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Case studies of technology transfer

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JAPAN

The contents of the lecture

- About the process of technology transfer
- Example of the activity experience of the technology transfer

Activity 1 The example of development of nanohydrooxyapatite.

The venture business was established for the applied research.

Activity The example of the development of pharmaceutical products to use for BNCT therapeutic method.

Activity The example of drug design development .

The research and development develop into a company and full-scale collaborative investigation.

- The important point of technology transfer

2004-2012 :

I was active as a technology coordinator of JST in Osaka,JAPAN.

I introduce the activity.

Process of the technology transfer

University

basic research

Established Venture

□□

possibility examination

Applied Study

Development

existing company

Esatblished intra-Venture

□□

introduce a new product into the market

New pharmaceutical products development

#3

SEARCHING CANDIDATE

PRECLINICAL TEST

CLINICAL TEST

Pharmaceutical approval

Hap Outline of the Research Project

□Development of the biocompatible nanohydrooxyapatite

□Target of activity□Development of devices interface harmony type transdermal skin bacterial infection prevention□

□**Representative** □Dr. Furuzono Tutomu

□Professor & Department Chair of Kinki University now.

□It was a section head of National cardiovascular Center Research Institute , Biomedical Engineering Department Head those days.

□**Corporate joint research partners, etc.** :

Tokyo Institute of technology, IMOTO MACHINERY CO.,LTD, Tokai Medical Products Inc. , SofSera Co.,

□**Coordinates period**□From April, 2004 to March, 2007

□**The coordinates activity**□ Adjustment of the participation in planning organization, holding of a periodical project meeting, patent consultation, examination of the study fund acquisition

Hap Technology seeds

Manufacturing of Hap

Technology of highly-dispersive nano-sized single crystal Hap

Form control, decentralized control technology

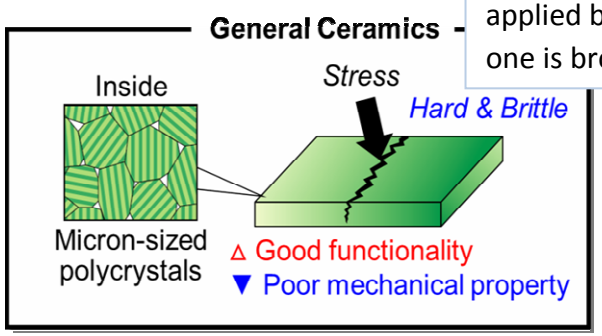
Composite technology

Composition of Silk and SHAp Graft Polymerization

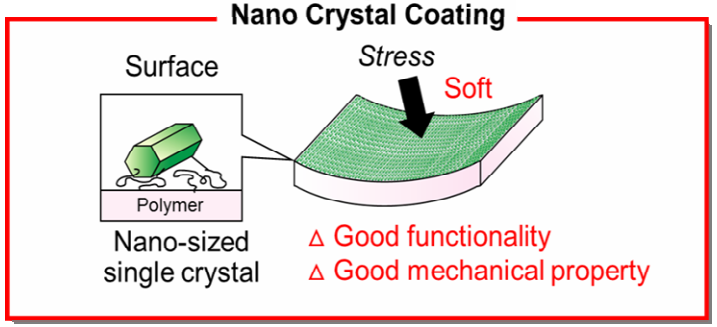
Composite Technology for Steel Surface Using Ozone Water

Soft ceramics□nano Hap

When the material is applied by stress, the one is broken.



To overcome the defect




Conventionally-Processed HAp


SHAp Processed by Our Original Technology

Hap Results

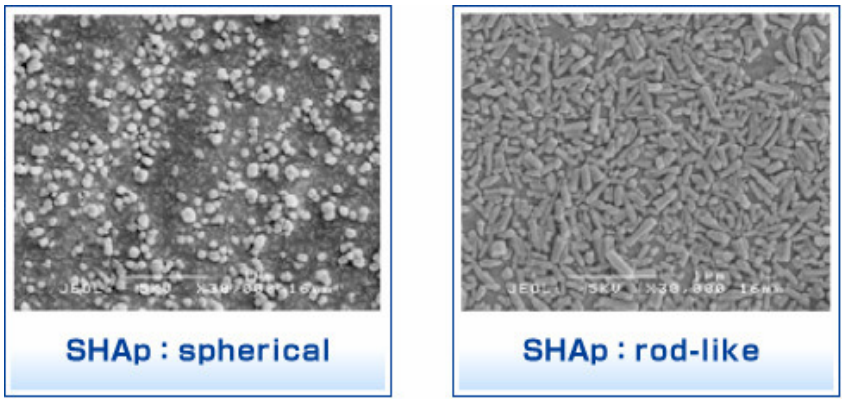
□The action of the study was conscious of practical use

□□This team was able to establish the large quantities manufacturing process of nanoHap-particles

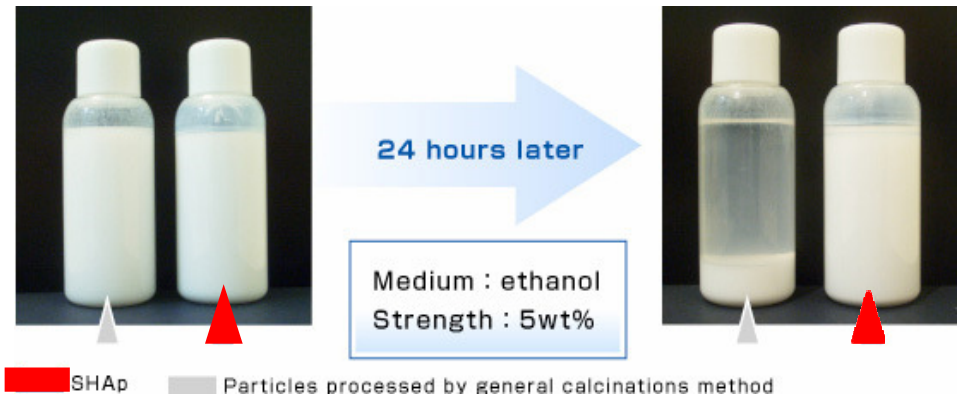
□□A technique to control particle size and a shape was able to be established

□□Enforcement of safe preliminary examination

•shape control



•High Dispersibility



Hap Results

The project developed original calcination method called *matrix-assisted calcinations method* to succeed in elaborating -dispersive nano-sized single crystal HAp.

1)Highly excellent bioaffinity

2)High Cell Adhesiveness

Established a venture in October, 2007

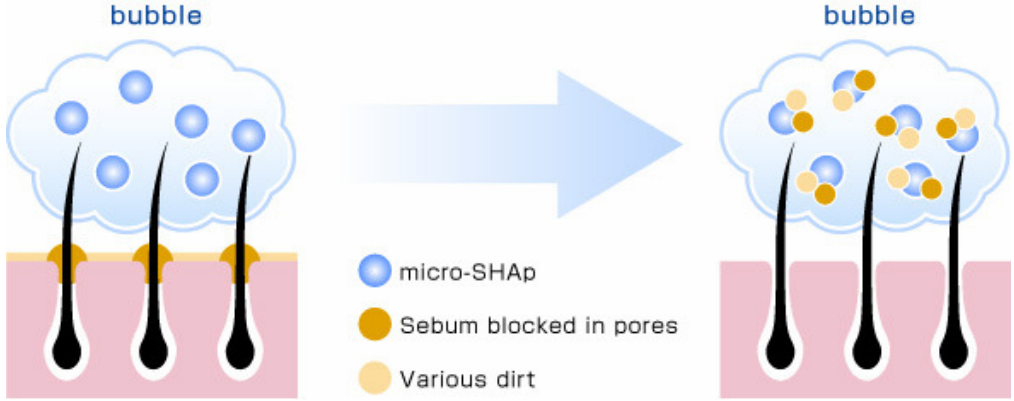
SofSera

Result in the applied study

1)A domain of dentistry: whitening paste with two kinds of particles

2)A basic cosmetics domain: high-protein adsorption performance and used it for a face wash

3)A medical equipment domain: utilize biocompatibility and use it for a catheter, a tube part



Application of 40nm SHAp to Basic Cosmetics

Hap Ripple effects

Technological Impact：Employment a project researcher in a venture company and planned the continuation maintenance of the study

Market Impact：Supplies materials to cosmetics, dentistry.
Under global medical equipment company and joint development

Social Impact：Established a venture company in October, 2007.
As of 2013, there are 16 employees

SofSera

Good point of the cooperation system：

1) The venture president is it in passion for the use development of the new technology.

2)The business divided the enterpriser, the fundamental researches into a researcher.

3) Understanding of the importance of the patent, patent management.

Hap History of the research funds

- 2001-2003　JST PRESTO　(Precursory Research for Embryonic Science and Technology)
- 2005-2007 JST (Innovaion Plaza Osaka R□D Program)
- 2008-2011　NEDO　(Nanotech advanced material development program)
- 2013-2014　NEDO (Innovation practical use venture support program)
- 2007□　　Support from venture capital

JST　□Japan science and technology agency□
NEDO□New Energy and Industrial Technology Development Organization□

Hap Future Prospect

Under a company and joint development global for the application to an interface harmony type catheter to realize prevention of infection

2015 The CE mark acquisition
2020 FDA approval

SofSera

代表取締役
カワベ　カーロカズシゲ
河邊　カーロ和重

Medical equipment development:

□A long-term action is necessary including the Pharmaceutical Affairs Law approval acquisition.

□The venture understood a technical future and marketability and pushed forward the applied development of original materials by the technology transfer.

For more information, contact□ President Kawabe Karl Kazushige
Phone□+81(0)3-5360-8668 **E-mail:**Kawabe_karl@sofsera.co.jp

BNCT □ Outline of the Research Project

□ Development of Boron Drugs for use in BNCT

□**Representative** □ PhD. Kirihata Mitsunori

Professor of Osaka Prefecture University

□**Participating company** □

STELLA CHEMIFA Co., Ltd. ,

STELLA PHARMA Co., Ltd.

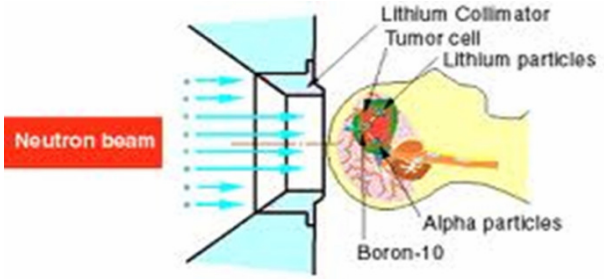
□ **Coordinates period** □

From April,2005 to March2009

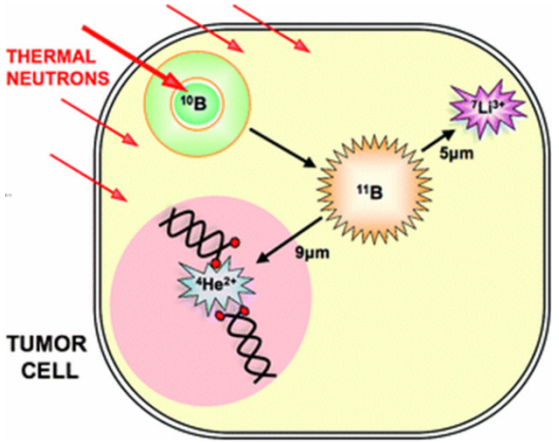
□ **Coordination Activity** □

Project coordination, Support of external funding, Support for patented

BNCT □ Born Neutron Capture Therapy



The Boron Neutron Capture Therapy (BNCT) consists of the injection of boron compounds into the human body, collecting them in tumor cells and then irradiating them with thermal neutrons in order to destroy these cells.



BNCT Goal of the Research Project

Materials: Development of plant production technology of ^{10}B-boric acid with high purity.

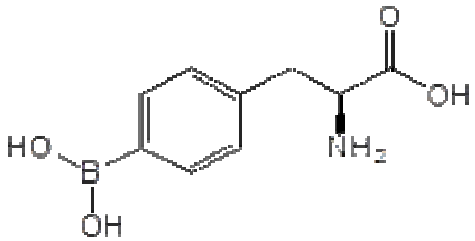
Manufacturing technology

Development of practical processing for industrial production of ^{10}B-boron drugs in GMP grade.

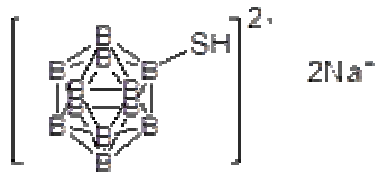
^{10}B-boron drugs: Two ^{10}B-boron compounds

- BPA (*p*-Boronophenylalanine),
- BSH (Disodium mercaptoundecahydro-dodecaborate)

Non-clinical tests including drug stability, distribution, metabolism, toxicity etc.



p-Boronophenylalanine
(L-BPA)



Mercaptoundecahydrododecaborate
(BSH)

BNCT Results

- Industrial production of ^{10}B-boric acid (^{10}B content > 99%) and its derivatives has been accomplished by use of specialized plant.
- Pharmaceutical production of two kinds of ^{10}B-boron drugs, ^{10}B-BPA and ^{10}B-BSH, was achieved by an efficient synthetic process.
- Non-clinical studies on the ^{10}B-boron drugs were examined *in vitro* and *in vivo.*

Speed up!

- **Accelerator development**: supported by Japanese government "Super Special Consortium for Supporting the Development of Cutting-edge Medical Care" ("tokku")
- The first clinical trial of accelerator based ^{10}B-BPA BNCT toward brain tumor has been started by Stella Pharma from October 2012 .
- The trial is currently progress and to be continued to 2015.

BNCT Ripple effects

Contribution to technology

- Development of simple measurement kit for boron drug in blood by ELISA
- Establishment of new measurement technique for neutron dose

Contribution to society

- Implementation of cell selective radiation therapy
- Treatment of brain tumors and melanoma by BNCT

Contribution to market

Market of boron drug

Estimation in 2020 :

24,000 patients(Japan)

cooperation/ Ripple effect

- Drug development Stella Pharma Co.
- Accelerator development Sumitomo Heavy Industries, Ltd.

- Movement of medical technology exports to Russia

Prime Minister Abe proposed the export of cancer treatment the most advanced equipment to Russia in April 2013.

BNCT History of the Research fund

- 2002 **METI** " Regional Revitalization Consortium R & D Projects "
- 2005-2008 JST "Practical Application Research"
- 2008: Cabinet Office "Super Special Consortium for Supporting the Development of Cutting-edge Medical Care" ("tokku")
- 2008-2014: JST "Contract development" (1.2 billion yen over six years)
- 2012: METI "The Innovation Center Establishment Assistance Program"
  Establishment of " Research Center for BNCT "
  Nakamozu campus (1,800m^2 of Osaka Prefecture University
- 2013: METI "Problem-solving medical equipment development projects "
  (General Zone promotion commission expense)

Research Center for BNCT

Image

*** METI : Ministry of Economy, Trade and Industry**

Long-term support is essential for drug development !!

BNCT Future Prospect

□2015□ Pharmaceutical application

□2017□ Pharmaceutical approval

Boron drugs will be provided to the advanced treatment

□ Expansion of adaptation disease

□ Brain Tumor → Mesothelioma, etc. □

□ Development research for the next-generation boron drugs.

For more information

Contact □ Stella Pharma Co.,

E-mail □ sp-info@stella-pharma.co.jp

Drug The outline of research Project

□Title□

Development of a therapeutic drug improving the neurological symptom due to diseases in the central nervous system such as the spinal cord injury

□Representative : DR Yamashita Toshihide

Professor of Osaka University

□Corporate joint research partners□

Mitsubishi Tanabe Pharma Co.

□Coordinates period□April,2009-March2012

□The coordinates activity□

Mitsubishi Tanabe Pharma

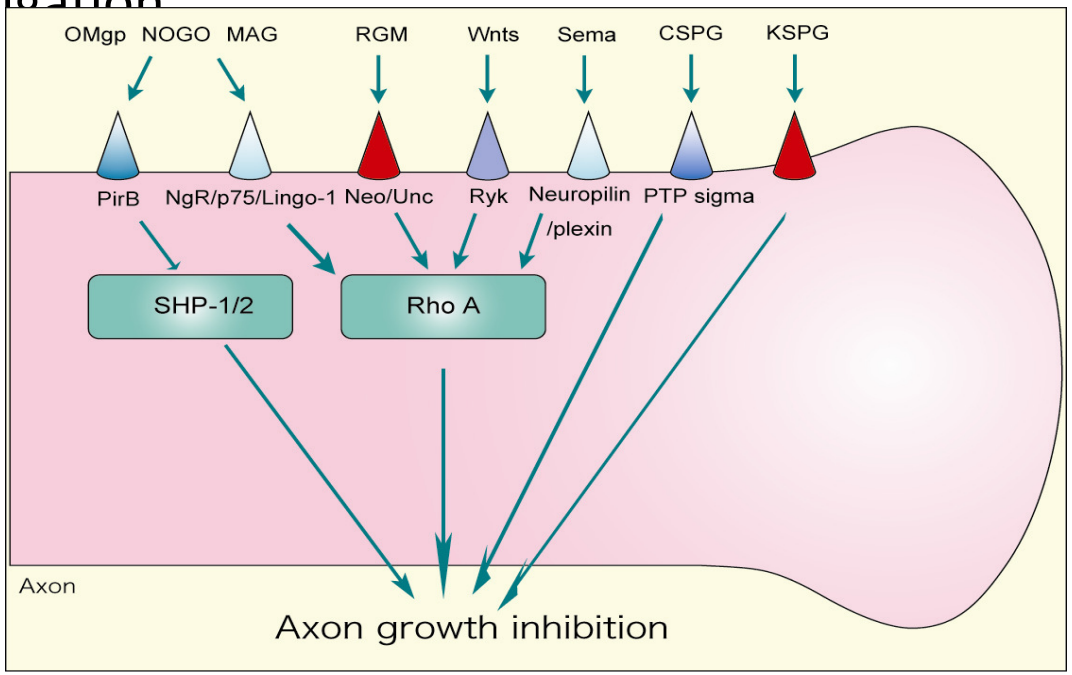
Adjustment of the participation in planning organization, holding of a periodical project meeting, patent consultation, examination of the study fund acquisition

Drug Technology seeds

The result in fundamental: Discovered p75 as the receptor for axon growth inhibitors and identified the downstream signal transduction mechanism

Matching: The antibody preparation technology of the Mitsubishi Tanabe Pharma Co. and basic researches of Dr. Yamashita performed matching and were tied to collaborative investigation

- By the development of the RGM antibody, the humanized antibody is made, too and performs the performance evaluations.
- Advance to the evaluation in the spinal cord injury model of the monkey, and a remarkable effect is observed.
- Under development for clinical application in cooperation with Mitsubishi Tanabe Pharma Co.



Molecular mechanism of axon growth inhibition in the adult CNS

Drug Results

□It became a mediation study to put technical seeds to practical use for innovative drug discovery.

□Developed into Tanabe Mitsubishi and genuine collaborative investigation.
□Dr Yamashita won American Ameritec Prize, and Osaka Science Prize
□Various talented people gather in the Yamashita lab , and talented scientists have been brought up.
□ It continues and gets many research funds, and basic research is accelerated.
□This study can expect that it is to antibody medicine called the neuronal regeneration with epoch-making spinal cord injury now because there is not a therapeutic strategy for the spinal cord injury.

Drug Patent □ Ripple effects

Patent□

□JP2006-510985□P3981148□

□PCT/JP2005/004246

□WO2005/087268

□Title :

AXON REGENERATION PROMOTER

Technologica□ impact :

Of the in vivo rating system of the central nerve reproduction was established

Market Impact :

□This therapeutic drug can contribute to the conquest of the aftereffects after the central nerve disorder.

□As a result, I enable the recovery from a need of nursing care state.

□Researchers put technical seeds to practical use and want to perform contribution to society.

Drug History of the research funds

□2009-2012 JST A-STEP(Adaptable & Seamless Technology Transfer Program through Target-driven R □ D□

□2010-2015 JST CREST (Core Research for Evolutional Science and Technology)

□2013-2017 JSPS: Grant-in-Aid for Scientific Research (S)

□2011-2014 JSPS□Grant-in-Aid for Scientific Research on Innovative Areas

JST □Japan science and technology agency□
JSPS□Japan Society for the Promotioni of science□

Drug Future Prospects

Target market:

□Spinal cord injury therapeutic drug □global market 7500 million dollars

□For cerebral infarction, stroke therapeutic drug □global market 5,300 million dollars clinical application.

Schedule:

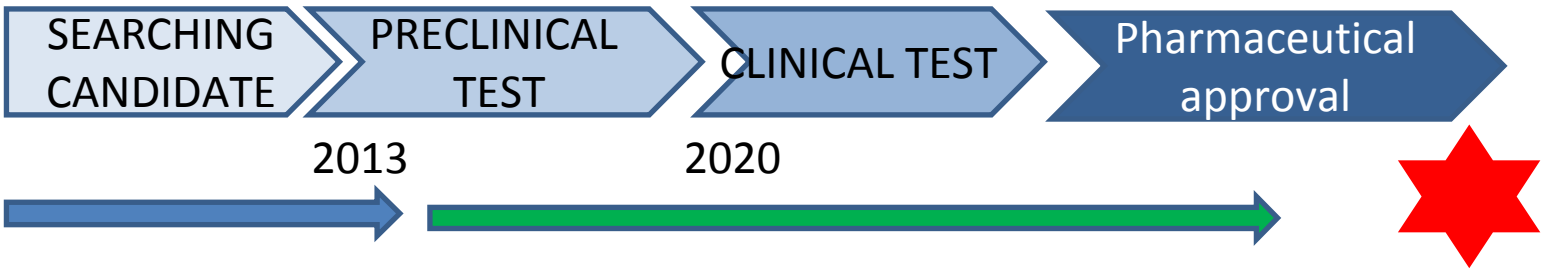
□The project is pushing forward Mitsubishi Tanabe Pharma Co. and joint development for clinical application.

□Clinical trial plan about 2020

Point : A long-term action is necessary, and big support is demanded from pharmaceutical Affairs Law approval acquisition.

Contact□ Professor of Osaka University , DR.Yamashita Toshihide

E-mail : yamashita@molneu.med.osaka-u.ac.jp



The important point of technology transfer

- In the practical use study, it is the most important condition that a university and the researcher of the company are eager for realization together.
- The securing of patent is important for practical use.
- The project can evade the risk of research and development of the mediation time by public support.
- The existence of a coordinator taking cooperation is important.

Acknowledgement

I thank Dr.Murai and Dr.Toyoda which had you instruct it by coordinator activity in JST Innovation Plaza Osaka and the person concerned.

Дякуємо за вашу увагу.

Thank you for your attention.