are there? Typically, an interested resident may spend a month or two with the laboratory director and staff, read intensively, and later take a position as laboratory director, their education and training to be rounded out during their first year or two on the job. Occasionally a resident or fellow may spend 6 months or more in cell therapy, but this is uncommon.

One also hears from institutions searching for laboratory director candidates. In more established specialties, a fresh crop of newly-minted faculty candidates appears each July, their formal subspecialty fellowship training completed. Lacking this regular supply, cell therapy programs must hope to find a laboratory director ready to change institutions, or failing that, someone amenable to on the job training.

The ISCT GMP and GTP workshops are invaluable in educating and training laboratory staff, supervisors, and directors, and can reach beyond workshop participants through the didactic material on CD-ROM. Even so, there is much that cannot be included in a 1-2 day workshop. I am pleased to see on page 9 of this issue, a notice regarding a new Masters Program in Cellular Therapies. It is these kinds of programs that will hopefully begin to fill the training void.

The recent NIH Request for Proposals for Somatic Cell Therapy Processing Facilities may provide an opportunity to develop more extensive training programs for staff and directors, if this is given priority by the participating centers. Core training facilities, with programs providing didactic and practical training courses, would provide fundamental infrastructure for the further development of cell therapies. Similarly, formal fellowship programs in cellular therapy are needed, and could be based in the NIH-funded Somatic Cell Therapy Processing Facilities. All this would require substantial investments in time, effort, and resources, and close cooperation between institutions. A daunting challenge, but one that we can ill afford to ignore.

With this issue of Telegraft we begin a concerted effort in globe-trotting. In this issue we hear from cell therapy laboratories in Asia and Australia. The next issue is planned to emphasize cell therapy in Europe, after which we turn to North and South America, and then begin the tour anew. It's the International Society for Cellular Therapy, after all.

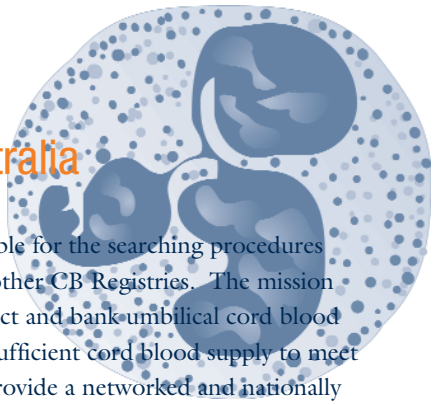
At present we are visiting Asia and Australia. Taira Maekawa, MD, DMSci, Professor of Medicine and Chairman of the Department of Transfusion Medicine at Kyoto University Hospital, tells us about the state of GMP cell processing facilities in Japan, and describes in particular the newly constructed Center for Cell and Molecular Therapy at Kyoto University Hospital. Makoto Yanagida, PhD, Senior Manager of the Cell Processing Center at Kirin in Gunma, Japan, discusses Kirin's Cell Processing Centers. Miles Prince, MD MRACMA FRACP FRCPA, Director of the Blood and Marrow Transplant Service at the Peter MacCallum Cancer Institute in Melbourne, has news about Embryonic Stem Cell legislation in Australia, as well as about the Therapeutic Goods Administration.

It wouldn't be Telegraft, of course, without the ever-useful Tech Talk column, or the update Just the FACTS, and naturally a preview of the programs for the GTP workshop and the annual meeting. All this and more. See you in Phoenix!

Scott Burger, MD
Telegraft Editor

AUSCORD

the National Cord Blood Banking Network of Australia



THE TRANSPLANTATION OF HAEMOPOIETIC STEM CELLS (HSC) IS WIDELY USED AS PART OF THE TREATMENT OF LEUKAEMIA, blood cell disorders, and other malignant and non-malignant diseases. Sources of HSC include bone marrow (BM), mobilised Peripheral Blood Stem Cells (PBSC) and, more recently, umbilical Cord Blood (CB). Each year a large number of patients are in need of a transplant of HSC from an allogeneic related (family) or unrelated donor. Allogeneic transplants are limited by the requirement for closely matching the patient and donor with respect to Human Leucocyte Antigen (HLA) expression in order to avoid severe immunological complications, in particular Graft versus Host Disease (GvHD). In the case of BM, about 30% of Australian patients have a suitable family donor. Of the remaining patients who search the worldwide BM donor registries for an unrelated donor only 20 to 30% proceed to receiving a transplant. The use of CB as a source of HSC has been shown to have the advantage of allowing a certain degree of HLA mismatching without increasing the risk of GvHD. This dramatically increases the chance of finding a suitable donor, the only limitation being the number of cells available in the CB donation (cells per kg patient body weight).

The efficacy of CB transplantation has now been well recognised and to date over 2,500 CB transplants have been reported worldwide. Early successes, more than a decade ago, triggered the establishment of cord blood banks worldwide currently containing over 100,000 CB Units (source: www.bmdw.org). Cord Blood can be collected immediately after childbirth, processed, tested, frozen and then stored for future use. The CB is then ready "off the shelf" and available on request for a transplant patient.

Cord blood banking in Australia commenced in 1995 by the Australian Cord Blood Bank at the Sydney Children's Hospital. This was followed by the establishment of the Bone Marrow Donor Institute National Cord Blood Bank at the Royal Children's Hospital in Melbourne (1996) and the Queensland Cord Blood Bank at the Mater Hospital in Brisbane (1998). The three cord blood banks (CBB) are networked under the name AUSCORD, while all CB data are centrally reported to the Australian Bone Marrow Donor Registry, which is responsible for the searching procedures and communication with other CB Registries. The mission of AUSCORD is "To collect and bank umbilical cord blood units in order to secure a sufficient cord blood supply to meet Australia's needs, and to provide a networked and nationally coordinated approach for the provision of suitably matched unrelated cord blood to patients requiring haemopoietic stem cell transplantation". It is estimated that a "stock" of about 20,000 cord blood units would provide >80% of Australian patients with a >5/6, and about 95% with a >4/6 HLA matched cord blood.

Currently the combined CBB's of AUSCORD have more than 6,500 CB Units listed on the Australian and international CB registries. AUSCORD is committed to providing safe and quality CB Units for transplantation. All CBB's have applied for accreditation by the Therapeutic Goods Administration (the Australian equivalent of the FDA). The quality approach not only applies to the specific CBB activities of donor selection, CB collection, processing and storage, but also extends to all (external) laboratories, companies and institutes that take part in the testing of CB including disease screening, tissue typing and stem cell testing. In addition, the FACT/NETCORD standards for CB banking have been taken into consideration to ensure international compliance.

With the increasing number of CB units banked, the AUSCORD CBB's are now effectively contributing in providing CB units to transplant centres. As at December 2002, 75 CB units have been released, 85% of these in the last 3 years. All AUSCORD CBB's operate on a not-for-profit basis, and are funded by the Australian Commonwealth, State and Territory Governments in combination with substantial financial support from individuals, community groups and charitable organisations.

Simon Bol (PhD)

Director
Bone Marrow Donor Institute National Cord Blood Bank
Royal Children's Hospital, Melbourne, Australia

From the Field: Kyoto University

GMP Cell Processing Facilities in Japan – status quo

Establishment of GMP-grade cell processing facility is mandatory to convert from basic research to clinical trials of advanced cell therapy. At the moment, in Japan, most medical centers and universities doing cell and gene therapy at last have come to recognize the importance of designing and building clinical laboratories capable of performing cell processing and viral vector production using current good manufacturing practice (cGMP) regulations. Unlike in the States, however, definite rules of cGMP-grade cell processing using human cell and tissue for advanced cell and gene therapy have not yet been issued by the Japanese government. Furthermore, few architects and engineers have sophisticated knowledge of how to appropriately design facilities for advanced cell and gene therapy. Of course, Japanese pharmaceutical companies have such knowledge, but for GMP-grade manufacturing of tablets or drugs. Cell processing for advanced cell therapy, using human tissues, is, however, quite different from the production of conventional pharmaceutical drugs.

My specialty is clinical hematology/oncology. Ten years ago, I was engaged in antisense research for hematological malignancies. At that time, no companies could make GMP-grade antisense compounds for clinical trials in Japan. Furthermore, there were no rules or systems for good clinical practices, or definite rules for informed consent for gene therapy, in Japan. Moreover, institutional review boards were not well organized. No infrastructures for translational research, or gene therapy clinical trials, existed in Japan at that time. Therefore, most clinical trials were performed outside Japan.

At the Institute of Medical Science, University Tokyo (IMSUT), I established the first cell processing facility for cell and gene therapy in Japan, in 1996. However, this first facility did not completely meet the criteria for GMP, so that we have improved and renovated it several times. In 1998, I visited several facilities in the States and discussed with many scientists and engineers how to design an appropriate facility for advanced cell and gene therapy. After I moved from IMSUT to Kyoto University in 2002, I again had to establish, with my colleagues, medical doctors, and technicians, a new cell and gene therapy facility named the "Center for Cell and Molecular Therapy" (CCMT), located in the university hospital. CCMT is approximately two hundreds square meters in width and has four rooms for cell processing. Temperatures of all refrigerators, CO2 levels in all incubators, airborne particle levels in all processing rooms, and temperatures and air pressures of all rooms can be monitored with a real-time system based in the monitoring room. We are now working to produce SOPs and other documents necessary to obtain ISO authorization. Within the year 2003, we are planning to commence cell processing for advanced immunotherapy and pancreatic islet cell isolation. In 2004 we may begin ex vivo culture of retina cells, inner ear cells, cardiac muscle cells, and other cell types.

To establish and operate an effective cell processing facility, it is mandatory to have good and close collaborations with medical doctors and researchers, technicians, pharmacists, engineers, GMP-consultants, and government officers. Since different participants come from different scientific, medical, technological, and political backgrounds, each must try to understand the other's point of view, and work with the same purpose, to produce novel cell and gene therapies for many patients with incurable diseases. Advanced cell and gene therapies cannot develop without effective and well thought out cell processing.

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From the Field: Kirin Cell Processing Centers

Production Department, Pharmaceutical Division
Kirin Brewery Co., Ltd.

Makoto Yanagida, Ph. D.
Investigational Product Security Manager

R&D activities of Kirin's pharmaceutical division are focused on kidney diseases, cancer, and immune-system/allergy-related diseases. Kirin has worked on the program of cell therapy to increase candidates in its product pipeline since 1998. Kirin has several cell therapy products in clinical trials or in preclinical development, including immunoselected cells produced using the CliniMACS cell selection device (licensed from AmCell), Provenge for the treatment of prostate cancer and Mylovenge for the treatment of multiple myeloma (licensed from and developing with Dendreon). With a view to the domestic development of cell therapy products, Kirin established its first Cell Processing Center (CPC) in Takasaki City (East Japan) in 2000, renovating a GMP facility that had been used for manufacturing investigational synthetic drugs. The second Kirin CPC was newly designed and constructed in Kobe City (West Japan) in 2002.

In Japan, the regulatory policy for cell therapy had been very ambiguous for a long time. However, the Japanese Ministry of Health, Labor and Welfare (MHLW) proposed a regulatory framework and core guidelines concerning cellular and tissue-based products during 1999-2000. According to the current regulation, good safety and quality of the products must be confirmed by MHLW through the review of submitted documents prior to IND application. Kirin gained the first green light for the confirmation of cellular products (Provenge and Mylovenge) in 2001 and started a clinical study of Mylovenge under IND in 2002.

The Takasaki CPC

The Takasaki CPC is located in the block adjacent to the Kirin Pharmaceutical Plant, where biotechnology products such as EPO (ESPO) and G-CSF (GRAN) are manufactured and released. The CPC is dedicated to GMP manufacturing and quality control of investigational cellular products for immunotherapy but is not eligible for gene therapy including vector production. Biological raw materials such as a leukapheresis product and peripheral blood are delivered into the CPC from a contract hospital and then the final product is released to the hospital and infused to the patient after clinical manufacturing.

The manufacturing and quality control of cellular products is performed in the "cell processing" designated space which is mainly comprised of four isolated cell processing rooms, three QC laboratory rooms and a material storage room. A large part of the building is reserved for future enlargement of the CPC. Material and personnel flows are carefully planned to prevent cross-contamination and mix-ups in every aspect of processing. The processing rooms are constructed with epoxy resin-based flooring, and surface-treated smooth walls and ceilings that are easily cleanable. Temperature and humidity are maintained approximately at 22°C and 40%, respectively.

Air quality is specified at class 10,000 in the aseptic processing rooms, where single-pass, terminal HEPA-filtered air is supplied under positive pressure. Cleaning, sanitization and environmental monitoring are performed regularly once weekly as well as each time rooms are used.

The areas for cell processing and material storage are equipped with ventilation and air conditioning systems, biological safety cabinets, carbon dioxide incubators, centrifuges, refrigerators, freezers, a central alarm system, etc. All instruments and equipments are regularly calibrated, validated, maintained and monitored. Each manufactured product is subject to quality control testing, including cell counts, cell viability, purity, potency and sterility. A radio-isotope facility shared with other groups also is available depending on needs for experiments. At present, the laboratory is staffed with 9 FTE facility members. All procedures are carried out with appropriate process control and documentation systems, including batch production records in compliance with GMP.

The Kobe CPC

Kobe City has made efforts to revitalize itself as an advanced medical industrial town since 1995, when it was badly damaged by a tragic earthquake. Kirin agreed with the idea of revitalizing Kobe City, and participated in the development project. The Kirin CPC subsequently was constructed in the compound of the Institute of Biomedical Research and Innovation (IBRI) last year. The CPC plans to promote the research and development of ex vivo cord blood stem cell expansion in collaboration with physicians, academic researchers and cord blood banks.

The facility is mainly comprised of two-line cell engineering suites, three QC laboratory rooms and a material storage room. These processing rooms are constructed and maintained based on similar policies to Takasaki CPC's. The CPC is still in the start-up stage. The construction of the facility, the installation of instruments and equipments and IQ/OQ have already been completed. The CPC is now working to prepare for actual operations, such as freeze/thaw of cord blood, CD34+ cell selection, cell culture/expansion, manufacturing and quality control, document control, and facilities management. Kirin aims to examine the clinical usefulness of expanded cord blood cells in the near future.

Tech Talk

Cord Blood Transplantation Where are we?

Several in our field were fortunate to have the opportunity to attend the CBER's Biological Response Modifiers Advisory Committee meeting on February 27, 2003 held in Silver Spring, MD. The agenda for the day focused on discussions regarding efficacy data for the use of minimally manipulated hematopoietic stem cells from placental/umbilical cord blood (UCB) for hematopoietic reconstitution. It was fascinating to observe the process. Oral presentations from leaders in the cord blood transplant field and patients were followed by a lengthy discussion of the efficacy of cord blood transplantation, clinical studies, and the degree and specifics of standardized recommendations vs. the requirement for an Investigational New Drug application (IND). Requiring the latter would necessitate clinicians filing for approval with FDA, as opposed to current status whereby this is not required for UCB transplants. Most of the attendees resided relatively close to the area or were from centers specializing in CB transplantation. There are over 60,000 UCB units available in the US, 30 UCB banks on the NMDP website, and over 130,000 UCB banks worldwide according to estimates presented.

Committee background

This Committee was established to provide counsel and data to the FDA regarding the safety and effectiveness of the use of biologics. The 11 member committee is selected by the FDA Commissioner and consists of experts in the field of biologic response modifiers (cytokines, lymphokines, growth factors, anti-proliferative biological agents), biostatistics, immunology, virology, molecular biology, biostatistics, immunology, virology, molecular biology, DNA technology, nuclear medicine, transplantation, gene therapy, infectious diseases, viral oncology; and cellular kinetics. This committee "reviews and evaluates available data relating to the safety, effectiveness, and appropriate use of biological response modifiers which are intended for use in the prevention and treatment of a broad spectrum of human diseases. The Committee also considers the quality and relevance of FDA's research program which provides scientific support for the regulation of these products, and makes appropriate recommendations to the Commissioner of Food and Drugs."

[REFERENCE http://www.fda.gov/cber/advisory/brm/brmchart.htm]

II. Review of Presentations: Members of this particular Advisory committee and speakers included physicians who are well known and respected in the field of cord blood transplantation as well as representatives from the Bone Marrow Transplant Registries (IBMTR/ABMTR), National Institutes of Health (NIH), and New York Blood and Tissue Resources (NY Dept. of Health). Guest speakers presented data on cell dose, engraftment kinetics, and clinical applications. These speakers represented Duke University, National Cord Blood Program, University of Minnesota and New York Cord Blood Program. Agenda, meeting transcripts and slides can be found at http://www.fda.gov/ohrms/dockets/ac/cber03.html#BiologicalResponseModifiers

III. Patient Testimonies: Former patients (UCB recipients) and their family members spoke next. Each had a unique story, situation, or point to stress. They ranged from children to full grown-large-past-middle-age adults. The main point they all had in common was the issue of timing. Identifying registry donors and completing the work up to marrow/PBPC collection process takes 3-6 months. Not all patients have this much time. With a cryopreserved, tested, released UCB unit in a freezer, this time frame can be decreased to 4 weeks. The patients' testimonies were intended to convince the FDA to expedite this process and permit it to be easily available to those in need. It served as a humbling and moving reminder of the importance of the work we do in the cell therapy community.

IV. Committee discussion of Questions. Factors for determining safety and effectiveness were discussed. They included age, disease, clinical condition (infections, etc), time to engraft, HLA disparity, CD34 dose and other indicators of quality and outcome. The FDA and committee were most interested in the data and asked good questions about the sources, testing methods, etc. Some noteworthy points follow. It was decided that there was a definite change in success between age 10 and 20 but the overall consensus appeared to be to avoid setting age limits due to patient variability. HLA matching was discussed and the conclusion was that data exists for up to 2 antigen mismatches but inadequate data exists for less than this. Additionally, some mismatching can be overcome by a higher cell dose in the UCB. Regarding cell dosing, much debate occurred regarding minimal dosing of nucleated cells. The consensus for recommendation was that a nucleated cell target of less than 1.5 x 107/kg resulted in delayed or non-engraftment according to the data. Many cord blood banks perform colony forming assays (CFU-GM) on cord products.

But the assays usefulness as a predictive measure of engraftment is limited by the fundamental shortcomings of the assay specifically lack of assay standardization and variability of colony morphology. Therefore, this aspect was not discussed.

REFERENCE http://www.fda.gov/ohrms/dockets/ac/03/briefing/3924B1_1.pdf

CD34 content as an indicator for peripheral blood progenitor cell transplantation has been well documented. Data was presented by Dr. John Wagner (University of Minnesota) to say that there is compelling evidence that demonstrates a minimum CD34 dose is necessary for engraftment*. It seems seems the data was quite variable. Wagner's data was on thawed samples, and Rubenstein (NY Blood Center) presented data on the banked product, since that is what is available at the time of

continue on page 9

Tech Talk *continued*

cord selection. After an abundance of stimulating conversation, it was left unspecified and noted that there is no currently licensed kit for CD34 measurements in cord bloods.

*[REFERENCE Wagner JE, Barker JN, DeFor TE, et al. Transplantation of unrelated donor umbilical cord blood in102 patients with malignant and nonmalignant diseases: influence of CD34 cell dose and HLA disparity on treatment-related mortality and survival. Blood. 2002;100:1611-1618].

What does this mean for the cord blood banking industry? First and foremost, all cord blood banks must register with the FDA as a manufacturer of UCB and demonstrate compliance with GTPs. If a cord blood bank is manufacturing and/or storing more than minimally manipulated products, (i.e., UCB is activated, expanded, genetically modified, etc.), or combining UCB with non-tissue components, the FDA requires an IND application and adherence to licensure application requirements. For minimally manipulated unrelated allogeneic peripheral and cord blood products the FDA believes that compelling clinical safety and that efficacy data may exist for the development of product standards and process controls by the FDA. In 1998 the FDA asked the public to submit clinical trial safety and efficacy data, non-clinical laboratory data, and proposed product standards and process controls including but not limited to donor selection, collection, processing, cryopreservation, packaging, labeling and product acceptance criteria.

During this time period in which the FDA is evaluating and developing standards the FDA has decided to "phase-in IND and licensure application requirements for minimally manipulated unrelated allogeneic hematopoietic stem/progenitor cell products." If adequate standards are developed, the FDA will likely forego IND and licensure requirements for banks who are certified as complying with the established standards. If at the end of this time period there is not sufficient evidence to establish standards, IND and pre-market applications will be required. It will be interesting to watch this unfold. It was also interesting to see our FDA process at work, they are commended for taking expert opinion and reviewing the raw data. Please visit the websites for additional details and helpful links.

Diane Kadidlo and Kathy Loper

Bioterrorism web pages

While budget deficits in the U.S. loom on the horizon and likely will affect funding for most biomedical research, one area of biomedical research that is sure to receive funding increases above average is in the area of Bioterrorism. Apart from emergency preparedness and public health initiatives, there is funding for traditional vaccine research, immunodiagnostics, and potentially for novel cellular vaccine research. For more information, see the following web pages:
http://www.niaid.nih.gov/biodefense/research/default.htm
http://www.niaid.nih.gov/publications/bioterrorism.htm

U.S. National Institutes of Health National Institute for Allergy and Infectious Diseases.
These pages contain information for scientists who want to become involved in NIAID's biodefense research efforts.
http://www.fda.gov/oc/opacom/hottopics/bioterrorism.html

US FDA BioTerrorism Information Page
http://www.fda.gov/cber/cntrbio/cntrbio.htm

FDA CBER page on countering Bioterrorism
http://www.acq.osd.mil/cp/dodcbdpbusinessopps.pdf

Defense Advanced Research Projects Agency
http://www.slu.edu/colleges/sph/csbei/bioterrorism/index.html

St. Louis University School of Public Health Center for the Study of BioTerrorism
http://www.slu.edu/colleges/sph/bioterrorism/

MS Program

MS PROGRAM. University-based regional blood center and transfusion service is accepting applications for Fall quarter 2003. This two year graduate program culminates in a Master of Science degree in Cellular Therapies. The program emphasizes the biology and therapeutic use of hematopoietic stem cells and other somatic cell therapies. The program also includes significant hands-on laboratory experience in selection and genetic manipulation of stem cells and in the development of novel cell therapy treatment protocols. An independent research project with faculty guidance is part of the curriculum. Application deadline: April 1, 2003.

Contact: Cathy Beiting, MS, MT(ASCP)SBB, Hoxworth Blood Center, University of Cincinnati Medical Center, 3130 Highland Avenue, PO Box 670055, Cincinnati, OH 45267-0055, (513) 558-1275, email: catherine.beiting@uc.edu

ISCT 2003

Meeting Introduction

It is with great pleasure that I welcome you to the ISCT annual meeting in Phoenix. As you are aware, our society has not only undergone a name change in the last year, but our focus has significantly expanded to include the entire discipline of somatic cell therapy. In that regard, I urge you to come to Phoenix and participate in an experience designed with your needs in mind. I emphasize this because the organizing committee has seriously considered the critique supplied by all ISCT members in designing the meeting format. Suggestions to the educational committee, the last 2 year's post- meeting evaluations and the recent ISCT web-based poll were invaluable in choosing topics, speakers and format. The format has a familiar scientific meeting structure in providing our members with state-of-the-art plenary and scientific sessions. However, the topics have been re-designed to include newly emerging fields in cellular therapy along with other aspects of hematopoietic stem cell research which differ from many of the major "blood and transplant" meetings that many of us also attend. Equally important to ISCT and the meeting is the growing field of nonhematopoietic stem cell research. Considerable thought has been taken to arrange topics in simultaneous sessions such that closely related disciplines do not compete for registrants. For many ISCT members, this yearly meeting becomes the only opportunity to attend a uniquely focused program in their area of expertise. The breakfast workshops, which we believe are one of the best opportunities to immerse oneself in a specific aspect of cellular therapy, have been chosen based on ISCT member input. There was a great demand for basic topics such as cryopreservation, CD34 determination, etc which have been given duplicate slots. These sessions are a significant opportunity to engage in dialogue with renowned experts in the field and in discussions with your peers. They are designed for you, and we hope that we have listened to your needs. I would be remiss if I didn't also mention the pre-meeting cGTP, and Flow Cytometry Workshops and Miltenyi Biotec Corporate Symposium, which meet the special needs of a large proportion of our members. The AABB will also conduct a special session on donor safety issues. In closing, I want to again emphasize that the 2003 ISCT Annual Meeting is a major opportunity for laboratorians, scientists, physicians and those involved in the regulatory/ corporate administrative fields of cellular therapy to meet with peers and network with individuals on a global scale. All facilities (and countries for that matter) from academia and industry are dealing with similar issues with an exponentially expanded discipline that is being surrounded by an ever-closing regulatory net. This meeting can only be successful if our members both attend, and as important, participate. Become part of the future of this scientifically exciting and socially active field. I look forward to greeting you in Phoenix!

ISCT President

Cytotherapy

Upcoming Issue Volume 5, Number 1

cGTP 2003 Workshop: Program

WEDNESDAY, MAY 28, 2003		
TIME	**TOPIC**	**PANEL CHAIR**
7:00pm | 8:00pm	Overview and History of FDA's Perspective	Joyce Frey, PhD *FDA, CBER*
8:00pm | 8:45pm	Introduction and Update of the Proposed GTP Rule	Ruth Solomon, MD *FDA, CBER*
8:45pm | 9:00pm	BREAK	
9:00pm | 9:45pm	Donor Rules	Ruth Solomon, MD *FDA, CBER*

THURSDAY, MAY 29, 2003			
TIME	**TOPIC**	**PANEL CHAIR**	**PANEL MEMBERS**
7:30am | 8:00am	BREAKFAST		
8:00am | 9:15am	Development of a Quality Management Program	Donna Przepiorka, MD, PhD *University of Tennessee*	Mary Malarkey *FDA, CBER* Donna Regan, MT(ASCP)SBB *St. Louis Cord Blood Bank* Linda Kelley, PhD *University of Utah Medical Center* Shelley Heimfeld, PhD *Fred Hutchinson Cancer Research Center*
9:15am | 9:45am	Discussion		
9:45am | 10:00am	BREAK		
10:00am | 11:15am	Adverse Reactions/Deviation Reports/ Corrective Actions	Cindy Elliott, BA, MT HP(ASCP) *AABB*	Mary Malarkey *FDA, CBER* Robert Preti, PhD *Progenitor Cell Therapy* Brenda Alder, MT(ASCP)SBB *Northside Hospital, Georgia* Diane Kadidlo, MT(ASCP)SBB *Fairview University Medical Center* Elizabeth Read, MD *National Institutes of Health*
11:15am | 11:45am	Discussion		
11:45am | 1:00pm	LUNCH		
1:00pm | 2:15pm	Validation of Computerized Systems	Scott Burger, MD *Advanced Cell & Gene Therapy Consulting*	Diane Gubernot *FDA, CBER* Safa Karandish, MT(ASCP) *MD Anderson Cancer Center* Elizabeth Read, MD *National Institutes of Health* Janis Halvorsen *EduQuest, Inc.*
2:15pm | 2:45pm	Discussion		
2:45pm | 3:00pm	BREAK		
3:00pm | 4:15pm	Product Import and Export Issues	Chatchada Karanes, MD *NMDP*	Mary Malarkey *FDA, CBER* Michael Strong, PhD *Puget Sound Blood Center* Carolyn Keever-Taylor, PhD *Medical College of Wisconsin* John McMannis, MD, PhD *MD Anderson Cancer Center*
4:15pm | 4:45pm	Discussion		

Due to circumstances beyond the control of the organizers, some speakers and/or topics may change in the Final Program.

WORKSHOPS

The cGTP 2003 Workshop Organizing Committee is finalizing plans for the workshop to be held immediately prior to the annual meeting in May. The cGTP meeting will begin on Wednesday, May 28th at 7 pm. The evening will feature Dr. Ruth R. Solomon, MD, from the Division of Human Tissues, Office of Cellular, Tissue and Gene Therapies, CBER, FDA. Dr. Solomon will introduce the proposed cGTP rule and discuss the status of the rule. The second day of the meeting will consist of four panel discussions. Each topic will be discussed in relation to the proposed cGTP rule. The four leaders and topics are: Dr. Donna Przepiorka (Quality Management Programs), Cindy Elliott MT(ASCP) HP (Adverse Reactions & Deviation Reports), Dr. Scott Burger (Validation & Computers) and Dr. Chatchada Karanes (Product Import/Export Issues). Each leader will introduce their topic and then speakers will discuss the issue in relation to their laboratory configuration (e.g. centralized, university-based). Each session will end with a discussion/question/answer period moderated by the panel leader. Shown below is a current list of confirmed speakers. The committee's goal was to create a program that is informative as well as interactive for the attendees. With a topic as current as the proposed cGTP rule, the 'open' discussion following the lectures can be equally educational and the program format was designed with this in mind. We look forward to an exciting meeting in Phoenix.

Janice Davis-Sproul, MAS, MT(ASCP)SBB
Organizing Committee Chair

DAY ONE WEDNESDAY MAY 28

9:00 am — MEETING REGISTRATION OPENS

12:30 pm – 6:00 pm

4TH BIENNIAL WORKSHOP ON APPLICATIONS OF FLOW CYTOMETRY IN MARROW AND STEM CELL TRANSPLANTATION

This workshop will be offered as an Intermediate Level program. The workshop will cover topics relating to the Standardization of Cytometric Testing, a Report from the Working Group on High Speed Cell Sorting for Clinical Use and Cytometric Applications in Biotherapy/Immunotherapy.

BD BD Biosciences · BECKMAN COULTER · DakoCytomation

SESSION I 12:30 - 2:30 PM

Standardization of Cytometric Testing

Mark Pittenger
Chair:

Lawrence S. Lamb, Jr., Ph.D., South Carolina Cancer Center

Speakers:

Jan W. Gratama, MD, PhD., Daniel Van Hoed Cancer Center, Rotterdam, The Netherlands
"Standardization of enumeration of antigen-specific cd8+ T cells by tetramer technology"

Nicholas J. Greco, PhD., American Red Cross Holland Laboratories, Rockville, MD, USA
"Characterization of cord blood CD34+ cell subpopulations: appearance of apoptotic cells after cryopreservation"

Michael Keeney, ART, FIMLS, London Health Sciences Centre, London, ON, Canada
"Issues in Standardization of CD34 counts in Hematopoeitic Transplantation"

SESSION II 2:30 - 3:30

Report from the Working Group on High Speed Cell Sorting for Clinical Use

Speakers:

Gerald Marti MD, PhD, Center for Biological Evaluation and Research, FDA, Bethesda, MD, USA

SESSION III 4:00 PM - 6:00 PM

Cytometric Applications in Biotherapy/Immunotherapy

Chair:

Maryalice Stetler-Stevenson, MD, PhD., National Cancer Institute, Bethesda, MD, USA

Speakers:

Sivasubramanian Baskar, PhD., National Cancer Institute, Bethesda, MD, USA
"Immunotherapy of human follicular lymphoma: T cell responses to tumor associated antigens"

Robert Kreitman, MD, National Cancer Institute, Bethesda, MD, USA
"Recombinant immunotoxins for treatment of hematologic malignancies"

Mark W. Lowdell, PhD, Royal Free and University College Medical School, London, UK
"Flow cytometric assays to monitor immune responses to leukaemia"

Maryalice Stetler-Stevenson, MD, PhD, National Cancer Institute, Bethesda, MD, USA
"The role of clinical flow cytometry in antibody based therapies"

ISCT 2003 ARIZONA

DAY ONE WEDNESDAY MAY 28

7:00 pm – 10:00 pm

ISCT CURRENT GOOD TISSUE PRACTICES WORKSHOP

This Workshop will be offered as an Intermediate Level program. The objectives of the workshop are to differentiate between the proposed cGTP and cGMP requirements for somatic cells, to apply the proposed cGTPs to laboratories based in academic centers, collection facilities, hospitals and contract facilities, and to understand the requirements for GTP compliance.

The first evening of the workshop will consist of presentations from members of the Food and Drug Administration on the following topics:

- Overview & History of the FDA's Perspective on Cellular Therapy
- Introduction & Status Update on the proposed cGTPs
- Proposed Donor Regulations for Cell/Tissue Products.

The second day of the workshop will be presentations and open discussions on the following topics:

- Development of a Quality Management Plan
- Adverse Reactions/Deviation Reports/Corrective Actions
- Validation of Computerized Systems
- Product Import and Export Issues

DAY TWO THURSDAY MAY 29

7:30 am – 4:45 pm

ISCT CURRENT GOOD TISSUE PRACTICES WORKSHOP (CONTINUED)

5:00 pm – 7:00 pm

Miltenyi Biotec

THE POTENTIAL FOR CELLULAR ENGINEERING AND THERAPY

Strategies in cellular therapy using highly purified progenitor or immune effector cells show promising perspectives that may improve disease-management and quality-of-life of patients suffering from a variety of pathologies including malignant, viral and cardiac diseases. In this symposium, investigators will report about dendritic cell vaccination currently under investigation in solid tumors and leukemias and on adoptive immunotherapy using natural killer cells or antigen-specific T cells. The symposium will also discuss evolving new concepts of cellular therapy such as regenerative treatment in heart diseases supported by stem cells.

Learning objectives:

- Outline various potential applications of cellular immunotherapy
- Discuss the therapeutical potential of immunological strategies using dendritic cells, natural killer cells and antigen-specific cytotoxic T lymphocytes
- Review stem cell support in ischemic heart disease
- Discuss magnetic cell separation as a means of obtaining pure cell preparations according to cGMP guidelines for cellular therapy trials

This program has been designed to meet the educational needs of hematologists, oncologists immunologists and cardiologists. Also, medical technicians, research technicians, scientists and physicians specializing in BMT, hematology, oncology and cellular therapies will benefit from attending.

7:00 pm – 8:00 pm

WELCOME RECEPTION AT THE ARIZONA BILTMORE HOTEL

THURSDAY MAY 29

INNOVATIVE APPROACHES TO CELLULAR THERAPY

Baxter DYNAL BIOTECH XCYTE

Description: "Session will focus on driving science from the lab to the clinic and the application of certain technologies to obtain a GMP product."

Topics:
Clinical Scale Selection of Dendritic Cells
Isolation of Antigen Specific T-Cells and their Therapeutic Role
Expansion of T-Cells using a CD3 CD28 Coated Immunomagnetic Bead

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PROGRAM

DAY THREE FRIDAY MAY 30

9:00 am – 8:00 am	TB 1 Storage and cryo-preservation of cell products **Carlos Lee**	TB 2 Evaluation of the apheresis product – from collection to reinfusion **Robert Sutherland and Michael Keeney**	TB 3 Facility design **Douglas Padley**	TB 4 In vitro assays for hemopoietic progenitors (CFC, CAFC, LTCIC, etc.) **Rob Ploemacher and Emer Clarke**	TB 5 Analysis of immunoreconstitution post-transplant, i.e., spectratyping, TREC assays, eli spots **Paul Schlegel**	TB6 Meet the FACT Experts **Linda Kelley, Shelly Heimfeld & Helen Heslop**
8:00 am – 9:20 am	**PLENARY SESSION I** Immunotherapy and Tumor Evaluation/Minimal Residual Disease **Lawrence Fong** Dendritic cells as a cellular vaccine for tumor immunotherapy **Klaus Pantel** Molecular signatures related to bone marrow micrometastasis in breast cancer					
9:20 am – 9:45 am	**BREAK AND EXHIBITS**					
9:45 am – 12:00 noon	**SIMULTANEOUS PLENARY SESSION A** Immunotherapy **Krishna Komanduri** CMV-specific immune reconstitution and immunodominance **Robert Negrin** Real-time modeling of adoptive immunotherapy **Robert Vonderheide** Adoptive immunotherapy targeting universal tumor antigens **Albert Donnenberg** Reconciling vaccines with dose-intensive therapy		**SIMULTANEOUS PLENARY SESSION B** Tumor Evaluation/MRD **John Park** Comparative analysis of immunocytochemistry (ICC), automated ICC, flow cytometry and RT-PCR in breast cancer patients **Michael Speicher** Advanced cytogenetic analysis of metastatic tumor cells **Gunnar Kvalheim** Latest clinical data on the Scandinavian breast cancer micrometastases study **Graham Sharp** Clinical significance of non-hodgkin's lymphoma MRD		
12:00 noon 1:00 pm	**LUNCH AND CYTOTHERAPY EDITORIAL BOARD MEETING**					
1:00 pm – 2:00 pm	**EDUCATIONAL SESSION 1** Immunotherapy	**EDUCATIONAL SESSION 2** Tumor Evaluation/MRD	**EDUCATIONAL SESSION 3** AABB HPC Donor and Recipient Safety			
2:05 pm – 3:05 pm	**WORKSHOP 1** Immunotherapy	**WORKSHOP 2** Tumor Evaluation/MRD				
3:05 pm – 3:30 pm	**BREAK AND EXHIBITS**					
3:30 pm – 4:30 pm	**ORAL ABSTRACT PRESENTATIONS** Ex Vivo Expansion	**ORAL ABSTRACT PRESENTATIONS** Tumor Evaluation/MRD	**CPT CODE REVISIONS**	**ORAL ABSTRACT PRESENTATIONS** Regulatory/Process Control		
4:30 pm – 5:35 pm	**ORAL ABSTRACT PRESENTATIONS** Immunotherapy	**ORAL ABSTRACT PRESENTATIONS** Cord Blood	**ORAL ABSTRACT PRESENTATIONS** Hematopoietic Stem Cell Transplantation	**STERILITY TESTING VALIDATION**		
5:35 pm – 7:00 pm	**POSTER VIEWING**					
7:00 pm – 10:00 pm	**COMMITTEE MEETINGS**					

ISCT 2003 ARIZONA

DAY FOUR SATURDAY MAY 31

7:00 am – 8:00 am	TB 7 Storage and cryo-preservation of cell products **Carlos Lee**	TB 8 Evaluation of the apheresis product – from collection to reinfusion **Robert Sutherland and Michael Keeney**	TB 9 Facility design **Douglas Padley**	TB 10 In vitro assays for hemopoietic progenitors (CFC, CAFC, LTCIC, etc.) **Rob Ploemacher and Emer Clarke**	TB 11 Analysis of immunorecon-stitution post-transplant, i.e., spectratyping, TREC assays, eli spots **Paul Schlegel**	TB 12 Ask the experts: Regulatory **Michele Sugrue**
8:00 am – 9:20 am	**PLENARY SESSION II** Gene Therapy and Hematopoietic Stem Cell Transplantation **Malcolm Brenner** How may gene transfer contribute to cellular therapies **Rainer Storb** The future of allogeneic hematopoietic stem cell transplantation					
9:20 am – 9:45 am	**BREAK AND EXHIBITS**					
9:45 am – 12:00 noon	**SIMULTANEOUS PLENARY SESSION C** Gene Therapy **Michel Sadelain** Translating lentiviral vectors to the clinic **Claudio Bordignon** Gene therapy of immunodeficiency using subablative conditioning regimens **Kim Lyerley** Clinical studies using RNA transfer into dendritic cells **Mike Jensen** Genetic modification of T cells			**SIMULTANEOUS PLENARY SESSION D** Hematopoietic Stem Cell Transplantation **Crystal Mackall** Potential role of Interleukin 7 in allogeneic transplantation **Vanderson Rocha** Cord blood transplantation **Richard Champlin** Minitransplantation **Yair Reisner** Crossing HLA barriers by megadose stem cell transplants: immune regulation by early hematopoietic progenitors		
12:00 noon 1:00 pm	**LUNCH AND ISCT COMMITTEE MEETINGS**					
1:00 pm – 2:00 pm	**EDUCATIONAL SESSION 4** Gene Therapy		**EDUCATIONAL SESSION 5** Hematopoietic Stem Cell Transplantation		**WORKSHOP 6** Non-Hematopoietic Stem Cells	
2:05 pm – 3:05 pm	**WORKSHOP 4** Gene Therapy		**WORKSHOP 5** Hematopoietic Stem Cell Transplantation			
3:05 pm – 3:30 pm	**BREAK AND EXHIBITS**					
3:30 pm – 4:30 pm	**EDUCATIONAL SESSION 7** Graft Evaluation	**EDUCATIONAL SESSION 8** Cord Blood	**EDUCATIONAL SESSION 9** Ex Vivo Expansion	**HOW TO PREPARE A CLINICAL IND** Legal & Regulatory Affairs		
4:30 pm – 5:35 pm	**WORKSHOP 7** Graft Evaluation	**WORKSHOP 8** Cord Blood	**WORKSHOP 9** Ex Vivo Expansion	**CRYOPRESERVATION CONTAINER DISCUSSION**		
5:40 pm – 6:40 pm	**ORAL ABSTRACT PRESENTATIONS** Graft Evaluation		**ORAL ABSTRACT PRESENTATIONS** Gene Therapy		**ORAL ABSTRACT PRESENTATIONS** Non-Hematpoietic Stem Cell Transplantation	
7:30 pm	**ISCT GENERAL BUSINESS MEETING/GALA EVENT**					

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PROGRAM

ISCT 2003 ARIZONA

DAY FIVE SUNDAY JUNE 1

7:00 am – 8:00 am	TB 13 CD 34 selection **Shelly Heimfeld**	TB 14 Dendritic cell preparation **Charles Carter**	TB 15 Characterization of T cell products for immunotherapy **Helen Huls**	TB 16 Detection and primary culture of tumour cells from patients with epithelial malignancies **Amy Ross and Panteli Theocharous**

8:00 am – 9:20 am — **PLENARY SESSION III**

Non-Hematopoietic Stem Cells & Evaluating Grafts for Long-Term Outcomes

Ed Horwitz
Mesenchymal Stem Cell Therapy: The New Frontier

Andrew Pecora
Replication competent viruses as adjuncts to cell based immunotherapy

9:20 am – 9:45 am — **BREAK**

9:45 am – 12:00 noon

SIMULTANEOUS PLENARY SESSION E

Non-Hematopoietic Stem Cells

Mark Pittenger
Mesenchymal stem cells as progenitors of cardiac myocytes

Jonathon Hill
Data of clinical trials using MSCs as cell therapy for the heart

Peter Wernet
Myocardial regeneration with autologous bone marrow derived progenitor cells following infarction in men

Donald Orlic
Stem cells for myocardial regeneration: mouse and monkey models

SIMULTANEOUS PLENARY SESSION F

Evaluating Grafts for Long-Term Outcomes

Carolyn Keever-Taylor
Establishment of treatment algorithm for recipients of alternative donor grafts for the treatment of hematologic malignancies

Francesco Lanza
Which phenotypic subsets may predict transplantation patient outcome?

Hans E. Johnsen
Clinical registration studies on quality assessment of autografting

Shelly Heimfeld
HLA-identical transplantation: how important is CD 34 in cell dose?

ISCT 2003 ARIZONA MAY 29 · JUNE 1

IMPORTANT DEADLINES

Abstract Submissions: February 14, 2003

Early Registration: April 4, 2003

Hotel Registration: April 17, 2003

Just the FACTs

New FACT Website

FACT is pleased to announce the launch of their new website at www.factwebsite.org. The site features a comprehensive listing of all FACT-accredited facilities along with program director names and services provided. Soon to be included on the site in downloadable PDF format will be frequently used forms in the accreditation process (applications, fee structure, document checklists, guidance for applicants, and the Inspection Checklist). Individuals are encouraged to log on and provide feedback for improvements to the site as well as additional topics to include.

FACt Collection Inspectors

FACT Collection Inspectors are needed to conduct quality, comprehensive FACT inspections. Prospective and current inspectors are invited to attend the FACT Collection Inspector training course at the Annual ASFA Meeting in Lake Tahoe, Nevada on May 6, 2003. Inspectors of progenitor cell collection facilities are not required to hold a doctoral degree. Nurses or technologists with the appropriate supervisory experience affiliated with FACT-accredited or applicant facilities are welcome. The course will highlight the second edition of the FACT Standards. To register for the workshop, please contact the FACT Office at 402-561-7555.

Annual Accreditation Payments

In order to provide accredited programs with a mechanism to budget annually for renewal accreditation fees, an annual payment plan has been instituted. Programs may choose between two payment options:

1) Lump Sum Payment: Facilities may elect to pay the entire sum, due the final year of their accreditation prior to the renewal inspection.

2) Annual Payments: Facilities may elect to pay one-third of the renewal fee each year following their initial accreditation at a 10% discount for pre-payment. The final payment is due prior to the renewal inspection.

All FACT-accredited programs will receive an invoice for their annual payment prior to their accreditation anniversary date.

Timeline for Renewal Accreditations

FACT-accredited facilities will receive renewal information approximately seven months prior to expiration of their accreditation. This will allow programs a full six months to complete the entire application, on-site inspection, review and reaccreditation prior to their expiration date.

Renewal Accreditation

The accreditation renewal cycle continues for facilities that previously achieved FACT accreditation. The following facility has completed the reaccreditation process and is listed below along with their Program Director:

Autologous peripheral blood progenitor cell transplantation, including collection and laboratory processing:

- Providence Portland Medical Center, Portland, Oregon

  Program Director: Stacy K. Lewis, MD

FACT-Accredited Facilities

Two additional facilities have gained FACT accreditation since the last issue of the Telegraft. Currently, there are 111 FACT-accredited facilities. Another 102 facilities are in various stages of the accreditation process.

The latest facilities to gain voluntary accreditation, along with their Program Directors are listed in the categories below:

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

- Kansas City Blood and Marrow Transplant Program, Kansas City, Missouri

  Program Director: Joseph McGuirk, MD

Allogeneic & autologous peripheral blood progenitor cell transplantation, including collection and laboratory processing:

- University of Maryland Greenbaum Cancer Center Blood and Marrow Transplant Program, Baltimore, Maryland

  Program Director: Barry Meisenberg, MD

For a complete list of accredited facilities, please visit the FACT website.

FACT Accreditation Office: (402) 561-7555

Facilities Registered	213
Facilities Completing Checklists	56
Facilities Scheduling Inspections	11
Facilities Inspected	146
Inspected/Pending Accreditation	32
Accredited	114
Renewal Accreditations	8

Upcoming Meetings

11th Annual Meeting on Recent Advances in Stem Cell Transplantation

March 8 – 10, 2003
San Diego, CA

Registration fee discount for ISCT members. For further information contact: Office of Continuing Medical Education, Ph 858-534-3940, Fax 858-534-7672, ocme@ucsd.edu.

Commercialisation of Tissue Engineering & Regenerative Medicine

April 9 – 10, 2003
London, UK

For further information, please refer to www.melifesciences.com/tissueengineering.html

Development of Therapeutic Cancer Vaccines Conference

April 27-29, 2003
Los Angeles, CA

Registration fee discount for ISCT members. For further information, please refer to www.jwci.org.

4th International Symposium on Minimal Residual Cancer

May 2 – 5, 2003
Homenkollen, Oslo, Norway

Full program and registration is available on-line at www.celltherapy.org. For further information please contact Moya Berli by e-mail at moyab@klinmed.uio.no.

4th Biennial Workshop: Applications of Flow Cytometry in Marrow and StemCellTransplantation

May 28, 2003
Phoenix, AZ

For more information, please contact the ISCT Head Office: Ph 604-874-4366, Fax 604-874-4378, isct2003@celltherapy.org. Full program information is available on-line at www.celltherapy.org.

cGTP Workshop

May 28 – 29, 2003
Phoenix, AZ

For more information, please contact the ISCT Head Office: Ph 604-874-4366, Fax 604-874-4378, isct2003@celltherapy.org. Full program information is available on-line at www.celltherapy.org.

2003 ISCT Annual Meeting

May 29 – June 1, 2003
Phoenix, AZ

For more information, please contact the ISCT Head Office: Ph 604-874-4366, Fax 604-874-4378, isct2003@celltherapy.org. Full program information is available on-line at www.celltherapy.org.

2003 World Congress of Cryobiology and Cryomedicine

July 27 – 31, 2003
Beijing, China

For further information, please refer to http://128.163.176.7/cryobiology/

3rd Annual Somatic Cell Therapy Symposium

September 13 – 15, 2003
Chesapeake Bay

For more information, please contact the ISCT Head Office.

3rd Annual Conference on Nonhematopoietic & Mesenchymal Stem Cells

October 9 – 11, 2003
New Orleans, LA

For more information, please contact the ISCT Head Office.

Cell Culture & Separations for Cell & Gene Therapies Course: 16th Annual Bioprocess Technology Seminars

October 20 – 24, 2003
New Orleans, LA

For further information, please refer to http://www.asme.org/education/techsem/bio/index.html

2002-2003 AABB-ISCT Audioconference Series

ISCT has joined with AABB again this winter to provide you quality audioconference education. Registration is done through AABB (www.aabb.org or ph: 301.215.6482). ISCT members receive the member discount on all AABB audioconferences.

Practical Applications in the Daily Operation of the Cell Engineering Laboratory
April 16, 2003
2:00 pm – 3:30 pm (ET)
6:00 pm – 7:30 pm (UT)
Program #034538

Moderator: John D. McMannis, PhD, professor, University of Texas-MD Anderson Cancer Center
Speakers: Janice Davis-Sproul, MAS, MT(ASCP)SBB, process development project manager, Johns Hopkins Oncology Center; Shelley Heimfeld, PhD, director, associate member, cellular therapy, Fred Hutchinson Cancer Center

Description: Cell processing facilities deal with SOPs, validation, quality control and routine processing on a daily basis. There are some techniques, however, that are requested infrequently. How does the laboratory determine the optimal conditions for using unusual procedures? This program focuses on rarely used procedures that are important to the cell processing facility such as short-term storage of cellular products, red blood cell or plasma depletion of ABO incompatibilities and reduction of cell clumps during processing. The presenters will discuss the current techniques for these requests along with the regulatory requirements that the cell processing laboratory must consider when developing/validating these techniques. In addition, there will be time for the participants to bring up additional infrequent procedures that they would like the panel to discuss.

Objectives:

- Describe the methods available to process ABO-incompatible cellular products
- Discuss the pros and cons associated with the ABO-incompatible processing procedures
- State the process and the regulatory issues associated with short-term storage of cellular products
- Discuss the validation requirements for short-term storage procedures
- Describe the methods used to reduce cell dumping

Audience: Technologists, medical directors and managers/supervisors
Program Level: Intermediate to Advanced
Content for this program was developed in cooperation with the International Society for Cellular Therapy.

Contributing Authors

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