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Using millions of years of cell evolution in the fight against cancer

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As the medical community continues to make positive strides in personalized cancer therapy, scientists know some dead ends are unavoidable. Drugs that target specific genes in cancerous cells are effective, but not all proteins are targetable. In fact, it has been estimated that as few as 10 to 15 percent of human proteins are potentially targetable by drugs. For this reason, Georgia Tech researchers are focusing on ways to fight cancer by attacking defective genes before they are able to make proteins.

Professor John McDonald is studying micro RNAs (miRNAs), a class of small RNAs that interact with messenger RNAs (mRNAs) that have been linked to a number of diseases, including cancer. McDonald's lab placed two different miRNAs (MiR-7 and MiR-128) into ovarian cancer cells and watched how they affected the gene system. The findings are published in the current edition of the journal *BMC Medical Genomics*.

"Each inserted miRNA created hundreds of thousands of gene expression changes, but only about 20 percent of them were caused by direct interactions with mRNAs," said McDonald. "The majority of the changes were indirect – they occurred downstream and were consequences of the initial reactions."

McDonald initially wondered if those secondary interactions could be a setback for the potential use of miRNAs, because most of them changed the gene expressions of something other than the intended targets. However, McDonald noticed that most of what changed downstream was

functionally coordinated.

miR-7 transfection most significantly affected the pathways involved with cell adhesion, epithelial-mesenchymal transitions (EMT) and other processes linked with cancer metastasis. The pathways most often affected by miR-128 transfection were different. They were more related to cell cycle control and processes involved with cellular replication – another process that is overactive in cancer cells.

"miRNAs have evolved for millions of years in order to coordinately regulate hundreds to thousands of genes together on the cellular level," said McDonald. "If we can understand which miRNAs affect which suites of genes and their coordinated functions, it could allow clinicians to attack cancer cells on a systems level, rather than going after genes individually."

Clinical trials for miRNAs are just beginning to be explored, but definitive findings are likely still years away because there are hundreds of miRNAs whose cellular functions must be fully understood. Another challenge facing scientists is developing ways to effectively target therapeutic miRNAs to cancer cells, something McDonald and his Georgia Tech peers are also investigating.

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