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Rethinking the Genetic Theory of Inheritance

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Scientists at the Centre for Addiction and Mental Health (CAMH) have detected evidence that DNA may not be the only carrier of heritable information; a secondary molecular mechanism called epigenetics may also account for some inherited traits and diseases. These findings challenge the fundamental principles of genetics and inheritance, and potentially provide a new insight into the primary causes of human diseases.

Your mother's eyes, your father's height, your predisposition to disease--these are traits inherited from your parents. Traditionally, 'heritability' is estimated by comparing monozygotic (genetically identical) twins to dizygotic (genetically different) twins. A trait or disease is called heritable if monozygotic twins are more similar to each other than dizygotic twins. In molecular terms, heritability has traditionally been attributed to variations in the DNA sequence.

CAMH's Dr. Art Petronis, head of the Krembil Family Epigenetics Laboratory, and his team conducted a comprehensive epigenetic analysis of 100 sets of monozygotic and dizygotic twins in the first study of its kind. Said Dr. Petronis, "We investigated molecules that attach to DNA and regulate various gene activities. These DNA modifications are called epigenetic factors."

The CAMH study showed that epigenetic factors - acting independently from DNA - were more similar in monozygotic twins than dizygotic twins. This finding suggests that there is a secondary molecular mechanism of heredity. The epigenetic heritability may help explain

currently unclear issues in human disease, such as the presence of a disease in only one monozygotic twin, the different susceptibility of males (e.g. to autism) and females (e.g. to lupus), significant fluctuations in the course of a disease (e.g. bipolar disorder, inflammatory bowel disease, multiple sclerosis), among numerous others.

"Traditionally, it has been assumed that only the DNA sequence can account for the capability of normal traits and diseases to be inherited," says Dr. Petronis. "Over the last several decades, there has been an enormous effort to identify specific DNA sequence changes predisposing people to psychiatric, neurodegenerative, malignant, metabolic, and autoimmune diseases, but with only moderate success. Our findings represent a new way to look for the molecular cause of disease, and eventually may lead to improved diagnostics and treatment."

An advance online publication of this study will be available on the *Nature Genetics* website on January 18, 2009.

Source: Centre for Addiction and Mental Health

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