

What I'd like to achieve here at Keio

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Introduction

In the 20th century, organ transplant medicine has become an ultimate treatment to cure the patients in danger of death due to the organ malfunction who could be completely healthy after the operation. However, this ultimate medicine is always accompanied by the donor; human being. I strongly believe that the science for creating transplantable human organ (I name it “Organ Fabrication”) will be an epoch-making research in the long history of Keio University School of Medicine. In the future, not only the development of treatment method without organ transplant but “fabrication of transplantable organs” without relying on donors’ organs from brain death or living tissues will become eligible.

I dare welcome the upcoming challenges with all the knowledge and experiences I have acquired so far, to give a birth to “Be a vanguard toward the dawn of Organ Fabrication” on this research here at Keio University School of Medicine. “Inishie in Japanese : Precedent in English” is the cornerstone of Teacher Yukichi Fukuzawa, the

founder of Keio University who represented it as an implicative meaning of courage and mission that he would pioneer it even though he would confront with difficulties and trial. This is a dream that I am destined to achieve with young fellow students like you.

The lecture this time has brought you how our ancestors acknowledged the essence of medical science. Therefore, I referred to the paintings of mythology with the highlights of organ transplantation and regenerative medicine in order to make it easier how the essence has been translated. Also I have picked up two persons actually in charge of transplantation therapy so that you can grasp the idea why I have been elaborating intensively to fabricate organs.

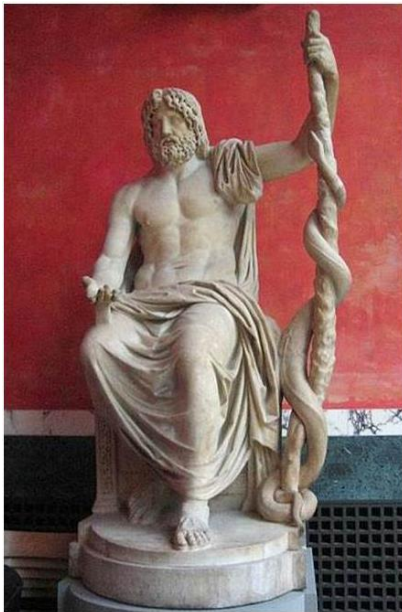
The essence of medical science implicated by mythology

(1) Why the rod coiled by a snake represent medicine and medical science?

Do you know the symbol of medicine and pharmaceutical science? Let me talk about the origin of the

myth.

Aesculapius' secret technique to reincarnate the dead derives from the usage of Medousa whose hair consists of snakes. In the ancient Greece the snakes were the symbol of eternal animal. It means that medical treatment itself was the way to bring back life to the patients in danger of death. In order to control the snake, it should be coiled by the rod to prevent the snake from moving freely. It exactly leads us to the medical ethics and guidelines for treatments in the present days (Figure 1).



(Obtained from internet)

Aesculapius was the son of *Apollon* and *Koronis*. Apollon made the white feather crow as a messenger with Koronis. One day the crow confessed the affair of Koronis to Apollon. He killed her by an arrow with furious anger. There were two different background stories about the crow; it lied to Apollon because it wasted

time on the way or it took Koronis affair mistakenly due to its carelessness. Either way, Apollon took away the human language literacy from it and changed the color of the feather from white to black. Koronis told Apollon that she was pregnant before the death, Apollon saved the unborn baby and asked the *Sage Cheiron* in shape of *Centaurus* to take care of him. He was Aesculapius. Aesculapius grown at Cheiron's place had shown his talent in medical science which exceeded even Cheiron's. His state of medical technique reached to the degree to reincarnate the dead by using the blood of *Medousa* given by *Athena*. Using this technique, Aesculapius brought the son of the king *Theseus* of Athenai, *Hippolytus* back to life.

The king of underworld, Hippolytus appears in the Greek Mythology. The son of the king Theseus of Athenai. The mother was *Hippolyte* of Amazon or Melanippe or Antiope. She strongly protested against *Zeus* that bringing dead back to life disrupted "Universal ethics of death (death of elderly or disease)". Zeus accepted the complaint and killed Aesculapius by a thunder. As Apollon whose son was killed by incomprehensive reasons, could not criticize Zeus directly, his anger reached to the extent that he killed all the one-eyed *Cyclops*, one of the Giant races who made thunders for Zeus. Zeus punished Apollon and asked him to take

care of live stocks as a shepherd.

In the ancient Greece, the hospital was called "*Aesculapia*". Aesculapius's children were all involved in medical sciences; his sons were good at medical knowledge who became famous for their endeavors at Trojan War; *Machaon* and *Podairius*, his daughters *Hygieia* in charge of hygiene, *Panakeia* in charge of healing. Hygieia has become a symbol of Pharmacy. Hippocrates is said to be their descendant. The crow killed by Apollon has become the constellation "Corvus". One saying goes that "Corvus" is located close by "Crater", its bill never reaches the water in "Crater". Aesculapius after the death was sent to the Heaven and became Ophiuchus as a member of Gods.

(2) The painting on the Miracle of Transplantation

Organ transplantation is as strong as the medical technique of Aesculapius in terms of saving the patients in danger of death. It seems a mere fact that the dream of transplanting organs has derived from ancient days. There is a myth of miracles that took place in collaboration between medical and pharmaceutical sciences.

In the ancient Roman period there were twin brothers, *Cosmas* and *Damian*, the elder Cosmas mastered Medicine and the younger Damian, Pharmacy and they were all welcomed for their loving-care

treatments. However, due to the Christianity persecution policy by the Roman emperor *Diocletianus*(284~305) the brothers were condemned to death in 290. Cosmas and Damian, even after the death they continued miracle treatments and further increased the number of Christians. Eastern Roman Emperor *Justinian 1st* (483~565) built the church under the names of St. Cosmas and St. Damian in Constantinopolis due to the fact that his fatal disease was miraculously cured through the belief in the brothers.

In 6th century at the church where the twin brothers were worshiped, a priest was suffering from the leg gangrene. The brothers appeared in his dream and advised him "This leg should be replaced". The leg was replaced for the leg of the black person who died on the day. There was another story about it that transplanted person was a judge and the donor was the Ethiopian prisoner condemned to death. Regardless the above two different views, the recipient who was transplanted, the leg was completely treated after he woke up. The transplanted leg color was black with his gangrene leg put beside him. This is the painting to evoke the origin of modern transplantation (Figure 2).



(Obtained from internet)

Not only Aesculapius sons and daughters but also the twin brothers, St. Cosmas and St. Damian, they are adored as “Saints to protect doctors and pharmacists”

(3) The painting on the myth of Organ Regeneration

Let me talk about the myth concerning medical care and humanism.

Prometheus taught the usage of fire to human and it led to the enormous anger of Zeus, he was condemned to be hung with iron chain to the rock of *Caucasus* mountain for thousands of years and his abdomen torn off and internal organs picked by vultures (Figure 3).



(Obtained from internet)

This painting was drawn by *Jordanens* in 1640.(Wallraf-Richartz Museum, Cologne) The vultures living in the mountain of Caucasus came one after another during the day to eat the internal organ of Prometheus on the right side where the liver was located. It led to the implicative theory that the liver was known as a regenerative organ.

When Prometheus watched down to the human world from the Gods' place, human being was in the middle of ignorance and darkness. Then, he went to Almighty God Zeus and consulted with him. However, Zeus implicated “Ignorance means they know nothing about sin. Human being is happy forever unless otherwise they notice somebody else is unhappy” and had no ears to listen to Prometheus. Zeus also added “If human being got to know how to use fire, as same as Gods ourselves, they would try to be strong and invade Olympus someday”. Prometheus was not satisfied with Zeus in regard to his suggestion and he was said to have stolen the fire of the dawn in the following morning and handed it over to human being.

Human has become happy with such an enormous sacrifice? For sure, they got a torch to lighten the ways in the dark night out of the caves. And they became able to eat cooked foods. But on the other hand, they brought it in the smithy and forged plow, sword and spear. Then they put helmets to the wars. In the

mythology the brave hero Hercules killed vultures and released Prometheus from pain. The donors of living tissue transplant are exactly as same as Prometheus for philanthropy. It might be us who persist in researching “Fabricating transplantable organs” to save Prometheus.

(4) Two important persons who have shown us the mindset how we deal with transplantation therapy.

Admirable surgeon solely in pursuit of his dreams ; Alexis Carrel

Carrel is a surgeon born in 1873 in Lyon, France. He became famous for the Nobel prize of physiology and medical science honored on his research “Angiography and Organ Transplant” when he dwelled in the US in 1912 (Figure 4).



(Obtained from internet)

In France evidences showed that he was a mere surgeon and scientist who had carried out his will without obeying old practices.

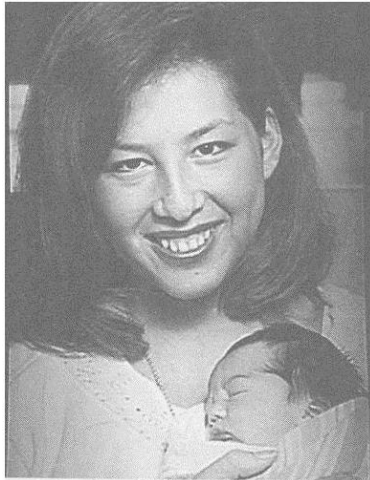
In late 19th century, while enhancing his experiences as a surgeon, he had been experimenting proboscis hooking of dogs’ kidney and thyroid blood vessel with common carotid artery and external jugular vein. In 1902 he reported in the Lyon medical association journal “30 minutes after enucleating of kidney with blood vessel and proboscis hooking with external jugular vein, the urine came out from the urinary duct”. In the end of the paper he concluded “Thanks to a series of animal tests, organ transplant is technically possible but I have not come to a conclusion yet. However, it is clear that by using this method, anastomosis in organ transplant becomes much easier”. This conclusion in the paper is astonishing to me over 100 years of time difference as a surgeon and researcher for this field of science.

In the following year he was exiled from Lyon medical association due to the case report on the elderly woman with pneumonia at “Sanctuary of Lourdes”. It led him to immigrate to the US.

Further in later years with *Charles Lindbergh* he tried on organ culture and published a book entitled “The Culture of Organs”. The book might implicate the “Transplantable Organ Fabrication” I have been elaborating at the moment.

Anissa & Marissa: Savior sisters

The photograph shows Ms. *Anissa Araya*, Hispanic American (Figure 5).



(Obtained from internet)

Currently her profession is a bone marrow transplant coordinator. The following is the common example of worries in line with the development of live donor transplant technology.

Spring in 1988 she got leukemia when she was 2nd grade of the high school. No one in her relatives has matched the type of her bone marrow. There was a match at the bone marrow donor registry, however, she was rejected. Then her parents made a decision to give a birth to a baby for using its bone marrow for Anissa. And they prayed for 25% of the match adaptability among brothers and sisters from the same mother. The challenge was made between the father Abe 45 years old and the mother Mary 42 years old, luckily Mary got pregnant. The family was fortunate because the bone marrow tissue of the unborn baby was found to be adaptable by the amniotic diagnosis of Mary at her 9-month pregnancy. April 2nd in 1990 she gave a birth to a baby girl named *Marissa*. And

when she completed 1-year birthday, the bone marrow transplant from Marissa to Anissa was done in a success. Anissa's leukemia was completely cured.

On the other hand there was a strong criticism such as "Is it justified to give a birth to a baby with the purpose of saving another child?"(Chicago Tribune) "Is it legal to have a baby to get a sort of spare organ?"(Los Angeles Times) Nowadays, assisted reproductive technique has been further implemented and there have been lots of brothers and sisters born thanks to the technology. (It is called "Designer Baby")

The transplant methodology without relying on donors; human being might be a challenge for us researchers towards an ultimate human love.

Discussion

Keio Akakura Academy(KAA) is organized by the students from medical, pharmaceutical and nursing departments for the purpose of showing the real meaning of being medical-related personnel and acting professionally as a team. The 9th KAA took place between Sept. 20 and 21, 2014. Despite the fact that I was appointed to be a project professor here at Keio University School of Medicine in April this year, a murmuring talk, a sort of teasing "There are nice students" from Mr. Soeda of Nursing School to which I reacted immediately. I made a nice excuse in

order to join rationally by telling him that I am good at “Dodge ball” because I did it many times with my kids when they were small.

In the morning of Sept. 20 we got together and left for Akakura in two buses with the encouraging shouting out “Daaaah” from the dean, Prof. Suematsu. The transit time was about 5 hours. On the way there were several coffee breaks. Each time Dr. Fukagawa a member of the alumnus association named “3-4-Kai” gave students something to have such as ice cream. It was very kind of him. In the bus we tried on the quiz with prizes by teams. Our team name was “Mitral Valve” and positioned in the 2nd place in the middle of the game but in the end we won the first prize by getting high points through drawing Prof. Suematsu portrait.

As soon as we get Akakura villa, all of us we played a skit entitled “The difficulty to choose donors for Living Donor Liver Transplantation”. Also it

took place a brainstorming focusing on “Think of you in 10 years from now” representing “Work-life balance” hosted by Dr. Satoh of alumnus association named “3-4-Kai” who supports especially female doctors. I could foresee my 10 years as same as now being supported by a family and concentrating on researches. After dinner, I gave a lecture on the above. I fell asleep under the zillions of stars looking for the symbol of medical science “Aesculapius” constellation Corvus.

Next morning on Sept 21 we won the first place for the Dodge ball games as promised while overcoming the hangover from last night with Prof. Kuroda of pediatric surgery who nicknamed me “Zaccheroni Kobayashi”. After lunch, we held winners’ ceremony for a series of games held in 2 days and took a picture of “Get Together”. (See the attached photograph)



On the way back by bus, I felt like sleeping with snore but on the contrary we held “Bingo” game. Luckily I got a bingo and won a cleaning robot “Moppy” which I was aiming at in mind. In the meantime, the bus arrived at Keio, Shinano-machi before falling asleep. Two-day KAA lodging in Akakura has passed like a flash.

Acknowledgement

The 9th KAA has been well planned and organized by the students from Medical Department (Y Akiba, M Wada, K Ishikura, H Sasaki, S Nozaki, H Sakurai) , those from Pharmaceutical (S Hirakura, Y Sakuma, H Kawaguchi, E Ohomura) and those from Nursing (Y Uenaka, S Miyamoto, M Miyajima). It was my great pleasure to have spent time with these young, promising and talented students because they are already endowed with the basic qualifications for doctors, pharmacists and nurses because one of the hosts of the lecture trip, Mr. Akiba and everybody involved held a meeting for reviewing right after coming back to Shinano-machi, Research Park building at Keio University School of Medicine.

I have been emotionally moved by the unlimited back-up care for the above students by the School of Medicine alumnus association named “3-4-Kai”; Drs Fukagawa, Satoh, Yoh, Akine and Takahashi. And I'd like to extend my

utmost gratitude toward Professor Kuroda of Pediatric Surgery and Dr. Soeda of School of Nursing for having invited me as a tutor with the theme “Organ Transplantation”.

Wrapping up the review of my KAA lecture, I also thank my laboratory manager Mr. Kita for his translation skills into English for the students who would make successes as cosmopolitans and my secretary Ms. Takahashi for her putting my draft writing in order.