Medical Xpress

Cancer drugs may help treatment of schizophrenia

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Researchers have revealed the molecular pathway that is affected during the onset of schizophrenia and successfully alleviated symptoms of the illness in mice, using a commonly used cancer drug.

The research, published online in the journal *Brain*, is from a group led by Professor Peter Giese at King's College London, and offers new avenues for drug discovery.

Schizophrenia is one of the most common serious mental health conditions in the UK, and affects about 24 million people worldwide. The illness is a long-term mental health condition that causes a number of psychological symptoms, including hallucinations and delusions as well as behaviour changes. The exact cause of the illness is unknown, although it is generally believed to be a combination of genetic and environmental factors.

According to the World Health Organization, 90% of people with untreated schizophrenia are in developing countries. Current treatments for schizophrenia include both psychological treatments such as psychotherapy, counselling or cognitive behaviour therapy and/or medication. However, many of the antipsychotic drugs or major tranquillisers used to treat or manage the illness have very bad side-effects.

Professor Giese, based at the Institute of Psychiatry at King's, said: 'For the first time we have found that an enzyme activator called p35 is

reduced in patients with schizophrenia and moreover, modelling this reduction in mice led to cognitive impairment typical for this disease. This gives us a better understanding of the changes that occur in the brain during the onset of schizophrenia.'

Proper brain development is ensured, in part, by the activation of a protein in the brain called Cdk5. The activation of Cdk5 requires the presence of an enzyme in the brain, called p35. The research found that in human post-mortem brains, there was approximately 50% less p35 in the brains of patients who had suffered from schizophrenia.

These molecular changes were then modelled and monitored in mice that had been modified to contain a comparable reduction in the p35 enzyme. As a result of this reduction in p35, the mice showed a reduction in synaptic proteins – important in maintaining neural connections – and displayed symptoms associated with schizophrenia, including learning impairments and inability to react to sensory stimuli.

Understanding this signalling pathway and the impact of low levels of p35, is important in finding potential future treatments for the disease.

Professor Giese continues: 'We noted that the reduction in p35 affects the same molecular changes targeted by a cancer drug called MS-275, so we administered this drug to the mice. We were excited to find that MS-275 not only addressed the molecular changes but also alleviated the symptoms associated with schizophrenia.'

He concludes: 'Our findings encourage the future exploration of these types of drugs for treating impaired cognition in schizophrenia.'

More information: Schizophrenia is associated with dysregulation of a Cdk5 activator that regulates synaptic protein expression and cognition, *Brain*, DOI: 1093/brain/awr155

Provided by King's College London