Maximizing the potential of 3D-patient tumor avatars for next-generation precision oncology

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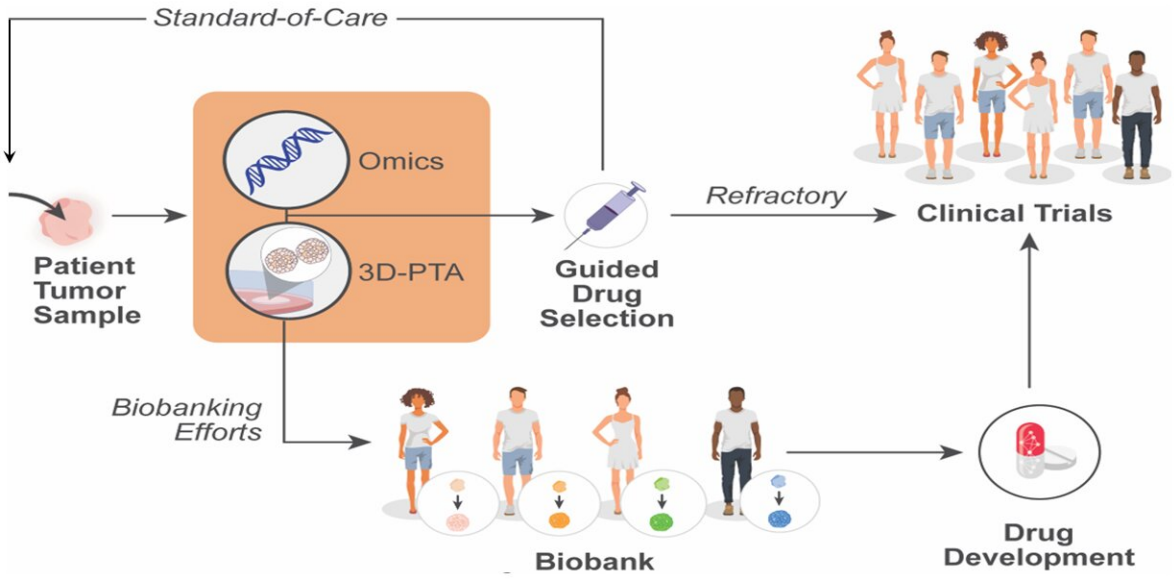

3D Patient Tumor Avatars (3D-PTAs) are part of a proposed integrative platform to provide optimal treatment selections for cancer patients. Such a platform combines omics and 3D-PTA data with standardized criteria and prospective clinical trial designs. Credit: Terasaki Institute for Biomedical Innovation

At any time, most cancer patients are receiving a treatment that does not

significantly benefit them while they endure bodily and financial toxicity. Aiming to guide each patient to the most optimal treatment, precision medicine has been expanding from genetic mutations to other drivers of clinical outcome. There has been a concerted effort to create "avatars" of patient tumors for testing and selecting therapies before administering them into patients.

A recently published *Cancer Cell* paper, which represents several National Cancer Institute consortia and includes key opinion leaders from both the research and clinical sectors in the United States and Europe, has laid out the vision for next-generation, functional precision medicine, by recommending measures to enable 3D patient tumor avatars (3D-PTAs) to guide treatment decisions in the clinic.

According to Dr. Xiling Shen, the corresponding author of the article and the chief scientific officer of the Terasaki Institute for Biomedical Innovation, the power of 3D-PTAs—which include patient-derived organoids, 3D bioprinting, and microscale models—lies in their accurate real-life depiction of a tumor with its microenvironment, and their speed and scalability to test and predict the efficacy of prospective therapeutic drugs.

To fully realize this aim and maximize clinical accuracy, however, many steps are needed to standardize methods and criteria, design clinical trials, and incorporate complete patient data for the best possible outcome in personalized care.

The use of such tools and resources can involve a great variety of materials, methods, and handling of data, however, and to ensure the accuracy and integrity for any clinical decision making, major efforts are needed to aggregate, standardize and validate the uses of 3D-PTAs. Attempts by the National Cancer Institute's Patient-Derived Models of Cancer Consortium and other groups have initiated official protocol

standardizations, and much work needs to be done.

The authors emphasize that in addition to unifying and standardizing protocols over a widespread number of research facilities, there must be quantification using validated software pipelines, and information must be codified and shared among all the research groups involved.

They also recommend that more extensive and far-reaching clinical patient profile be compiled, which should encompass every facet of a patient's history, including not only medical but demographic information as well; these are important factors in patient outcome. To achieve standardization in this regard, regulatory infrastructure provided by the National Institutes of Health and other institutes and journals must additionally be included to allow reliable global data sharing and access.

Clinical trials are also a major part of the 3D-PTA effort, and to date, studies have been conducted to examine clinical trial workflows and turnaround times using 3D-PTA. The authors advise on innovative clinical trial designs that can help with selecting patients for specific trials or custom treatments, especially when coupled with the patient's clinical and demographic information.

Combining these patient omics profiles with information in 3D-PTA functional data libraries can be facilitated by well-defined computational pipelines, and the authors advocate the use of relevant consortia, such as NCI Patient-Derived Model of Cancer Program, PDXnet, Tissue Engineering Collaborative, and Cancer Systems Biology Centers as well as European research infrastructure such as INFRAFRONTIER, EuroPDX)

Integrating data from existing 3D-PTA initiatives, consortia, and biobanks with omics profiles can bring precision medicine to a new

level, providing enhanced vehicles for making optimum choices among approved therapeutic drugs, as well as investigational, alternative, non-chemotherapeutic drugs. It can also provide solutions for patients experiencing drug resistance, and expand opportunities for drug repurposing.

"The integration of the 3D-PTA platform is a game-changing tool for oncological drug development," said Ali Khademhosseini, Director and CEO for the Terasaki Institute for Biomedical Innovation. "We must combine it in a robust fashion with existing cancer genomics to produce the most powerful paradigm for precision oncology."

More information: Margarida Barroso et al, A path to translation: How 3D patient tumor avatars enable next generation precision oncology, *Cancer Cell* (2022). DOI: 10.1016/j.ccell.2022.09.017

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