The University of Maryland’s Center for Stem Cell Biology and Regenerative Medicine is driven by a single imperative—providing better diagnoses, treatments and preventions for disease. That’s really what biomedical research is all about. Our currency as scientists consists of the published papers we write which become the historical record of our discoveries. These are the products that stand out as the objective landmarks of our careers. However, I believe the long-lasting impact of what each of us in biomedical research truly accomplishes should be measured, not by papers, but by the benefits to patients and community health.

I’m reminded of a young man I think of as a poster child for purified stem cell therapy. He was just 18-months-old when he became my first patient in a pilot Phase I trial I had just started. He had a soccer ball-size tumor in his belly, and the cancer had spread to his bone marrow. There was no option other than the one offered through the clinical trial testing purified stem cells. Today, this young man plays soccer, is a sophomore at the University of Maryland, and is living proof of the impact of stem cell research.

Our directive at the Center is to work toward human benefit—and to work quickly. We are targeting research that will go from lab bench to bedside to community, and then back again to the lab with the next health problem. The founding of the Center
in 2008 comes at a pivotal time in stem cell research. The repeal of federal restrictions will open up National Institutes of Health funding of stem cell research projects. Scientists will be free from the burden of ensuring that non-federally-sponsored experiments don’t trivially utilize restricted federal resources. One of the most important consequences of the repeal of restrictions will be the emergence of a global stem cell research community made possible by the removal of artificial boundaries between those of us under the previously restrictive U.S. guidelines, and researchers in other countries able to pursue scientific discoveries within standard policies governing all animal and human research. We anticipate the benefits of such energized research efforts, and eagerly invite the interaction of scientists worldwide who will be partnering with us in the joint pursuit of discovery.

On still another front, we look forward to the first clinical stem cell trials for spinal cord paralysis authorized by the Federal Drug Administration’s clearance of Geron’s investigational drug GRNOPC1. Some of the first patients in this Geron clinical trail may be treated in the University of Maryland Medical System’s Shock Trauma Center.

My laboratory’s 1984 discovery of a way to isolate stem cells provided a critical step for studying and transplanting them. This and other similar tools developed in the laboratory are currently used in leukemia diagnosis and clinical bone marrow stem cell transplantation. They lay a foundation for our young Center, and corroborate our ongoing studies focusing on the genes expressed in stem cells, and the modification of specific properties of stem cells to increase their therapeutic capability.
We are fortunate that the Center is supported by a continuing alliance with colleagues from my 30 years at Johns Hopkins, as well as by scientists at the National Cancer Institute, other National Institutes of Health and leading research organizations in Maryland and beyond. Here in Maryland, we have the solid support of our Governor and legislature, partly because of the presence of one of the largest biotech industrial components in the country. A Bio-Park, located on the University of Maryland Baltimore campus, houses several biotech companies explicitly relevant to stem cell research, some with manufacturing facilities. As we get closer to commercialization, these companies will be a decisive asset for us. Maryland is a life sciences-rich state, continually being made more prosperous by having two leading academic medical entities, whose scientists’ discoveries provide their physicians and medical caregivers with new clinical tools. One example is the University’s Shock Trauma system, recognized as the most advanced in the world. This, together with the University’s recent appointment of a world-class trauma researcher, Alan Faden, MD, leads one to consider stem cell therapies for spinal cord paralysis, and possibilities inherent within stem cell biology to prolong the “golden hour,” the current time limit for preventing severe organ injury or death.

There is a broad and deep research culture at the University that enhances the Center. The University of Maryland Baltimore campus receives nearly $400 million per year in research grants, and the College Park campus receives a similar amount. For example, Ricardo Feldman, PhD recently received a large grant from the Maryland Stem Cell Research Fund (MSCRF) for his studies into the generation of potent-specific induced pluripotent stem (iPS) cells for modeling and treating Gaucher disease. Last year, a major MSCRF grant went to Richard Eckert, PhD for his work on epidermis (skin)-
derived multipotent cells for cell therapies. Another scientist with a large MSCRF grant award is Laure Aurelson, PhD, who works on stem cell transplantation for severe Herpes Simplex Virus (HSV) skin infections.

The vision at our Center is to create a stem cell research environment that fosters a broad range of interdisciplinary research designed to fully understand stem cell biology, while at the same time affecting human health and disease. Right now, in stem cell research, it is as if we understand some of the words, but we need to learn the whole sentences and paragraphs of the stem cell biology book. For example, we have identified some of the genes whose products are necessary for stem cells to make blood. We know that if these genes are mutated or knocked-out, we won’t get blood. But what we don’t yet have is the full system of molecules needed to grow clinically useful amounts of blood from stem cells.

An example of research aimed at such understanding is my own laboratory’s current research on hematopoietic (blood-forming) stem cells. We seek to understand the regulation of stem cell function at the fundamental molecular level. However, our reasons for seeking this understanding are clinical. We want to manipulate stem cell regulation to grow these cells outside the body, then direct their differentiation into blood cells for better transplantation and transfusion therapies. Further, we want to block stem cells that sustain leukemias and other cancers. Once we have nailed the basic understanding, we will translate the lab bench discoveries to bedside patient treatments.

Bone marrow transplantation has been around for 50 years, but is still an expensive and high risk procedure. Blood transfusions, which are widely used, remain risky if one contemplates the possible intrusion of some new unknown virus, for which
we have no way of testing. In fact, I’m amazed that, in the 21st century, we continue to do transfusions of blood from donors.

What if we could take stem cells from the bone marrow, purify them, then grow them like yeast in a fermentor? Currently, when we try to do this, the stem cells will proliferate, but at the price of differentiating, resulting in our quickly running out of them. However, what would happen if we were to grow them as stem cells, allow them to divide, and divide, and divide? Then, if a patient required a red blood cell transfusion, we could add the right molecules to a few of the stem cells, changing their condition so that they will differentiate into blood cells sufficient for transfusion. The other possibility is that of creating universal donors to be available when needed for a sick patient. We can’t do any of this now. But we are hopeful that we will be able to do so as we understand more about the early stages of stem cell development, and learn how to keep a cell at the stem cell stage, and have it divide but not become leukemic. These are the kinds of challenges we are taking on at the Center. We have made strides, as have others. The first step was to purify the stem cells. Now we need to expand them significantly.

Evidence surrounding the correlation between basic understanding and therapy is seen in a successful collaboration of my laboratory with a colleague at Johns Hopkins, Donald Small MD/PhD. It’s possible to improve diagnosis, treatment and prevention, not by transplanting the cells, but by working with purified hematopoietic stem cells in the lab. Dr. Small and I identified a molecule that is key to stem cell growth, and later it was shown that this molecule mutates in leukemia. This led to Dr. Small’s development of drugs against the mutant molecule that are now used to treat leukemia patients. Stem cell research isn’t only about transplantation. In this case, the understanding provided by stem
cell research led to a very specific “targeted” therapy which we hope will be more effective, less toxic, and far less expensive than a transplant.

In order to further approach our mission of increasing understanding while attacking disease, Center investigators work with all kinds of stem cells—adult, embryonic, and iPS—and using multiple species as models. Our purpose is to pair the type of stem cell and model system with the application to get the most accurate results in the shortest possible period of time.

In that regard, as a result of reorganization by the Regents of the Maryland University System, the Center of Marine Biology (COMB) is now integrated into the University. COMB investigators’ continuing interest is in preserving the fish of the Chesapeake Bay, including for example, genetically re-engineering the fish for enhanced fertility. Our Center’s interests in utilizing simpler model systems for stem cell biology has opened up new opportunities for interaction.

While much of what we know about human cells emanates from work with bacteria and yeast, these microorganisms have only one cell and no tissues or organs. However fish share most of the genes and have many of the tissues and organs of humans, and so fish, especially the transparent zebrafish, are excellent models for stem cell biology. Compared to mice, they can be bred quickly and in large numbers inexpensively. Many of the genes that play a role in human stem cells play roles in the stem cells of fish as well. So we can use these fish as models to quickly figure out how genes are involved in development and in stem cells—and as a bonus, zebrafish can be used for drug treatment and toxicity studies.
One specific comparison involves the knock-out mouse, which takes a year to develop, contrasted with the fish in which large numbers of fish with the knocked-out gene can be generated much more quickly. Whereas a mouse or human cell has layers of protection that can replace a knocked-out gene, a fish cell may have no more than one or two family members of a gene that can compensate for each other, making it easier for stem cell biologists to determine the action of a given gene. Another promising fish model is the lamprey, which has a primitive type of immune system, and which is of interest to us in developmental biology of the immune system. We are particularly excited about our new association with Yonathan Zohar, PhD, a world-class fish biologist at COMB. Undertaking research in fish without the collaboration of COMB scientists would require our recruitment of a top investigator with Dr. Zohar’s credentials. Our plans for late summer include setting up a stem cell core laboratory at the COMB Inner Harbor facility, staffed by human stem cell biologists who will interact with Dr. Zohar.

Our interactions within the University system are expanding even further with recognition of the need to educate undergraduates, graduates and postgraduate trainees about stem cell biology. We have been fortunate in engaging enthusiastic participation that includes a student stem cell organization founded by a student with a severe irreversible spinal cord injury sustained in a swimming accident. Our involvement with the ethical, legal, and societal issues associated with stem cell research includes important interactions with the faculty and students of the University of Maryland School of Law. A highly technical subject like stem cell biology can be misregulated if lawyers (many of whom are legislators) don’t understand the science, and scientists don’t understand the legalize.
A key component of our Stem Cell Center is the development of core resources for our research that will enhance stem cell production, differentiation and banking of the cells. Human embryonic cells are among the most difficult of any cells to grow in the lab. In fact, many researchers avoid or abandon work with human embryonic stem cells because of this. In many centers including our own, there is a core laboratory of cell biologists who artistically nurse the cells and provide the human embryonic stem cells to university-wide scientists for research. The specific team of scientists who work exclusively on the technically demanding problems of growing these cells makes possible the experiments of many other scientists. Instead of working for a year to grow stem cells, a biochemist can order the cells needed to obtain and study the RNA for new stem cell genes and pathways. The other core we are currently creating is one that can modify the gene expression in stem cells, for example, to induce them to better differentiate into blood cells.

In the final analysis, it is by understanding the inner mechanics of how stem cells work that we will be successful in diagnosing diseases earlier, curing them more effectively, and someday preventing them. In addition, by modifying the key properties of stem cells, we may enable better transplantation and transfusion therapies. Our scientists continue to work toward these aims.

It is likely that the goals of many attending this World Stem Cell Summit are similar. We are all working toward the defeat of disease as we know it today. I believe the assembly here of so many scholars and other interested parties working in different realms toward the same objectives provides hope that we will achieve these dreams. I
look forward to the chance to interact with many of you at this meeting in the months and years of progress ahead of us.