



High Energy Accelerator Research Organization (KEK)

Astellas Pharma Inc.

KEK and Astellas begin collaborative research to discover new drugs for neglected tropical diseases

- Design of pharmaceuticals based on the three-dimensional structure of proteins using synchrotron^{※1} X-ray crystallography-

Tokyo, Japan, September 20, 2012 –The High Energy Accelerator Research Organization (KEK) and Astellas Pharma Inc. (Tokyo:4503,“Astellas”) have today concluded an agreement to begin collaborative research to discover new drugs for the treatment of neglected tropical diseases^{※2} (“NTDs”) through the use of synchrotron X-ray crystallography.

Background Information

NTDs, prevalent mainly in poor remote rural areas, are infectious diseases spread by parasites or bacteria. Approximately one billion people are affected worldwide and some 500,000 die each year as a result. NTDs are a serious healthcare issue that is being addressed on a global scale.

A valuable approach to new drug development that has evolved rapidly in recent years is the design of pharmaceuticals based on the three-dimensional structure of proteins. This method involves designing drugs for the target protein by analyzing and comparing the structure of various compounds and complex conjugates in order to develop an overall understanding of the mechanism by which protein activity is inhibited (or activated). Since 2006, KEK and Astellas have been progressing drug discovery research using synchrotron X-ray beams. The synchrotron radiation beam produced in the Photon Factory in KEK has high-brilliant and high-energy properties conferring advantages such as the ability to conduct experiments on small crystals that would have been difficult to analyze using conventional X-rays and to acquire data in an extremely short period that would otherwise take vast amounts of time.

Nature of the Research

The target of this research is infectious diseases caused by parasitic protozoans, namely leishmaniasis^{※3}, Chagas disease^{※4} and Sleeping sickness^{※5}, and will be divided into two major phases. The first phase involves elucidating the three-dimensional structure of parasitic protozoan proteins that are potential drug targets, allowing the identification of inhibiting compounds that block the action of pathogenic proteins. The second phase consists of the

structural analysis of target proteins in complex with the inhibitory compound. Crystallization robots and dedicated beamlines^{※6} developed by KEK will be employed with structural analysis performed efficiently and over a short time period.

Structural data obtained through the successful application of this collaborative research will contribute to the discovery of new drugs for the treatment of parasitic protozoan diseases.

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Note on Technical Terminology

※1 Synchrotron

Synchrotron is an accelerator facility to radiate a high-brilliant light with a wide range of energies (wavelengths). Ultra-violet light, soft X-rays and X-rays are used to investigate the configuration of the atoms and the behavior of its electrons in materials. These special properties of synchrotron radiation are widely used in research in both the materials and life sciences.

※2 Neglected Tropical Diseases (NTDs)

NTDs are tropical infections caused by parasitic worms and bacteria, which are mainly endemic in tropical areas of developing countries. It is estimated that over 1 billion people are affected worldwide with the 17 diseases* of NTDs on which currently WHO is focusing on. Since these patients do not have enough access to medicine and healthcare, NTDs are not only a global health challenge but are said to affect economic growth and poverty in developing countries.

* Group of 17 diseases : Buruli Ulcer, Chagas disease (American trypanosomiasis), Cysticercosis, Dengue/Severe dengue, Dracunculiasis (guinea-worm disease), Echinococcosis, Foodborne trematode infections, Human African trypanosomiasis, Leishmaniasis, Leprosy, Lymphatic filariasis, Onchocerciasis, Rabies, Schistosomiasis, Soil transmitted helminthiasis, Trachoma, Endemic treponematoses (including yaws)

※3 Leishmaniasis

Leishmaniasis occurs in 98 countries, and 350 million people are exposed to risk worldwide. The parasite that leads to this infection is called *Leishmania* and is transmitted by a sandfly. Leishmaniasis is a poverty-associated disease with several different forms. Visceral leishmaniasis, which is fatal without treatment, and cutaneous leishmaniasis are the most common.

※4 Chagas disease (American trypanosomiasis)

Chagas disease is endemic in 21 countries across Latin America and kills more people in the region than any other parasite-borne disease, including malaria. In total, 100 million people are at risk worldwide and patient numbers are growing in non-endemic countries such as the United States and Australia, as well as some European countries. The disease is transmitted by an insect known as the 'kissing bug' and, without treatment, is potentially fatal.

※5 Sleeping sickness (human African trypanosomiasis, or HAT)

Sleeping sickness threatens millions of people in sub-Saharan Africa. The disease is transmitted by the bite of the tsetse fly. Without treatment in the initial phase, which causes general symptoms, the disease progresses to a second stage where mental debilitation occurs, and the patient often dies within six months to three years. Existing treatments are toxic, difficult to administer, and/or have severe side effects. The disease is fatal if left untreated.

※6 Beamline

Beamline is a full set of equipment that extracts synchrotron radiation and directs it to each piece of experimental apparatus. Equipment placed in the beamline includes a slit for modulating light, a mirror to condense light and a monochromator to extract specific wavelengths (energies).

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