Astellas and Johns Hopkins University researchers identify a novel action of quetiapine in the regulation of cell-cycle related p21/Cdkn1a gene expression in CD-1 mice

～Data Reported in U.S. Scientific Journal, Translational Psychiatry～

TOKYO, April 10, 2013 - Astellas Pharma Inc. ("Astellas"; Tokyo:4503) announced today that its collaborative research project with Johns HopkinsUniversity School of Medicine ("JHU"; Baltimore) identified a novel action of quetiapine in the regulation of a cell-cycle related gene in CD-1 mice. The study results were published in Translational Psychiatry, a Nature Publishing Group journal focusing on the translational science in psychiatry between basic research and clinical.

The research team found that the chronic treatment with quetiapine, which was designed by the clinically-relevant pharmacodynamics examination of antipsychotics, uniquely down-regulated the cell-cycle related p21/Cdkn1a gene expression in the mouse frontal cortex when compared to the treatment with a typical antipsychotic haloperidol. The reduction of gene expression was observed in post-mitotic neurons and oligodendrocytes in the quetiapine treated-mice.

It is commonly accepted that the pharmacological actions of typical antipsychotics are mainly based on the blockade of dopamine D2 receptor in the striatum and could affect the positive symptoms of schizophrenia. Newly introduced atypical antipsychotics are acknowledged for additional clinical benefits. The clinical use of quetiapine in bipolar depression and major depression in addition to schizophrenia has been approved by the many countries. Although it is postulated that the modulation of neurotransmitter receptors including dopamine D2, serotonin 5HT2A, and adrenergic alpha 1 contributes to the clinical benefits of quetiapine, its affect on brain regions and intracellular functional pathways are not fully understood. The present study demonstrated that, in CD-1 mice, quetiapine regulates intracellular gene expression in both post-mitotic neurons and oligodendrocytes. In human, the aberrant regulation of cell-cycle is supported by the fact of genetic, pathological, and gene expression analyses of post-mortem brains of patients and the white matter abnormality attributable to oligodendrocyte dysfunction have been suggested as common pathophysiologies across schizophrenia, bipolar disorder, and major depressive disorder., the present discovery of a potential novel action of quetiapine in frontal cortex may shed additional light on its mode-of-action.

Astellas expects to identify new drug targets and conduct translational science research to create innovative pharmaceuticals in the field of neuroscience by building on the research reported in this paper.

<Reference>
The title and authors of the article reported in Translational Psychiatry published on April 2, 2013 (local time) are as follows:

Title： Unique pharmacological actions of atypical neuroleptic quetiapine: possible role in cell cycle/fate control

Authors： Mari A. Kondo, Katsunori Tajinda, Carlo Colantuoni, Hideki Hiyama, Saurav Seshadri, Beverly Huang, Samantha Pou, Keiko Furukori, Caroline Hookway, Hanna Jaaro-Peled, Shin-ichi Kano, Nobuya Matsuoka, Katsuya Harada, Keni Ni, Jonathan Pevsner, and Akira Sawa

About Astellas Pharma Inc.

Astellas Pharma Inc. was created from the merger of Yamanouchi Pharmaceutical Co., Ltd. and Fujisawa Pharmaceutical Co., Ltd. in April 2005 and is a global pharmaceutical company with ethical pharmaceuticals as its core business. Astellas has already established its position as the world's leading company in the fields of urology and transplantation. Moving forward, Astellas has identified urology, immunology (including transplantation) and infectious diseases, oncology, neuroscience, and DM complication and kidney diseases as five focused areas of research for the company, and is promoting research to develop revolutionary new drugs that are needed for the treatment of diseases in these five areas. In order to continually create promising discovery projects and enrich the research pipeline, close collaborative research will be aggressively pursued with leading edge research institutions in addition to promotion of Astellas research.

About schizophrenia

Schizophrenia affects up to 1% of population world-wide. Patients start to have multifaceted symptoms in their early adolescent including positive and negative symptoms, and cognitive dysfunction. Currently, the positive domain is the primary target by dopamine D2 receptor blockade. The treatment opportunity for unmet medical needs has been waited

About quetiapine

Quetiapine is an atypical antipsychotic medication initially indicated for the treatment of schizophrenia and is commonly commercialized under the brand names of SEROQUEL and SEROQUEL XR worldwide.

Launched in 1997, SEROQUEL has been approved in 104 countries for schizophrenia, 100 countries for bipolar mania, in 74 countries for bipolar depression and in 51 countries for bipolar maintenance SEROQUEL is commercialized by Astellas in Japan for the treatment of schizophrenia.

SEROQUEL XR, an extended release version of SEROQUEL, has been approved in 85 countries for schizophrenia, 81 countries for bipolar mania, in 72 countries for bipolar depression, in 61 markets for bipolar maintenance, in 10 markets for Generalised Anxiety Disorder (GAD), and in 65 markets for Major Depressive Disorder (MDD).

For inquiries or additional information
Astellas Pharma Inc. Corporate Communications TEL: +81-3-3244-3201, FAX:+81-3-5201-7473 http://www.astellas.com/en