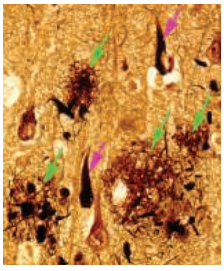

Takeshi Iwatsubo

Preventative Medicine: Predicting Alzheimer's Disease

Japan—like many other industrial nations—is dealing with a rapidly aging population. In particular, the limitations of present-day medical care and social support infrastructure make coping with increases in Alzheimer's disease (AD) a challenge. **Takeshi Iwatsubo** in the Department of Neuropathology is the principle investigator of the Japanese Alzheimer's Disease Neuroimaging Initiative (J-ADNI). "J-ADNI was launched in 2007 to establish a complete set of biomarkers to predict the onset of AD, in particular the progression from mild cognitive impairment to AD," explains Iwatsubo. "The goal is to develop disease-modifying drug treatments."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Researchers at Todai have contributed to understanding the causes of Alzheimer's disease through the discovery of amyloid ß42 in senile plaques (green arrows) and tau protein in neurofibrillary tangles (pink arrows).

As of 2012, J-ADNI had tested approximately 600 subjects at 38 clinical sites throughout Japan and has collected a plethora of MRI, brain activity, pathology, and biomarker data. These results will be analyzed for patterns indicative of disease progress and also used to track patient response to treatment.

Researchers at J-ADNI are collaborating with 11 major drug manufacturers to identify and test promising therapies, including Japan's Takeda Pharmaceutical Company Limited, from which Todai obtained the license for TAK-070—a β-secretase inhibitor—for phase 1 clinical trials scheduled to start in March 2013. "There are at least two million AD patients in Japan alone," says Iwatsubo. "We expect preemptive medical diagnosis in preclinical AD to improve the quality of life for millions of people worldwide."




Clockwise from left: Hidenori Ichijo, Takayoshi Okabe, Hirotatsu Kojima

The Open Innovation Center for Drug Discovery

Hidenori Ichijo is director of the Open Innovation Center for Drug Discovery (OCDD) and with his colleagues, Takayoshi Okabe and Hirotatsu Kojima, manages the OCDD, a central facility for drug screening in Japan. In contrast to other institutions providing complete screening services, the OCDD offers facilities and training but requires researchers to conduct screening themselves, giving them more control over their own research.

"We store a huge range of chemical compounds—approximately 210,750 as of 2012—that are available for screening to identify new drugs, including so-called orphan drugs for treating rare diseases," explains Ichijo. In addition to shipping samples to researchers around Japan, the OCDD also provides advice and the use of its facilities. "Through the end of 2012, we have accepted 646 applications for use of the OCDD library, provided 3.6 million samples, and held 629 advisory meetings," says Okabe.

A recent research highlight is an important finding by Ichijo concerning amyotrophic lateral sclerosis (ALS)—a rare motor neuron disease. Ichijo and colleagues used the OCDD library to tease out some of the biochemical pathways in ALS. "This was the first study focusing on the general relationship between superoxide dismutase-1 [SOD1] mutants and the onset of ALS," says Ichijo.

Looking Ahead and Abroad

"Education and research are evolving at Todai," states executive vice president Shimizu. "President Junichi Hamada has stated the need to 'change the whole education system'," he continues. "So we will start our academic year in September to synchronize with overseas universities." This shift symbolizes the emphasis that Todai places on internationalization, taking an outward-looking stance as the University meets, in Shimizu's words, "the daunting challenges facing the next generation." Shimizu also strongly believes "that student and faculty diversity and mobility are vital for the university to nurture students able to take on those challenges."

Basic Research Seeds for Translational Medical Research

Kohei Miyazono

Department of Molecular Pathology

Research into the autocrine signaling of the cytokine transforming growth factor beta (TGF-β) has led to the discovery that it can regulate the ability of so called glioma-initiating cells to produce tumors in the brain. Importantly, Miyazono and colleagues found that TGF-β receptor inhibitors could act as effective antitumor agents.

Yasuteru Urano

Department of Chemical Biology and Molecular Imaging

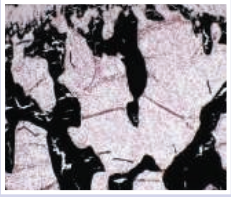
Urano has developed a method for rapid in vivo cancer detection using a novel γ-glutamyltranspeptidase-activated fluorescent probe. The probe 'switches on' when taken up by tumor cells. His research was featured on the 23 November 2011 cover of *Science Translational Medicine*.

Hiroshi Takayanagi

Department of Immunology

Takayanagi and colleagues initiated osteoimmunological studies into the molecular mechanisms of bone destruction in arthritis. They found that an antibody against the proangiogenic semaphorin 4-D molecule promoted bone formation, but did not impact resorption. Related patents have been licensed to a U.S. company that plans to perform clinical trials on its use for the treatment of arthritis, osteoporosis, and cancer.


Hiroshi Takayanagi


Augmented bone formation (black) in a Sema4d$^{-/-}$ mutant (below) in contrast to a wild type mouse (above).

ADDITIONAL RESOURCES

22nd Century Medical and Research Center
www.h.u-tokyo.ac.jp/english/center22/index.html

Center for Disease Biology and Integrative Medicine (CDBIM)
www.cdbim.m.u-tokyo.ac.jp/english/center.php

Cooperative Unit for Medicine and Engineering Research
www.ikourenk.umin.jp

Graduate Program for Leaders in Life Innovation (GPLLI)
square.umin.ac.jp/gplli/

Japanese Alzheimer's Disease Neuroimaging Initiative
www.j-adni.org/etop.html

Open Innovation Center for Drug Discovery
www.ocdd.u-tokyo.ac.jp/index_e.html

Translational Research Initiative
tri.u-tokyo.ac.jp/en/

University of Tokyo Hospital
www.h.u-tokyo.ac.jp/english/

University of Tokyo Hospital Clinical Research Support Center (UT-CresCent)
www.cresc.h.u-tokyo.ac.jp/en/index.html

Todai Research
www.u-tokyo.ac.jp/en/todai-research/

University of Tokyo
www.u-tokyo.ac.jp/en/