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Small molecules shed light on cancer therapies

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Patients suffering from an aggressive brain cancer will benefit from the results of a University of Illinois study that could advance the development of targeted gene therapies and improve prognosis.

"We have advanced the understanding of the role of microRNAs on glioblastoma multiforme, a deadly brain cancer, by studying the networks between the microRNAs and their target genes associated with different stages of cancer development and progression," said Kristin Delfino, a U of I doctoral candidate in animal science with a focus in genetics and bioinformatics.

What exactly are microRNAs? microRNAs are small, non-coding RNA molecules that regulate the expression of genes such as oncogenes or tumor suppressor genes. U of I researchers used a novel approach to identify the simultaneous association between tens of thousands of microRNAs, target genes, and glioblastoma progression and survival.

Delfino integrated clinical information such as race, gender, therapy, survival, and cancer stage from 253 patients together with genome-wide microRNA and gene expression data.

"We looked at the big picture and how microRNAs work together," Delfino said. "When you look at a single microRNA alone, it can seem significant. But when you evaluate it in the context of all other microRNAs, some turn out to be more significant and others may not be as significant as they appear on their own. The systems biology approach

that we implemented is critical for understanding the gene pathways influencing cancer."

The study evaluated 534 microRNAs together, unlike the typical method of studying one at a time. They confirmed 25 microRNAs previously associated with glioblastoma survival and identified 20 other microRNAs associated with initiation or growth of other cancer types such as breast cancer, ovarian cancer and gastric adenocarcinoma.

"These findings suggest common pathways that can be targeted with similar drugs already developed and tested for other cancers," said Sandra Rodriguez Zas, co-researcher and U of I professor of animal science and bioinformatics.

In addition, researchers found that some of the microRNA biomarkers of survival are personalized, Rodriguez Zas said. This means that they are particularly useful for patients of a specific race, gender or therapy. Other microRNAs are equally effective regardless of the clinical conditions of the patient.

"These biomarkers can serve as the basis to dig deeper into cancer studies," Delfino said. "Cancer affects us all in one way or another. Unfortunately, we still don't know how it's caused, what takes place when it is caused and how to cure it. But these biomarkers give us guidance into developing specific gene therapies to target glioblastoma."

Today patients can easily and cheaply be screened for microRNA and target gene levels, Rodriguez Zas said.

"Based on our research, that information can be used to select the most effective therapy and develop prognosis strategies," Rodriguez-Zas said.

More information: This study, "Therapy-, Gender- and Race-specific

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microRNA Markers, Target Genes and Networks Related to Glioblastoma Recurrence and Survival," was published in *Cancer Genomics & Proteomics.*

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