CONFERENCE SUMMARY

Conference summary of the First International Association of Neural Restoration Annual Conference (IANRAC)

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The First International Association of Neural Restoration Annual Conference (IANRAC) was held on May 15 ~ 18, 2008 in Beijing, China. It was sponsored by the International Association of Neural Restoration (IANR), and co-sponsored by the Beijing Hongtianji Neuroscience Academy, the Neuroscience Institute of Taishan Medical University, and the Chinese Journal of Reparative and Reconstructive Surgery. The representatives came from China, United Kingdom, United States, Spain, France, Australia, Japan, Argentina, Jordan, and the Hong Kong Special Administrative Region.

With the purpose of "establishing neurorestoratology and promoting basic and clinical research on neural restoration" and with the theme of "Neurorestoratology", the conference reviewed the past, faced the present, and prospected the future on neural restoration; carried on the discussion on related issues of neural restoration, discipline construction, and the impetus strategy as well. Many world renowned experts in the field gave exciting special reports, including basic and clinical research on neural restoration, basic and clinical research on peripheral nerve restoration, cell transplantation on spinal cord injury, topics on stem cells, various intervention strategies on neural restoration, basic research on neural restoration, and clinical application of cell transplantation.

As the only international specialized academic organization in this field, the IANR has been given a historical mission, professional tasks, social responsibility, and the goal of meeting patients' expectations. The successful conclusion of the 1st IANRAC moved the new subject, neurorestoratology to the international academic platform. The conference also elected the 1st Council of the IANR for a term of 3 years.

Association and Subject Creation

Professor Huang Hongyun, as the president of this conference's organizing committee, emphasized in his speech that Neurorestoratology is a sub-discipline of neuroscience which studies neural regeneration, remodeling, restoration and functional recovery. Its purpose is to promote the recovery of neural function of all patients with neural degenerative diseases and damages. Its strategies are to stress the close combination and organic integration between basic research and clinical research, to emphasize the solution of practical problems of clinical medicine and preventative medicine, and to insist on always setting the direction according to clinical research while constantly enriching the knowledge gained from basic research. Its main goal is to promote a coordinative effort to improve both basic and clinical research rapidly; to break the barrier between basic research, pharmacy development and clinical medicine while establishing the direct links between them; and to shorten the process from bench to bed, thus transferring the basic research achievements of neurorestoratology into new methods for the clinical treatment and faster patient benefit from medical, scientific, and technological advances.

Establishing the IANR would create a broad professional platform of exchange for global basic scientific researchers and clinicians working in the neural restorative field. It would be beneficial to increase the depth of basic theoretical research related to its subjects, to

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improve and perfect the intervention strategies, to raise the effectiveness of the restorative functions, and to promote the development of neurorestoratology.

Topics on Olfactory Ensheathing Cells (OECs)

The world renowned experts in the field of olfactory ensheathing cell research came to Beijing to attend this conference. Prof. Almudena Ramón-Cueto from Spain gave a presentation titled, "Auto-transplantation of olfactory bulb glia to repair spinal cord injuries: clinical perspectives". She pointed out the following: traumatic spinal cord injuries (SCI) have a big impact on our society. Several attempts have been made to find a repair strategy in experimental animals that could be translated into human application. In 1990, researchers started a series of experiments, and their studies demonstrated that adult olfactory bulb-olfactory ensheathing glia (OB-OEG) transplants could functionally and structurally repair spinal cords completely sectioned for adult mammals. To elucidate the feasibility of OB-OEG use in humans, they carried out animal experiments with primates. The studies showed that *ex vivo* expansion of one single primate adult OB-OEG for up to 2.5 months *in vitro* could yield enough OEG (2×10^{10}) to guarantee both auto- and allo-grafting, with excess cells to be stored in banks for future therapeutic use. In addition, they have developed medical and surgical procedures for autologous (and heterologous) OEG transplantation in rhesus monkeys, compatible with human application. Strikingly, in the first paraplegic monkey transplanted autologously with OB-OEG using their technique, they observed a tangible functional recovery by objective neurophysiologic assessment, and step-training on a treadmill promoted neurological functional recovery. As an important marker of olfactory ensheathing cells, p75 positive rate accounted for about 35 percent in Ramón-Cueto's laboratory. She believed that this was a major part of executive function. She summarized that olfactory ensheathing cells have four unique abilities to repair nerve injuries as follows: can be used for autologous transplantation, can integrate with other natural glial cells, will not form tumors, and can express a variety of regeneration associated factors. Professor Meng Inn Chuah from Australia introduced the restorative functional mechanism of olfactory ensheathing cells: ① OECs express growth factors and membrane-associated molecules that are known to promote axon growth. ② OECs are able to mingle with astrocytes, regulate GFAP expression in astrocytes mediated by FGF family member. ③OECs and microglia interact in the inflammatory response, OECs function as phagocytes. ④ OECs express cytokines and molecules of the innate immune system such as Cebpb, Lyz, Ccl2, Gro1, Ctgf for example. As a scientist having a tremendous impact on this field, Geoffrey Raisman, the researcher from the British Royal Academy of Sciences, proposed the tunnel theory of nerve regeneration. He explained the complexity of neural remodeling and the importance of neural rearrangement. He believes that cell transplantation strategy should be used in clinics, and more work should be done. Researcher Ying Li, who worked in his lab, introduced their work in which they had transplanted OECs into the damaged spinal cord to promote neural regeneration. The transplanted OECs could help restore the integrity of the original pathway, and promote some functional recovery. She suggested that it was better to perform cell transplantation with all types of cells under physiological status. She agreed that people should use different animal models of spinal cord injury for different research purposes. Wei Kai-bin (Shandong) proposed that the combination of OEC transplantation and methylprednisolone might effectively treat acute spinal cord injury. Liu Yan (Beijing) studied the Low-affinity NGFR positive OECs in the human fetal olfactory bulb. She compared fetal olfactory ensheathing cells' development in rats and humans and discussed their distribution, effects, and culture technique. Her data strongly suggests that p75-positive OECs participate in glomerular formation in the fetal human olfactory bulb. This behavior differed from OECs in the rat olfactory bulb. About 40% of the cells expressed p75 in culture. This result is similar to the results of OECs cultured in primates by Professor Ramón-Cueto. Professor Alan Mackay-Sim's (Australia) presented the experience of three patients with chronic spinal cord injury receiving autologous transplantation of adult OECs from olfactory mucosa after three years follow-up, and suggested that the procedure of OECs autografting transplantation was

safe. Professor Huang Hongyun (Beijing) reviewed the functional restoration by OEC transplantation for spinal cord injury, ALS, cerebral palsy and stroke in 1,255 cases. All the data strongly suggests that OEC transplantation for these damages and diseases is a safe and effective procedure. Zheng Zuncheng (Shandong) reported the clinical treatments of SCI with OEC transplantation. He suggested that the ASIA rating scale could not comprehensively reflect the changes of a patient's quality of life, so a new evaluating scale which was proper for clinical application needed to be designed.

The Theory of Evolution and Neural Restoration

Professor Wang Dajue (British) explained the restorative mechanism of a spinal cord injury by evolution theory. Spinal cord injury is part of biology, so it is closely related to the evolution theory. It is unwise to ignore the evolution theory; both the species and the cell germination are controlled by molecular evolution. Evolved into the more advanced stage, the participation of factors was increased, thus control was more difficult. From the viewpoint of evolution theory, the neural cells with regenerating ability in the human body have to be the most ancient structures in the mature nervous system (the olfactory system, the limbic system, and the network structure). According to Professor Wang Dajue's observations, most patients treated by Professor Huang Hongyun's OEC transplantation sweat on the day after surgery, so this was the short-term response to the treatment. The restorative functions still existed on long-term follow-up. He analyzed that the older the system, the easier it is to be restored. The higher developed species are less likely to be restored. The order of easily restoring spinal cord injury is precisely the same as the order of treatment preferred. The first priority is survival; the second is improvement in the quality of life. He believes that we should rethink whether the strategic principle that overemphasizes body movement is correct.

The Central Nervous Restoration

Professor Liu Enzhong (Heilongjiang) introduced the pathological process and the changes in molecular biology following an injury to the central nervous system. The self-protective body response occurs with injury, so he explored the time window of intervened treatment and the prospects of restoration in CNS. He believes that neurorestoration of CNS should include not only nervous structure reconstruction, but also neurological functional recovery. Professor Luan Zuo (Beijing) reported the strategies on pediatric neurorestorative intervention. They selected eleven cases of children with cerebral palsy accompanied by visual impairment, and did human neural progenitor cell transplantation. Three to six months after transplantation, they found that the children had visual functional progress. Their primary conclusion was that the neural progenitor cell transplantation is a safe and effective method for children with cerebral palsy accompanied by severe visual impairment.

The Peripheral Nervous Restoration

Professor Zhang Shaocheng (Shanghai) reported the experimental and clinical research of the side-to-side anastomosis between the nerve tracts. It has been found that the clinical effect is better by using side-to-side anastomosis than by using broken ends anastomosis. This method was effective for the patients with brachial plexus injury, peripheral nervous injury and local spastic cerebral palsy. Professor Liu Song from French Pasteur Institute reported his experimental therapeutic research about brachial plexus injury. After establishing the rat C6, C7 dorsal root cut model, peripheral nerve tissue transplantation was done below the injured region. Histological data showed that grafts could go through the strong GFAP positive gliosis region and measurement of toe to toe distance and the weight distribution of different toes improved after transplantation.

The History and Current State of Neurorestoratology

Dr. Chen Lin (Beijing) reported on many important historical events and scientists who have conducted basic research of neurorestoration over the last 100 years. He showed the neurorestorative intervening strategies' processes of CNS on a panoramic display.

Professor Huang Hongyun (Beijing) believes that the clinically exploratory treatment of neurorestoration was the major driving force for promoting the development of neurorestoratology. Neurological functional recovery and improvement in the quality of life have become realistic goals through neurorestorative intervention strategies. Though embryonic and fetal brain tissue transplantation were controversial, they were critical to the development of clinical neurorestorative treatments. Cell transplantation; biological, genetic and tissue engineering; medicine and other physical factors; and neurological rehabilitation's intervention strategies might help neurological functional restoration. So it should be objective and fair to evaluate these achieved results through active exploration. Scientists and physicians should focus on how to improve the neurorestorative effect in the future. The strategies were the following: (1) optimizing results by combining the methods which have been proven effective, and (2) actively exploring new methods. Professor Wise Young (USA) reported the functional recovery of spinal cord injury and assessing methods, such as ASIA, SCIM II, and WISCI. He introduced the application prospects of cell transplantation using many kinds of cells and focused on the advantages and the mechanism of OEC transplantation to restore spinal cord injury, prospects of the stem cell applications, and the distribution of China SCI Net. He believes that combination therapies can be approved if the combination therapy is more effective than each individual component on its own. The aspects of cell transplantation which should be paid attention to are safety, quantity, efficacy, side-effects, and complications. As for the question of how to design the control group, Young's reply was, "This is a very good question, because it is hard to explain the effectiveness of the treatment without control. However, is the design of control group the only way to explain effectiveness? We have not seen the data with control over years, such as organ's surgical resection or transplantation. Of course, because there is no sham control, people will believe that the effect of functional improvement is the process of spontaneous recovery. The design of sham surgery is really a very complex issue."

Topics on Stem Cells

Professor Gustavo Moviglia (Argentina) proposed that the combination of adult neural stem cells with the intervention strategies of protective immunity have an effect on patients with spinal cord injury, amyotrophic lateral sclerosis, pseudo-hypertrophic muscular dystrophy and Becker muscular dystrophy. Bao Jian-ling (Beijing) reported the culture and identification of human fetal olfactory stem cells *in vitro*. She also analyzed the misuse of the term, neural stem cells. Professor Ding Jigu (Hubei) reported his experiment on the differentiation of the mesencephalic neural stem cell by GDNF and IL-1β *in vitro*-induced. The M-NSC could be successfully induced and differentiated by GDNF, IL-1β or both *in vitro* into a sufficient number of dopaminergic neurons that are both morphologically and functionally mature. Professor Chi Feng and Xu Yinghui (Liaoning) suggested that neural stem cell transplantation done under sub-hypothermic conditions was more effective than neural stem cell transplantation done at normal room temperature. Associate Professor Liang Peng (Heilongjiang) proposed that neural stem cells can promote the neurorestoration for spinal cord injury. Wang Jiming (Tianjin), chief physician of Chinese medicine, introduced the effect on proliferation and differentiation of the bone marrow stromal cells into nervous cells by application of traditional Chinese medicine. He also reported on the beneficial exploratory treatment of motor neuron disease by combining bone marrow stromal cells and traditional Chinese medicine.

During the discussion, Professor Huang Hongyun stated that the definition of neural stem cells used by some scholars is inaccurate. The effects of neural stem cell transplantation reported in basic and clinical research are mainly from mature functional cells with transplantation, but not from neural stem cell transplantation. Neural stem cells play important roles in two ways; one is the functional gene transfer to neural stem cells *in vitro* causing the cells with transferring functional gene from stem cells to proliferate and differentiate after transplantation; the other one is that the stem cells induced to differentiate functional neurons or glia *in vitro* or *in vivo*. But the process of inducing stem cells *in vivo* has not even been started. Although currently there are still some

differences of viewpoint about the definition and identification of neural stem cells, it is generally agreed that neural stem cells have three unique characteristics. One is that they keep the marks of primeval neural cells, such as Nestin. The second is that they do not have the marks of mature neural cells. The third is that they can self-renew, self-replicate, differentiate multipotentially and stably continue to passage, and later differentiate into nervous tissue *in vitro*. Neural stem cells are one of the most important potential intervention strategies for neurorestoration. In order to unite the scientific community to correctly identify and exploit stem cells' role and value, it is urgent for neurorestoratology to create a standard definition and identification methods for neural stem cells. Achieving this will help to advance and increase the amount of stem cell research.

The Comprehensive Intervening Strategies for Neural Restoration

Professor Wagih S EI Masry (United Kingdom) proposed that spinal cord injury should be treated conservatively, so that patients can maximize their nervous functional recovery. But other doctors suggested that he not only show a case report, but present all of the data. Professor Albert Bohbot (France) introduced experiences with laser acupuncture that promoted functional recovery. He preliminarily confirmed that the combination of laser acupuncture and rehabilitation training for patients with chronic spinal cord injury played a very important role in functional improvement after OEC transplantation. Dr. Tang Zhouping (Hubei) introduced the concept of biologically engineering materials and its future application prospects in the central nervous system. Professor Wu Chengyuan (Shandong) mainly introduced his research during which fetal nervous cells and transgenic cells were transplanted into the striatum of a primate monkey with Parkinson's disease. The results showed histological and functional improvements in the subjects. Dr. Li Xiangdong and Professor Hui Guozhen (Jiangsu) reported on the application of the amniotic epithelial cell and the transfer of BDNF amniotic epithelial cell transplantation to treat primates with acute spinal cord hemitransection. The motor functions in the cell transplantation group improved significantly better than the control group, and best in the transfer of BDNF amniotic epithelial cell group. Dr. Chen Renhui (TianJin), on behalf of Professor Feng Shiqing, reported that a low-dose X-ray promoted neurorestoration in rats with SCI. Professor Xu Shaoting (Beijing) proposed that promoting motor neurorestoration by the current strategies of cell transplantation should still be under suspicion. The key points for restoration of spinal cord injury are to provide the channels of axon growth, nerve growth factors, and to remove the inhibition factors. Dr. Zhu Zhenzhong (ShanXi), on behalf of Professor He Xijing, reported on the neural protection and regeneration by the injury reactive astrocytes in the subventricular zone (SVZ) of adult rats. Professor Li Gang (Hong Kong) proposed the new technological concepts of distraction osteogenesis which can increase brain blood supply; thereby improving the functions for patients with stroke.

Patients' Wishes

As the representative of patients with spinal cord injury, Mr. Wen Jun put out the following call to action: "Currently it is more realistic for us to improve the quality of life and reduce complications if the dream of walking again cannot be achieved. I hope that future research can achieve greater success and I believe that scientists should present patients with realistic expectations."

At the conclusion of the conference, attendees all agreed to make the ***International Association of Neural Restoration*** (***IANR***) ***Spinal Cord Injury Functional Rating Scale***, ***SCI-FRS*** (***Seeking Suggestions***), ***International Association of Neural Restoration*** (***IANR***) ***ALS/MND Self-Assessment Scale*** (***Seeking Suggestions***), ***and The Neural Restorative Cell Transplantation Clinical Practice Principle*** (***Seeking Suggestions***) public and seek more advice and suggestions from other experts in the field. The IANR promised to donate one million Yuan to support neurorestorative treatments for those who suffered spinal cord injury and brain damage in the Wenchuan earthquake in southwest of China. The IANR also declared that the 2nd IANRAC will be held in Beijing on April 24-26, 2009.

International Association of Neural Restoration (IANR) Spinal Cord Injury Functional Rating Scale, SCI-FRS (Seeking Suggestions)

1. **UPPER LIMB MOVEMENT**

(1) **Eating and Drinking**

3 Normal

2 Finish independently with difficulty

1 Some assistance

0 Total dependence

(2) **Grooming**

3 Normal

2 Finish independently with difficulty

1 Some assistance

0 Total dependence

(3) **Writing**

3 Normal

2 Slow or sloppy; most words legible

1 Many words not legible

0 Unable to grip pen

2. **LOWER LIMB MOVEMENT**

(1) **Standing without brace**

3 Normal

2 Stand independently but unsteady

1 Some assistance

0 Cannot do

(2) **Walking without brace**

3 Normal

2 Walk independently but slow or unsteady

1 Some assistance

0 Cannot do

3. **TRUNK MOVEMENT**

(1) **Sitting**

3 Normal

2 Stable when still, but unstable when moving

1 Unstable when still

0 Cannot do

(2) **Turning body over**

3 Normal

2 Finish independently with difficulty

1 Some assistance

0 Total dependence

4. **GENERAL MOVEMENT**

(1) **Transfers: bed to chair/wheelchair**

3 Normal

2 Finish independently with difficulty

1 Some assistance

0 Total dependence

(2) **Bathing**

3 Normal

2 Finish independently with difficulty

1 Some assistance

0 Total dependence

(3) **Dressing**

3 Normal

2 Finish independently with difficulty

1 Some assistance

0 Total dependence

5. **SPHINCTER CONTROL**

(1) **Bladder Control**

3 Normal

2 Reflex voiding with partial sensation or control

1 Reflex voiding without sensation or control

0 Totalincontinenceorurethralcatheterization/cystostomy needed

(2) **Bowel Control**

3 Normal

2 Partial control with sensation

1 Partial control without sensation or no control with partial sensation

0 Total incontinence

6. **MUSCULAR TENSION (refers to the amount of tension or resistance to movement in a muscle.)**

3 Normal

2 Slight increase /decrease or mild spasm

1 Large increase/ decrease or significant spasm

0 Extreme stiffness or spasticity

7. **SWEATING**

3 Normal

2 Slight decrease

1 Significant decrease

0 Absent sweating

8. **SKIN CONDITION**

3 Normal

2 Partial breakdown

1 Significant breakdown, often associated with edema

0 Enduring bedsore or skin damage; severe edema

9. **PAIN**

3 No pain

2 Mild pain, ordinary pain killer effective

1 Severe pain, narcotics required

0 Extreme pain, uncontrolled

SEXUAL FUNCTION (Rate for males only; do not include in overall score)

3 Normal

2 Can achieve erection and sexual penetration, but problems with sensation or ejaculation

1 Can achieve erection, but no sexual penetration, sensation or ejaculation

0 Unable to achieve erection

Establishing a Functional Rating Score:

This scale includes 9 categories with 16 items in total (plus one optional category).

The maximum possible score is 48; the lowest possible score is 0. Below is an explanation of the functional rating scale scores:

48: Normal functioning across all categories

34 – 47: Slight degree of functional handicap (mostly independent)

17 – 33: Medium degree of functional handicap (some dependency indicated)

0 – 16: Severe degree of functional handicap (significant impact on daily life)

The total score is 48 **points, the lowest score is** 0 **point.**

International Association of Neural Restoration (IANR) ALS/MND Self-Assessment Scale (Seeking Suggestions)

Ranking: 0 – 10 points. 0 is the worst condition; 10 is the best condition.
(**Note: For evaluation of Pain and Discomfort, 0 is the bad pain/discomfort, 10 is no pain/discomfort**).

Please fill out the appropriate score in the blank below.

The total score is 180 points.

Bulbus Medullae Function

Speech _____

Swallowing _____

Salivation _____

Stick out tongue _____

Limbs Function

Left arm movement _____

Left hand movement _____

Right arm movement _____

Right hand movement _____

Left leg movement _____

Right leg movement _____

General trunk movement _____

Bend head up and down _____

Walking _____

Climbing stairs (one flight) _____

Others

Breathing _____

Muscular tone _____

General pain _____

Muscle discomfort _____

TOTAL SCORE _____

The neural restorative cell transplantation clinical practice principle (Seeking suggestions)

International Association of Neural Restoration

As cell transplantation is a valuable theme of neural restoration research, several countries have already succeeded using it for clinical practices. In order to bring the therapeutic strategy of cell transplant to a higher neural repair research application standard while conform to the internationally recognized criterion, follow the relevant policies, combine translational medicine idea, and also promote the healthy and fast development of neural restoration research, thus further safeguard the clinical safety and make it more effective, the association proposes the following application principles:

1. Any researches involve human fetal cells must follow host country's laws and regulations while conducting clinical scientific research and providing treatment. The pregnant woman need to know the exact circumstances and written permission must be obtained.

2. Any researches involve cells from human body must follow host country's laws and regulations while conducting clinical scientific research and providing treatment.

3. Prior to cell transplant clinical practice, primate animal models experiment is not an absolute requirement. For acute and subacute life threatening disease, the physician should act quickly to explore clinical intervention methods, in order to prolong patients' survival duration as far as possible.

4. In the treatment of a patient, where proven prophylactic, diagnostic and therapeutic methods do not exist or have been ineffective, the physician, with informed consent from the patient or his/her family, must be free to use unproven or new prophylactic, diagnostic and therapeutic measures, if in the physician's judgments it offers hope of saving life, re-establishing health or alleviating suffering.

5. Phase Ⅰ clinical trials should include 5 ~ 10 patients, Phase Ⅱ clinical trials should include 20 ~ 40 patients, Phase Ⅲ clinical trials should include 120 ~ 200 patients. The experimental design should pass through rigorous examination and obtain permission from ethics committee. The physician should cease any investigation if the risks are found to outweigh the potential benefits. If there is conclusive proof of positive and beneficial results, the clinical trial can be stopped and it can be used as a conventional clinical treatment method.

6. Currently, the clinical research has confirmed the following cells are effective or have clinical application prospect. The cell types include the embryo brain cell (for example mesencephalic nigral cells), olfactory ensheathing cell, the neural stem cell, the neural progenitor/precursor cell, the bone marrow stromal cells, Schwann cells, umbilical cord blood mononuclear cell, the embryo stem cell, the retinal pigment epithelial cells, the embryo spinal cord cell, the amnion cell and so on. The physician should conduct thorougher research regarding cells' safety, validity, and the mechanism while enlarge the foundation and clinical research dynamics.

7. Presently, the neurological diseases intervened by using cells therapy in clinic mainly involves Parkinson's diseases, spinal cord injury, amyotrophic lateral sclerosis, cerebral palsy, stroke, brain injury, dystaxia, multiple sclerosis, Huntington's disease, dementia, persistent vegetative state, sequela of myelitis, spinal muscular atrophy and so on. For some of those diseases, the definite short term benefits have been found, the future research should be emphasized on discussing the middle and long term treatment results.

8. Currently, the cell injection methods include: intracerebral (cerebral parenchyma and ventricle), intra spinal cord, intrathecal as well as in the vein or in the artery and so on. As diseases are different and types of transplanted cells are different, theoretically there is a most suitable way for each type of disease. However, the physician should base their research on animal experiments; while gradually establish the standard regarding the location of cell implant and the best amount of cells used.

9. Although the animal experiments result supports the use of immunosuppressant, but on the clinical application, the physicians are still debating whether it is necessary to use immunosuppressant after the central nervous system cell transplantation. It should be considered an important research topic in the future.

10. All medical files and the recent information should be record, at a suitable time it could be published. Regarding the comparison findings of cell transplants' neural regeneration, the physicians should act promptly to analyze and summarize the results. The physicians should publish results by clinical phases for other researchers to refer, to compare, and further to confirm.

11. Continuously to enhance "translational medicine" awareness, when the physician proved two kinds of cells have the certainly clinical effects, he should conduct combination transplant research as soon as possible. The physician should follow the mindset of always exploring new ways to enhance treatment's effectiveness. At the right moment, the physician should be encouraged to combine medicine, physical, chemistry, biological, the bio-engineering and other kinds of regimes to improve therapeutic outcomes.

12. The physicians should also be promoted to carry out multi-centers international cooperation regarding cell transplant research.

Reference:

Declaration of Helsinki (2000)

(Editor Wu)