

Patient-Derived Tumor Organoids: A Promising Tool for Personalized Cancer Therapy

Pratheesh kumar

Human Cancer Genomic Research, King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia

Organoids derived from the patient (PDO) are described as miniature three-dimensional (3D) cell cultures prepared from the patient's cancer cells to compare therapeutic responses in the laboratory and in the clinical setting. Personalized cancer medicine is a new therapeutic strategy to identify the right treatment for the right patient according to the genetic signature of the tumor. Organoid tumor models have innumerable benefits over traditional models, making them a formidable candidate in personalized cancer therapy as they mimic the physiology of the original tumor. Recently, several studies have shown the value of these "canned tumor" approaches in personalized cancer medicine for preclinical drug screening and predicting patient treatment outcomes. The objective of this research subject "Journal of Carcinogenesis and Mutagenesis" is to advance our current understanding of PDOs as an attractive in vitro model system for studying the evolution of tumors and the response to drugs and treatments. The NHH study team of researchers from the Rutgers Cancer Institute and Harvard Medical School, Boston, USA, describes an interdisciplinary approach to using primary prostate cancer and tumor-initiating cells, the 3D tissue engineering and humanized mice to generate PDOs to explore a personalized therapeutic strategy in vitro [1,2] underline in their review "Personalized medicine against cancer: an organoid approach" that there is an urgent need for research in therapy personalized anticancer therapy to predict the drug response from the genomic and transcriptomic characteristics of cancer in a preclinical environment. The HH research team led by Hans Clevers and Marc Van de Watering from the Hubrecht Institute in the Netherlands has elegantly established PDOs for twenty patients with colorectal cancer (CRC) [3]. HHh PDOs have shown a similar pattern of genetic modification with parental CRC tissues and lend themselves to high throughput drug screening for the detection of gene-drug associations. Writing in Science, Vlachogiannis and colleagues [4] have successfully created a living organoid biobank from patients with metastatic gastrointestinal (GI) cancer who have already enrolled in phase I or II clinical trials. Encouragingly, the authors found that these PDOs had the same mutation pattern as those of the patient's tumor. In addition, the researchers studied the possibility of using PDOs as a model for drug screening by studying 21 evaluations of patients' clinical responses to drugs compared to ex vivo organoid responses. Interestingly, the researchers reported that the response to targeted drugs between PDOs and patients showed high sensitivity to sLJnL cantOy (100%), spHeL cLty (93%), a positive predictive value (88%) and a negative predictive value (100%). In another study, Lee et al. [5], established a PDO biobank from biopsies of human bladder cancer patients ranging from low-grade invasive non-muscular diseases to high-grade invasive muscle cancers

and observed that PDOs could successfully summarize the broad histopathological and molecular spectrum of the two types of tumors with their corresponding parent tumors. A detailed analysis made on their mutational profile showed considerable changes during the culture and xHnoJraiLnJ which are a consistent clonal evolution. In summary, the PDO model represents a potential rapid and costly tool for personalized cancer treatment for preclinical drug screening and predicting individual response to treatment.

Cancer treatment, particularly radiation therapy and chemotherapy, is often hampered by inherent resistance to cancer cells. Cancer stem cells, in particular, have previously been shown to be more resistant than other cells in a tumor and are thought to repopulate the tumor after therapy. Therefore, it is of utmost importance to develop tools and techniques that can be used to study the resistance mechanisms of cancer stem cells as potential targets for treatment. Organoids (and cancer-derived organoids) are three-dimensional cell clusters resembling tissues derived from tissue or tumor-specific stem cells that mimic in vivo (tumor) characteristics, as well as cell (tumor) heterogeneity. Cancer organoids can further improve the in vitro and in vivo models that

References

1. Bartucci M, Ferrari AC, Kim IY, Ploss A, Yarmush M, et al. (2016) Personalized Medicine Approaches in Prostate Cancer Employing Patient Derived 3D Organoids and Humanized Mice. *Front Cell Dev Biol* 4: 74
2. Aboulkheyr EH, Montazeri L, Aref AR, Vosough M, Baharvand H (2018) Personalized Cancer Medicine: An Organoid Approach. *Trends Biotechnol* 36: 358-371.
3. van de Wetering M, Francies HE, Francis JM, Bounova G, Iorio F, et al. (2015) Prospective derivation of a living organoid biobank of colorectal cancer patients. *Cell* 161: 933-945.
4. Vlachogiannis G, Hedayat S, Vatsiou A, Jamin Y, Fernández Mateos J, et al. (2018) Patient-derived organoids model treatment response of metastatic gastrointestinal cancers. *Science* 359: 920-926.
5. Lee SH, Hu W, Matulay JT, Silva MV, Owczarek TB, et al. (2018) Tumor Evolution and Drug Response in Patient-Derived Organoid Models of Bladder Cancer. *Cell* 173: 515-528