Random chance may explain hereditary disease

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(Medical Xpress)—A new study from Karolinska Institutet and the Ludwig Institute for Cancer Research shows that random chance decides whether the gene copy you inherit from your mother or the one from your father is used something which in turn may determine your risk of hereditary illnesses. The research, which is presented in the journal *Science*, may explain why an illness only afflicts some individuals even if they are carrying the same gene copy as their healthy relatives.

We are all genetic mixtures of our parents. There are two copies of each gene in our body, one inherited from our mother and one from our father. Most studies conducted in this field have shown that both gene copies (i.e. the mother's and the father's) are used to the same extent. With the aid of new technology, a research group at Karolinska Institutet in Sweden and the Ludwig Institute for Cancer Research has now been able to show that gene activity is more dynamic and unpredictable than what was previously believed. There is often only one single, randomly chosen, gene copy active in each individual cell. Which gene copy is active may also change over time.

"This dynamic phenomenon inside cells has not previously been described, as the methods for studying gene activity have been based on analysing hundreds to thousands of cells at a time", says study leader Dr Rickard Sandberg. "This gives you an average, where the contribution of the copies from the father and mother of the same gene, known as the alleles, are mixed together. We have instead developed a method that allows us to analyse the gene activity in individual cells, which enabled this discovery."

The discovery casts new light on many issues in biomedical research, according to Rickard Sandberg. For example, the discovery could help explain how apparent differences can arise in identical twins, despite having nearly identical genes. The inherent randomness of how the parents' copies are used in the cell might account for their phenotypic differences. Many diseases have previously been hard to explain as they have only developed in a subset of patients at risk, or caused symptoms of varying severity. Stochastic expression of a healthy and disease allele might help account for such variability in disease outcomes.

"This discovery is also interesting for basic research regarding gene activity and regulation",says Dr Sandberg. For example, it highlights the fact that studies and models of gene activity should be made using resolution for both the maternal and paternal alleles."

More information: "Single-Cell RNA-Seq Reveals Dynamic, Random Monoallelic Gene Expression in Mammalian Cells." Qiaolin Deng, Daniel Ramsköld, Björn Reinius, and Rickard Sandberg. *Science* 10 January 2014: 343 (6167), 193-196. DOI: 10.1126/science.1245316

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