Team finds markers related to ovarian cancer survival and recurrence

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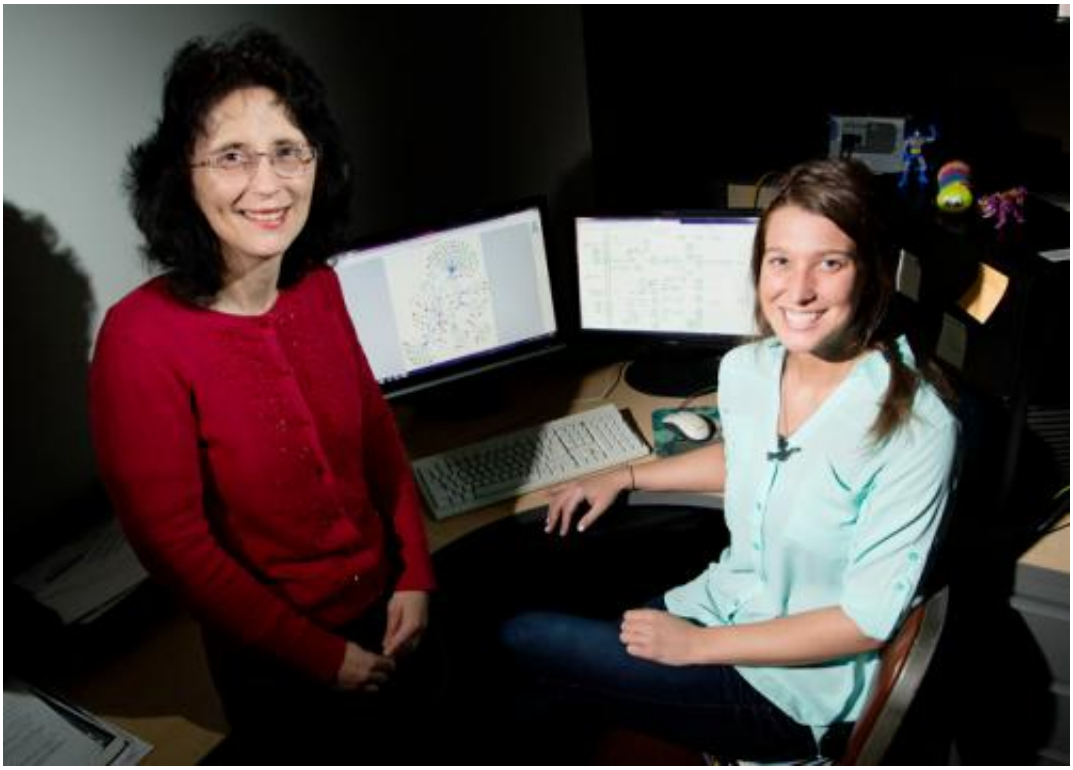

Illinois animal sciences professor Sandra Rodriguez-Zas, left, and graduate student Kristin Delfino identified biomarkers that are used to determine ovarian cancer survival and recurrence and showed how the interactions between these biomarkers affect these outcomes. Credit: L. Brian Stauffer

(Medical Xpress)—Researchers at the University of Illinois have identified biomarkers that can be used to determine ovarian cancer survival and recurrence, and have shown how these biomarkers interact

with each other to affect these outcomes.

Their findings appear in the journal *PLOS ONE*.

Researchers try to find molecules called biomarkers that help determine a person's likelihood of getting a disease or, if they have already been diagnosed, how far the disease has advanced. Genes, transcription factors and microRNAs are often used as biomarkers because these molecules can be heralds of disease or portents of susceptibility.

Genes are segments of DNA that code for proteins or other molecules that perform the functions of the cell. Transcription factors regulate these genes by binding to specific DNA sequences, preventing or inducing the genes to be "expressed" at higher or lower levels. MicroRNAs, as their name suggests, are small RNA molecules that regulate an intermediate stage of gene expression. Transcription factors and microRNAs also can regulate each other.

The relationships among transcription factors, microRNAs and target genes can be visualized as interconnected networks. These intricate webs are often used to determine how diseases such as cancer proceed. Analyzing how these networks function in cancer can offer insight into how tumor cells proliferate and differentiate, undergo (or resist) programmed cell death, and how likely they are to become invasive.

According to the American Cancer Society, an estimated 22,240 women will be diagnosed with ovarian cancer in 2013, and 14,230 will die of the disease; this makes ovarian cancer the fifth most common cause of cancer death in women.

The high prevalence of ovarian cancer and ovarian cancer deaths in the U.S. prompted U. of I. animal sciences professor Sandra Rodriguez-Zas and doctoral researcher Kristin Delfino to search for biomarkers

associated with ovarian cancer survival and recurrence.

"We knew that there are specific biomarkers that have been associated with ovarian cancer, but we were looking at whether we could more accurately predict survival or age at cancer recurrence considering hundreds of interacting biomarkers simultaneously," Rodriguez-Zas said.

The team used data from the Cancer Genome Atlas, which contains information about ovarian cancer patients' age, survival, cancer recurrence, treatment, tumor stage, tumor grade and genomic expression. The researchers then performed statistical tests to tie these factors to patients' survival time, measured in months from diagnosis to death, and their recurrence time, measured in months from diagnosis to recurrence.

"The networks change for people who have different rates of survival, so we looked at what's being expressed in high-survival patients compared to what's being expressed in low-survival patients," Delfino said.

The team was able to confirm the association of 21 microRNAs with ovarian cancer. They also found 838 target genes and 12 transcription factors associated with ovarian cancer survival and 734 target genes and eight transcription factors associated with ovarian cancer recurrence.

"We were able to find many biomarkers that held the same relationship with survival no matter the cancer treatment, as well as some that were unique in their relationship with survival depending on the treatment the patient had received," Rodriguez-Zas said.

Delfino said that a network-based approach is more predictive of ovarian cancer survival and recurrence than a single-molecule-based perspective.

"We took a step back and looked at everything from a network point of view instead of just individually to see how the components interacted

with each other and how the biomarkers were associated with ovarian cancer survival and recurrence," Delfino said.

"This demonstrated that the consideration of networks of microRNAs, transcription factors, and target genes allows us to identify reliable indicators of cancer survival and recurrence and serves as the basis for effective prognostic tools," Rodriguez-Zas said.

Delfino believes this study opens the door to the creation of less invasive diagnostic tests and more specialized treatment options for women with ovarian cancer.

"In the future we'd like to be able to just take a little sample of your DNA and be able to tell you what's going to happen, what we can do to prevent it, and how to cut cancer off before it ever reaches that point," Delfino said. "Everyone is different, and hopefully, we will be able to specify the treatment that will best treat the individual patient."

The paper, "Transcription Factor-MicroRNA-Target Gene Networks Associated With Ovarian Cancer Survival and Recurrence," is available online.

Provided by University of Illinois at Urbana-Champaign

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