Cancer-metabolism link runs deep in humans

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Eighty years ago, the medical establishment believed cancer was caused by a dysfunction of metabolism, but the idea went out of vogue. Now, scientists are again looking at metabolism and its role in cancer and other common diseases. Metabolism is a highly connected network of reactions that are arranged in parallel and interacting pathways. Such parallelism can mask how genes are linked with disease traits and make it difficult to treat conditions.

In a paper in the journal *CHAOS,* which is published by the American Institute of Physics, researchers at Harvard Medical School and Boston University analyzed ways to "break" the multiple parallel pathways of a metabolic network. The team applied a novel network algorithm to a published genome-scale model of human metabolism to design minimal "knockouts" for a wide variety of metabolic functions, such as phospholipid biosynthesis and the role of fumarase in suppressing human cancer.

The research suggests that the many pathways in the human metabolic network buffer each other to a striking degree, inducing "deep" epistasis -- the suppression of a mutation by one or more seemingly unrelated genes. Their results identify specific in vivo perturbation experiments that could confirm this deep parallelism in human metabolic pathways. "The results of our analysis could also be used to statistically probe complex relationships between genetic variation and disease," says co-author Marcin Imielinski.

More information: The article "Deep epistasis in human metabolism"

by Marcin Imielinski and Calin Belta was published in the journal CHAOS on June 30, 2010. See: chaos.aip.org/chaoeh/v20/i2/p026104_s1

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