

Keio University Global Research Institute
Longevity Initiative
April 14, 2018

Longevity Research in Keio University.

Hideyuki Okano

Dean, Keio University Graduate School of Medicine
Professor and Chair, Department of Physiology
Keio University School of Medicine

**Global Future Council on the Future of Biotechnologies,
World Economic Forum**

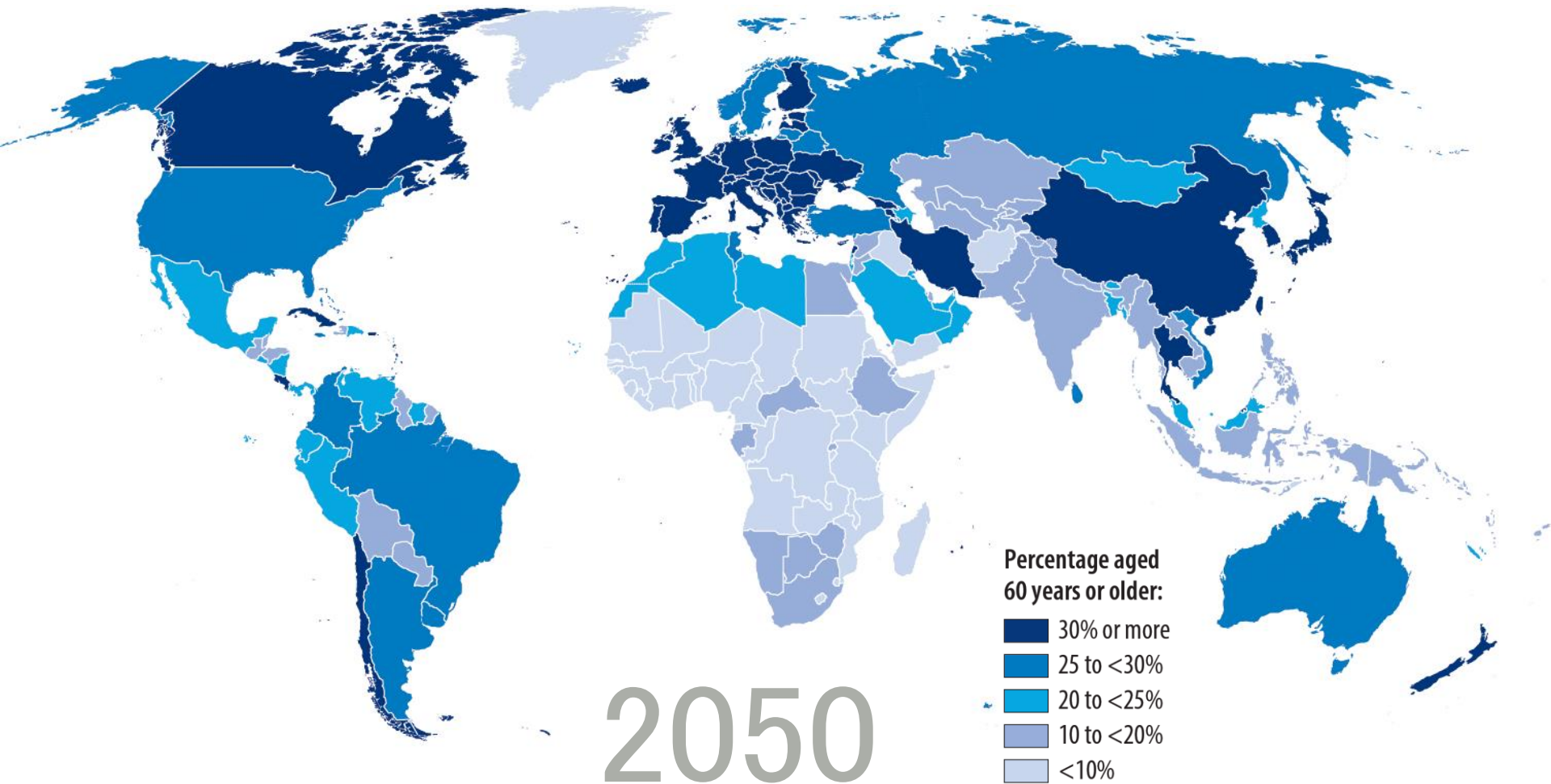


Keio Global Initiatives

Longevity, Security, Creativity



Populations are getting older





Keio Longevity Initiative



1. Dementia

2. Supercentenarian Study

3. Neurodegenerative Disease Model Marmoset

SOCIAL COSTS FOR DEMENTIA IN JAPAN

- 14.5 trillion Yens per Year (~3% of GDP)

Including

Medical Expenses (1.9 trillion Yens)

Care Costs (6.4 trillion Yens)

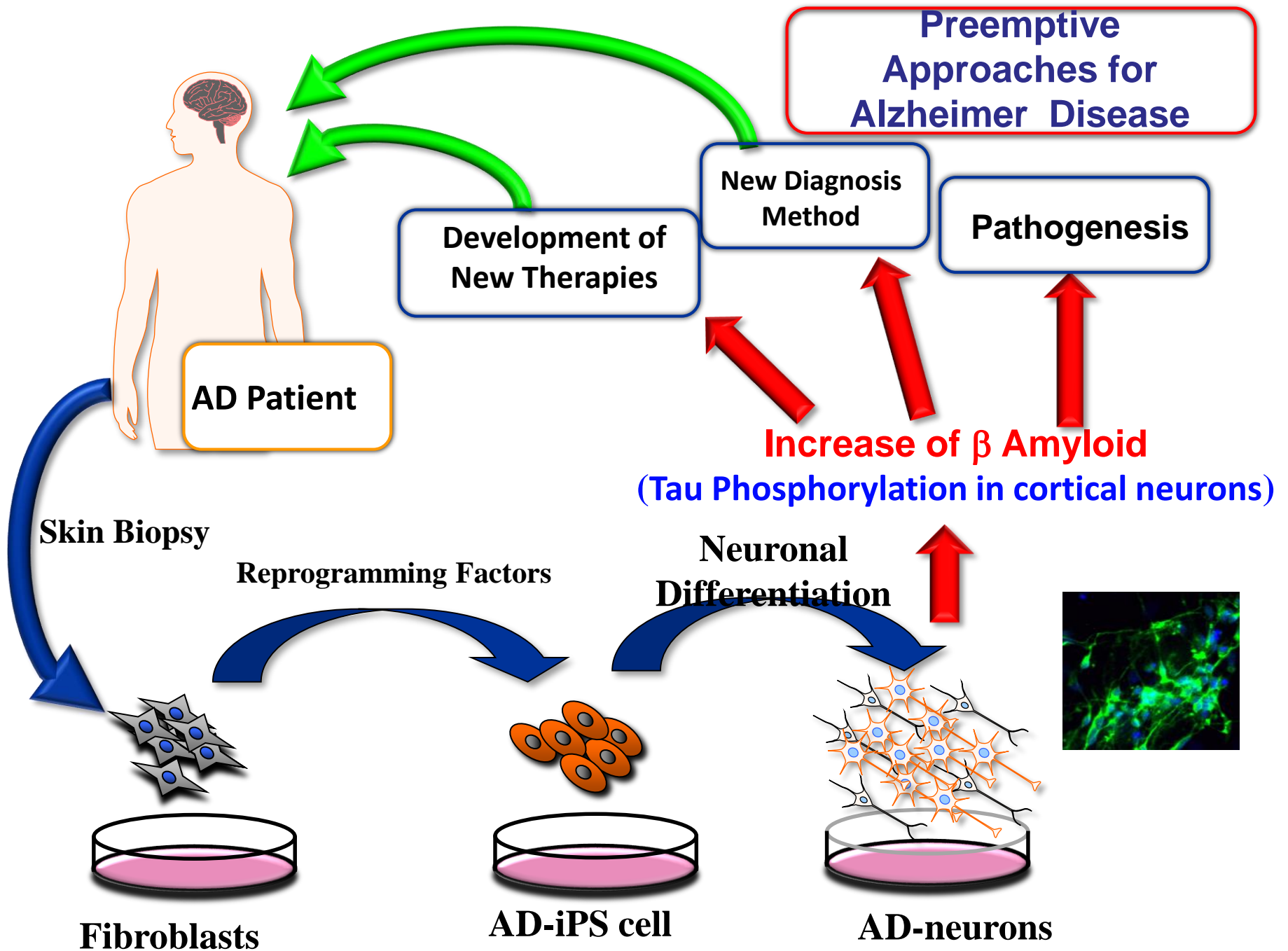
Informal Care Costs (6.2 trillion Yens)

Dr. Michihiro Sado at Keio University School of Medicine



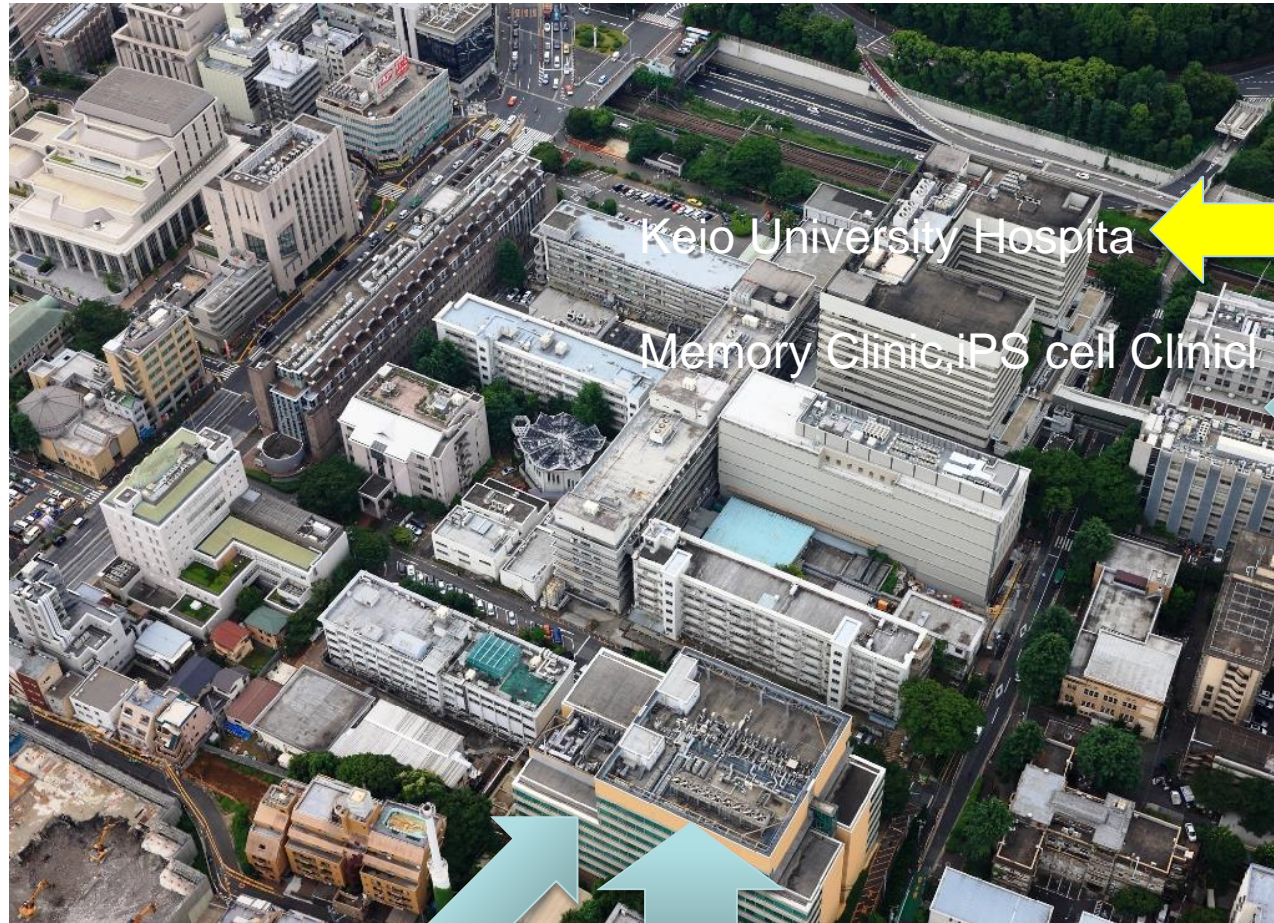
To prevent the increase of this ratio, preemptive approaches against dementia are indispensable.

Preemptive Medicine includes **Early Detection** of the diseases and **Early Interventions**.



Preemptive Medicine for Alzheimer Disease in Keio

Keio University
Shinanomachi Campus
2015-June



Keio University Hospital

Memory Clinic, iPS cell Clinic

Early Intervention

**Amyloid β , Tau
PET imaging**

(Preventive Medicine Center)

Early Diagnosis

iPS cells (iPS cell Research Center)

Whole Genome Sequencing (Keio Center for Supercentenarian Medical Research)



Keio Longevity Initiative



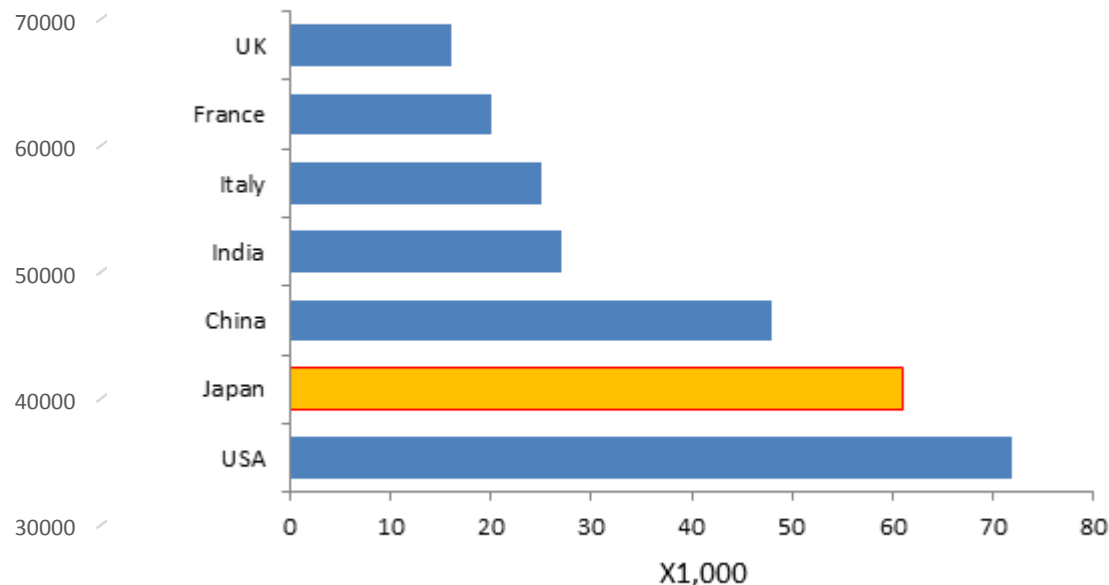
2. Supercentenarian Study

Toward a comprehensive understanding of healthy longevity

Yasumichi Arai, Hideyuki Okano, Nobuyoshi Hirose,
Center for Supercentenarian Medical Research
Keio University School of Medicine

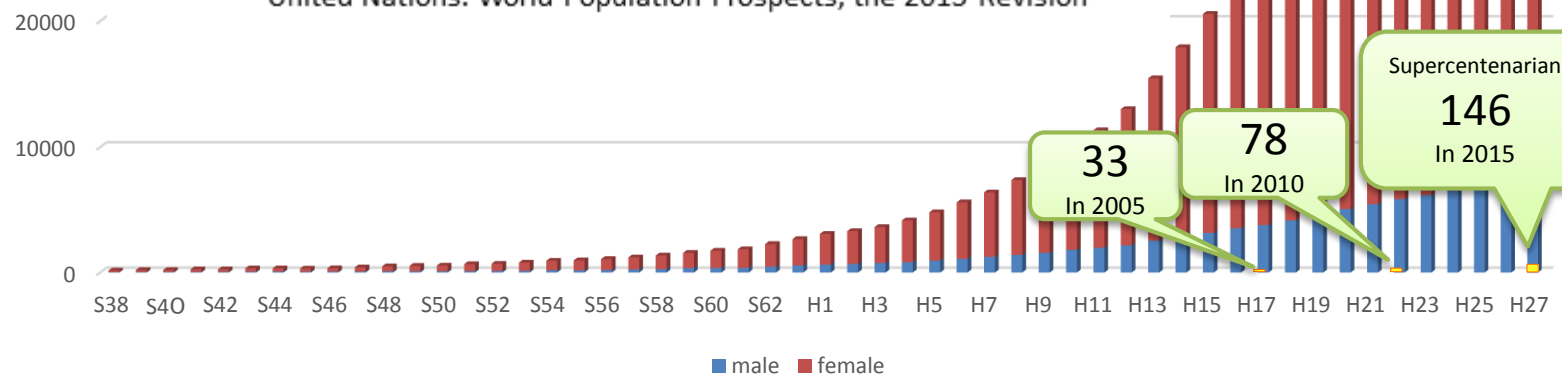
Number of Centenarians in Japan from 1963 to 2015

The Number of Centenarians in Selected Countries in 2015



61,763 in 2015

United Nations. World Population Prospects, the 2015 Revision



Number & ratio of SSC and SC in Japan in 2015

Increase from 2010

-0.8%

129%

153%

187%

Total Population
127,000,000

Centenarian
61,763

Semi-SC
3,916

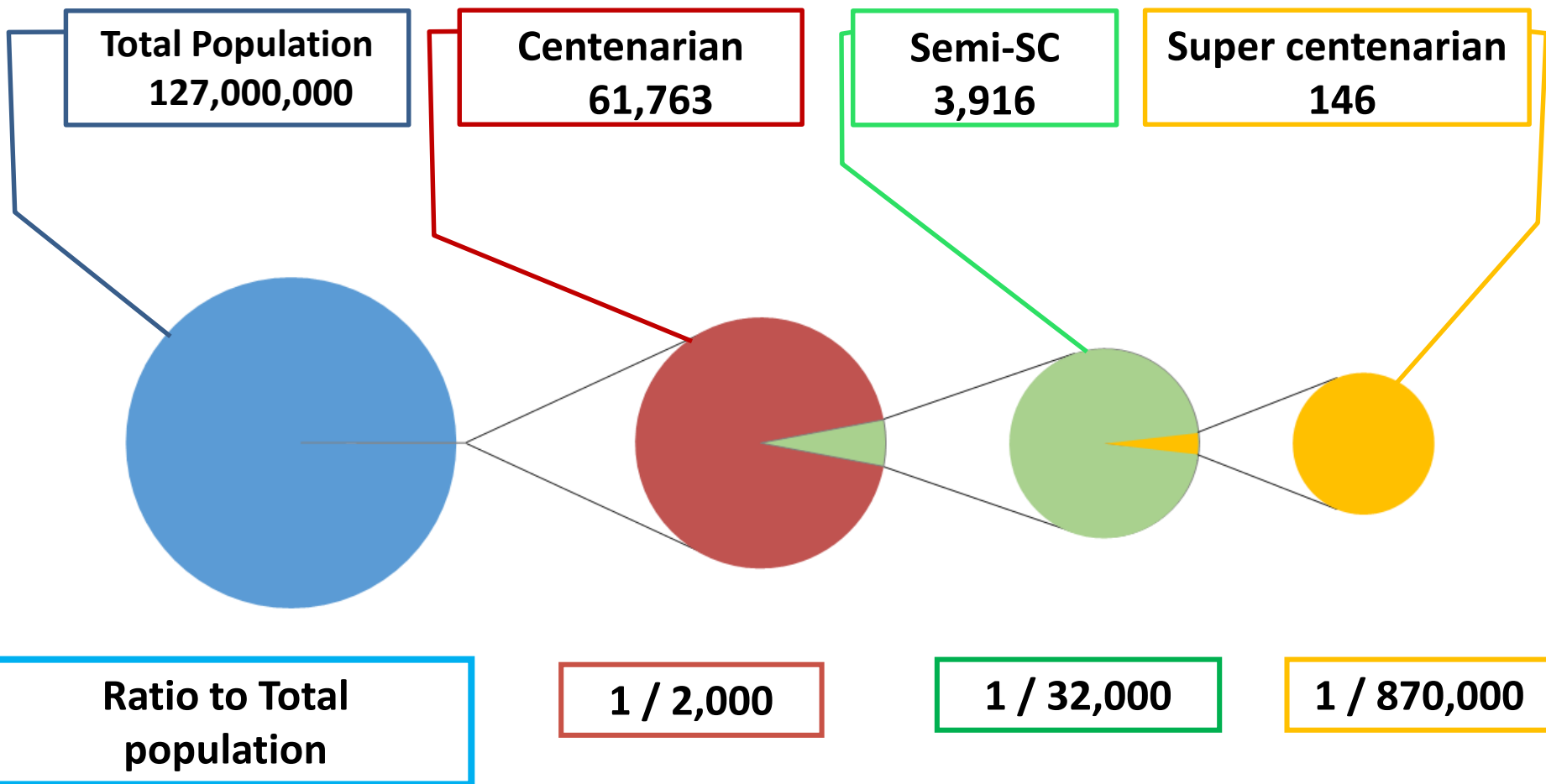
Super centenarian
146

**Ratio to Total
population**

1 / 2,000

1 / 32,000

1 / 870,000

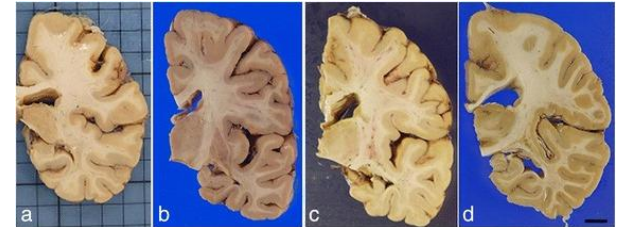


Nation-wide recruitment of Japanese Semi-supercentenarian Study



Successful Brain Aging in Supercentenarians

~ Four Brain Autopsy Cases ~



	Case 1 (111 yo)	Case 2 (111 yo)	Case 3 (114 yo)	Case 4 (110 yo)
Past medical history	HT-, DM-	HT-, DM-	HT-, DM-	HT+, DM-
Apo E	2/3	2/3	3/3	3/3
CDR	0.5	NA	0	NA
Brain weight (fresh)	460 (left hemisphere)	925	1,015	1,115
Atrophy	F, T	F, T	F, T	T
AD pathological changes (NIA-Reagan)	Intermediate	Intermediate	Unclassified	Intermediate
AD pathological changes (NIA-AA)	Intermediate	Intermediate	Low PART possible	Intermediate
Lewy body pathology	None	None	None	None
Vascular injury	Multiple cortical infarcts	None	None	None
Arteriolosclerosis	Mild to moderate	Mild to moderate	Mild to moderate	Mild to moderate

Possible Implications of Supercentenarian Study

<Supercentenarian Study>

Deep Phenotyping
Biomedical and Psychosocial
aspects

Demography

Multi-omics



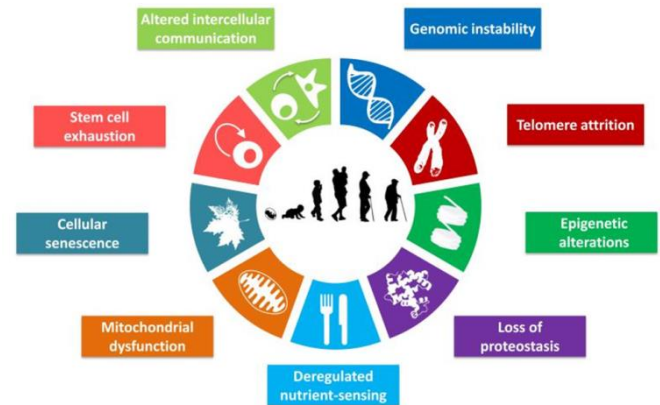
Genome
Sequencing

iPS
technology

Autopsy
Healthy tissue



<Basic Aging Science>



Identification of
“Biological pathways &
Molecular markers”
for healthy Longevity



- Validation in the general elderly population
- Screening for high risk population
- Health Promotion Program
- Active participation & contribution

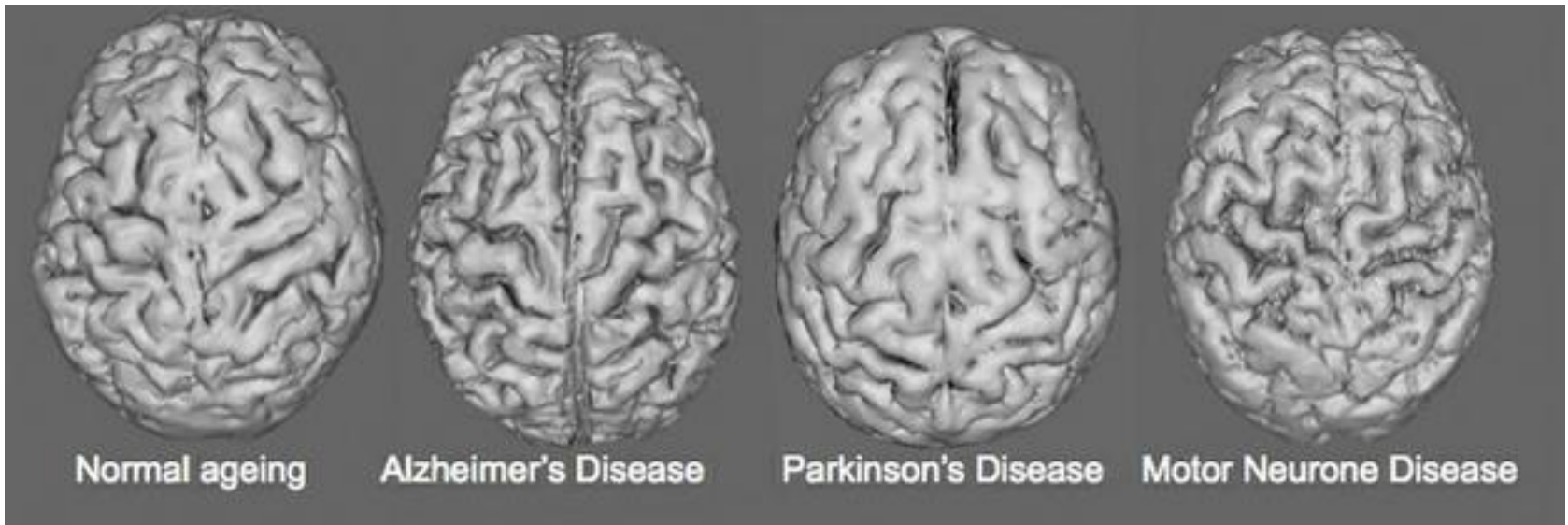


Comprehensive Approach to healthy Aging Society

<Kawasaki-Tomomachi Wellbeing Project>



3. Neurodegenerative Disease Model Marmoset

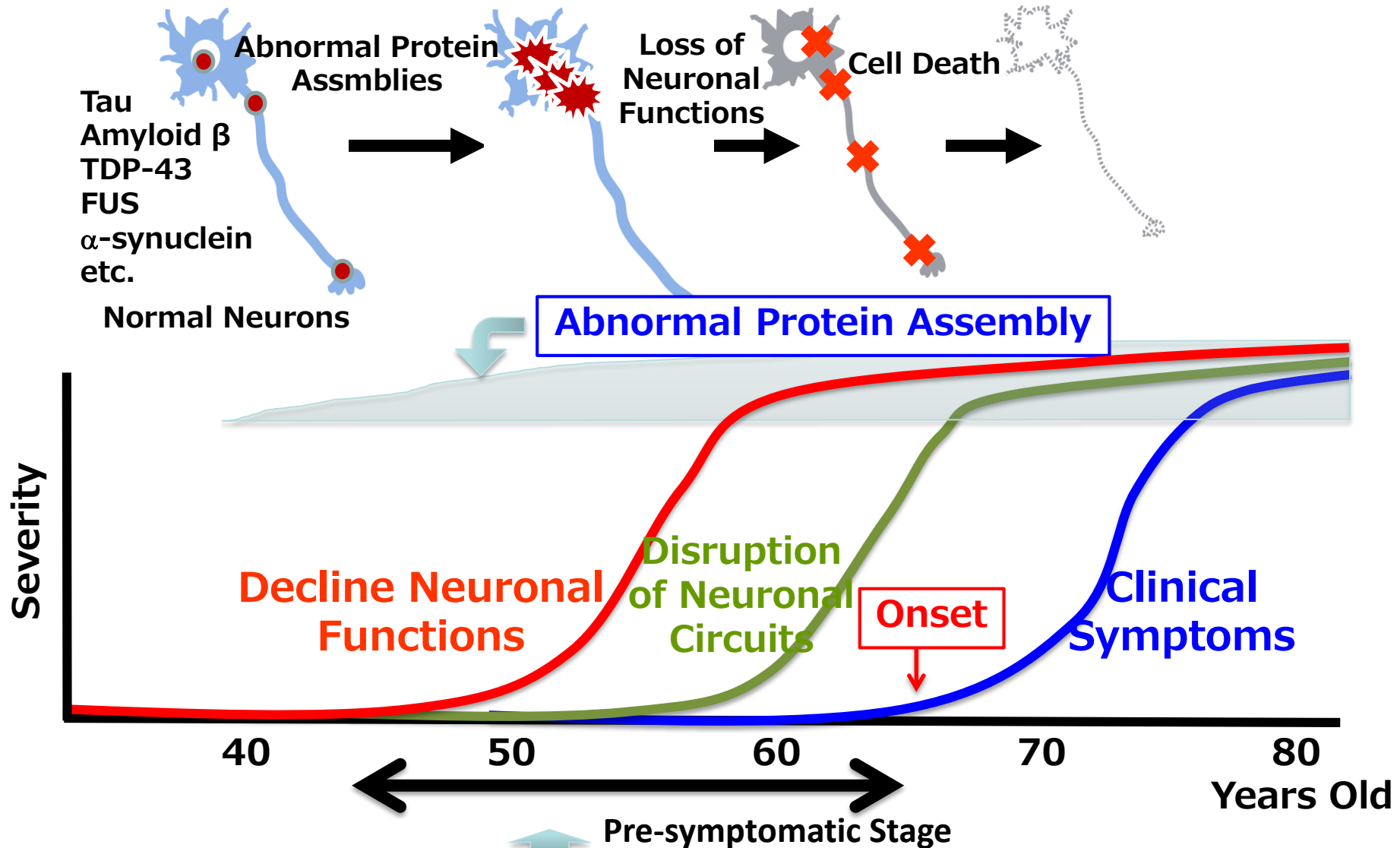


Hideyuki Okano,

Department of Physiology

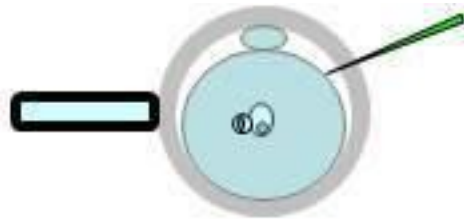
Keio University School of Medicine

Abnormal Protein Assembly is a Common Mechanism for Triggering Neurodegeneration including Alzheimer D, Parkinson D, ALS and etc.

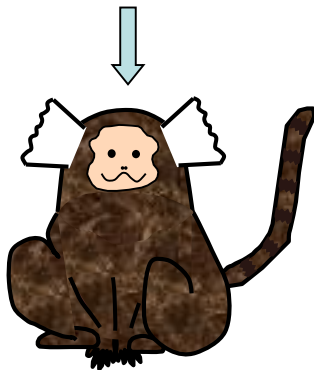


Preemptive Approach: Early Therapeutic Interventions to prevent Disease Progression

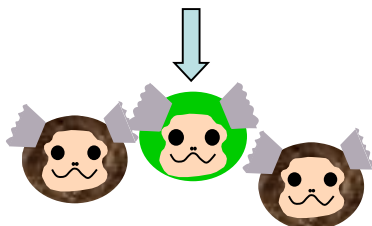
Generation of Genetically Modified Marmoset



Lentiviral vector injection



Embryo transfer to surrogate mother



Transgenic marmoset



Lentivirus: Sasaki et al., *Nature*, 2009

Genome Editing: Sato et al. *Cell Stem Cell*, 2016

Patented in USA, Europe, China, Korea, Singapore, Australia and Japan



Motor symptoms in patients with PD



Symptoms of Parkinson's Disease in human

extremely early stage

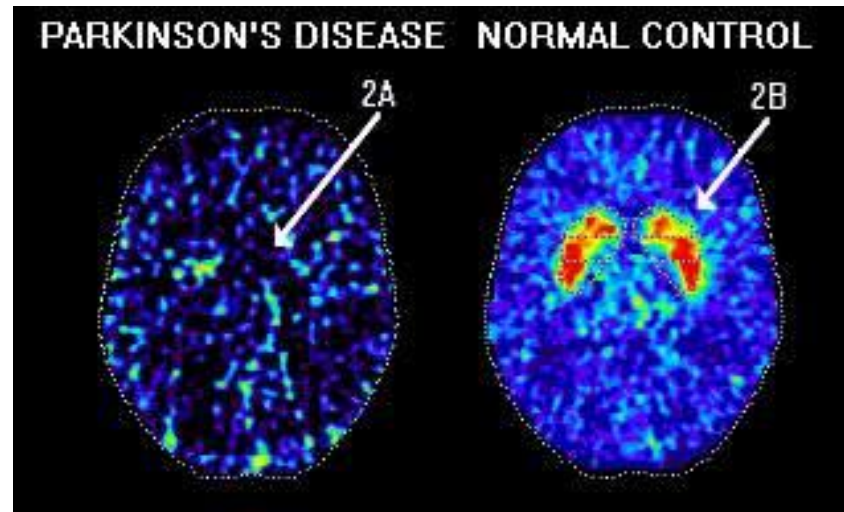
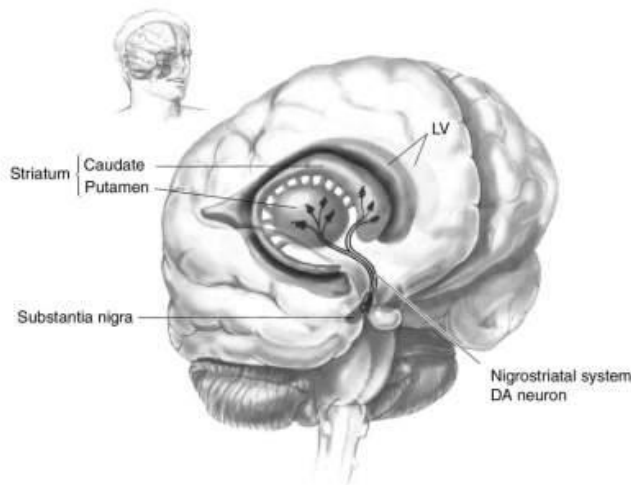
- sleep disorder
- olfactory disturbance

early stage

- tremor
- akinesia
- muscle rigidity
- gait disturbance

advanced stage

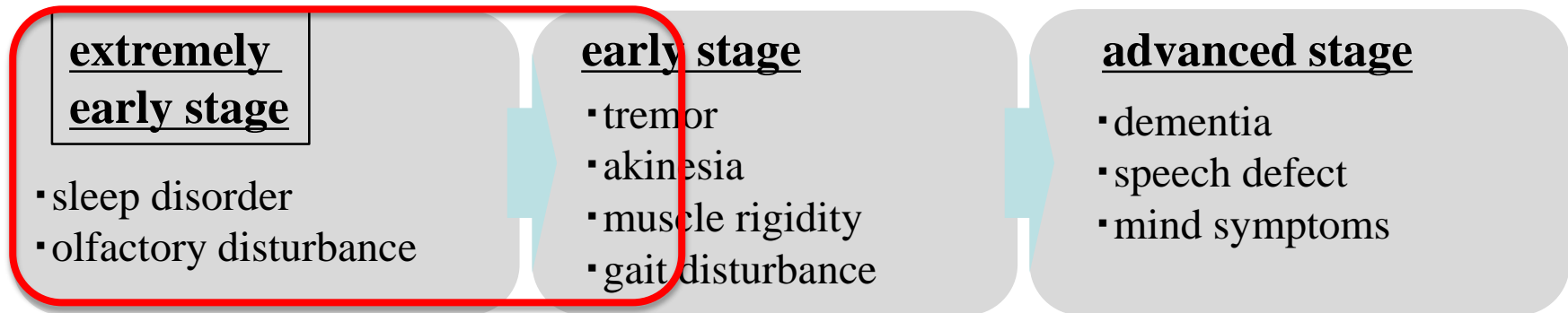
- dementia
- speech defect
- mind symptoms



It is said that motor symptoms of PD appear when more than 80% of DA neurons at Substantia Nigra are lost by the disease.



Symptoms of Parkinson's Disease in human



Future issues to be addressed using PD model transgenic marmoset

- What are the neuronal circuits damaged at the each clinical stage?
- Any relationship between the Pathogenic protein accumulation and each clinical symptom?
- Prediction of the Onset of each clinical symptom
- Development of the drugs to slow-down the Disease Progression as a Preemptive Approach

Development Plan 2020



Haneda International Airport

Tama River

Kanagawa
Life Innovation Center
(Regenerative medicine)

J&J Tokyo Science Center

Innovation Center of
Nano Medicine
(iCONM)

Central Institute for
Experimental Animals
(CIEA)



KeioTonomachi campus
(planned 2017)