

The “A New Dawn for the Treatment of Schizophrenia” project won the 2022 Future Tech Award.

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The prevalence of schizophrenia approaches 1 percent worldwide and the incidence is about 1.5 per 10,000 people. It is very costly for families and society. However, currently existing antipsychotics mainly target dopamine D2 receptors and more or less result in many unwanted adverse effects. Our team developed J4, a novel adenosine analogue. J4 simultaneously modulates equilibrative nucleoside transporter 1 (ENT1) and A2A adenosine receptors (A2AR). Oral or intraperitoneal administration of J4 increases synaptic adenosine concentration and activates A2ARs in the brain. Our preclinical data revealed that J4 can suppress hyperdopaminergic activity and alleviate methamphetamine-induced psychosis in mice. Our results open a new avenue for the development of a first-in-class non-dopamine antipsychotic drug for the treatment of schizophrenia without dopamine-related bothersome side effects.