Cell Society, La Jolla, CA - February 18 and 19, 2011

Opening Keynote and Welcome

Kiyoshi Kurokawa, MD / 2,150 words

Our body has been a wonder and miracle to all of us. Just think, one fertilized egg, through cell multiplications in an amazingly orderly and coordinated manner, becomes a baby and comes out of the mother in 10 months. It continues to grow for 15–20 years when it becomes almost an adult with some 50 trillion cells, with distinct forms and functions of very complex organs and complete body systems. AND OUR BRAIN FUNCTION, to think and to create – it made our civilization what it is today.

Hundreds of millions of cells die every day, replaced by a similar number of new cells – thus the size of the entire system will remain stable and our body size will remain more or less constant after around the age of 20.

We knew about these things for years, but could not understand HOW they happened. As our indigenous knowledge about health, disease and body systems increased and accummulated, we began to understand HOW.

Nonetheless, we recognize major scientific discoveries were made in the last 100 years or so. They were built upon many years of prior critical observations, knowledge, and experiments of many – aided by a variety of scientific discoveries and technological and engineering advances:

- 1. Edward Jenner's small-pox vaccination of 200 years ago is a major breakthrough in the human history of medicine.
- 2. We learned of sanitation, hygiene, nutrition, and they become a major force to improve health.
- 3. We could see major breakthroughs of the past 100 years or so in the list of Nobel laureates which began in 1901; the first year of the 20th century.
- 4. They included discoveries of the existence of ABO blood types, the nature of various infectious diseases by bacteria, virus, and other forms like malaria, vitamins and hormones, cell function and regulation, molecules to DNA and many

other breakthroughs.

Indeed, now detailed anatomy, function, regulatory mechanism of body system have most been clarified to the level of organs and body systems, of cells and molecules, of genomes, and even at the level of chemical and atomic compositions.

While many cells die and regenerate, which is the dynamic process of our body, many organs may have their own resident STEM CELLS · as the origin of its own cell types, generating new cell types; such stem cells may sometimes attach to dead spaces from circulation with some specific signaling interaction.

Stem cells have been found in many organs, and could be used under certain conditions, to become pluripotent – the ability to become many different cell type.

1. Stem cells for a patient could be obtained by the enrichment of organs such as adipose tissue for potentially several distinct diseases, e.g., cardiac infarction, liver disease, or reconstruction of a removed organ, e.g., breast reconstruction after surgery.

This is the focus of this conference and we will hear great deal of progress in its science as well as their clinical applications. Thus, I will briefly touch upon the other stem cell types described below.

- 2. Embryonic stem or ES cells; created via in vitro fertilization and thus contains the eggs of a donor along with its related ethical issues—— this ES cell was particularly genuine since it could become a baby and thus a human being.
- 3. Umbilical cord blood cells
- 4. Induced pluripotent stem cells; or iPS by Dr. Yamanaka and others.

This iPS or re-programming ordinary cell of our body, e.g., a small piece of our skin, opened a new way, bypassing the use of embryonic stem cells and thus the ethical issues of securing human eggs.

However, because of various issues, including markings of DNA of the original well

differentiated cells, or epigenetics, there may still be more rigorous steps needed for its clinical use. Nonetheless, iPS provide various clinical utility for cell function, screening for drug action, specific disease cell types from patients with specific diseases and genetic disorders.

We are not certain of the impact and mid- to long-term consequences, thus we have to be very careful in balancing the potential benefits and risks to patients until more be known through various studies and data. Such prudent and transparent processes are the key to securing public trust and support.

## CHANGING WORLD

Internet and connectedness have changed the way we communicate and engage in social activities and life style. Many of you had PC's and laptop computers in the 80s and 90s. The internet has become more and more accessible and connected every year since the introduction of the world wide web in 1991.

Initial barriers for access to internet, have been overcome very fast – year after year so that now, almost everyone uses and carries at all times one, two and even three computers in their pockets. Technologies like the iPhone, iPad and BlackBerry are used constantly, wireless in a completely mobile manner.

We have become more and more inter-connected. Increasingly, the general public has access to a lot more information and those who suffer from various diseases are desperate to have the 'dream therapy' like those related to stem cells.

The research results are not owned only by the science community, but shared with a large public across national borders. Nonetheless, scientists must be careful to pursue research in the labs and with patients.

Potential risks, safety, efficacy, quality of research as well as clinical studies and other elements for the new discovery of stem cells to patients are tedious and carefully conducted through a critical analytic process. Transparency and rigorous, critical assessments are of vital importance.

This forum of the Cell Society is aimed at exactly that; to provide such progress and

to share with you, the scientists, clinicians, patients and their families as well as the general public, the frontier and the state-of-the art of stem cell research.

Further the forum should promote better understanding and stronger support from the public and various stakeholders and, as situation permits, an opportunity for investment —— I will come back to this a bit later.

When such therapy becomes clinically available, then who will pay? Health and reimbursement policies differ by various countries. Even with a well-established public health policy, a question always remains – who pay for what disease and in what condition.

Even in this era with a wide range of ability to travel, many patients will go abroad to receive such treatments. This may create a situation where only the rich can afford such treatment. Is this ethical? What should be the guideline? Is it just?

A few days ago, we learned that Watson, IBM's supercomputer scored a major victory over two human champions in a quiz-show called 'Jeopardy'.

What does this mean? It may mean that the ability of computing system went NOW, to real artificial intelligence. Watson takes questions in spoken in English, recognizes spoken language, searches thru a massive database, matching back and forth through vast databases and picking up the most likely answer in just a few seconds.

The implications are huge. When you think of some question, how do you find the answers? Many of us now use Google, but you still have to think of your answers. NOW, this Watson will do it for you.

You may say it's expensive. Of course, but remember your lap-computers of 90s? Its size, cost, functions and speed?

In these days, there were many search engines and some have gone, some have survived. Google was founded in 1998, just 12 years ago, and went public in 2006. Its service was, in principle, provided at no cost to users (recently on newspapers and books, they proposed a new business model based on the tough competition with

## Apple).

Watson's database could become available sometime in the not-so-long future - hopefully. How about cloud computing? Microprocessor becomes faster, smaller, and cheaper. The speed of progress in IT and its associated technologies and business models has been very, very fast and similarly unpredictable. Just think of FaceBook. Its history is only a few years old, yet the speed of its spread is very, very fast indeed.

You may argue biomedical science is more complex and difficult since their applications are for humans. That is true, but many unexpected things could happen in very unpredictable way in this global world with more competitors.

Just think of the human genome project. It began as an international collaborative effort headed by Dr. Francis Collins, now Director of the NIH. This consortium was supported, in principle, by public money. Then, Craig Ventor jumped in with the new 'shot-gun approach', but he began his attempt as a private venture company. The fund? Of course, it came from private investors.

But, because of this competition, the human genome project was almost completed in 2000 with President Clinton, Francis Collins, Craig Ventor and Tony Blair on TV together.

Originally, the Human Genome Project was expected to reach this stage of decoding around the year 2005. However, it can be said that Ventor saved a great amount of tax payers' money by shortening the time period for decoding.

The same could apply to stem cell research. And now there are more and more competitors with rising new economies.

Everyone will want to have the right cure for various diseases. Stem cells are a big hope for many very difficult diseases such as spinal cord injury, various neuronegenerative diseases, stroke, and many other conditions you hear about today and tomorrow.

Stem cells could eventually eliminate organ transplants by repairing the heart, liver,

and kidney directly as well as skin grafts, tissue engineering and many more.

Even stroke – by replacing lost brain cells, ie, neurons and glia. Great hope.

We all wish to live a good and long life. What kind of life? Healthy, stay young; look, feel and live long young life. All of course.

How about if you could never look over 50 years-old, even though you may actually be 80, 90 or even 100? Skin texture and hair? That is really, really super, and it is a big possibility. Thus, internal organs, organ system and external body system may artificially regenerate at certain intervals. Many may eventually live longer than 100 or even 130 while staying healthier and looking no more than 50 or 60 year-old. This is great stuff, but this may not be a medical issue, but cosmetic one.

Suppose if you receive stem cells after brain stroke, recovering from paresis or paralysis. This is great.

As you live longer you may receive such procedures more than few times – eventually losing a considerable portion of your original brains?

Is this still you? You may lose a lot of old memories replaced with perhaps new memories?

NEW YOU may be someone else?

Such things are not beyond imagination.

How about a combination with robotics? Many robots or humanoids already do many human functions. You can make something just like humans or even you. There are a few devices that support a fragile musculoskeletal system of the aged and those who suffer from stokes.

You may eventually have your own 'second life' or 'avatar'.

This may not be as far-fetched as you may think. Watson is a major decision maker for you - to choose the right answers whenever you have a question. You already

do this quite often everyday – by Googling your questions using keywords and finding your own answer. Now, you can speak to Watson who will immediately find the right one for you.

With ICT, nanotech and nano-materials and biotechnology, Ray Kursweil, a futurist and entrepreneur, predicts in his book 'Singularity is Near' that in coming 20-30 years, all knowledge currently learned through college could be embedded on a very tiny chip which you could simply implant into your brain.

It is amazing the speed at which science, technology and engineering progresses. Now, with more and more such experts involving in this process, thus tougher competition, many unpredictable things will happen.

Think of Steve Jobs, who created a tabletop computer, animation movie at Pixar, music business by iTune and iPod, mobile phone by iPhone, and now a publishing house and newspaper by the iPad.

How about Google, Facebook, twitter?

They are the forces behind recent major and unpreditables in Tunisia and Egypt as well as several other places in the Middle East. How about Wikileaks? Clearly, the world has become seemingly quite fragile.

Even this frontier of stem cell research with great and various implications, its impacts on human life and societal changes may be unpredictable and quite interesting.

Unpedictables could always happen in sciences.

I am very much looking forward to listening to the presentation today and tomorrow, on what you are exploring in this new frontier of biomedical sciences.

Your effort and dedication are very much appreciated and Cell Society is committed to connect this area of research to the patients and their families inviting participation of multistakeholders of our global society at large

THANK YOU.