SOUTHWESTERN NEWS

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COLD VIRUS WITH *P53* GENE TESTED TO COMBAT OVARIAN CANCER

DALLAS – October 28, 1998 – Researchers at UT Southwestern Medical Center at Dallas are using the p53 gene, inserted into an inactive common-cold virus, as a novel way to attack ovarian cancer in a patient.

Drs. Carolyn Muller and Robert Coleman, assistant professors of obstetrics and gynecology, said p53 is known as the housekeeper gene because it patrols for damaged cells, and if the cells cannot be repaired or are growing out of control and can't be contained, the *p53* gene turns on its second line of defense: a built-in cell-death program, a process called apoptosis. The *p53* mutations are the most common mutations in solid tumors and are found in 50 percent to 79 percent of ovarian cancers.

Muller said the normal *p53* genes are replicated in the laboratory and inserted into adenoviruses, which act as carriers. During the treatment procedure, the patient's large amount of abdominal fluids, caused by the cancer, is withdrawn, and a therapeutic mixture of engineered *p53* genes floating in saline is injected into the abdominal cavity. There the viral "geneboats" deliver the *p53* gene to all cells. Once the gene is turned on in cancer cells, the invading "housekeeper" goes to work, recognizes the cancer cell's DNA damage and condemns it to death.

Muller and Coleman, who work in the Harold C. Simmons Comprehensive Cancer Center and the Nancy B. and Jake L. Hamon Center for Therapeutic Oncology Research, said that this trial will determine several things. They include the appropriate mixture of engineered viruses in the solution, the sequence of doses, the length of treatment and the manner in which the patient reacts to it. The first patient's treatments are occurring in three weekly visits with two-week intervals between them. Patients will continue treatments as long as a positive response occurs unless significant side effects develop. Fifteen to 18 patients are expected to be treated in this study.

Nancy Ruff, a 65-year-old wife, mother and grandmother, never intended to be a pioneer. But

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when she was referred to Coleman and Muller to discuss the first human *p53* trial for ovarian cancer, she had run out of treatment options. Ruff had gone through two surgeries and six different chemotherapies in the last two years. She said that after each chemotherapy series she felt better for a while, but signs of the cancer would reappear.

Ruff's ovarian cancer was discovered when she had an endoscopy for an ulcer that wouldn't heal. Later she learned that she also suffered from a hernia, so she hadn't connected the "bloaty feeling," often symptomatic of ovarian cancer, with any other illness.

"The first time I went to see the Southwestern doctors, I took six pages of typewritten questions in with me, so I wouldn't forget anything I wanted to ask," Ruff said.

Ruff said that "so far the treatment at its worst is like a bad case of the flu. And I know what I'm talking about since I've had a lot of chemotherapy." She's also delighted that the *p53* treatment doesn't cause her to lose her hair.

The two researchers have been part of a large medical team that has been looking at using the *p53* gene for four years – performing extensive studies with genetically engineered cells and animals – before receiving approval from the National Cancer Institute to treat women with "advanced, persistent or recurrent ovarian cancer."

The researchers hope that therapy with the engineered *p53* gene may provide a strong second front for fighting ovarian cancer because of the low survival rates with surgery and chemotherapy. "With this trial, we will learn a lot about the how the gene works in humans, and we will be able to improve the treatment strategy for future patients," Muller said.

For further information, stage III and IV ovarian cancer patients or their physicians should call clinical research nurse Paula Rogers at (214) 648-2806.

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