UNM Cancer Center researcher looks for genetic markers for ovarian cancer

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Ovarian cancer is a deadly disease. With no overt symptoms and no screening tests to catch it early, ovarian cancer is often detected at stage 3 or later. By then, it can be very aggressive and may have spread beyond the ovaries into other organs. Many women eventually succumb to it; the five-year survival rate for a stage 3 ovarian cancer diagnosis is only 34 percent.

"We're challenged on every front by this cancer," says Linda Cook, PhD, University of New Mexico Professor of Epidemiology and Biostatistics. "It's even challenging to find modifiable risk factors, such as behaviors that people can change." So Dr. Cook will soon examine a unique aspect of the disease using a rare resource. With the support of a large National Institutes of Health multi-year grant, she will study the mitochondrial DNA differences in several hundred women with and without ovarian cancer. "Our hypothesis is that we will see differences in the mitochondrial DNA," explains Dr. Cook. "Our preliminary data suggest that these differences may be related to survival." These genetic differences in the mitochondria could provide the basis for a screening test or possibly even a drug intervention.

Mitochondria are cellular structures that produce energy for the cell. They have their own set of DNA, referred to as mtDNA, which are passed down solely from the mother in the egg cell because sperm cells from the father carry only nuclear DNA. Although composed of the same set of nucleotide bases as nuclear DNA, mtDNA is much more susceptible to mutations. It contains only 16,500 bases while nuclear

DNA has over 3 billion bases in each cell; so while nuclear DNA can twist tightly to protect itself from mutations, mtDNA is too short to do so. Nuclear DNA gains additional protection from the nuclear membrane surrounding it and by associating with histones and other molecules in the nucleus except when it is being copied or transcribed. But like nuclear DNA, mtDNA has polymorphisms which are the variations in the sequence of the bases between different individuals. Dr. Cook's research will focus on understanding the role mutations and polymorphisms play in ovarian cancer.

To conduct this mtDNA population study, Dr. Cook and her colleagues will use a unique resource they have spent more than a decade to build. The resource is a database of information on over 4,200 Canadian women—almost 1,600 of whom have been diagnosed with ovarian cancer. The database gives Dr. Cook's team access to each woman's blood or saliva samples, tissue samples, medical records, and records from an in-depth interview on lifestyle. The researchers have followed each woman for at least 4 years so they have access to information on lifestyle changes, treatment responses, and cancer survival as well. "Because we're taking a very comprehensive look at ovarian cancer," says Dr. Cook, "we need to consider this multi-layer complexity of data on a single person. We're considering gene-environment interactions, gene-gene interactions, and interactions with treatment, so we've got to have a lot of information from a lot of people." The large number of women in the study gives Dr. Cook's team the ability to find enough people with the same set of interactions so that statistically significant predictions are possible.

The Canadian arm of Dr. Cook's research team will sequence mtDNA from the blood and saliva samples and will analyze the tissue samples. The New Mexico researchers will then use this information along with the other database information in their population analyses. The analyses will search for correlations between mtDNA sequences and incidence of

ovarian cancer, type of ovarian cancer, response to treatment, and survival probability. Such correlations strongly suggest genetic markers for the disease, which researchers could then use to create screening protocols and therapies.

Thus, finding mtDNA sequences that show promise as potential genetic markers will be crucial to ovarian cancer research. "We can't intervene on any population risk factors and the therapies for ovarian cancer just extend survival. Although we've made progress, ultimately these women are dying of ovarian cancer," says Dr. Cook. "So, if we can discover the basis for a screening test or a therapy that will prevent mortality, it will help. Any information we can get on this cancer will really help."

Provided by University of New Mexico Cancer Center