

CHIRONIAN

New York Medical College



Fall / Winter 2008

Inside:

Young Guns,
Old Pathogens

Defying Cancer's
Toll on Fertility

Dual Degrees Are
All That and More

Remembering
Melvin D. Freeman



A professor of obstetrics and gynecology is blazing a trail in the field of reproductive medicine: storing tissue to help cancer patients preserve their fertility.

Kutluk Oktay, M.D., puts ovaries away for safe keeping

By Marjorie Roberts

Without a doubt, chemotherapy is saving the lives of women with cancer, but at considerable cost: the toll it takes on their fertility. Giving up the ability to have children is too high a price to pay, believes Kutluk Oktay, M.D., so he has spent the last decade developing techniques to intervene *before* a patient's fertility is jeopardized. This pioneering research has earned him an international reputation as the leading authority on what is known as fertility preservation, an advance in reproductive medicine that New York Medical College has offered since January 2008, when Dr. Oktay joined the Department of Obstetrics and Gynecology (OB/GYN) as professor and director of its Division of Reproductive Medicine.

Fertility preservation is a program of innovative treatments, techniques and strategies to help patients cope with the rigors of cancer treatment. A woman's fertility is preserved by the freezing of eggs, embryos or ovarian tissues, and then returned to her body when chemotherapy and radiation are complete and the patient decides to get pregnant. Candidates are not only women of childbearing age who have breast or other cancers, but also young girls with leukemia and solid tumors whose parents want to keep safe their ability to have children later in life. While some cancer patients are happy just to survive their treatment, others desire a normal ovarian hormone production, and then to have fertility restored. Decades ago patients were in a quandary over breast reconstruction: should they remove the tumor or breast and be done with it, or let it heal and then have a surgical implant? Now surgeons can do both at the same time. Fertility preservation offers a similar choice of options to women who refuse to let a cancer diagnosis dash their hopes of having a child.



The highly pedigreed laboratory team of Kutluk Oktay, M.D., center, consists of Xingtao Wang, Ph.D., left, research associate professor of OB/GYN; Veronique Drouineaud, M.D., Ph.D., a visiting fellow from Dijon, France; and Samir Babayev, M.D., a post-doctoral fellow from Azerbaijan. The research group uses in vitro and xenografting models to investigate how chemotherapy damages ovarian follicles.



After laparoscopic removal of an ovary, pieces of ovarian tissue are covered in a cryoprotectant and frozen at -280°F. Dr. Oktay performed the first transplant of previously frozen ovarian tissue in 1999.

New chairman's coup

That fertility preservation is available here in Valhalla is due in large part to the efforts of Howard Blanchette, M.D., professor and chairman of the Department of Obstetrics and Gynecology, which has been revitalized under his leadership. In 2000 he left positions at Harvard and Metro West Medical Center in Boston for the top OB/GYN job at College-affiliated Danbury Hospital. Three years later he joined the College faculty, becoming full professor and chairman of the department in August of 2007.

"Many of my colleagues across the country spoke very highly of Dr. Oktay and his groundbreaking translational research," says Dr. Blanchette. "We are very lucky to have recruited him to our faculty. This is real cutting edge work that will greatly strengthen the academic mission of the department and enhance the reputation of New York Medical College."

Dr. Oktay spends three days a week on campus—in his laboratory at the College and as an attending at Westchester Medical Center. The rest of the week he divides his time between his consulting and hospital obligations at Memorial Sloan-Kettering Cancer Center, Memorial Hospital for Cancer and Allied Diseases, and the Institute for Fertility Preservation, a division he founded and directs for The Center for Human Reproduction in Manhattan. The variety of these assignments is something he covets:

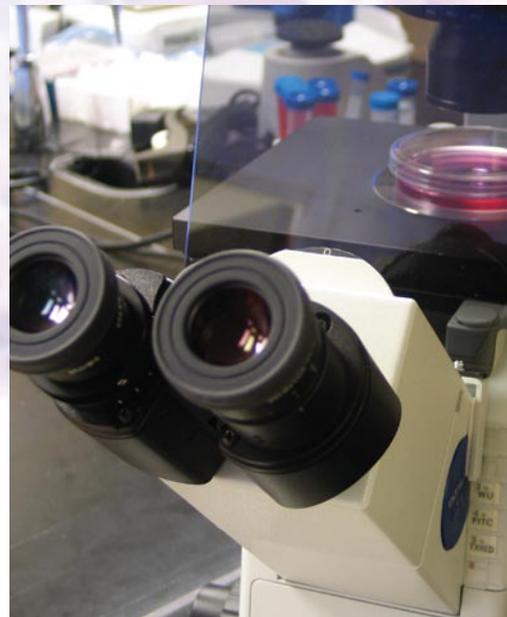
"I am a basic scientist, translational researcher, clinician and a surgeon. What I find exciting is the fact that I may be working on a molecular experiment in the laboratory during the morning, and by noon I'm doing clinical research. In the afternoon I may have a complicated laparoscopic surgery. To be able to experience the whole spectrum of medical science gives me the most I could get from life."

Global training

Born in Turkey, Kutluk Oktay graduated from Hacettepe University Medical School in Ankara in 1986. After two years of an internal medicine residency in Istanbul, he came to the U.S. and completed residencies in internal medicine and OB/GYN. A clinical fellowship in reproductive endocrinology and infertility followed at the University of Texas at San Antonio. An exchange research fellowship at the University of Leeds in the U.K. came next. Dr. Oktay had won a grant from the Royal College of OB/GYN and the American College of OB/GYN. Each university gives one grant annually to only one person from each country. In 1996 he returned for academic appointments at SUNY Health Science Center in Brooklyn and Weill Medical College of Cornell University in Manhattan. His hospital appointments were at New York Methodist Hospital in Brooklyn and New York Presbyterian-Cornell. In 1999 he performed the first frozen ovarian transplant at New York Methodist, taking it from animal studies to working with patients in only three years.

Dr. Oktay is married to Maja Hrzenjak Oktay, M.D., Ph.D., a cancer researcher at Montefiore Medical Center in the Bronx. If they talk shop at home it is not surprising because his work has attracted the attention of cancer doctors who see fertility preservation as an essential part of their treatment. This is Dr. Oktay's goal, and it looks

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like it is full steam ahead thanks to a new million-dollar RO1 Grant from the NIH entitled “Characterization and prevention of chemotherapy-induced damage to ovarian reserve.”

He has another NIH application working to test a number of agents to see if they can assist in revascularization to improve the survival of ovarian transplants. Some of these agents are sphingosine1 phosphate, vascular endothelial growth factor (VEGF), nerve growth factor (FGF), and bone marrow stem cells. He is also exploring alternative ways of freezing ovarian tissue. “It’s not so simple,” he says. “By the time the transplant is finished, you may have lost two-thirds of the eggs. What we are trying to do is develop medicines that will protect the transplanted ovary against initial ischemia until angiogenesis occurs.”

One might ask how New York Medical College, with its ties to the traditions of the Catholic Church, can promote fertility preservation when the Church is opposed to most forms of *in vitro* fertilization. Dr. Oktay responds, “We are protecting ovarian tissue from chemotherapy damage, which does not require assisted reproductive technology at all. By transplanting ovarian tissue we are restoring natural fertility and avoiding the need for assisted reproduction techniques.”

Dr. Oktay’s technique involves a laparoscopic removal of the ovary, which he then cuts into pieces. It is frozen that way, at minus 280 degrees Fahrenheit, covered with an antifreeze-like cryoprotectant. The transplant will go into one of two locations, neither involving the ovary’s original site in the body: the lower abdomen, just under the skin, or the forearm. The decision is made based on discussions with the patient, her medical needs as well as her preferences. In one of his earliest successes with this technique, the patient became

Of that number, 6 returned for transplant, but only 3 tried to have children. There is the woman who appeared on the Today show. She conceived normally and delivered a healthy child—and, she is pregnant again. Another woman died from her cancer. But in all 6 cases, their menstrual periods returned and they had normal hormonal function. In Europe and Asia there have been fewer than 40 ovarian transplants resulting in 6 or 7 babies.”

This is the world of oncofertility, to which Kutluk Oktay has devoted his entire professional life. He has also pioneered new ovarian stimulation protocols for embryo and oocyte freezing for breast and endometrial cancer patients. This is good news for the estimated 125,000 people under the age of 45 who are diagnosed with cancer each year, in particular, the 50 percent who will receive treatments that will affect their fertility. ●

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– Kutluk Oktay, M.D.

pregnant naturally when her remaining, inactive ovary began ovulating. In a television interview about the case, Dr. Oktay speculated that “the healthy ovary may contain signals or hormones that may enable the dormant ovary to regenerate eggs. At least, that’s the theory—other than a miracle.”

National recognition

For his pioneering accomplishments, Dr. Oktay was invited to join the National Cancer Institute’s President’s Cancer Panel and was given the task of writing the fertility preservation guidelines by the American Society of Clinical Oncology. It’s been a slow but successful start: “I have frozen ovarian tissues from around 100 patients.