Proposal of next generation measurement method of cells and tissues using quantum beam

Laser medicine, Photometry, Free electron laser, Quantum beam biology, Proteomics
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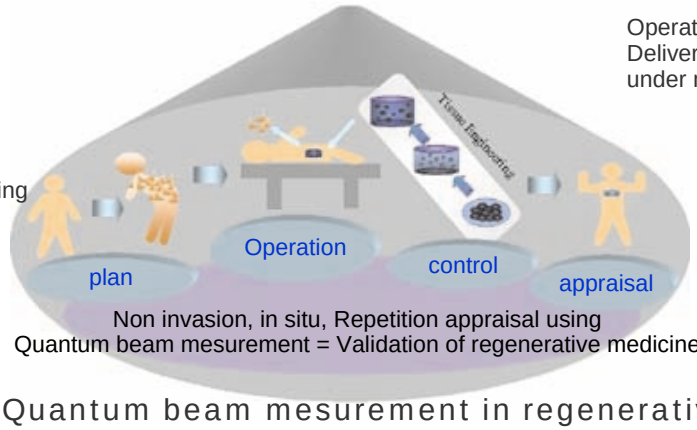
Free Electron Laser Research Facility, Department of Engineering Research

Integrated Cell and Tissue Reguration

Diagnosis before the Remedy and Remedy plan

Operation of Cell and Organization Delivery (using Endscope, Robot) under mesurement monitoring



Operation of Cell and Organization Delivery (using Endscope, Robot) under mesurement monitoring

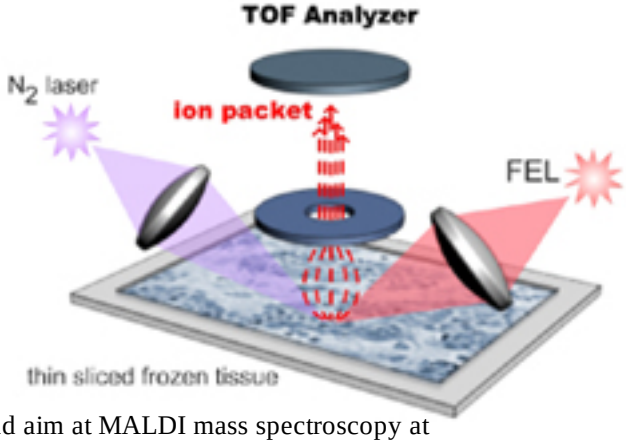
Observation of Progress and Servival State / Medical appraisal

Non invasion, in situ, Repetition appraisal using Quantum beam mesurement = Validation of regenerative medicine

The role of Quantum beam mesurement in regenerative medicine

1 Mass spectroscopy of biological tissues by UV/FEL-MALDI method

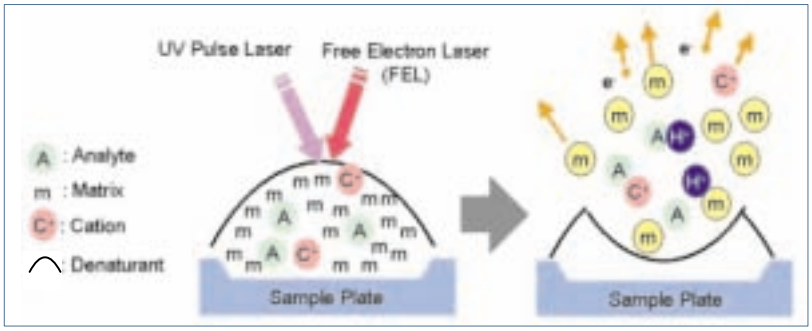
<Direct Proteome Profiling / Mass spectroscopy of biological tissues by MALDI method>



Laser soft ionization of protein, matrix-assisted laser detachment ionization (MALDI), is a technique that has accelerated the progress of mass spectroscopic proteomics. However, ionization using ultraviolet lasers, which is currently used widely, is incapable of analyzing complex mixtures of slightly soluble proteins and lipids such as cell membranes and biological tissues.
The UV/FEL-MALDI mass spectroscopy system for analysis of slightly soluble proteins being developed by our laboratory has achieved ionization of slightly soluble proteins in a mixed environment by simultaneous irradiation by 2 types of laser: an ultraviolet laser and a tunable middle infrared free electron laser (MIR-FEL). In this COE, we target the realization of efficient laser ionization using this method, and aim at MALDI mass spectroscopy at the cell and tissue level, which has not yet been achieved. We will also perform development studies of an apparatus for cell and tissue analysis.
Concretely, the following subjects are considered.

- UV/FEL-MALDI mass spectroscopy of complex systems
- In-situ MALDI mass spectroscopy and mass imaging of cells and tissues
- Elucidation of the ionization mechanism of UV/FEL-MALDI and achievement of very high efficiency of ionization

Ionization of UV/FEL-MALDI method



Targets (mixture of sample, matrix, and solubilizer) are simultaneously irradiated with an ultraviolet pulse laser and a middle infrared free electron laser (MIR-FEL). The ultraviolet laser induces an excited state in the electrons, and rapidly superheats the matrix, inducing proton donating-receiving reactions upon evaporation. MIR-FEL induces a vibrational excited state and assists ionization by weakening the aggregating action of the solubilizer that inhibits the ionization process.

Proposal of next generation measurement method of cells and tissues using quantum beam 2/3

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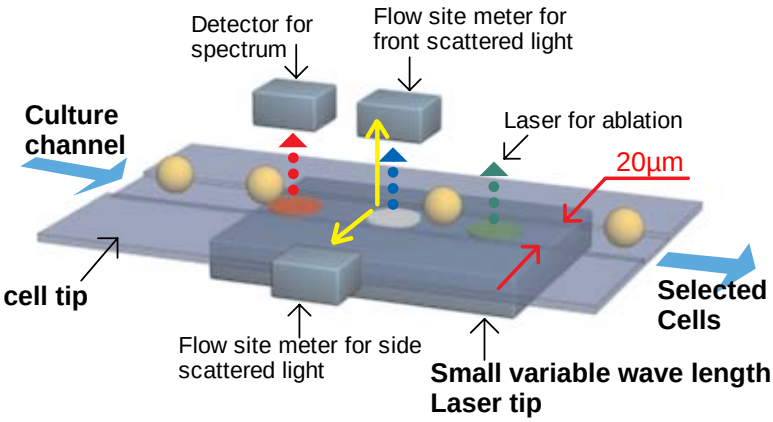
2 Development of an on-chip cell culture management system using light

Currently, the quality and function of cells and tissues are evaluated using direct destructive methods such as biochemical techniques. Moreover, limited amounts of cells and tissues are available for transplantation in regenerative medicine. Thus, development of a screening technique capable of performing nondestructive rapid functional evaluation and quality control is necessary. Our laboratory performs quality control of cells and soft and hard tissues, mainly ES cells, stem cells, regenerated tissues, and regenerated bone studied in this COE, using photometric methods, mainly laser fluorescence excitation and infrared spectroscopy, aiming at the establishment of a novel method of evaluating the functions of cells and tissues.
For recovery of cells of interest after analysis of cell types and functions, currently large and expensive instruments such as flow cytometers and cell sorters are necessary. Downsizing and generalization of the cell sorting technique is necessary for the clinical application (generalization) of cell studies. Thus, our laboratory will develop a 'cell chip', on which quality control of cells can be performed eg. cell culture (measurement (sorting (improvement of quality) (recovery. Cell chips aim at advancement in culture capacity, simplification of measurement and control, and high recovery efficiency for construction of an integrative cell culture management system.

The image of cell quality controle with Laser cell tip

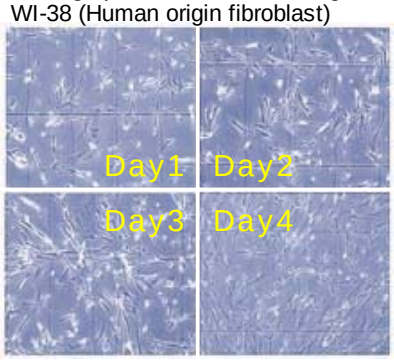


Cell chips that allow the culture, measurement, selection, and sorting of cells on chips will be developed, and quality of cells will be controlled using the cell chips. Measurement and selection of cells will be controlled using quantum beams (laser, light, etc.).

Photograph of Cell tip

Laser processing designing the optional passage on the plastic basis / Processed 20um Flow width

Photograph of Cell culture using Cell tip
WI-38 (Human origin fibroblast)



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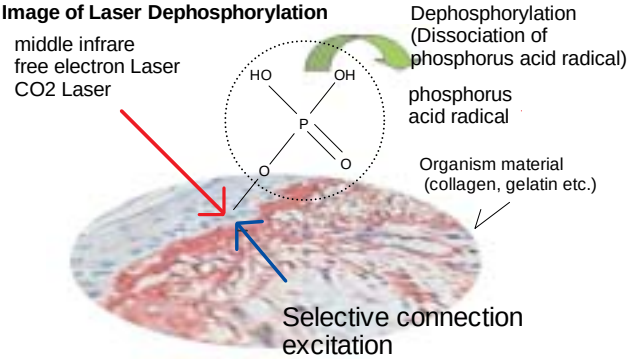
3 Compatibility control of biomaterials by nondestructive measurement method of phosphorylation using infrared and laser dephosphorylation

For reconstruction of tissues located in the boundary between hard and soft tissues such as tendons, intervertebral discs, and periodontal tissues, material techniques capable of accurate control of compatibility with soft tissues and adherence to hard tissues are necessary. Regarding biocompatibility and adherence, it has been reported that bases possessing phosphate groups promote formation of hydroxyapatite, the main component of hard tissues.
Our laboratory is performing a development study of non-contact and nondestructive methods of protein phosphorylation using infrared spectroscopy and laser dephosphorylation method using free electron laser in the 9-(m wavelength zone and CO2 laser. The laser dephosphorylation methods will control the phosphorylation level on biomaterial surfaces, and the surface phosphorylation level will be measured with no contact using infrared spectroscopy to achieve desired adherence and compatibility of biomaterials for optimization of biomaterial designs.

Image of Laser Dephosphorylation



- Through this COE program, we make efforts to develop human resources capable of highly understanding and studying the 2 fields, quantum beam engineering, mainly laser, and medicine.

Other study contents of Awazu laboratory

- Development of novel laser angioplasty for atherosclerosis therapy by selective removal of cholesterol
- Development of hollow optical fiber system for guiding light in the body cavity
- Removal of new blood vessels by ICG-PDT using femtosecond laser
- Development of DDS using laser percutaneous absorption
- Infrared spectroscopic analysis of phosphorylation and laser dephosphorylation
- Prevention of dental caries by improvement of surface quality of tooth hard tissue
- Development of real-time monitoring method using laser-induced sound
- Elucidation of the biological soft tissue excision mechanism for low-invasive laser surgery