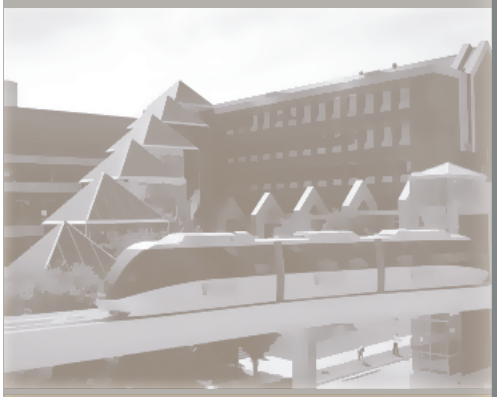

Report of the Indiana University School of Medicine Task Force on Establishing an Adult Stem Cell Research Center

Hal Broxmeyer, Ph.D.
Distinguished Professor
Chairman & Mary Margaret Walther
Professor of Microbiology/Immunology
Professor of Medicine
Scientific Director of the Walther Oncology Center

Eric M. Meslin, Ph.D.
Director, Indiana University Center for Bioethics
Assistant Dean for Bioethics, IU School of Medicine
Professor of Medicine, Medical & Molecular Genetics, and Philosophy

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H.B.
E.M.M.

Executive Summary

In June 2005 Indiana University School of Medicine (IUSM) Dean D. Craig Brater, M.D., appointed Hal Broxmeyer, Ph.D., (Director, Walther Oncology Center) and Eric Meslin, Ph.D. (Director, Indiana University Center for Bioethics) to co-chair a Task Force charged with assessing the feasibility of establishing an Adult Stem Cell Center at Indiana University. The origin of Dean Brater's request was the passage of Indiana Bill, S-268, signed into law by Governor Mitch Daniels on May 20, 2005. The law affects the conduct of research involving human cloning, embryonic stem cells and adult stem cells, and includes a provision (Chapter 29.7.2) permitting the "the board of trustees of Indiana University [to] establish an adult stem cell research center". The Dean's establishment of the Task Force is intended to provide the first of what may be several assessments that will be needed to provide a full picture of the opportunities.

The Task Force met with approximately 40 IUSM-affiliated investigators on eight separate occasions between July-September 2005, including a half-day retreat on September 29. This report, which is an outgrowth of those encounters, provides seven conclusions and seven recommendations that are provided below. Additional information is contained in four accompanying Appendices.

Conclusions

1. The IU School of Medicine has a well-established and diverse base of stem cell investigators working in several areas. This suggests that the necessary foundation exists at IUSM on which to build a Center. [See Appendix 1]

2. Many potential disease targets are being studied by IUSM investigators, involving seven different cell sources. Among these, three areas of prominent research focus have shown promising potential as therapeutic foci for adult stem cells: cancer and its many variants, cardiovascular disease, and neurodegenerative disorders.

3. There is evidence of the capacity to obtain external support for stem cell research at IUSM. Over $23 million from public and private sources has been obtained by IUSM investigators who self-identified as working with adult stem cells.

4. There is evidence of positive clinical results from current research efforts and emerging clinical trials in other areas, including blood and bone marrow transplants, an FDA approval of a stem cell selection device based on work done at IUSM, and an FDA-approved clinical trial involving endothelial progenitor cells used to stimulate angiogenic growth in deteriorating limbs.

5. Many potential scientific benefits are likely to arise from establishing an Adult Stem Cell Center, including: attracting new investigators to IUSM and in so doing increase the likelihood of attracting additional external funding; ,enhancing synergistic collaboration, bringing multiple cell fields and sources into contact, and translating scientific work into clinical trials. This increased activity may, if successful, translate into additional intellectual property.

6. There are several domestic and international initiatives that will have an impact on any IUSM (or state-wide) initiative, including state and federal legislation that provide funding for stem cell initiatives, and the recent announcements in other countries to build capacity. [See Appendix 2]

7. There is growing agreement that advances in stem cell investigation are now being made with an eye to cooperative efforts in research, rather than competitive ones. Time is of the essence if Indiana and IUSM are to attract and retain quality researchers and promote leading contributions to knowledge about stem cells.

<u>Recommendations</u>

Recommendation 1. **The IUSM should move forward expeditiously with plans to develop and establish an Adult Stem Cell Center.** If a Center is not established soon, much of the opportunity for Indiana to take a leading role in adult stem cell research may be lost.

Recommendation 2. The Center should approach research from the perspective of both cell-type and disease target, building from those areas in which IUSM has already demonstrated progress: Hematopoiesis, Cardiovascular disease, and Cancer.

Recommendation 3. The Center should promote research at all levels, from basic science through therapeutics. However, emphasis should be given to the promotion of

translational research, and should encourage and enable any application of stem cells for patient treatment and cure.

Recommendation 4. **The Center should have a multidisciplinary structure**, involving basic science investigators, clinicians, imaging experts, and geneticists, among others. This would allow stem cell research to draw on many areas of science, medicine, and technology to ensure that all the potential therapeutic benefits of adult stem cells are realized. Take for example the involvement of radiologists and biological microscopists for imaging. It would be feasible and tactical to recruit additional researchers to capitalize on existing strengths in imaging who are capable of following the migration/insertion of labeled stem cells into the targeted organ in 3-D rendering, or following dynamic events in 4-D (time); and genomic analysts using RNA arrays as a particularly good way to look at global changes in gene expression during differentiation.

Recommendation 5. **The Center should work to address applications for stem cells in research on which IUSM, as yet, has not been able to focus**. There are several examples of this, such as diabetes mellitus, recognized as a fast-growing and very important area of research. Also in this category are certain neurodegenerative disorders, among them, spinal cord injury, Parkinsonism, and auditory cell replacement.

Recommendation 6. While describing the potential scientific and clinical merits of such a Center are necessary for moving forward with plans for its establishment, other logistical and financial issues must be addressed separately**. The IUSM should seek additional input on the following issues:**

- Costs and sources of financing for both start-up and long-term support;

- Logistics, including the space (whether virtual or concrete) in which a Center would be located;

- Administrative structure, including whether the Center will function as its own department, be housed within an existing department or school, and other factors related to reporting relationships;

- Organization of the Center, involving status of faculty (full or part time), and possible cross-appointments; and

- Operational focus, both initially and also as expansion and development occur.

Recommendation 7. The IUSM should develop a database (or refine an existing one) that can identify investigators, publications, and grant support directly related to stem cell research. As the Task Force discovered, there are little data to accurately inventory investigators who are conducting stem cell research, how productive they are, or how much stem-cell specific support they are receiving. More accurate data will be invaluable in developing excellence in this area.

Personal Comments by the Co-Chairs

One of the challenging features of our efforts to provide advice on the establishment of an Adult Stem Cell Center at the IU School of Medicine was the need to describe the opportunities and potential in a way that did not compromise the scientific freedom and integrity of IUSM scientists who wish to work on embryonic stem cells. For example, it is one thing to recommend that IUSM undertake the steps necessary to fully realize the potential of researchers working in (or planning to work in) the many areas of adult stem cell research—which we jointly and unequivocally do—it is another thing to make this recommendation knowing that some will interpret it as simultaneously recommending that adult stem cells *and only adult stem cells* can be studied in the proposed Center. The latter interpretation of our recommendations would be wrong. Since it is currently legal in the United States to use federal funds to support research on embryonic stem cells (under very specific conditions and limitations), we would be remiss if we were to recommend that an Adult Stem Cell Center at Indiana University be established that would prohibit what the White House, the NIH, the US Congress and Indiana law permit. Therefore, in making the recommendations contained in this report we wish to make clear that any progress towards establishing an Adult Stem Cell Center should be mindful of the risk that is manifest in unduly limiting the resources to scientists that only work on adult stem cells. Some investigators will also want to work with embryonic stem cells in addition to adult stem cells, or may only wish to work with embryonic stem cells, and as such may feel uncomfortable with or excluded from the resources of the Center. This could lead to problems in retention and/or recruitment of outstanding scientists. Given these considerations we personally feel strongly that every consideration be given to establishing an *IU Stem Cell Research Center*, without specifying (in name) the specific type of stem cells that will be studied therein.

REPORT OF THE INDIANA UNIVERSITY SCHOOL OF MEDICINE TASK FORCE ON ESTABLISHING AN ADULT STEM CELL RESEARCH CENTER

A. History, Mandate, and Process of Adult Stem Cell Center Task Force

In June 2005, Indiana University School of Medicine (IUSM) Dean D. Craig Brater, M.D., appointed Hal Broxmeyer, Ph.D., (Chairman, Department of Microbiology and Immunology, and Scientific Director, Walther Oncology Center Director) and Eric Meslin, Ph.D. (Director, Indiana University Center for Bioethics) to co-chair a Task Force charged with assessing the feasibility of establishing an Adult Stem Cell Center at Indiana University. The origin of Dean Brater's request was the recent enactment of Indiana Bill, S-268, signed into law by Governor Daniels on May 20, 2005. The law affects the conduct of research involving human cloning, embryonic stem cells and adult stem cells, and includes a provision (Chapter 29.7.2; see Box A) permitting the "the board of trustees of Indiana University [to] establish an adult stem cell research center". Further provisions contained in Chap 29.7 provide general guidance for the establishment of such a Center. In a separate appropriation, the State provided $50,000 to allow for the process of establishing the Center to begin.

Box A

Indiana Senate Bill S-268

Chapter 29.7 Adult Stem Cell Research Center

Sec. 1 As used in this chapter, "center" refers to an adult stem cell research center established under section 2 of this chapter to carry out the duties specified by this chapter.
Sec. 2 The board of trustees of Indiana University may establish an adult stem cell research center.
Sec. 3 The center must be under the administration of the school of medicine
Sec. 4 The dean of the school of medicine shall appoint the director of the center.
Sec. 5 The board of trustees of Indiana University may receive, accept, hold, and apply donations, bequests of funds, property, gifts, and other income in support of the center's purposes.
Sec. 6 The center shall:
(1) conduct a thorough and comprehensive needs assessment of the state of science of adult stem cell research; and
(2) develop strategies to move Indiana University into the forefront of the nation in its capacity to attract and retain adult stem cell researchers.

While it is assumed that the Legislature's vision for such a Center may include other institutions and regions of Indiana, the IUSM Task Force mandate and focus was limited to Indiana University School of Medicine. Our mandate there was to:

- **Identify those researchers at IUSM who were active in adult stem cell research;**

- **Identify the opportunities and potential benefits (for science and for patient care) that the establishment of such a Center at IUSM might provide;**

- **Identify any challenges or impediments to the establishment of such a Center.**

Moreover, while it is well recognized that no Center can be established without a concrete vision for how it will be funded, this report intentionally focuses on the scientific potential and opportunity to bring that capacity to fruition, not on the type or amount of financial investment needed. Suffice it to say, the investment needs to be sufficient to catalyze the kind of scientific potential that exists when groups of this kind are organized, and for which IUSM already has experience through the Indiana Genomics Initiative (INGEN).

Following consultation with Dean Brater and Executive Associate Dean for Research Ora Pescovitz, Drs. Broxmeyer and Meslin agreed that they would constitute a two-person Task Force with the expectation that extensive input would be sought from active stem cell research at IUSM (and in other IUPUI schools). The Task Force met with approximately 40 IUSM-affiliated investigators on eight separate occasions between July-September 2005: five separate meetings with individual investigators, two meetings with research programs whose work involves adult stem cells, and a half-day retreat on September 29 involving approximately 35 participants. The goals of the retreat were to have a focused discussion about the prospects for a Center on the IUSM campus, to assess how a Center would affect the current stem cell research at IUSM, and to identify unique projects that might serve as illustrative examples for how a Center might accomplish what could not be accomplished under current arrangements.

This report is an outgrowth of those encounters, and especially of the retreat. A draft was shared with all who participated in the Task Force process. Thus, the information presented represents a collaboration of many individuals who are directly involved in the field of stem cell research, and as such the report is an integration of many ideas, thoughts, and opinions expressed during the task force process. In the end, of course, the final conclusions and recommendations are those of the Task Force Co-Chairs.

B. Current Stem Cell Research Activity at IUSM

No assessment of the feasibility of establishing a new Center can begin without first determining the present status of activity. By "status of activity" we are referring to:

- The quality of faculty working on adult stem cell research, including their productivity (peer-reviewed publications and grant support).
- The types of cells being investigated.
- The diseases being targeted for treatment with stem cells.
- Other approaches to assessing research such as biological processes.
- Types of research (from basic to therapeutics).

1. Faculty

The IU School of Medicine has a diverse group of stem cell investigators working in several areas and targeting multiple diseases. In rough numbers, **there are more than 30 self-identified adult stem cell researchers affiliated with IUSM,** with backgrounds in surgery, medicine, genetics, immunology, microbiology, biochemistry, and cell/molecular biology. [See Appendix 1] Most prominent is the work currently done that studies hematopoietic, cardiovascular, and cancer stem cells. These researchers have enjoyed success in publishing in the peer reviewed literature including more than 450 publications in the last 6 years. In addition, these investigators have reported success in obtaining funding for their work. Over $23 million has been obtained by IUSM investigators, with $18.9 million from the NIH, $3 million from private corporations, and $1.1 million from philanthropic sources. However, it is important to note that while these numbers are impressive, exact figures are not possible to obtain. For example, some publications mention the use of stem cells even though the focus of the research was not on stem cells per se. Similarly, it is not known what portion of all grant funding is devoted exclusively to research on stem cells.

2. Adult Stem Cell Types under Investigation as IUSM

The Task Force identified 7 stem cell sources currently under investigation by IUSM researchers: Adipose, Epithelial, Endothelial, Hematopoietic, Mesenchymal, Muscle, and Neural. [See Table 1] The majority of IUSM-based research involves the study of three major cell types:

- Investigators from the IU Cancer Center, the Walther Cancer Center, and the programs in hematopoiesis and immunology at the IU Cancer Center are investigating **hematopoietic**, or blood-related cells. Indeed, the largest number of investigators, publications, and grant funding is attributed to research associated with these cell types.

- A second area of work involves vascular biology and investigates **stem cells derived from the endothelium of blood vessels**, as well as stromal and adipose tissues. This is an important area for work since the cell sources have potential applicability in multiple disease states. These include, but are not limited to, diabetes, nervous system disorders, coronary and vascular disease, and cancer. Investigators from the IU Center for Vascular Biology and Medicine are using these cell types.

- Finally, an area that currently promises much in the way of potential treatment is that of **neural stem cells**. At IUSM, a small group of investigators from the Stark Neuroscience Research Institute are currently working on the basic science behind these cells and are performing studies on animal models.

In addition to tissue-focused differentiation, many investigators at IUSM are examining the pluripotential differentiation of these cells into more than one cell type. This is an attractive area of research in the field of adult stem cell biology, and its development is becoming more and more a primary objective for the future.

3. Disease Targets

The Task Force found that there are many potential disease targets now being discussed by investigators, however, three in particular have shown promising potential as therapeutic foci for adult stem cells:

- **Cancer and its many variants**
- **Coronary and vascular disease**
- **Neurodegenerative disorders**

Present scientific knowledge indicates that these three disease targets show especially promising clinical treatment potential. Further, there is some evidence of effective therapeutic use at least in the area of transplantation of bone marrow, peripheral blood, and umbilical cord blood stem cells for patients with blood disorders, such as leukemia and those with other tumors or genetic disorders whose hematopoietic system is compromised by treatment (chemotherapy and radiation).

Cancer is an especially important disease in which the important role of tumor stem cells for disease initiation and maintenance has now been recognized. Cancer serves as a target for correction of disease through intensive treatment and replacement of normal hematopoietic stem cells. It is now believed that it is not the total burden of tumor that initiates and maintains cancer, but rather a rarer population of tumor stem cells that produce malignant cells. Researchers are ultimately looking to stem cell research as a way to discover a means to target these 'cancer stem cells.' This differs from existing cancer treatment, and in fact may fill a gap left where current therapies actually spare the stem-like cells in cancer to the detriment of treatment efficacy. The majority of the current success using adult stem cells is in the treatment of cancer, especially through transplant procedures. In fact, some of the groundbreaking research in this area was first done at IUSM. For example, work that has been done in the Walther Oncology Center includes the original research demonstrating that umbilical cord blood collected at the birth of a baby contained hematopoietic stem cells that could be used to transplant and cure recipients undergoing treatment for malignant and non-malignant disorders. In addition, the first proof of principle as to the utility of a cord blood bank that supplied cells for the first cord blood transplant was initiated at IUSM.

Cardiovascular disease is the focus for multiple new developments in adult stem cell research. There are various causes for coronary and vascular damage, among them poorly controlled diabetes mellitus, hypertension, and hypercholesterolemia. The Indiana Center for Vascular Biology and Medicine is involved in several new studies to promote angiogenesis through use of progenitor and stem cells. Most recently, an FDA-approved trial has begun at IUSM in which bone marrow mononuclear progenitor cells are being

used to stimulate angiogenic growth in deteriorating limbs. This trial is the first of its kind to be approved in the United States, and will serve as the platform for multiple clinical and laboratory investigations, which might, in turn, lead to development of intellectual property material.

Neurodegenerative disorders are also among the most prominent targets for adult stem cells, with spinal cord injury and certain diseases such as Parkinson's as a focus of research efforts. The Stark Neurosciences Research Institute and other neurology researchers in the School of Medicine have worked to differentiate certain adult stem cells (neural, stromal) with the goal of practical application for degenerative disease. The stem cell approach to these diseases has potential in generating large quantities of brain and neuron cells by amplifying or immortalizing the primary neurons in culture. These cells could then be used for regeneration, repopulation, and transplantation into a damaged central nervous system. Most recently, the Institute has had success in using differentiated neural stem cells to help create a trophic environment to increase neuron reinnervation in a targeted region.

4. Beyond Cell Type and Disease: Biological Processes

Another important perspective for understanding the potential and future for stem cells is that of natural biological processes in response to disease stimuli and the effects of temporal change. These processes include:

- **Inflammation:** unwanted side effects encompassing cell production of cytokines and chemokines due to insults to the body
- **Recruitment:** movement to and retention of cells in the appropriate tissue site
- **Proteomics and genomics:** study of proteins and genes in cells
- **Aging:** the decline in physiological and cell function that is associated with time

A further process, **Regeneration,** is among the more exciting areas of investigation on the IUPUI campus, especially due to the work of the IU Center for Regenerative Biology and Medicine. [See <www.regen.iupui.edu>]. Regeneration involves the production of

new cells and tissues. Due to the ongoing difficultly in distinguishing between stem and progenitor cell types, the field of regenerative medicine provides a well respected set of research tools and approaches for understanding the prevention and treatment of disease, There is much evidence demonstrating that stem cells may act at least in part by a paracrine effect, where a trophic environment is created that acts via chemokine/cytokine signaling. The most valuable effect of stem cells, from this perspective, is to interact with and integrate into the normal functions listed above. As research and knowledge increase, this may become even more prominent in understanding the therapeutic applications for adult stem cells.

5. Types of Research

Current research at IUSM can be grouped into four categories (See Table 1).

- **Basic science:** the initial research that studies the character and properties of stem cells

- **Animal model:** the first line for testing the effects of stem cells when introduced into living tissue

- **Clinical/Translational:** the research that studies the effects of stem cells in the context of disease in human subjects

- **Therapeutics:** the study of stem cells used for the purpose of replacement and cure in disease states

While the majority of IUSM-based research involves basic science and animal model research, this is not dissimilar to the current state of stem cell research in general. In addition, some clinical and translational efforts are indeed beginning to take shape and we now have an established study for therapeutic applications. Presently, our scientific investigators are attempting to collaborate closely with clinicians and clinical investigators in identifying specific targets and focusing existing knowledge into therapeutic application. Of the 40 self-identified stem cell investigators who are involved in the basic science research, all but three work with animal models, while a quarter are involved in translational efforts. Only a few are investigating adult stem cells in therapeutic application.

Table 1

ADULT STEM CELL TISSUE SOURCES

DISEASE TARGETS

	Hematopoietic	Epithelial/Endothelial, Mesenchymal, Muscle	Neural	Stromal/ Adipose
Cancer/ Transplant	C. Chang[1] C. Orschell[1, 2, 3] K. Pollok[1, 2] L. Pelus[1, 2, 3] M. Yoder[1, 2] H. Broxmeyer[1, 2, 3] S. Fukuda[1] S. Goebel[1, 2] R. Kapur[1, 2] K. Pollok[1, 2] E. Srour[1, 2] E. Chan[1, 2, 3] R. Chan[1, 2, 3] R. Kapur[1, 2]	E. Srour[1] (Muscle stem cells) S. Goelbel[1, 2] H. Nakshatri[1, 2, 3] E. Srour[1, 2, 3]	F. Zhou/Anthony[1, 2] (Dopamine and serotonin stem cells for Parkinsonism (motor neurons))	K. March Lab[1, 2]
Coronary & Vascular Disease	E. Srour[1, 2, 3] K. March Lab[1, 2, 3] M. Murphy[1, 2, 3]	D. Hou[1, 2] J. Rehman[1] M. Yoder[1, 2] M. Clauss[1] E. Srour[1, 2] K. March Lab[1, 2, 3, 4] D.Ingram[1, 2] M. Murphy[1, 2, 3, 4]		D. Hou[1, 2] J. Rehman[1] E. Srour[1, 2] K. March Lab[1, 2, 3] M. Murphy[1, 2, 3]
Neuro-degenerative Disorders			E. Hashino[1] F. Zhou/Anthony[1, 2] (Adult spinal cord, retinal, and sensory stem cells) Y. Du[1, 2]	E. Hashino[1, 2] E. Srour[1, 2] Y. Du[1] K. March Lab[1, 2]
Regenerative		J. Ruiz[1, 2] M. Yoder[1, 2] D. Stocum[1, 2] (Derived by dedifferentiation) E. Chernoff[1, 2] S. Rhodes[1, 2] A. Mescher[1, 2] A. Neff[1, 2] M. King[1, 2] J. Rehman[1]	F. Zhou/Anthony[1, 2] E. Chernoff[1, 2] T. Belecky-Adams[1, 2]	K. March Lab[1, 2] M. Sturek[1, 2]

Key: **1** – basic science research
2 – animal model research
3 – clinical/translational research
4 – therapeutics

C. Potential Benefits and Challenges

There are many potential benefits that might become available to Indiana and IUSM with the creation of an Adult Stem Cell Center. The Task Force has identified four in particular. Among them, recruitment of new researchers is a necessary and attainable possibility. Also, the opportunity for collaborative work will be greatly enhanced. Greater collaboration will enable increases in cross-disciplinary studies. Additionally, promoting the ability to translate basic scientific research into tangible clinical benefits for patients is of high importance. A Center would contribute to all of these goals by creating an environment that fosters collegiality and collaboration among adult stem cell investigators. It would also establish a core of activity that could become a haven to attract other scientific investigators with interests and expertise in the area of adult stem cells.

Box B
Proposals for Tissue Repositories

Umbilical Cord and Placental Tissue

The use of somatic stem cells, particularly those stem cells derived from umbilical cord and placental tissues, as a therapy to treat human disease and aging is rapidly approaching and a need for banked clinical grade stem cells of many types, including endothelial and mesenchymal, will be the rate-limiting step. The proposed Center might not only serve as nationally recognized center for stem cell investigation but would be a recognized center for banking umbilical cords and placental tissue in order to harvest various cell types found within.

A key feature of the Center could be the statewide initiative to **S**AVE **O**UR **S**TEM **C**ELLS (**SOSC).** The focus of would be to develop a statewide infrastructure that will permit the collection, distribution, and harvesting of umbilical cord and placental tissue for somatic stem cell isolation, characterization, testing, cryopreservation, and banking. The frozen stem cells are prepared for both research and clinical use to permit ongoing advances in the field of adult stem cell research and for banking these various cell types in a way that permits statewide and national distribution for clinical treatments.

Adipose tissue

Another feasible banking opportunity might include the establishment of a broad-based repository for saving adipose-derived stem cells. This development of a novel resource could serve as a bank for IUSM as well as outside investigators involved in stromal/adipose stem cell research. The collection of these cells would be enabled by the fact that they are made available by one of the most commonly practiced surgical procedures, and as a result could be accessible for collection, typing, and storage to be used in research contexts.

As a central organization for research activities, the Center would provide an ideal situation in which to house various peripheral components of work relating to adult stem cells. One such possibility has been suggested involving the storage and use of umbilical cord and placental tissues that are usually discarded after birth. Another opportunity would involve establishing a broad-based repository for saving adipose-derived cells. Normally discarded tissue from already common surgical procedures could be collected,

typed and stored. [See Box B] In terms of producing benefits to patients, the Center would provide a preexisting apparatus for moving ideas begun at the laboratory level into clinical trials, and thus speed the development of treatment. It would allow important scientific progress to be developed into treatment trials in Indiana and in so doing, open up new opportunities to attract and retain clinician-scientists.

One of the challenges facing a center of this kind is to overcome delays that would inhibit the translation of bench to bedside proposals. In the past, a number of basic laboratory research findings made at IUSM were not first translated to clinical use here, but rather were translated elsewhere. Examples include but are not limited to: (1) the concept and research demonstrating that umbilical cord blood collected at the birth of a baby contained hematopoietic stem and progenitor cells that could be used to transplant and cure recipients undergoing conditioning regimens to treat malignant and non-malignant disorders, (2) the concept and research demonstrating that a small molecular weight compound, AMD 3100, could be used alone to mobilize hematopoietic stem and progenitor cells to the blood, and used in combination with Granulocyte Colony Stimulating Factor (G-CSF) to enhance mobilization of these stem and progenitor cells. Mobilized stem and progenitor cells are used to transplant patients with malignant and non-malignant disorders. Having an ACS Center that encompasses basic pre-clinical and clinical research should allow IUSM to quickly facilitate translation of the findings that are made here into therapeutic benefit.

A separate challenge for the Center would involve enhancing the development of new partnerships with commercial aspects as a funding resource. This potential might be present over the longer timeframe, and could include collaboration with existing organizations or even the creation of new entities.

D. Conclusions and Recommendations

Conclusions

1. The IU School of Medicine has a well established and diverse base of stem cell Investigators working in several areas. There are more than 40 adult stem cell researchers affiliated with IUSM, with backgrounds in surgery, medicine, genetics, immunology, microbiology, biochemistry, and cell/molecular biology. This suggests that the necessary foundation exists at IUSM on which to build a Center. However, it should

be noted that since these researchers self-identified, and because stem cell research is a broad category, these numbers are only approximations. [See Appendix 1]

2. Many potential disease targets are being studied by IUSM investigators, involving seven different cell sources. Among these, three areas in particular are dominant in terms of the weight of current efforts: cancer and its many variants, cardiovascular disease, and neurodegenerative disorders. These three areas of prominent research focus have shown promising potential as therapeutic foci for adult stem cells, and they form a basis from which the research capacity at IUSM can be grown and developed.

3. There is evidence of the capacity to obtain external support for research at IUSM. Over $23 million has been obtained by IUSM investigators who self-identified as working with adult stem cells, with $18.9 million from the NIH, $3 million from private corporations, and $1.1 from philanthropic sources. However, since it is not known what percentages of the grants are for stem cell research, these numbers are only approximations of funding for stem cell work.

4. There is evidence of positive clinical results from current research efforts and emerging clinical trials in other areas. For example:

- Umbilical cord blood, pediatric, and adult blood and bone marrow hematopoietic stem cell transplants are now an accepted treatment that has helped cure patients with leukemia, other cancers, and non-malignant genetic disorders whose hematopoietic systems have been compromised by chemotherapy and radiation. While this is an accepted treatment, there remains much work to be done in investigating hematopoietic stem cell potential and how to most efficiently use these cells

- An FDA approval of a purification protocol involving a stem cell selection device based on the work done by IUSM researchers

- An FDA-approved clinical trial is underway in which endothelial progenitor cells are being used to stimulate angiogenic growth in deteriorating limbs

- There are also two other related trials that are pending approval

5. Many potential scientific benefits are likely to arise from establishing an Adult Stem Cell Center, including:

- Providing the opportunity for existing investigators to expand into cross-disciplinary studies, bringing multiple cell fields and sources into contact;

- Attracting new investigators to IUSM with unique and complementary abilities and in so doing;

- Increasing the likelihood of attracting additional external funding from grants, contracts, and philanthropy;

- Enhancing synergistic collaboration that promote the exchange and progress of ideas; and

- Translating scientific work into clinical trials. This will occur by developing an organized structure for translating scientific research so that stem cell efforts would be more quickly and easily brought to the patient's benefit.

Moreover, the scientific benefits may translate into new jobs and have considerable intellectual property potential.

6. There are several domestic and international initiatives either underway or planned that will have an impact on any IUSM (or state-wide) initiative in this area. For example:

- Eight states have passed legislation that provide funding for stem cell initiatives, with almost as many others considering similar measures in the next year. Three of these are looking exclusively at adult stem cell research, while the others are addressing both embryonic and adult stem cells. [See Appendix 2 for a more detailed overview].

- Federal legislation regarding stem cell research is also being considered. In May 2005, the US House of Representatives passed HR 810, "to amend the Public Health Service Act to provide for human embryonic stem cell research." This bill, if enacted, would expand the number of eligible

embryonic stem cell lines for federal funding. Competing legislation is also pending, including HR 3144, the "Respect for Life Pluripotent Stem Cell Act of 2005," which focuses on techniques that do not require destruction of an embryo.

- In October, 2005, South Korea announced its intention to establish a world stem cell hub aimed at making their country the center of a global initiative for adult and embryonic stem cell banking and research. The United Kingdom and Singapore also have announced broad initiatives.

7. There is growing agreement that advances in stem cell investigation are now being made with an eye to cooperative efforts in research, rather than competitive ones. However, the rapid pace with which stem cell centers of excellence are being considered and then established in the United States and elsewhere leads the task force to conclude that time is of the essence if Indiana and IUSM are to attract and retain quality researchers and promote leading contributions to knowledge about stem cells.

Recommendations

Recommendation 1. **The IUSM should move forward expeditiously with plans to develop and establish an Adult Stem Cell Center.** If a Center is not established soon, much of the opportunity for Indiana to take a leading role in adult stem cell research may be lost.

Recommendation 2. The Center should approach research from the perspective of both cell-type and disease target, building from those areas in which IUSM has already demonstrated progress: Hematopoiesis, Cardiovascular disease, and Cancer.

Recommendation 3. The Center should promote research at all levels, from basic science through therapeutics. However, emphasis should be given to the promotion of translational research, and should encourage and enable any application of stem cells for patient treatment and cure.

Recommendation 4. **The Center should have a multidisciplinary structure**, involving basic science investigators, clinicians, imaging experts, and geneticists, among others. This would allow stem cell research to draw on many areas of science, medicine, and

technology to ensure that all the potential therapeutic benefits of adult stem cells are realized. Take for example the involvement of radiologists for imaging; other researchers capable of following the migration/insertion of labeled stem cells into the targeted organ in 3-D rendering, or following dynamic events in 4-D (time); and genomic analysts using RNA arrays is a particularly good way to look at global changes in gene expression during differentiation.

Recommendation 5. **The Center should work to address applications for stem cells in research on which IUSM, as yet, has not been able to focus**. There are several examples of this, such as diabetes mellitus, recognized as a fast-growing and very important area of research. Also in this category are certain neurodegenerative disorders, among them, spinal cord injury, Parkinsonism, and auditory cell replacement.

Recommendation 6. While describing the potential scientific and clinical merits of such a Center are necessary for moving forward with plans for its establishment, other logistical and financial issues must be addressed separately**. The IUSM should seek additional input on the following issues:**

- Costs and sources of financing for both start-up and long-term support.

- Logistics, including the space (whether virtual or concrete) in which a Center would be located.

- Administrative structure, including whether the Center will function as its own department, be housed within an existing department or school, and other factors related to reporting relationships.

- Organization of the Center, involving status of involved faculty (full or part time), and possible cross-appointments

- Operational focus, both initially and also as expansion and development of the Center occur

Recommendation 7. The IUSM should develop a database (or refine an existing one) that can identify investigators, publications, and grant support directly related to stem cell research. As the Task Force discovered, there are little data to accurately

describe which investigators are conducting stem cell research, how productive they are, or how much stem-cell specific support they are receiving. More accurate data will be valuable in describing the potential for excellence in this area.