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1. 助成金額： 800,000 円

2. 研究テーマ

高齢者のQOLを改善するナノバイオマテリアルの開発

3. 成果の概要(100字程度)

高齢者のQOL、とりわけ口腔環境の改善を図るため、ナノ構造の導入により新たな機能を付与した、生体にやさしい/耐摩耗性人工歯根、骨再生用スcaffolds、歯周組織再生用傾斜機能型GTR膜等の生体材料の開発を行った。

4. 研究組織

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## 高齢者のQOLを改善するナノバイオマテリアルの開発

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### Abstracts

To improve the QOL of the aged people, especially their oral environment, the biomaterials endowed with new functions by nano-structure formation were developed such as highly biocompatible/abrasion resistant implants, scaffolds for bone regeneration and functionally graded GTR membranes.

**Key Words:** Nanotechnology, Biomaterial, Implant, Biocompatibility, Composite, Carbon nanotube

### Introduction

Health and environments are the major problems confronted in the 21st century. Tissue regeneration and biomaterials will be two main approaches to respond to these problems and realize the quality of life (QOL). In this point the micro/nano-structured biomaterials and their composites have a large possibility for further development. Especially nanotechnology has made the most important contributions in recent years. The present study has brought together the subjects, which are important to establish the QOL of the aged people, especially their oral environment, from several aspects including implants, surface modification treatments, tissue regeneration, scaffolds, dental materials, composites and carbon nanotubes shown in the followings:

- (1) A three-layered nano-carbonated hydroxyapatite/collagen/PLGA composite membrane for guided tissue regeneration (S.Liao et al.<sup>1,2,3,7,12</sup>)
- (2) Fabrication and properties of sintered carbon nanotubes (W.Wang et al.<sup>4,5,10,14</sup>)
- (3) Surface carbide formation on titanium for abrasion resistant implant material (Y.Zhu et al.<sup>11,13,15</sup>)
- (4) Preparation of Mineralized Fibroin Fiber (X.Kong et al.<sup>9</sup>)
- (5) One-step synthesis of Fe(II,III)-doped MCM-41 nano-rod (Y.Geng et al.<sup>8</sup>)
- (6) New Observations to Hierarchical Structure of Human Enamel from Nanoscale to Microscale (F.Z.Cui et al.<sup>6</sup>)

### Results and Discussions

- (1) A three-layered nano-carbonated hydroxyapatite/collagen/PLGA composite membrane for guided tissue regeneration (S.Liao et al.<sup>1,2,3,7,12</sup>)

Functional graded materials (FGM) provided us one new concept for guided tissue regeneration (GTR) membrane design with graded component and graded structure where one face of the membrane is porous thereby allowing cell growth thereon and the opposite face of the membrane is smooth, thereby inhibiting cell adhesion in

periodontal therapy. The goal of the present study was to develop a three-layered graded membrane, with one face of 8% nano-carbonated hydroxyapatite/collagen/poly(lactic-co-glycolic acid) (nCHAC/PLGA) porous membrane, the opposite face of pure PLGA non-porous membrane, the middle layer of 4% nCHAC/PLGA as the transition through layer-by-layer casting method. Then the three layers were combined well with each other with flexibility and enough high mechanical strength as membrane because the three layers all contained PLGA polymer that can be easily used for practical medical application. Fig. 1. shows the schematic representation of three-layered membrane. Fig.2 is the microscopical view of the cross section (b). This high biocompatibility and osteoconductivity of this biodegraded composite membrane was enhanced by the nCHAC addition, for the same component and nano-level crystal size with natural bone tissue. The osteoblastic MC3T3-E1 cells were cultured on the three-layered composite membrane, the primary result shows the positive response compared with pure PLGA membrane.

#### (2) Fabrication and properties of sintered carbon nanotubes (W.Wang et al.<sup>4,5,10,14</sup>)

A novel bulk multi-wall carbon nanotubes (MWCNTs) sintered with polycarbosilane (PCS) as a binder agent was fabricated by spark plasma sintering (SPS), and their microstructure and properties were investigated. Sintering was done with the pressure in a range 20MPa to 60MPa at 1200°C. SEM and TEM observations showed that the nano-sized tube microstructure was preserved even after sintering and tubes were adhered each other with the nano-sized nodules of SiC pyrolyzed form PCS as revealed by X-ray diffraction. The bulk density and Vickers hardness were increased and the specific surface area was reduced with the content of PCS and sintering pressure. The inflammatory reaction of CNTs/PCS material was slightly increased with PCS content in the animal experiments. Sintered CNTs with the physical and mechanical properties close to bone and biocompatibility would be suitable as implant materials.

#### (3) Surface carbide formation on titanium for abrasion resistant implant material (Y.Zhu et al.<sup>11,13,15</sup>)

Physical and mechanical properties of carbide coated Ti were investigated to examine its possible use as an abrasion resistant implant material. Carbide layer was formed on the surface of Ti by heating in the hydrocarbon atmosphere (benzene C<sub>6</sub>H<sub>6</sub>) at 1000-1200°C. XRD showed that the specimens were consisted of TiC and Ti. SEM showed that the surface of Ti was covered with fine-grains of 1-7µm, depending on heating conditions. Carbide layer of about 4-20µm thickness was observed on the cross section by SEM and EDS. The rate of carbide particle size and layer thickness was increased with heating temperatures. The Vickers hardness of surface carbide was more than 2000. Martens scratch test showed the smaller indentation depths for carbide coated Ti than pure Ti, which confirms its high abrasion resistance.

#### (4) Preparation of Mineralized Fibroin Fiber (X.Kong et al.<sup>9</sup>)

Fibroin gel was prepared and used to regulate the biomineralization of calcium phosphate in this paper. We obtained one kind of mineralized fibroin fiber with the length of 1-2 millimeter, which has the potential to be used to enhance the strength of tissue engineering scaffold. Scanning electron microscopy (SEM) results showed that hydroxyapatite (HA) was mainly deposited on the surface of the mineralized fiber. Fourier transform infrared spectroscopy (FTIR) results displayed the red shifts of absorption bands of amide II and amide III (9cm<sup>-1</sup> and 5cm<sup>-1</sup>, respectively), which were related to the strong chemical interaction between HA and fibroin. It was also found that HA was at low content (12.5%) and the ability of gelled fibroin to induce mineralization decreased greatly because of the formation of β-structure in gelled fibroin molecules, which showed the importance of molecules structure to biomineralization.

(5) One-step synthesis of Fe(II,III)-doped MCM-41 nano-rod (Y.Geng et al.<sup>8)</sup>)

Morphogenesis of periodic mesoporous SiO<sub>2</sub> material has attracted much attention, due to the important effects of morphology on their properties, such as catalysis, adsorption/separation, photochemistry, drug delivery, and so forth. Since doping transition metal (TM) in the framework of mesoporous silica is an important subject in such a wide range of field, study on the self-assembly involving morphogenesis of TM-doped mesoporous silica may be helpful for understanding the role(s) of TM on morphogenesis, and for finding a convenient route to prepare materials with complex morphology. In this paper, we described a convenient route for preparing Fe-doped periodic mesoporous silica (MCM-41) nano-rod from the diluted surfactant reaction system. The nano-rod Fe-doped MCM-41 powder was obtained through assembly from a diluted surfactant solution of high pH value (pH=12). The material was characterized by X-ray diffraction pattern (XRD), The thermogravimetric analysis (TGA), transmission electron microscopy (TEM), and the UV-Vis absorption spectrum techniques. The sample was featured with a rod-like morphology with diameter of about 150 nm, length of about 400 nm, and the aspect ratios (length/width) of about 3. It can be substantially proved that the addition of Fe ions can play a significant role on the morphology of MCM-41 from the diluted surfactant solution. This method enriches the strategy for preparing metal-doped MCM-41 of specific morphology.

(6) New Observations to Hierarchical Structure of Human Enamel from Nanoscale to Microscale (F.Z.Cui et al.<sup>6)</sup>)

Enamel refers to the outmost crest of tooth that is mostly built up of hydroxyapatite (HA) crystals in well controlled assembly manners. In the present study, human enamel distilled from the mature third molars was investigated by Atomic Force Microscope (AFM), Scanning Electron Microscope (SEM) and High Resolution Transmission Electron Microscope (HRTEM) from macroscale to nanoscale indicating the high complexity of enamel microstructure in regard to hierarchy. Based on the observations, 7 hierarchical levels of the microstructure were proposed and described with the scheme representing a complete spectrum of the organization in detail. Meanwhile, we discussed the most possible matching between the hierarchical structure of enamel and its mechanical properties at each level.

#### Conclusions and Acknowledgements

The present subject is related to the health and environment of all over the world, which must be discussed and developed with the international point of view and collaboration. In this point of view it was a good opportunity to have the international symposium, the 5th Asian Bioceramics Symposium (ABC2005), held on Oct. 1-3, 2005 at Hokkaido University, Sapporo, Japan (Organizing Chaiman: F.Watari). The symposium brought together the top researchers worldwide to exchange research results and address open issues in all aspects of bioceramics and their related topics. The details of the symposium can be found at the homepage (<http://www.den.hokudai.ac.jp/rikou/events/ABC/index.html>). Prof.Cui, invited speaker, and two young researchers in Tsinghua University made important contributions as well as three Chinese postdoctor and graduate students in Hokkaido University. The Proceedings, Archives of BioCeramics Research (Volume 5), were published with the compilation of 104 papers. Fig.3 is the group photograph of the whole participants in the symposium. The authors appreciate Japan-China Medical Association greatly for the financial aid of Collaboration Research Project Grant.

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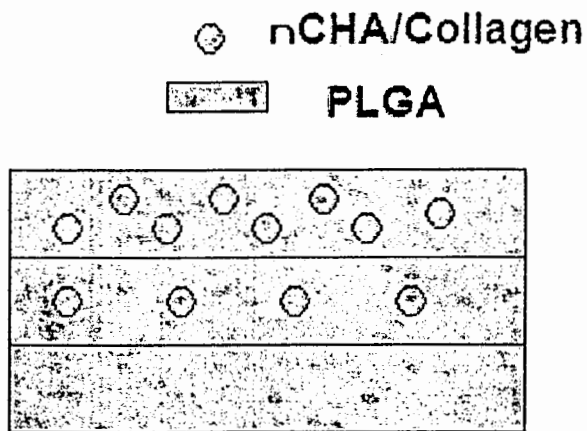


Fig. 1. Schematic representation of functionally graded GTR(Guided Tissue Regeneration) membrane



Fig. 2. Cross section of three-layered GTR membrane of nCHAC/PLGA composite with graded concentration of apatite (Thickness 0.4mm)

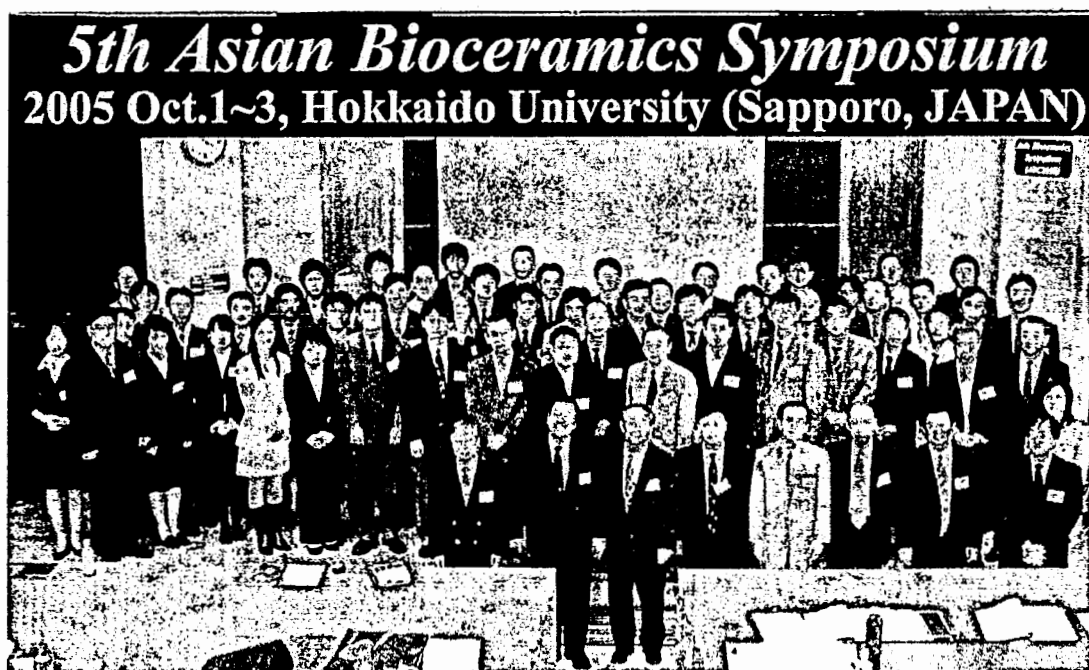


Fig.3 Group photograph of the whole participants in the ABC2005 symposium

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