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HKUST Researchers Unlock Mystery of Schizophrenia

Researchers at the Hong Kong University of Science and Technology (HKUST) have made a major breakthrough in revealing the cause of schizophrenia, discovering a key genetic link that will pave the way for the finding of an effective treatment of the disease.

The HKUST research group led by Dr Hannah Hong Xue, Associate Professor of Biochemistry, has identified the fifth gene associated with schizophrenia in the global race to find the root and treatment of the disease. In the past decade, scientists all over the world have been searching for genes linked to schizophrenia and four were found. The HKUST group searched out the fifth one in the past year.

This is also the first time in the scientific world that a gene strongly associated with a complex disease was first pinpointed in ethnic Chinese, prior to being established in other ethnic groupings. HKUST's findings were published in the latest issue of the prestigious journal *Molecular Psychiatry* of the Nature Publishing Group.

"As long as the causative genes of schizophrenia remain unidentified, medicinal therapies are given on a trial-and-error basis. The discovery of the causative genes will open a completely new way to a more effective approach. And when the mechanisms are fully understood, effective cure and some degree of prevention of schizophrenia will become possible," said Dr Xue, a specialist in the biochemistry of neuroreceptors and the genetics of schizophrenia.

What Dr Xue and her team have uncovered is a haplotype - a pattern of DNA sequence variations between individuals that may be associated with predispositions to specific diseases - of five Single Nucleotide Polymorphisms (SNPs) in a gene that is strongly associated with schizophrenia.

"Our work provides the first direct genetic evidence, at the single DNA base level, that a gene of the $GABA_A$ receptor in the Central Nervous System is likely to be involved in the development of schizophrenia," said Dr Xue.

Schizophrenia affects almost 1% of world population and has a broadly equal prevalence across ethnic groups. The disease manifests itself in a range of ways, including delusions, disordered thought, hallucinations, blunted emotions, paranoid ideation, and motor abnormalities.

Dr Xue obtained her MD from Shanghai and PhD from the University of Toronto. After two years of post-doctoral work in Glasgow, she joined HKUST in 1995.

She is also one of the HKUST scientists taking part in the international project to construct the haplotype map (HapMap), which represents the next generation of the human genome blueprint. The project aims to define the detailed genetic differences among individuals, thereby allowing the mapping of genes that predispose humans to such common diseases as diabetes, cancers and mental disorders. HKUST scientists and other Hong Kong experts will team up with their counterparts from Beijing and Shanghai in constructing the part of the HapMap that centers on human chromosomes No. 3, 8 and 21.

SNP and Haplotypes

- The DNA sequences of any two individuals are 99.9% identical. The 0.1% variations, however, may greatly affect an individual's risk of contracting diseases.
- Sites in the DNA sequence where individuals differ are called single nucleotide polymorphisms (SNPs).
- Sets of nearby SNPs on the same chromosome may be inherited in blocks.
- This pattern of SNPs on a block is a haplotype.
- Such a block may contain a large number of SNPs.
- A few SNPs are enough to identify the haplotypes in a block.
- The HapMap is a map of these haplotype blocks.

Receptor and GABA

- A receptor is a protein in the cell membrane with which a transmitter substance or drug can interact to produce a biological response.
- GABA (gamma-amino butyric acid) is a major inhibitory neurotransmitter, and interacts with $GABA_A$ receptor in the membrane of brain cells.