Research Center for Advanced Science and Technology, The University of Tokyo
Fujitsu Limited
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University of Tokyo's RCAST, Fujitsu, and Kowa Successfully Generate a Novel Active Compound Targeting Cancer Using IT-based Drug Discovery Technology

Tokyo and Nagoya, Japan, August 7, 2014 - The University of Tokyo's Research Center for Advanced Science and Technology (RCAST), Fujitsu Limited, and Kowa Company, Ltd. today announced that they have used IT-based drug discovery technology to successfully generate a novel pharmacologically active compound with the potential to be developed into a candidate for an anticancer drug. The compound, generated using computer-based virtual design and evaluation, inhibits the activity of cancer-causing protein (target protein).

In addition to the IT-based drug discovery of this new active compound, the research collaboration yielded multiple low-molecular-weight compounds that provide important information in advancing drug discovery research. The three parties have decided to pursue the optimization of the low-molecular-weight compounds generated by their research with the aim of moving forward to preclinical evaluation (*1) of the compounds.

Background and Division of Responsibility
RCAST and Fujitsu began their IT-based drug discovery research collaboration in June of 2011, and Kowa joined the collaboration in July of the same year.

Based on RCAST's research on proteins thought to cause specific diseases, the research collaboration moved forward on two methods of drug discovery research targeting cancer indications. One method is IT-based drug discovery, while the other combines conventional low-molecular-weight drug discovery technologies with computer-based compound screening. In the IT-based drug discovery effort, Fujitsu's main role was to design low-molecular-weight drug candidates, while Kowa primarily synthesized compounds and ran assays to estimate inhibitory activity.

In addition, during this collaboration Fujitsu worked with Fujitsu Laboratories to make iterative enhancements to their IT-based drug discovery technology to improve its precision and performance.

Research Results to Date
With conventional low-molecular-weight drug discovery technology, researchers look for compounds that exhibit a certain threshold of inhibitory activity (*2). They do this by screening a reagent company-supplied commercial library of existing low-molecular-weight compounds against a target protein. Development of the compounds identified by the screening to drug candidate compounds requires manipulation into a novel structure, but the problem has been that the method does not necessarily provide compounds suitable for the manipulation..

The current research collaboration, however, used drug candidate compound design technology (*3). This technology leveraged a computer to design a variety of compound structures that would bind to the target protein. Those were then filtered using high-precision activity prediction technology (*4) to predict their inhibitory activity. Afterwards, they were synthesized and their inhibitory activity was measured through assays. This method yields novel chemical structures that are not easily generated using conventional drug discovery techniques involving manipulation of known compounds. The aim was to generate, with a high degree of probability, drug candidate compounds with potent inhibitory activity.

The collaborative efforts produced a variety of computer-designed chemical structures, of which 22 were selected on the presumption that their interaction with the target protein would lead to the formation of a stable complex structure with the target protein. Eight of those compounds were then synthesized and

their inhibitory activity was measured in assays. Of these, one low-molecular-weight compound showed inhibitory activity that met the target threshold, representing the successful generation of a new active compound. Accordingly, the rate of one in eight compounds, or 12.5%, is a much higher ratio than conventional low-molecular-weight drug discovery technologies yield.

In addition to the IT-based drug discovery of a novel active compound, the research collaboration of RCAST, Fujitsu, and Kowa identified multiple low-molecular-weight compounds that provide important information in advancing drug discovery research.

Next Stage in the Research Collaboration
RCAST, Fujitsu, and Kowa will continue their current research collaboration and plan to optimize the generated compounds quickly to initiate preclinical evaluation.

Overview of the Research Collaboration
1. Timeframe:
April 2014 to March 2015

2. Structure:
RCAST: Laboratory for Systems Biology and Medicine
Fujitsu: Bio-IT Business Development Unit, R&D Division, Center for the Future of Medical Care
Kowa: Tokyo New Drug Research Laboratories of the Pharmaceutical Business Division

3. Location:
RCAST, Fujitsu's office within RCAST, and Kowa Company, Ltd.'s Tokyo New Drug Research Laboratories

4. Respective Responsibilities
RCAST: Provision of information on proteins thought to cause specific disease indications
Fujitsu: Design and evaluation of small molecule compounds using IT-based drug discovery technology
Kowa: Synthesis of small molecule compounds and measurements of their inhibitory activity with assays, and screening of small molecule compounds using a computer

Glossary and Notes
1. Preclinical evaluation
A phase of drug development in which studies are conducted prior to clinical testing in human subjects. These studies test safety and efficacy in animals.

2. Inhibitory activity
The degree to which a compound binds to a protein thought to cause a specific disease indication and inhibits the function of the protein. Usually expressed in terms of the concentration of the compound.

3. Drug candidate compound design technology
Optimum Packing of Molecular Fragments (OPMF), a software module developed by Fujitsu that designs small molecule compounds that bind to the functional site of proteins that are believed to cause specific disease indications and inhibit the activity of the proteins.

4. High-precision activity prediction technology
Software developed by Fujitsu Laboratories comprised of MAPLE CAFEE, a module that, based on molecular dynamics calculations, predicts the inhibitory activity of drug candidate compounds with a high level of precision that is equivalent to that of biochemical assays, and Force Field Formulator for Organic Molecules (FF-FOM), a module that generates highly detailed parameters for the force fields between atoms.

Related Links
"University of Tokyo's RCAST and Fujitsu Collaborate in Race to Develop New IT-based Drug Discovery Technology" (press release dated June 10, 2011):
http://www.fujitsu.com/global/about/resources/news/press-releases/2011/0610-01.html

About Fujitsu
Fujitsu is the leading Japanese information and communication technology (ICT) company offering a full range of technology products, solutions and services. Approximately 162,000 Fujitsu people support customers in more than 100 countries. We use our experience and the power of ICT to shape the future of society with our customers. Fujitsu Limited (TSE: 6702) reported consolidated revenues of 4.8 trillion yen (US$46 billion) for the fiscal year ended March 31, 2014. For more information, please see http://www.fujitsu.com.

About Kowa
Kowa is a privately held multinational company headquartered in Nagoya, Japan. Established in 1894, Kowa is actively engaged in various manufacturing and trading activities in the fields of pharmaceuticals, life science, information technology, textiles, machinery and various consumer products. Kowa's pharmaceutical division is focused on research and development for cardiovascular therapeutics (dyslipidemia, type 2 diabetes, and atherosclerosis), ophthalmology and anti-inflammatory agents. Global sales of the company's flagship product, pitavastatin (known as LIVALO and LIVAZO in different markets) was over 80 billion yen (US$800 million) in 2013
For more information, please see http://www.kowa.co.jp/eng/