

Engineering bio-inspired tumor niches at a scale: from microfabricated sensors to nanoscale drug delivery

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Tumoroids are three-dimensional tumor models derived directly from patient biopsies that retain key features of the original tissue and hold considerable promise as patient-specific models for cancer research. Their broader adoption, however, is limited by poorly defined animal-derived matrices, limited reproducibility, and the lack of quantitative, real-time analytical tools.

This work presents a materials engineering approach based on fully synthetic, xeno-free hydrogels microfabricated into arrays of microniches with independently tailorable architecture and biomechanical properties. These engineered microenvironments provide standardized culture conditions while functioning as intrinsic mechanical sensors: forces generated by individual tumoroids deform the surrounding material, enabling continuous, label-free monitoring of single tumoroid growth, mechanics, and therapeutic response. Combined with label-free holotomography, the platform enables dynamic, subcellular-resolution visualization of tissue morphology together with real-time tracking of drug trafficking and penetration in living patient-derived tumoroids.

To illustrate the platform's versatility, a bladder cancer case study examines the transport limitations of the antibody-drug conjugate enfortumab vedotin. Using the microengineered platform, self-propelled urease-powered PLGA nanomotors were evaluated as a strategy to generate local microscale convection and enhance intratumoral drug transport. Real-time holotomographic imaging revealed significantly improved drug penetration and therapeutic efficacy, independent of target expression.

Together, these results establish an instrumented tumoroid platform that enables quantitative, real-time analysis of tumor mechanics, drug transport, and therapeutic response at the level of individual patient-derived tumoroids. By combining standardized synthetic microenvironments with dynamic, label-free imaging, the platform addresses the growing need for reproducible, human-relevant preclinical models aligned with the evolving regulatory landscape for New Approach Methodologies (NAMs).

