

Is Human Society Evolving In a Sustainable Way? -What I Can Do As a Research Student At Sophia-

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Abstract

To evolve in a sustainable way, there are two issues to be solved. First, the world had developed on the mass production and consumption during the 20th century. But natural resources are now showing signs of depletion and the ecological balance is getting of. Second, the development had not proceeded without distinction, but with unevenly and locally distributed trend. There are only a handful of people who are blessed with the current development. It is absolutely essential to challenge from two sides to evolve as a sustainable society. Environmentally sensitive technology from the side of natural science nurtures earth-friendly environment. From the side of social and human science, development of an equitable society is expected. The aim of my study is to fabricate bone materials that can be used by anybody. I am trying to coat hydroxyapatite on metal substrates by a unique method. This method reduces the environmental load and allows anybody to have treatments on account of its simplicity.

Also, it is very important to think about education. Cross-fertilization of arts and science should be achieved for developing a sustainable society. It is a great advantage for me to have opportunities to study at Sophia University. I must become a person of vast attainments and make efforts to evolve human society in a sustainable way.

What I Can Do As a Research Student At Sophia

Evolving our human society in a sustainable way is what each person must involve in according to each person's situation, without wondering if one can do or not. From Oct. 26th till Sept. 4th, World Summit on Sustainable Development (WSSD) was held at Johannesburg in South Africa. Prime Minister Koizumi delivered a speech to the effect that the key factor for ensuring the sustainable development be people and stressed the importance of people's health as much as their education.

I, as a graduate student performing a development research on artificial substitutable bones,

have taken thought for a sustainable human society. I believe that there are two big problems to evolve the human society in a sustainable way; the system of finite consumption society and its unequal development.

The world had developed on the mass production and consumption during the 20th century. The budget of fossil fuel and the amount of industrial production swelled to more than ten-fold and twenty-fold, respectively. Furthermore, 80% of the increase was achieved after 1950, indicating these had increased at an exponential rate. But the development had not proceeded without distinction, but with unevenly and locally distributed trend. Advanced industrial countries with no more than 20% of world population consumed almost 80% of all the resources and energy exclusively. This fact means that hierarchical society had been built up on a global basis. A picture book titled "If The World Were a Village of a Hundred People" commanded public attention with such a background. Sustainable development is feasible if the two paradoxes mentioned above are broken down. In other words, we must outgrow from conventional infinite-like growth pattern to work out environmentally pertinent society and eliminate the global discrepancies to achieve social equity. It is absolutely essential to challenge from two sides to evolve as a sustainable society; from the side of natural science to nurture earth-friendly environment and the side of social and human science to develop a system for all people to live happily and equally.

I am studying artificial bone materials. When a bone receives damage, it is possible to repair the damaged place by transferring a part of bone from another less important part. However, a patient is obliged to endure operations twice for bone extraction, suffering from discomfort and pain for the bone removing. It is also possible to implant a donated bone from a late person, but donors are very few and there could be an infection disease induced. Recently, methods based on tissue reconstruction using undifferentiated cells attract much attention. But this would not be a treatment technique for anyone at anytime, because it requires a huge facility and a long time. On the other hand, some inorganic materials can activate cells surrounding tissues in a human body, regenerate the tissues and unite with living bones. They are relatively cheap and available for anyone at anytime. The problem is the difficulty of fabricating artificial bones to satisfy all the recipients. There are more than 200 bones in a human body and each is very different from others in shape, size and composition. They are designed in a very complicated and ingenious way with calcium phosphate called hydroxyapatite (HAp) and collagen, fibrous organic constituent. The surfaces of bones are compact and covered by thin periosteum. The insides consist of porous cancellous bones. The proportion of compact bone and cancellous bone is different from bone to

bone. Osteoid cells (osteogenic cells, osteoblasts, osteocytes, and osteoclasts) function as osteogenesis and bone resorption. Bones are inorganic/organic/cell composites highly performing with a huge variety. Additionally, cartilages are needed at joint parts, and the relevancy among bones, ligaments, and muscles is also considerable. On the basis of these facts, designing artificial bones requires aggressive adoption of technologies from various interdisciplines such as life science, tissue engineering, genome engineering and biomechanics.

Generally, artificial bones require biocompatibility and functionality as substitutes for natural bones. When we look back at the history of human bones' substitutes, the mechanical property was the first requirement, but, of course, not all the artificial bones satisfying this requirement were harmless to human body. The development of artificial bones has worked out on a tenuous balance of biological and mechanical conditions coupled with the lifetime and costs problems.

The mechanical properties required for artificial bones depend on the parts of use, but need to be tougher than living bones in general. Especially, high-loading parts such as femurs, tibias, and roots of teeth require high fracture toughness. Thus, I am now trying to coat hydroxyapatite (HAp) on metallic substrates since most metals meet this mechanical requirement. For practical use of those metals as biomaterials, non-toxicity should be certified. Toxic substances eluting from materials may kill cells or turn them cancerous. Developing a fever, excessive inflammation and acute allergy should strictly be avoided. It goes without saying that biomaterials need good biocompatibility for clinical application. When a piece of material is implanted in a living body, a reaction will more or less take place between the surfaces of the material and of the living body, indicating the importance of biocompatibility of the interfaces. At first, there would be an acute inflammation and a foreign-body reaction, followed by encapsulation of the material with fibrous tissue by fibroblasts. Through these processes, the living body will gradually accord the material. However, the materials with the best biocompatibility can bond directly to bones without any interpositions of fibrous tissue. Ceramics have generally better biocompatibility than metals do. The bioactive ceramics are innovative materials bonding directly to bones with much better biocompatibility compared to other artificial bone materials. The problem is that the fracture toughness of those bioactive ceramics is lower than that of human cortical bones, and none of the metals having high fracture toughness can bond directly to living bones. Although ceramics have better biocompatibility, metals are used for implantation of artificial femur considering the total balance of mechanical and biological properties. Coating bioactive ceramics onto tough metals is therefore a

popular method to provide the metals with bone-bonding ability. For the loading parts of the skeleton being replaced, titanium and its alloys coated with hydroxyapatite (HAp) by plasma spray are now usually used. By this method, however, the materials are heated over 10,000°C instantaneously and coated HAp might partly melt or degrade. It is very difficult to control the composition and structure of the coated layer and resorbable molten phases contained in coated ceramics, which will accelerate the film peeling. Some melted components even have toxic consequences. Plasma spray coating requires special and costly equipments and very high temperature that is a burden on earth environment. In contrast, the method I am trying is very easy and simple. The process is only that Immersing heated metallic substrate (i.e. Ti metal) at 200-300°C into simulated body fluid (SBF) and soaking in it for a week. The SBF is an aqueous solution prepared by dissolving the reagents NaCl, NaHCO₃, KCl, K₂HPO₄ · 3H₂O, MgCl₂ · 6H₂O, CaCl₂, Na₂SO₄ and HCl to make the ion concentrations, pH and temperature adjusted to almost equal to those of human plasma. The soaking temperature is set at 37 or 50°C to evoke intravital environment outside of a body (*in vitro*). Accomplished specimens are usually analyzed by thin film X-ray diffractometer (TF-XRD) and scanning electron microscope (SEM). The XRD peaks newly found after soaking in the SBF were identified as HAp. The SEM photos showed plate-like HAp crystals covering the substrate uniformly.

Bone formation and resorption are continuously taking place in a human body and my experimental process may be regarded as a method mimicking this bone forming mechanism (biomimetic method). As an approach from the side of natural science to nurture earth-friendly environment that had been mentioned at the beginning, permanent use of resource and environment should be sought. Holding back the consumption of exhaustible resource as much as possible, switching to regenerable resource, limiting the amount of consumption in the amount of regenerable resource, and abating emissions of environmental pollutant to decomposable, sorbable or regenerable amount to minimize or defuse them are the examples in concrete terms. The advantage of my coating method is to reduce the load on environment by modeling after mild reactions occurring in a human body, which will correspond to an approach satisfying the above-mentioned conditions.

My study will come to be useful also from the viewpoint of social equity. The experimental technique for the coating is very simple and no special equipment is needed. A coated material can be fabricated anywhere without discrimination. This means that anybody can be treated with this material according to need whenever and wherever. The mechanism of this coating method consists of two steps:

nucleation of HAp onto metallic substrate and its crystal growth. When a metallic substrate is immersed into SBF with a certain amount of urea and its hydrolytic enzyme, urease, nucleation of HAp will occur on the surface of the substrate on immersing impact. Enzyme reaction leads to pH increase and HAp nucleuses precipitated on a metallic substrate grow to HAp crystals. After 24 hours since immersing, the pH becomes constant and then the substrate should be soaked in SBF without urea and urease, renewing it every other day. SBF is supersaturated for calcium and phosphate, providing ions for crystal growth of HAp. A thin HAp film about 10 μm thick can be observed on a substrate after a week soaking. The purpose of the coating is to provide bone with bonding ability, and therefore implanting a material just after nucleation and contriving natural crystal growth in a body is also thinkable. In such a case, only heating and immersing metals into surface treatment solution (SBF + urea + urease) are the two simple procedures, and fabricating a material just before a surgery may be possible. This will make a likely scenario for anyone to receive medical treatment. The coating method is costless and therefore satisfies social equity, as well.

I have evaluated the biocompatibility of the coating both *in vitro* and *in vivo*. I used osteoblastic cells from rat calvaria to examine the cell initial adhesion, proliferation and differentiation. It became clear from the result of its initial adhesion and proliferation that the coating was a little hard for cells to attach on very firmly, but not toxic at all. The great alkaline phosphatase value as an indicator of differentiation demonstrated that fabricated coating has osseous conductionability, which will indicate the coating might bond directly to living bone. Thus I have implanted Ti rods coated with HAp by this method in rabbits' tibias and back of rats to study the *in vivo* reaction. All implanted rods were collected from the living body with the surrounding tissue, and the undecalcified sections were prepared for microscopic observation. These experiments using animal models were ran at animal experiment laboratory in Keio University. The sections were stained and observed with a light microscope. During the whole implant period, all the animals were healthy and any inflammation or infection was not detected. The rods implanted in the back of rats were covered with fibrous tissue by fibroblasts. This encapsulation revealed good biocompatibility of the coated materials. Meanwhile, the rods implanted in rabbits' tibias were found to have bonded directly to bones. It is clear from these results that I succeeded in creating bioactivity on a Ti metal surface.

There remains a problem, however. Adhesive strength of the HAp films on the Ti substrate was $14.61 \pm 1.03 \text{ M Pa}$, not strong enough for practical application. This is the biggest problem to be overcome.

The evaluation using osteoblastic cells and animal models indicated that the biocompatibility of coated Ti substrates were significantly better than that of non-treated Ti substrates. Based on this result, the credibility of safety and stability of the material should be enhanced for clinical application. Furthermore, this coating method succeeded on Ti metals but not on stainless steel which is the most applied material as bone substitute. Ti metal is better material than stainless steel in terms of corrosion resistance and biocompatibility, but the cost of stainless steel is about 5 times lower than that of Ti metal; the price of rod stock per ton is 5 million yen for commercially pure Ti metal and 1.1 million yen for stainless steel (SUS316L). Coating on stainless steel is now carried on in practice.

The goal of artificial bones is still difficult to configure. The goal would be wide-ranging depending on patient's life style and philosophy, whereas the goal of usual industrial products is well defined. The goal settings after a treatment may differ from person to person, even if the symptoms are much the same. A patient may have a choice of a treatment. A young child would wish to be cured to have his (or her) daily life to come unaffected even the treatment takes a good amount of time, and on the other hand, an elderly person might wish for a treatment with less pain to live his (or her) relatively limited life as happily as possible. That is the reason why QOL (quality of life) has been advocated.

It should be pointed out that there is room also for social improvement. Putting such biomaterials to practical use is difficult, unless regulation of environment and for use and economic support such as bounty are configured. It is absolutely essential to develop the insurance institution further. In our country, one cannot use biomaterials without "an approval number for the medical device" and at the same time, health insurance benefits cannot be extended without recognition as "medical product for specified health use" by Ministry of Health and Welfare; neither the artificial bone for use nor the related medical treatment costs such as hospital and surgical expenses can be covered by insurance. At present, we have only a few biomaterials as medical products for specified health use, and a patient has only a few choices. Additionally, only material cost can be calculated but the accompanying technical fees are not. Thus, it is very unclear how much it may cost for an implantation of an artificial bone.

Also, education whose importance Prime Minister Koizumi appealed in his speech at the summit should be cogitated. The importance of education for solutions of the global problems has been widely acknowledged since United Nations Conference on the Human Environment at Stockholm in 1972 and various environmental educations have been practiced, but not achieved full success yet. After United Nations Conference on the Global Environment at Rio de Janeiro in 1992 where the "sustainable

development” became the keyword, it was stated that environmental education should be carried on as education for sustainability with themes of development, gender, poverty, human rights and world peace. In the international practice of environmental education up to now, it has transpired that conventional ideals and systems of education and development of educational materials are insufficient. People including even children who face the problems in their local society have to play a primary role for the solution. They should evaluate once and change the existing system, value and stereotyped knowledge to work out newly coordinated education. This recognition resulted in the agreement of “10 years education for sustainable development” at the last summit at Johannesburg that Japan proposed. Although Japan is not well blessed with natural resources, it has become a nation creating the world’s 1/7 wealth by the well-nurtured people. For developing a country, there are some necessary essential qualifications. The peace, security and good governance come first. One cannot acquire a good education without peace. The first step for a sustainable society is the peace of the world. The brilliant development of Japan with the war-renouncing article of the Constitution has proven this principle.

I have thus far mentioned as a beginner of biomaterial research that human health is *sine qua non* to develop in a sustainable society. Now, I would like to think about another important theme, the education, as a graduate student at Sophia University. In my study, I have to master scientific technology from various disciplines such as life science, tissue engineering, genome engineering and biomechanics. I think that medical science and engineering have not mingled enough yet. Not only materials but also disciplines have to be conjugated. In this respect my study which includes material fabricating, evaluation of its characteristics, evaluation of its biocompatibility using osteoblastic cells and animal models, and gene mapping in future will surely help in my deep consideration of the way of being in the future study. Additionally, cross-fertilization of arts and science should be achieved for developing a sustainable society. It is a great advantage for me to be able to study at Sophia University where the entire departments centered in one campus and in the neighbor enable students to take various classes. I could deepen my knowledge about fine arts, literature, psychology, etc., other than my major, chemistry. It requires a lot of effort to establish a leadership position and to have more of a voice in international framework, mainly because education in Japan is short on improving the capability for advocating, and partly because Japan was a defeated country at the beginning of the present international framework established about half a century ago. But Japan has the potential called “actual results.” We have to appeal it in the world community. Sophia University is advantageous in the field of languages, a

fundamental tool for communication. There are many foreign students and teachers from abroad in our university. I have had a number of occasions to speak with them. I took special English classes for returnees. I was involved in the volunteer to meet foreign students at the airport. My French class was conducted in English. Many researchers from abroad visit our lab and I have had pleasant talks and instructive discussions with them. Now I am thinking of taking a class at the Department of Cross-cultural next year. The lectures will be delivered in English there and I have to study English to catch up with it.

Sustainable society cannot take a shape unless the whole human family become happy and live with a hope for the maintenance of the social status quo. Activities for the social equity seem to be going backward, hitting against the walls of fundamental human rights and of care for underdogs. In particular, synchronized terrorist attacks on Sept. 11th rub salt into wounds. There is a kind of atmosphere to allow even a war which denies human rights and democracy. Under such circumstances, our mission as technical experts is to state a way shifting the present industrial techniques to sustainable ones. We have to prefigure the sustainable society to determine the direction of future research and development. As a Japanese citizen and as a human being, I have to bring efforts for global peace up in my consciousness.

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