COXEN model picks the best drug for ovarian cancer

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There are three common drugs for advanced ovarian cancer: paclitaxel, cyclophosphamide, and topotecan. Like a shell game, if you pick the right drug a patient is likely to respond. And, unfortunately, picking the wrong drug can lead to treatment failure. As reported in this month's issue of the journal *PLoS ONE*, a University of Colorado Cancer Center and University of Virginia study used a sophisticated model of ovarian cancer genetics to match the right tumor with the right drug. Patients who were matched in this way lived an average 21 months longer than patients who were not matched.

Because it has been so difficult to predict which ovarian cancers will respond to each of these three drugs, doctors have largely been forced to guess which will work best – and so in this study of four groups of 783 patients each, some were accidentally given what would turn out to be the best possible drug whereas others were given one of the two other, less good drugs. The model, called COXEN (CO-eXpression gENe analysis), sorts through the massive genetic data of thousands of tumor samples to discover differences between tumors that responded and tumors that did not.

"The model allowed us to ask what would have been the right drug in each case, how could we have known from the tumor's genetics, and what difference it made," says Jennifer R. Diamond, MD, CU Cancer Center investigator and medical oncologist at the University of Colorado Hospital.

When COXEN looked back through this registry of advanced ovarian cancer, it first sorted tumors into those that had responded and those that had not responded to each drug ("what would have been the right drug in each case"). It then pinpointed genetic signatures of tumors that responded to each drug ("how could we have known from the tumor genetics"). And the study finally showed that patients who had been serendipitously given the drug that the COXEN model would have picked for them lived 21 months longer than the average patient with advanced ovarian cancer.

"We have traditionally considered site-specific cancer to be homogenous – one ovarian cancer is like the next ovarian cancer. But we are increasingly learning that isn't the case at all. The COXEN model allows us to identify the heterogeneity within the disease. It lets us see why some ovarian cancers respond and others don't," Diamond says.

Diamond is also quick to point out that while the current study shows that COXEN could have been used to predict the most useful drug in many of these cases of advanced ovarian cancer, the actual use of the model will be possible only after validation with a prospective clinical trial. In fact, a similar strategy led to similar results in bladder cancer, and a prospective clinical trial of COXEN in bladder cancer is underway at the CU Cancer Center and elsewhere.

"This study supports the idea that we could test ovarian cancer tumors and say they're more likely to respond to one or the other drugs," Diamond says.

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