Technology Transfer at Tokyo University of Science (TUS)

The 2nd JUNBA Summit Technology Fair

Tokyo University of Science (TUS)

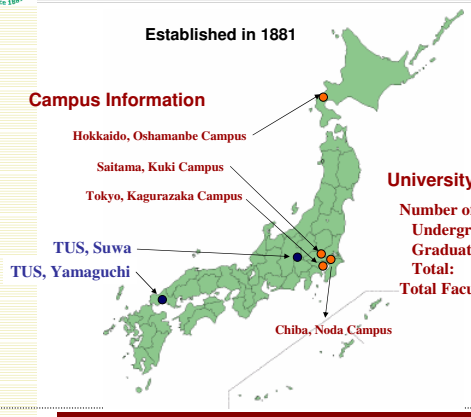
January 11th, 2008

1. About TUS Technology Licensing Organization (RIDAI SCITEC)
   Head of Global Division: Dr. Motoo Watanabe
2. Direct Thermal-to-Electric Conversion
   Faculty of Industrial Science and Technology
   Associate Professor: Dr. Tsutomu Iida
3. Nanoimprint technology, Electron beam lithography and Nano-mold fabrication process
   Faculty of Industrial Science and Technology
   Associate Professor: Dr. Jun Taniguchi
4. SQAG: Potent Novel Radiosensitizer
   Faculty of Science and Technology
   Professor: Dr. Fumio Sugawara

About Tokyo University of Science (TUS)

Established in 1881

President
Dr. Shin Takeuchi,



University Statistics

Number of Students
Undergraduate: 16,900
Graduate: 3,064
Total: 19,974
Total Faculty 524
(2006,TUS only)

About Technology Licensing Organization (RIDAI SCITEC)

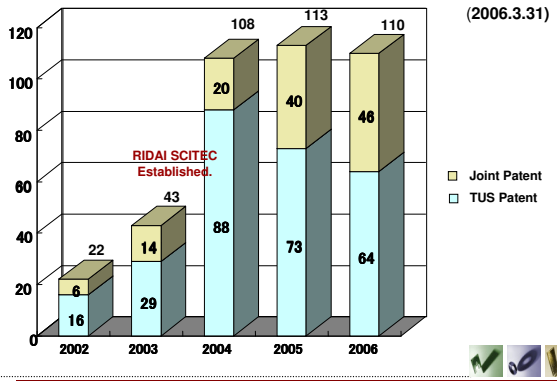
Basic Philosophy

To strive for the formation of new intellectual creation cycles based on return of activity achievements to TUS and further activation of education and research.

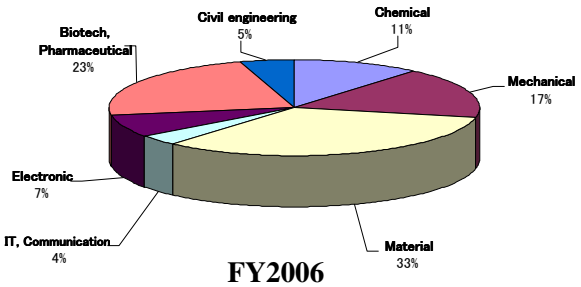
Main Functions

1 Recruit commercial-section partners
2 Negotiate contracts / agreements
3 Promote sponsored / joint research
4 Assist in protecting intellectual property
5 Support for regional collaboration with local government
6 Support for university-initiated ventures
7 Public relations pertaining to industry-academia-government collaboration

Patent Applications



Patent Applications by Technology Fields



FY2006

For more information

http://www.tus.ac.jp/tlo/

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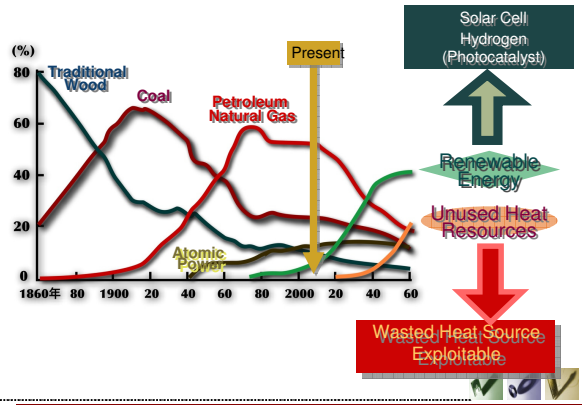
e-mail: tlo@admin.tus.ac.jp

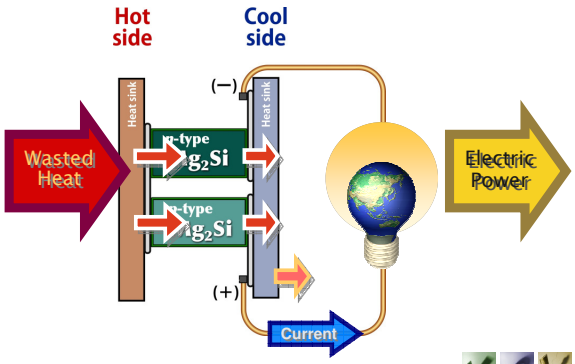
Mg_2Si

Direct Thermal-to-Electric Conversion
Environmentally Benign Semiconductor
Reused Silicon Source

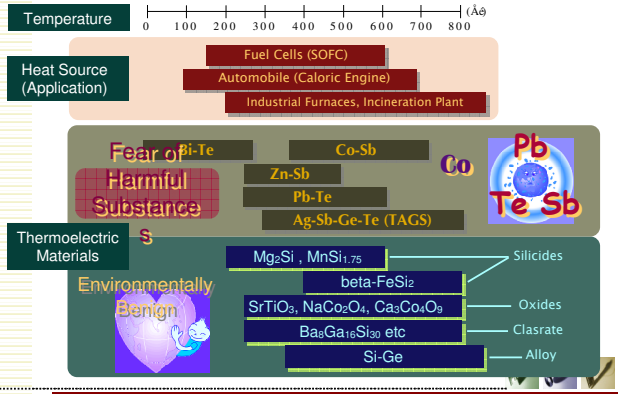
Forecasts for Energy Sources (Duetche Shell)



Direct Thermal-to-Electric Energy Conversion



Thermoelectric Materials and Applications



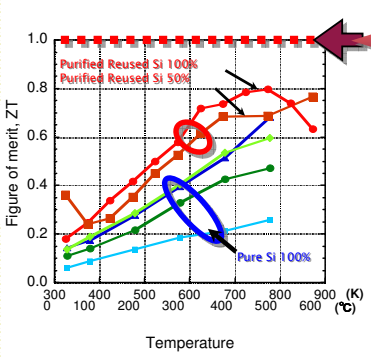
Reuse Process of discarded Silicon for Mg_2Si

Thermal-to-Electric Energy Conversion

Mg_2Si

Source Material
- 100% Reuse Si
- Less Pure Mg

Material Performance of Mg_2Si with 100% Reused Si



Material Conversion Efficiency ~10%

100 % Reused Si
Material Efficiency ~8%

Big Surprise!!
Big Impact!!

TUS is the birthplace of Nanotechnology

The basic concept of Nanotechnology and technical term of "Nanotechnology" were introduced in 1974 by Professor Norio Taniguchi (Faculty of Science and Technology, Department of Mechanical Engineering).

On the Basic Concept of 'Nano-Technology'

Norio TANIGUCHI
Tokyo Science University
Noda-shi, Chiba-ken, 278 Japan

Abstract

'Nano-technology' is the production technology to get the extra high accuracy and ultra fine dimensions, i.e. the preciseness and fineness of the order of 1 nm (nanometer), 10⁻⁹m in length. The name of 'Nano-technology' originates from this nanometer. In the processing of materials, the smallest bit size of stock removal, accretion or flow of materialsis probablyof one atom or one molecule, namely 0.1~0.2 nm in length. Therefore, the expected limit size of fineness would be of the order of 1 nm. Accordingry, 'Nano-technology' mainly consists of the processing of separation, consolidation and deformation of materials by one atom or one molecule. Needless to say, the measurement and control techniques to assure the preciseness and fineness of 1 nm play very important role in this technology.

In the present paper, the basic concept of 'Nano-technology' in materials processing is discussed on the basis of microscopic behaviour of materials andas a result the ion sputter-machining is introduced as the most promissing process for the technology.

Abstract of International Conference on Production Engineering (1974) Tokyo

World first "Nanotechnology"

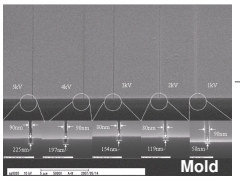
Nanotechnology activity in TUS

- **Nano-material**
  - Carbon Nano Tube, Nano-particle
- **Nano-positioning**
  - Machine element, Tribology, control system
- **Nano-chemical/bio material**
  - DDS
- **Nano-fabrication process**
  - MEMS (microelectromechanical system), NEMS

Nanoimprint technology, Electron beam lithography, Nano-mold fabrication process

3D Nanoimprint technology

- **Three dimensional nanoimprint lithography techniques. Using electron beam direct writing of mold and replication by UV-NIL. (Patterning area of 90 μm^2 is possible, in the case of nano-order pattern.)**

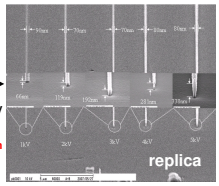


Mold is expensive

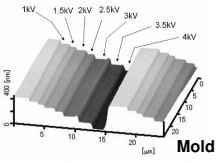
Different depth Mold (3D mold)

Replicated by UV-NIL

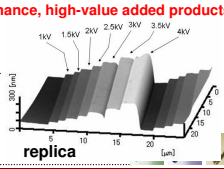
Mass production is possible!!



High performance, high-value added products !!

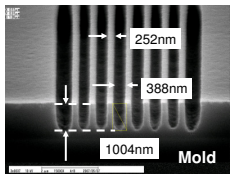


Blade-shaped binary optics mold

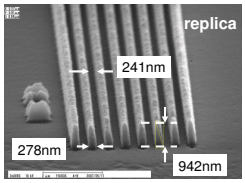


Nanoimprint technology for optical devices

- **Fabrication of submicron high-aspect-ratio structures using EB resist for NIL molds. And using this mold, pattern transfer is possible. EB resist is inorganic resist (SiO_2) which has enough toughness and durability for NIL molds. These kind of high-aspect-ratio structures are used for sub-wavelength plates and quarter wavelength plates which are one of the main components of an optical pickup at CD or DVD. (Patterning area of 900 μm^2 is possible, in the case of sub-micron pattern.)**



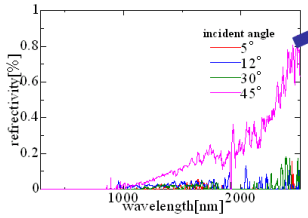
Sub-wavelength plates mold

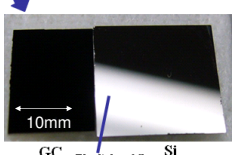


Sub-wavelength plates

Nanofabrication process

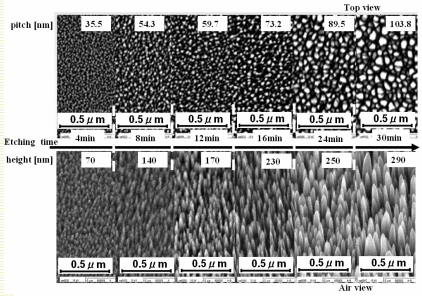
- **Anti-reflection structures (Moth eyes structures) were fabricated on glassy carbon (GC) surface by special ion irradiation method. This process is very simple and large area fabrication (up to 30 mm square) is possible. This structure indicates non-reflective (less than 0.1 % reflection) property over the range of visible light. Furthermore, with this method, oblique incident angle reflection has been suppressed.**





The light of fluorescent image of Si and etched GC

Anti-reflection structures (Moth eyes structures)



Applications possibility

- **Anti-reflection**
  - Flat panel display
  - Mobile phone
- **Large surface area**
  - Lotus effect (Super hydrophobic surface)
  - Adhesive tape
- **Life science**
  - Cell culture sheet
  - Substrate for Surface Plasmon Resonance (SPR)
- **Energy**
  - Solar cell window
  - Heat storage system

- **SEM images of top view and air view of anti-reflection structures at various irradiation times.**

SQAG: Potent Novel Radiosensitizer

a-Sulfoquinovosylmonoacylglycerol Is a Novel Potent Radiosensitizer Targeting Tumor Angiogenesis.

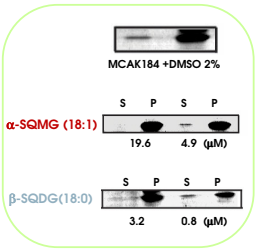
Fumio Sugawara, Professor of Chemical Biology, Genome & Drug Research Center.
sugawra@rs.noda.tus.ac.jp

Angiogenesis is a promising target for the treatment of cancer, and varying types of antiangiogenic agents have been developed. Although radiotherapy can be combined with antiangiogenic compounds, almost all previously known angiogenesis inhibitors could still cause side effects at effective doses, and only additive effects are seen in current combination therapy.

Here we identified that a-SQMG is a potent radiosensitizer. The agent synergistically inhibits angiogenesis at low doses when combined with ionizing radiation. Combined treatment seems to promote the adoption of a senescence-like phenotype by vascular endothelial cells. Finally, the agent remarkably enhances the radioresponse of human tumors transplanted into nude mice, accompanied by a significant reduction in the vascularity of the tumors.

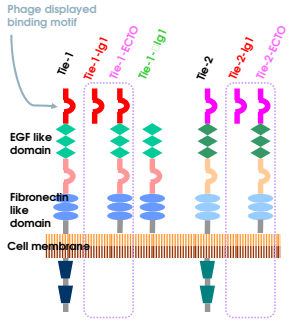
SQAGs target MCAK, inhibiting tublin depolimarization.

Tublin depolymerization assay



A screen for candidate target molecules using a T7 phage display method identified an amino acid sequence. An homology search showed this to be a mammalian mitotic centromere-associated kinesin (MCAK). An in vivo microtubule depolymerization assay, using EGFP-full length MCAK fusion constructs, indicated inhibition of the microtubule depolymerization activity of MCAK. From these results, we conclude that clinically promising SQAGs have several different molecular targets including MCAK

SQAGs target Tie1/2 signaling.



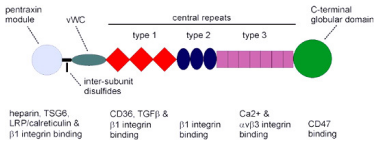
Second candidate target molecules obtained from using a T7 phage display method identified an amino acid sequence to be a signal domain of Tie 1 and 2.
An in vivo assay indicated down regulation of Tie signaling.

SQAGs are VEGF trap.

SQAG	VEGF-165 K_D (M)	PDGF-BB
β-SQDG (vesicle)	$1.0x10^{-10}$	$6.4x10^{-7}$
β-SQDG	$1.3x10^{-10}$	$8.1x10^{-7}$
β-SQMG	$1.9x10^{-5}$	$2.4x10^{-5}$
β-SQG	$5.3x10^{-6}$	$1.5x10^{-3}$
β-GDG	<1	<1
α-SQDG	$3.5x10^{-9}$	$1.6x10^{-6}$
α-SQMG	$1.7x10^{-5}$	$1.9x10^{-5}$
α-SQG	$5.3x10^{-5}$	$1.3x10^{-2}$

Third candidate target molecules obtained from using a T7 phage display method identified that an amino acid sequence was conserved in $VEGF_{165}$.
The obtained dissociation constants from SPR (Biacore) indicated the strong bindings of SQAG. We conclude that the angiogenesis inhibitors ,SQAGs, are strong VEGF trap.

SQAGs target TSP1.



Forth target is thrombospondin (TSP). From DNA microarray experiments, we found that THBS1 was identified one of highly expressed genes.

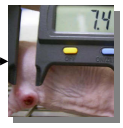
TSP-1 acts to inhibit angiogenesis, inhibiting the proliferation and migration of endothelial cells by interactions with CD36 expressed on their surface of these cells. Inhibitory peptides and fragments of TSP1 bind to CD36, leading to the expression of FAS ligand (FasL), which activates the expression of Fas. This leads to the activation of caspases and apoptosis of the cell. Since tumors overexpressing TSP-1 typically grow slower, exhibit less angiogenesis, and have fewer metastases, TSP1 is an attractive target for cancer treatment.

SQAG: Potent Novel Radiosensitizer

Control

X-ray (2Gy)

SQMG1 mg/kg



SQMG+X-ray
ER≧3.0

Significant reduction in the vascularity of the tumors

Radiation

X

SQMG

Angiogenesis
DNA replication & repair
Tie1/2 signaling
TSP1expression