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Affectis Pharmaceuticals AG Identifies Novel Target for the Treatment of Unipolar Disorder

Munich, Germany – Affectis Pharmaceuticals AG, a biopharmaceutical company developing novel drugs against depression and schizophrenia, announced today that it has identified a genetic variation associated with major depressive disorder. [1] As the variation may have consequences for the functioning of a receptor protein in the brain, it constitutes a promising target for the development of novel anti-depressants. In a previous paper published in May this year Affectis already had demonstrated that the variant is strongly associated with bipolar affective disorders. [2] According to WHO figures, in 2002 worldwide 154 million people suffered from unipolar disorder, while about 28 million suffered from bipolar affective disorders.

In the study, the researchers investigated 29 single nucleotide polymorphisms (SNPs) of the P2RX7 gene in a sample of 1000 German Caucasians suffering from recurrent major depressive disorder (MDD) and in 1029 healthy individuals from the same population. SNPs are DNA sequence variations that occur when a single nucleotide (A, T, C, or G) in the genome sequence is altered. The researchers found a significant association (p=0.0019) between MDD and an SNP codenamed rs2230912, which previously also had been found to be associated with bipolar affective disorders in another population.

The P2RX7 gene encodes for the P2X7 receptor, an ion channel that opens up on binding of extracellular ATP. The rs2230912 variation leads to an altered protein sequence in the cytosolic domain of the receptor with potential consequences for its function. The P2X7 receptor is thought to be involved in neuroprotection, the modulation of inflammatory processes, and in neurotransmission in the hippocampus region of the brain.

"The study provides further evidence for our hypothesis that a variation of the P2RX7 gene plays a causal role in the development of depression and bipolar disorders," said Herbert Stadler, CEO of Affectis AG. "And as the product of the gene is a receptor localised in the plasma membrane of cells, it is a promising drug target. We already have identified lead compounds, which we plan to take into preclinical development later this year."

"Our observations about the association of the P2RX7 variation with bipolar disorders and with major depressive disorders are consistent with the possibility that various mood disorders share some genetic origins," said Bertram Müller-Myhsok of Max-Planck-Institute of Psychiatry and lead author of the study. "Our data suggest that the variant in question might be a susceptibility factor for both disorders."

The research was published in this month's Human Molecular Genetics. The study was conducted at Max-Planck-Institute of Psychiatry (Munich, Germany).

1 Lucae S et al. (2006), P2RX7, a Gene Coding for a Purinergic Ligand-Gated Ion Channel, is Associated with Major Depressive Disorder. Human Molecular Genetics Advance Access published on July 5, 2006.

2 Barden N. et al. (2006), Analysis of Single Nucleotide Polymorphisms in Genes in the Chromosome 12Q24.31 Region Points to P2RX7 as a Susceptibility Gene to Bipolar Affective Disorder. Am J Med Genet Part B 141B:374-382.