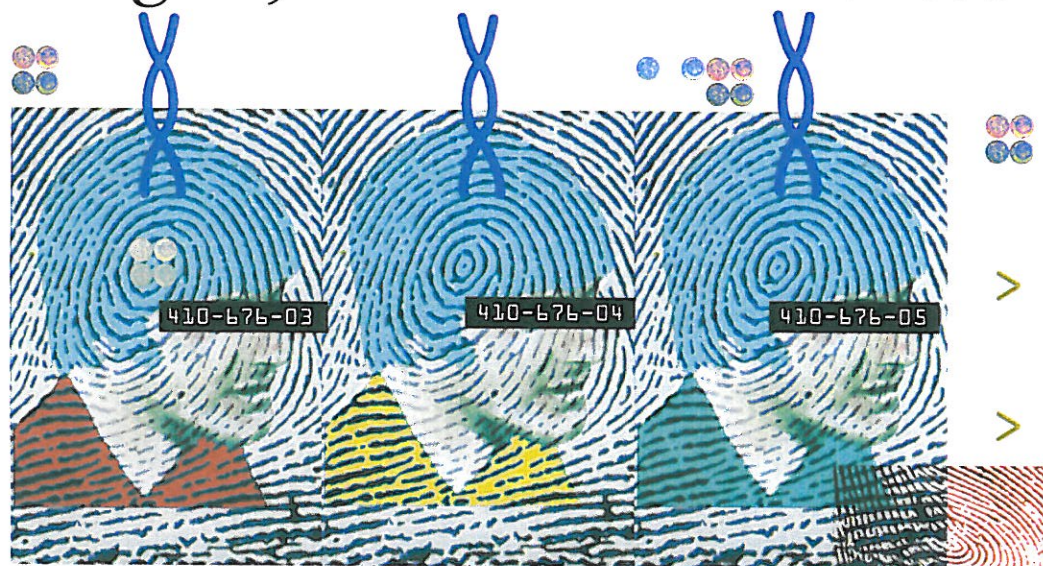


# the Winship REPORT

From the Winship Cancer Institute of Emory University

Fall 2001

## Personalizing Cancer Treatment with the World's Largest, Fastest Life Sciences Supercomputer



Imagine a supercomputer that uses 1250 IBM servers and processes information at 7.5 trillion calculations per second. While such a machine could be straight from the pages of science fiction, it is in fact being assembled now in midtown Atlanta at the headquarters of Nutec Life Sciences. When all 5,000 CPUs are installed, the supercomputer will be the fastest in operation outside a government agency.

The Winship Cancer Institute (WCI) recently joined NuTec and IBM to develop an integrated bioinformatics system. With the Nutec supercomputer, IBM technology, and WCI understanding of the disease process of cancer, this system will

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### Tackling Tubulin Mysteries

One of the major obstacles in cancer chemotherapy is drug resistance. Assistant professor of hematology and oncology Paraskevi Giannakakou investigates methods of drug resistance at the molecular level. "The more we understand about the molecular interactions between anticancer drugs and cells, the better we'll be at designing drugs that defy resistance," Giannakakou says.

While completing a fellowship at the National Cancer Institute (NCI), Giannakakou began working on the problem of drug resistance to compounds like Taxol (paclitaxel), which has been effective against many types of can-

cers, including breast and ovarian cancer. Taxol targets tubulin, the constituent protein of microtubules, which are structures in the cell's cytoplasm critical for cell growth and division, motility, and signaling. Among anticancer agents, drugs such as Taxol may be the most effective class of agents, according to Giannakakou. However, the development of drug resistance hampers Taxol's applicability in the clinic. With colleagues at the NCI, she has made important discoveries about the mechanism underlying Taxol resistance in cancer.

Giannakakou and colleagues were the first to show that acquired tubulin mutations are an important mechanism in Taxol resistance. Their work showed that cancer cells exposed to Taxol develop tubulin mutations that impair Taxol's anticancer activity.

Giannakakou's work focuses on mutations in microtubule processes of signaling and transporting. Her studies of the microtubule network showed that the p53 tumor-suppressor protein used microtubules as passageways to navigate through the cytoplasm in a highly organized process.

The inactivation of p53 is the most common alteration in human cancers and occurs through acquired mutations or abnormal localization in the cell. Giannakakou's study showed that in response to stress, p53 moves on microtubules with the help of a specific motor protein, dynein, and is translocated from the cell's cytoplasm to the nucleus. In the nucleus, p53 binds DNA and activates mechanisms leading to growth arrest or cell death. She also found that this transport mechanism requires an intact micro-

tubule network to work properly.

"We did not know until recently how p53 moves from the cytoplasm to the nucleus," Giannakakou says. "Now we know that it does so on microtubules, and it requires an intact microtubulin network to do so." This finding is significant for the use of Taxol-like agents to arrest cancer because they work by disrupting microtubules.

*Paraskevi Giannakakou takes on drug resistance at the cellular level by studying the microtubules.*



### RESEARCH

Her research on drug resistance and microtubule-mediated cellular trafficking could lead to novel and more effective drugs. "The more we understand the molecular interactions between drugs and tubulin," she says, "the better we can design drugs that effectively target tubulin."

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