Discovery and Assistance of Translational Research at Academia: from the experience of the Institute of Medical Science, the University of Tokyo.

Division of Advanced Medicine Promotion & Center for Translational Research, the Institute of Medical Science, the University of Tokyo

Fumitaka Nagamura
Content

- Introduction/History of the Institute of Medical Science, the University of Tokyo (IMSUT)
- Pipeline of IMSUT
- Incentive: discovery of SEEDs
Development of granulocyte-colony stimulating factor (G-CSF: lenograstim)

Leukocytosis of lung cancer patient → Leukocytosis was observed in tumor-bearing nude mouse of the patient → Demonstration of the existence of leukocytosis inducing factor

From bedside → G-CSF was purified from G-CSF producing cancer cell line by collaborative company → G-CSF was cloned → Clinical studies and clinical trials

Collaboration with pharmaceutical company → Basic research
Facilities of IMSUT

Focusing on cancer, infectious disease and other intractable diseases, our mission is to translate basic research findings to medical therapies.

**Biobank Japan**
Leading and largest biobank in Japan, database storage of DNA and serums provided by 200,000 general public and patients.

**Supercomputer**
Fastest supercomputer in the life-science section research in Japan.

**Core Facility for Therapeutic Vectors**
Systematic production and storage of viral vectors, oncolytic virus, and transfected cells in cGMP grade for clinical trials.

**Stem Cell Bank**
Establishing and storage of disease-specific iPS cells for a broad range of medical and pharmacological studies.

**Research Hospital**
135 beds, 6 level 100 clean rooms, 27 level10,000 clean rooms, 4 negative pressure isolation rooms.

**Cell Resource Center**
Oldest cell processing facility in Japan. Cell processing for regenerative medicines, cord blood mesenchymal stem cell banking.

**Center for TR**
Assistance from basic research obtaining intellectual property to conducting translational research and INDs by pharmaceutical companies.

**Department of Biopharmaceutical Safety Inspection**
Analysis to test for the presence of bacteria, fungi, endotoxins, and mycoplasma within biopharmaceuticals.

- Department of Microbiology/Immunology
- Department of Cancer Biology
- Department of Basic Medical Sciences
- Human Genome Center
- Center for Experimental Medicines/System Biology
- Advanced Clinical Research Center
- Center for Stem Cell Biology/Regenerative Medicine
- International Research Center for Infectious Diseases
- International Research and Development Center for Mucosal Vaccines
- Center for Gene/Cell Therapy
- Laboratory Animal Research Center
- Laboratory of Molecular Genetics
- Medical Proteomics Laboratory
# Representative Pipeline of IMSUT

**Supported under Translational Research Network Program**

<table>
<thead>
<tr>
<th>Preclinical phase</th>
<th>Phase I</th>
<th>Phase II</th>
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<tbody>
<tr>
<td>Genetically engineered Measles for cancer</td>
<td>Genetically engineered HSV-1 for advanced glioma</td>
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<td>Peptide vaccine for cancer</td>
<td>Peptide vaccine for NSCLC as adjuvant therapy</td>
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<td>Oligonucleotide therapy targeting cancer stemness using chimera RNAi for triple negative breast cancer</td>
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<td>Cancer</td>
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<td>Umbilical cord derived MSC banking for regenerative medicine, GVHD</td>
<td>Genetically engineered HSV-1 with hIL-12 for melanoma</td>
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<td>Engraftment acceleration using umbilical cord blood derived cells for pts treated with HSCT</td>
<td>Alveolar bone regenerative medicine</td>
<td>Cell Therapy/Regenerative therapy</td>
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<td>Lipid-based drug for the control of allergic or inflammatory bowel diseases</td>
<td>Regenerative medicine for gonarthrosis with hemophilia</td>
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<td>Gene therapy for neuromuscular junction diseases</td>
<td>Rice-based oral cholera vaccine</td>
<td>Others</td>
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<td>Antibody targeting nucleic acid-sensing Toll-like receptors for Rheumatoid/inflammatory diseases</td>
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<td>Nanogel nasal vaccine for pneumococcus</td>
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<td>Oligonucleotide therapy (STuD) for cancer/inflammatory diseases</td>
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<td>Cancer immunotherapy</td>
<td>Cancer immunotherapy (peptide)</td>
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<td>Oligonucleotide therapy (new form)</td>
<td>Oncolytic virus</td>
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<td>Oligonucleotide therapy (new form, novel DDS)</td>
<td>Regenerative medicine</td>
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<td>Rice-based vaccine</td>
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<td>Cell therapy (engraftment activation)</td>
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Novel concept

Many novel concepts
Coordination, Support and Training Program for Translational Research → Translational Research Network Program

2007-2011
Coordination, Support and Training Program for Translational Research

2012-2016
Translational Research Network Program

University of Tokyo
University of Tokyo Hospital
IMSUT Hospital
At the time of “Coordination, Support and Training Program for Translational Research”

- 7 seeds registered/ 5 yrs
- License out: 1, Diagnostic algorithm: 1, Non IND (under guideline) regenerative medicine: 1

I’m reluctant to register my seeds. Because, there is no benefit for me. I receive no money from the Program.
SEEDS pipeline system under Translational Research Network Program

Basic Research

SEEDS A
Basic research intending to apply intellectual property within 2 yrs
Research funding up to ¥5M + Intellectual property assistance

SEEDS B
Seeds intending to obtain preclinical PoC or submit IND application within 3 yrs
Research funding up to ¥50M + assistance to conduct preclinical studies, to obtain POC by preclinical studies

SEEDS C
Seeds intending to obtain clinical PoC within 3 yrs via clinical trial or advanced medical care
Research funding up to ¥80M + assistance to conduct clinical trial
Application for SEEDS from IMSUT under Translational Research Network Program

SEEDS A

2012 2013 2014 2015

SEEDS B

2012 2013 2014 2015

SEEDS C

2012 2013 2014 2015
Needs more efforts for seeking SEEDs

- “Mode of bioenergetic metabolism during B cell differentiation in the intestine determines the distinct requirement for vitamin B1”, Cell Reports (Professor Kunisawa)
- “Development of high-yield influenza A virus vaccine viruses”, Nature Communications (Professor Kawaoka)
- “An Ebola whole-virus vaccine is protective in nonhuman primates”, Science (Professor Kawaoka)
- “A Safeguard System for Induced Pluripotent Stem-Cell Derived Rejuvenated T-cell Therapy”, Stem Cell Reports (Professor Nakauchi)
- “An interleukin-33-mast cell-interleukin-2 axis suppresses papain-induced allergic inflammation by promoting regulatory T cell numbers”, Immunity (Associate Professor Nakae)
- “MCRIP1, an ERK Substrate, Mediates ERK-Induced Gene Silencing during Epithelial-Mesenchymal Transition by Regulating the Co-Repressor CtBP”, Molecular Cell (Professor Takekawa)
Summary

Progress
- By offering research funding, intellectual property consultation, and assistance of preclinical studies including management of Pharmaceutical Affairs Consultation on R&D Strategy of PMDA, researchers have recognized the importance of our assistance, and the number of SEEDs has been increasing.

Problems
- Researchers with huge research funds still have no curiosity of our activities.
- More and continuous incentives for researchers is required.
- Necessity of collaboration with companies.