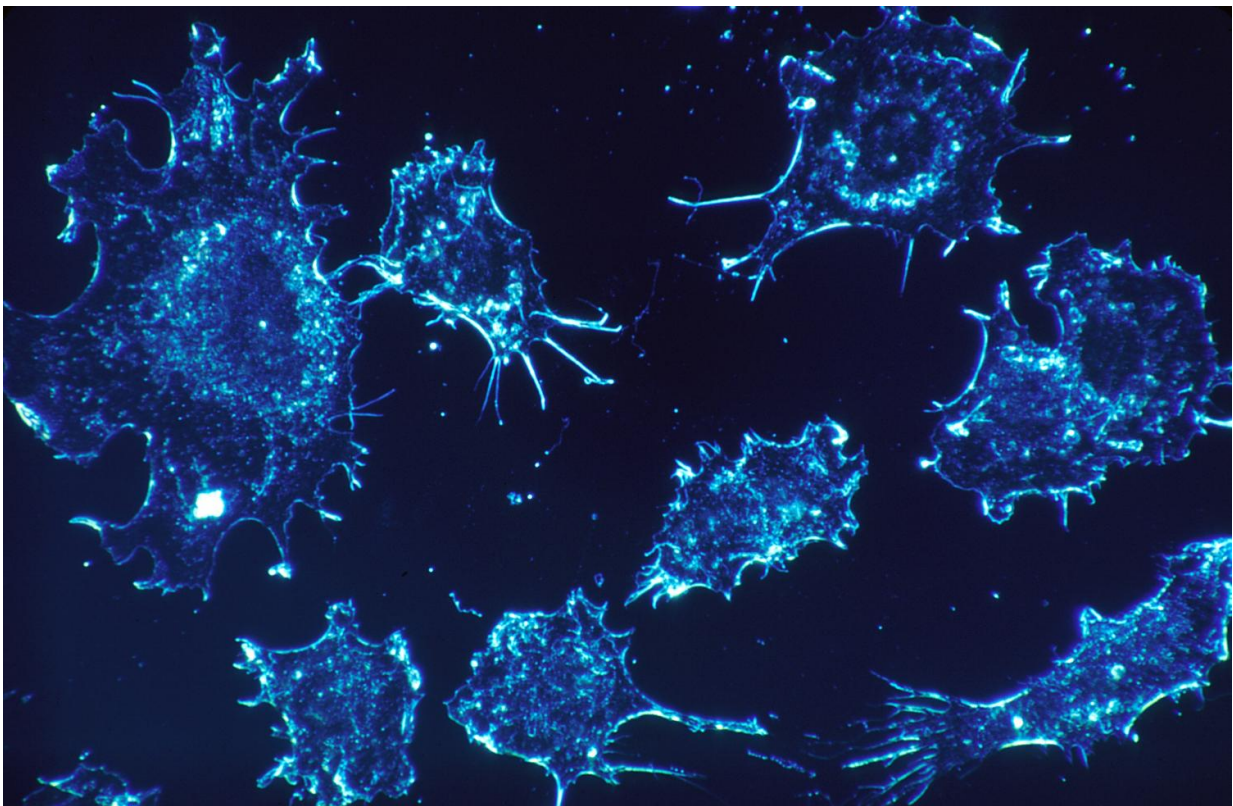


Study offers road map to personalized therapies for sarcoma, other aggressive cancers

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Sarcoma is a rare and deadly form of cancer occurring in the bones and connective tissue that affects people of all ages. Its aggressiveness, rarity

and diversity continue to hinder efforts to identify effective therapies for people with this malignancy. In a patient-derived orthotopic xenograft, human tumor fragments are transplanted into a mouse. Such xenografts have long shown great promise in modeling how sarcoma and other cancers can respond to and resist therapies, but their feasibility for use in people in clinical settings remains unknown.

A new UCLA study is the first to identify patient and [tumor](#) characteristics that predict the successful creation of patient-derived orthotopic xenograft models and which types of sarcomas are most likely to grow as xenografts. The research, which is also the first such xenograft study in sarcoma, gives physician-scientists a much-needed road map for personalizing therapies for the disease without placing people at risk for treatment-related complications or ineffective therapy.

There are up to 50 types of soft-tissue sarcomas, making each one rare. Consequently, it is challenging for scientists to design clinical trials to identify effective systemic treatments, such as chemotherapy or targeted therapy.

Recent research has shown that patient-derived orthotopic xenografts faithfully reproduce the biological behavior of the human tumor, including treatment response and resistance that accurately mirrors that of the individual. Given the overall promise of these xenografts, the UCLA team set out to assess the feasibility of developing patient xenograft models in a clinical setting and to determine potential factors that facilitate or prevent the successful development of xenografts from people with sarcomas.

In the yearlong study, the UCLA team collected tumor samples from 107 people with soft-tissue sarcomas. Tumor fragments were then surgically implanted into the mice in the anatomic site corresponding to the original tumor location in the patient. The researchers assessed the

ability of the models to successfully "establish," meaning that after implantation of the human tumor fragments in the mouse model, a new tumor grew. The tumor fragments could also be subsequently transferred and grown in additional mice for further testing, Eilber said.

Eilber and colleagues discovered that only the aggressive, or high-grade, tumors established but not the less aggressive, or low-grade, sarcomas. Of the high-grade tumors that did establish, the highest rates (62 percent) were from people whose tumors had not previously been treated with chemotherapy or radiation. Tumors from people who had undergone pre-operative radiation therapy for their sarcoma saw no successful establishment of xenograft models, and establishment was also lower when patients had received pre-operative chemotherapy (32 percent) compared with those who had untreated tumors.

More than 12,390 cases of soft-tissue sarcoma will be diagnosed in the United States this year, and nearly 5,000 Americans are expected to die from the disease. The use of traditional treatments such as chemotherapy in soft-tissue sarcoma cases continues to result in low response rates and poor survival outcomes, and there is an urgent unmet need for more personalized strategies for the disease.

The study demonstrates that patient-derived orthotopic xenografts are feasible for use in the clinical setting and can provide oncologists with a [road map](#) to accurately identify which people will and will not benefit from a specific therapy. This research has the potential to change the way that people with [sarcoma](#) and other cancers are treated.

UCLA researchers are conducting additional studies to learn if human xenograft models can be developed for needle biopsies, as well as determining the potential of patient-derived orthotopic xenograft models to guide patient therapy and outcomes.

More information: Tara A. Russell et al. Clinical Factors That Affect the Establishment of Soft Tissue Sarcoma Patient-Derived Orthotopic Xenografts: A University of California, Los Angeles, Sarcoma Program Prospective Clinical Trial, *JCO Precision Oncology* (2017). [DOI: 10.1200/PO.17.00071](https://doi.org/10.1200/PO.17.00071)

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