## Micro- and Nano-Biomechanics in Tissue Engineering (Application of Load Bearing Tissues to Regenerative Medicine)

### (1) Aims

Recently, the promise of regenerated tissue as a medical treatment in which biological and engineering approaches are combined has been realized through advances in and cross-disciplinary research in biochemical and physical sciences. In order to maintain the form and function of load bearing tissues (such as bones, tendons, ligaments, cartilage, and arteries) and power generating tissues (such as muscles, heart muscles, and the digestive tract tissues), proper mechanical stimulation needs to be maintained. This is especially true for tissue regeneration. From this point-of-view, we project the potential contribution of mechanical engineering to the field of tissue regeneration.

### (2) Social and technical needs

- To be able to replace biological tissues in which function has been lost with new tissues.
- Mechanical stimulation must be taken into consideration in any examination of regeneration of load bearing tissues.
- To be able to rearrange cells and basic structures three-dimensionally in regenerated tissues.
- Need to clarify mechanical factors that control cell differentiation and tissue regeneration as mechanical environments are closely linked to and affect differentiation of premature cells and the formation of living tissues (not only general formation but also vascular organization).

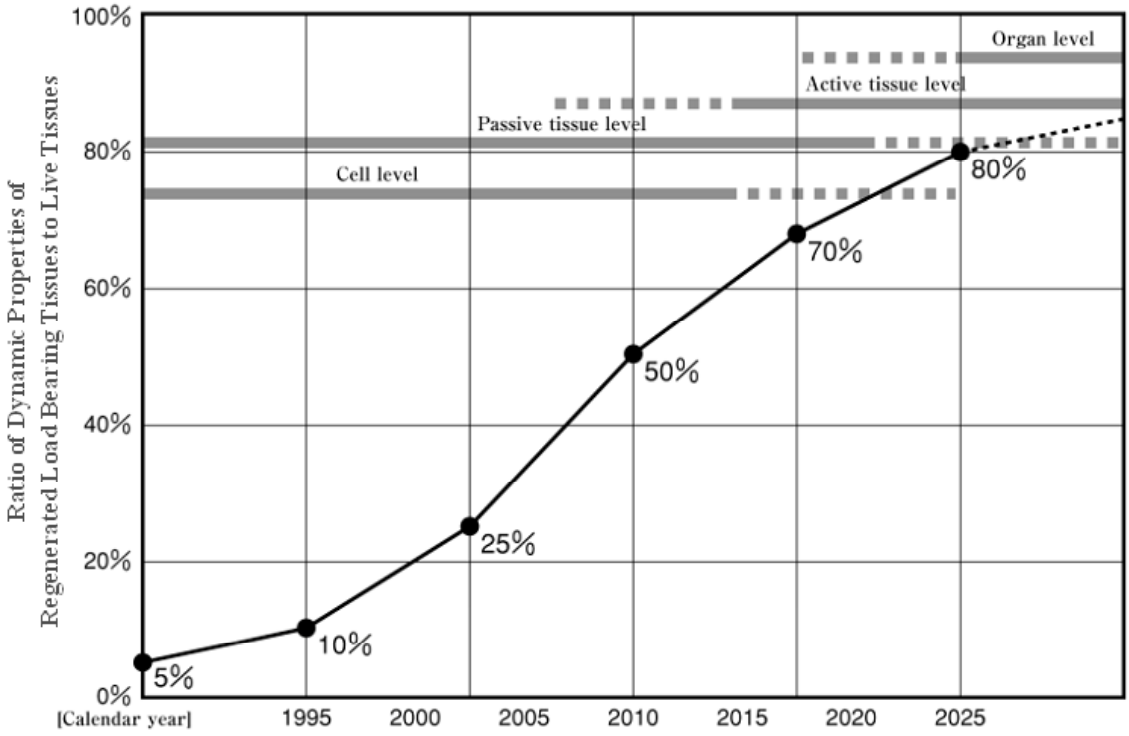
### (3) Future directions for determining key mechanisms and parameters

Use of regenerated tissues may be implemented first at the cellular level, then at the tissue level and finally at the organ level.

- Some crucial combinations of biochemical and physical stimulation necessary for the differentiation of ES cells and bone marrow stromal cells to tissue regeneration may be elucidated. Technology for controlling cell orientation in two-dimensional tissues and inducing capillary nets using various growth factors may be established (2005 and later).
- Many of the specific conditions necessary to stimulate cell differentiation and tissue regeneration may be clarified. Technology for controlling cell orientation in three-dimensional tissues and for forming capillary networks at a certain depth by combining growth factors and mechanical stimulations may be established (2010 and later).
- Appropriate stimulation conditions for the regeneration of several large tissues and organs may be clarified, and technology for forming capillary networks within the regenerated tissues may be established (2015 and later).
- Appropriate stimulation conditions for the regeneration of many large tissues and organs may be clarified (2020 and later).

### (4) Contributions to society

- Various tissues with functions equivalent to those of natural tissues generated using animals may be available for medical treatment.
- Various tissues with functions equivalent to those of natural tissues may be available for transplantation into humans.
- Various tissues with functions equivalent to those of natural tissues and regenerated from ones' own cells may be available.



## Social & Technical Needs

**Social and Technical Needs**

- To be able to replace biological tissues in which function has been lost with new tissues.
- Mechanical stimulation must be taken into consideration in the examination of regeneration of the load bearing tissues (such as bones, tendons, ligaments, cartilage, arteries, muscles, cardiac muscles, and digestive organs).
- To be able to rearrange cells and basic structures three-dimensionally in regenerated tissues.
- Need to clarify mechanical factors that control cell differentiation of premature cells and the formation of living tissues (not only general formation but also vascular organization).

## Technical Breakthrough

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| 2005～2010 | • Clarify the basic stimulation conditions necessary for cell ifferentiation and tissue regeneration.<br>• Establish technology for controlling cell orientation in two-dimensional tissues. |
| 2010～2015 | • Clarify stimulation conditions necessary for cell differentiation and tissue regeneration.<br>• Establish technology for controlling cell orientation in three-dimensional tissues. |
| 2015～2020 | • Clarify appropriate stimulation conditions for the regeneration of several large tissues and organs.<br>• Establish technology for forming capillary networks at a specific depth in three-dimensional tissues. |
| 2020～2025 | • Clarify appropriate stimulation conditions for the regeneration of large tissues and organs. |

## Changes in Society and Markets

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| 2005～2010 | • Start medical care system for elderly people over the age of 75 (completed).<br>• Generate human iPS (induced pluripotent stem) cells (completed).<br>• Establish method for culturing human ES cells in large quantities. |
| 2010～2015 | • Make various tissues with functions equivalent to those of natural tissues reproduced in animal experiments available.<br>• Establish medical technology for eyesight recovery with artificial retina chips embedded in eyes.<br>• Implement ability to determine various genome functions from DNA base sequence. |
| 2015～2020 | • Transplant various tissues with functions equivalent to those of natural tissues into humans.<br>• Put transplantation of artificially cultured heart muscle tissues and hepatocytes into practice.<br>• Regenerate heart muscles and vascular tissues with functions and structures equivalent to those of normal tissues and liver tissue with function equivalent to that of the natural liver. |
| 2020～2025 | • Reproduce various tissues with functions equivalent to those of natural tissues from ones' own cells.<br>• Establish technologies to predict high-order protein structures, interactions of proteins, interactions of DNA and RNA, and other living activities. |