Scientists identify liposarcoma tumors that respond to chemotherapy

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Liposarcoma, the most common type of sarcoma, is an often lethal form of cancer that develops in fat cells. It is particularly deadly, in part, because the tumors are not consistently visible with positron emission tomography (PET) scans that use a common probe called FDG and because they frequently do not respond to chemotherapy.

Now, using a strategy that tracks cancer cells' consumption of nucleosides, a team of researchers at UCLA's Jonsson Comprehensive Center has identified a group of liposarcoma tumors that can be imaged by PET scanning using a tracer substance known as FAC. Furthermore, they have found that these tumors are sensitive to chemotherapy.

The team's findings are published online in the journal *Cancer Discovery* and will appear in an upcoming print edition.

Led by Jonsson Cancer Center researcher Heather Christofk, an assistant professor of molecular and medical pharmacology at UCLA, the scientists employed a metabolomic strategy that detected nucleoside salvage activity in liposarcoma cells taken from patient samples, cells grown in the laboratory and cells grown in mouse models. The nucleoside activity was visible using PET with the UCLA-developed FAC probe (FAC PET), which measures the activity of the DNA salvage pathway, a fundamental cell biochemical pathway that acts as a sort of recycling mechanism to help with DNA replication and repair.

FAC was created by slightly altering the molecular structure of the

standard chemotherapy drug gemcitabine, and in the current study, the UCLA research team discovered that the liposarcoma cells with high nucleoside salvage activity were sensitive to gemcitabine chemotherapy.

In clinical practice, this strategy might be used to identify liposarcoma patients, at the time of diagnosis, who would respond well to gemcitabine chemotherapy, saving time on other treatments and possibly extending the lives of this sub-group of patients.

"It was a satisfying study because it has translational potential for liposarcoma patients now—and this is a deadly disease," Christofk said. "Our metabolomic strategy is also generalizable to treatment strategies for other cancers, and that is something we hope to do."

The study was a collaboration between basic scientists and clinicians, following the translational paradigm of bench-to-bedside discoveries.

"This was an outstanding transdisciplinary project between a diverse group of physician scientists and basic scientists that translates molecular oncology from the laboratory to the clinic in a rapid and clinically relevant manner," said Dr. Fritz Eilber, an associate professor of surgery and of molecular and medical pharmacology at UCLA and an investigator on the study. "The findings from this work can be used to directly impact the care of patients with this morbid and lethal malignancy."

Provided by University of California, Los Angeles