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TAAR1 ligands as prospective neuroleptics: From D-neuron study

Keiko Ikemoto
Iwaki Kyoritsu General Hospital, Japan

Recent pharmacological studies have shown the importance of trace amine-associated receptor, type 1(TAAR1), a subtype of trace amine receptors, as a prospective target receptor for novel neuroleptics. Endogenous ligand producing neuron of TAAR1 is the D-neuron, i.e., trace amine neuron, defined as "the aromatic L-amino acid decarboxylase neuron, neither contains dopamine (DA) nor serotonin". We found significant decrease of D-neurons (trace amine neurons) in the nucleus accumbens (Acc) of autopsy brains of patients with schizophrenia. Animal model studies have shown that reduced stimulation of TAAR1 on DA neurons in the midbrain ventral tegmental area (VTA) increased firing frequency of VTA DA neurons. Thus, D-neuron reduction and consequent trace amine decrease, causing TAAR1 stimulation reduction on terminals of midbrain VTA DA neurons has been shown as the molecular basis of mesolimbic DA hyperactivity of schizophrenia. D-neuron decrease in Acc of postmortem brains is supposed be due to neural stem cell (NSC) dysfunction in the subventricular zone of lateral ventricle (cf. NSC dysfunction hypothesis of schizophrenia).The new "trace amine hypothesis" ("D-cell hypothesis"), of schizophrenia in which D-neuron and TAAR1 is involved, is in agreement with recent reports showing effectiveness of TAAR1 ligands for schizophrenia model animals. This hypothesis links DA hypothesis of schizophrenia with NSC dysfunction hypothesis. D-neuron reduction in the Acc, an anatomical area known for an antipsychotic acting site, would let us assume TAAR1 ligand searching study being pivotal in novel neuroleptics discovery.

Biography

Keiko Ikemoto, MD, PhD, graduated Shiga University of Medical Science in 1985, specialized in Psychiatry and Neuroscience. She studied monoamine neuronal system and sleep as Boursiere du Gouvernement Francais in the Department of Experimental Medicine, Claude Bernard University (1995-1996). She continued research in Department of Anatomy, Fujita Health University, Hanamaki National Hospital, Fukushima Medical University, School of Medicine, Shiga University of Medical Science, and Iwaki Kyoritsu General Hospital, in Japan. She organized the 1st Symposium for Brain Bank, in Fukushima in 2006. Now she chairs the Department of Psychiatry, Iwaki Kyoritsu General Hospital, Japan.

ikemoto@iwaki-kyoritsu.iwaki.fukushima.jp