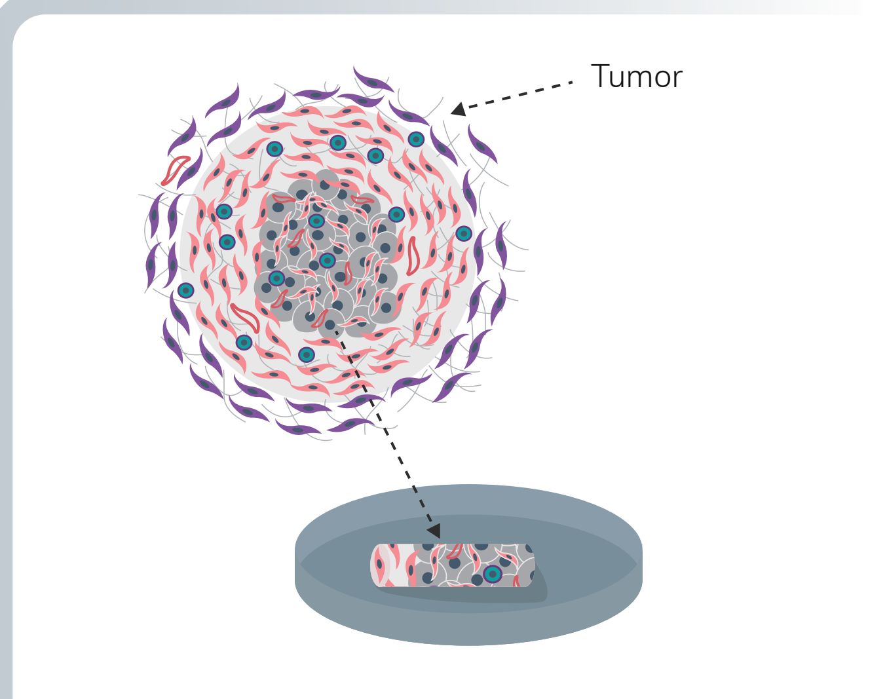
Tissue- vs iPSC-derived tumor organoids for cancer research

Organoid models for cancer research can largely be differentiated into two types: tissue-derived organoids and iPSC-derived organoids. Here, we detail the differences in their preparation, the pros and cons of each type, and provide key tips for their development and implementation.

Workflows for the generation of:

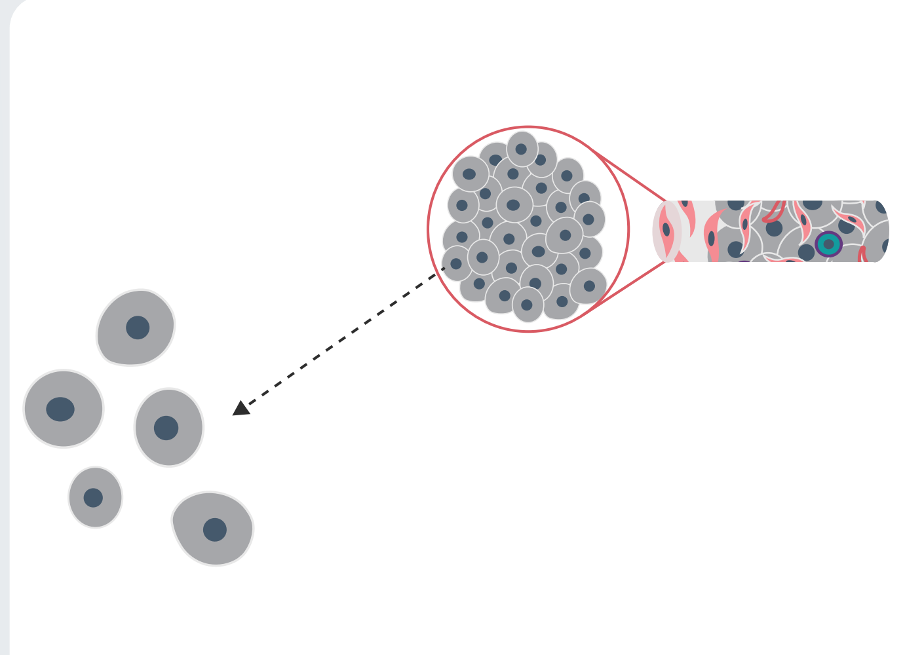
Tissue-derived tumor organoids



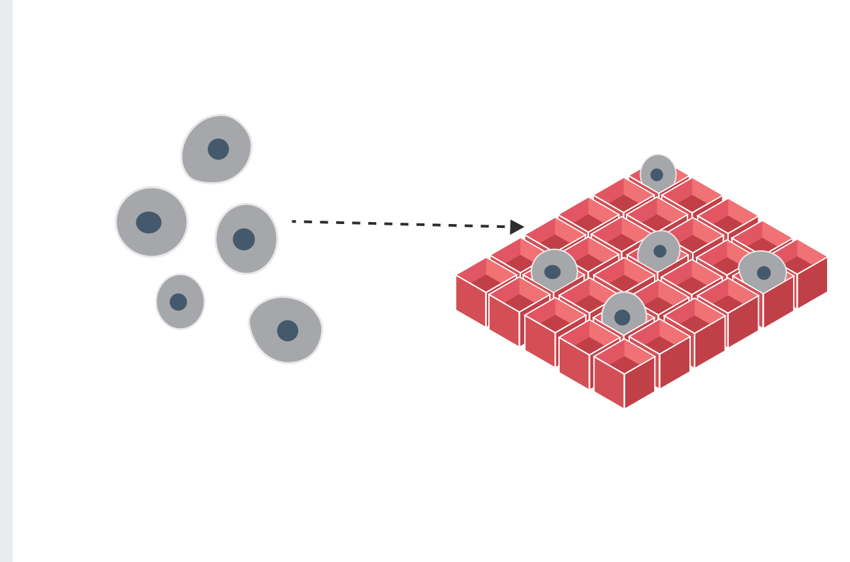
Sourced from a biopsy or surgical aspiration of a tumor.

Sartorius' top tip:

Circulating tumor cell-derived organoids can be derived from circulating tumor cells in the blood and can be used to study metastasis.

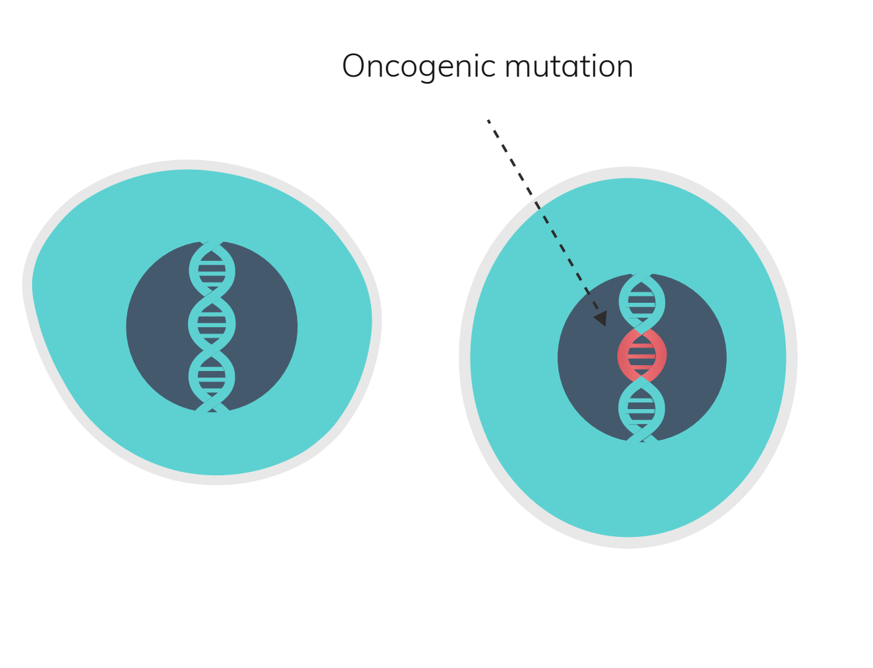


Cancer cells are extracted from tumor biopsies.

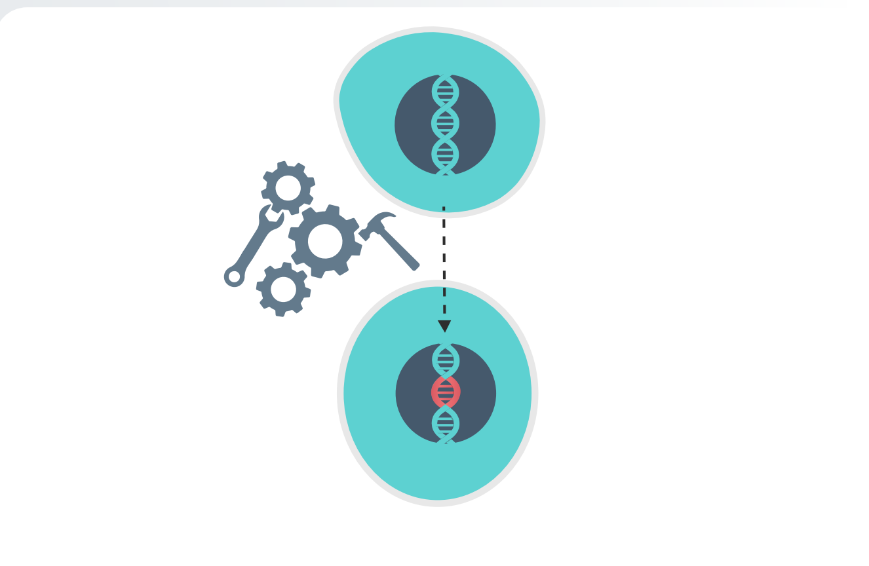


Adult tissue-specific cancer stem cells are seeded into a specialized 3D matrix to grow.

iPSC-derived tumor organoids



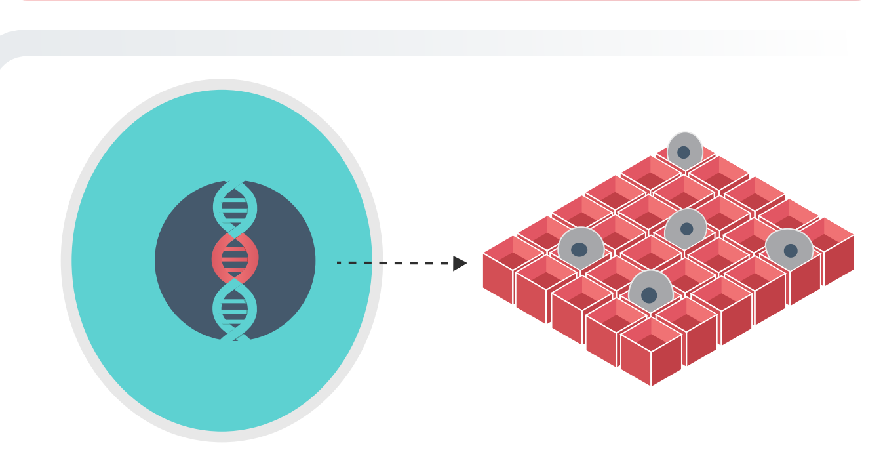
Sourced from healthy cells or cells containing an oncogenic mutation.



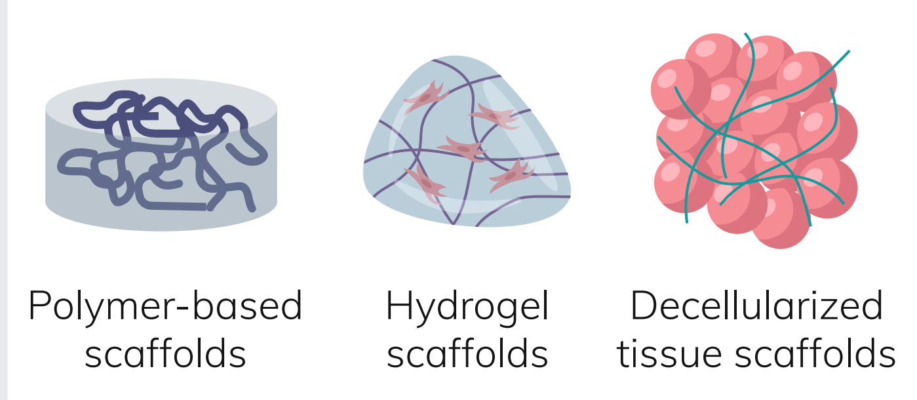
iPSCs from healthy cells are then manipulated with gene editing techniques to contain an oncogenic mutation.

Sartorius' top tip:

This is often a lengthy process that involves multiple technical steps. Make sure you have the right phenotype and function of the iPSC lines moving forward.



Once established, oncogene-carrying iPSCs are then seeded into an extracellular matrix.

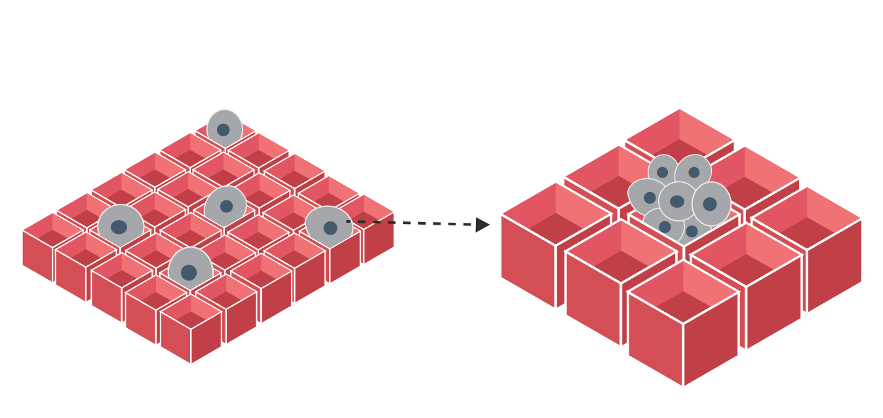


Polymer-based scaffolds

Hydrogel scaffolds

Decellularized tissue scaffolds

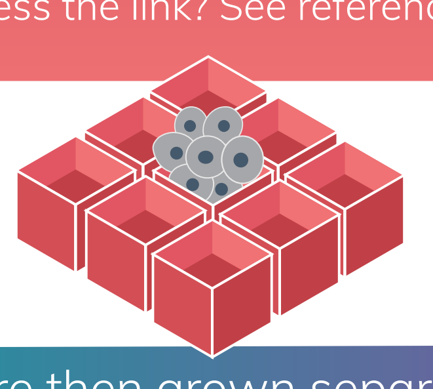
There are three types of 3D matrix materials.



After initial growth, emerging organoids can be extracted from the matrix.

Sartorius' top tip:

Even distribution of nutrients and oxygen throughout organoids optimizes their growth, complexity and longevity. Automated platforms are available to deliver these conditions for organoid growth [can't access the link? See reference 4].



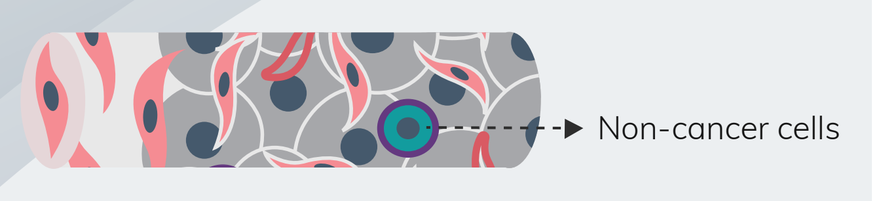
They are then grown separately to avoid them interacting and disturbing each other's growth. This allows the formation of high-density organoids.

Sartorius' top tip:

Required culture conditions vary for different tumor types and are highly specific. Fine tuning the composition of tumor organoid induction medium is the most crucial part of tumor organoid culture.
This table provides a detailed breakdown of the conditions required for 14 different cancer types [table included in reference 5].

Tissue-derived tumor organoids

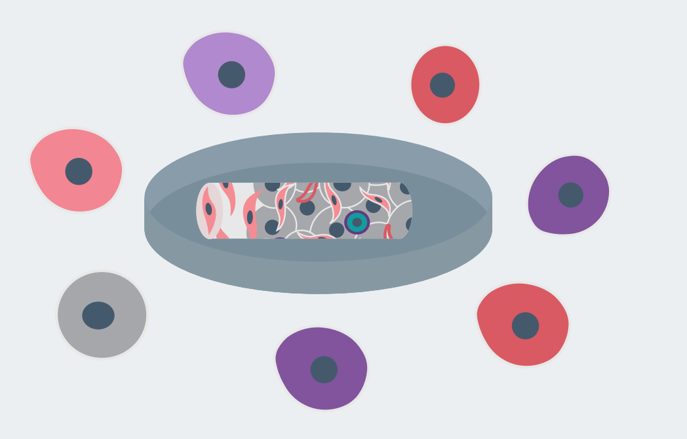
Pros



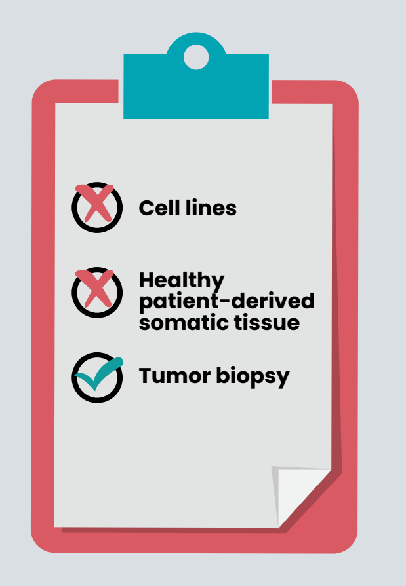
Cells of the tumor microenvironment, including immune cells, can be extracted from the biopsy and added into the 3D matrix, creating highly representative environments.

Simple and well-established method.

Cons



Total heterogeneity and cellular hierarchy of cancer cells is not always present in the initial tumor biopsy, so may not be represented in the resulting organoid.



Requires available tissue samples.

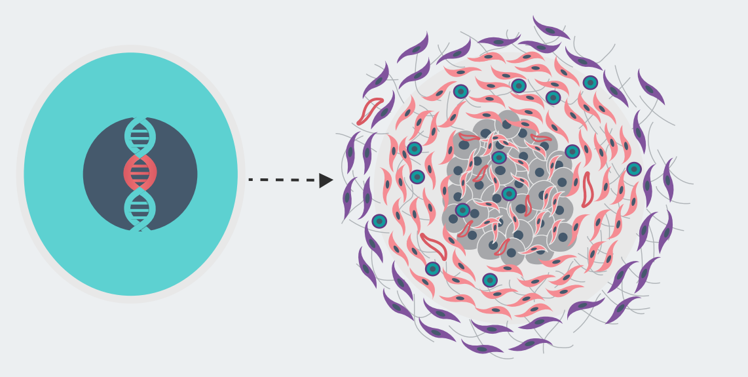
Less genetically stable than iPSC-derived organoids, making them less amenable to long-term cultures and gene editing.

iPSC-derived tumor organoids

Pros

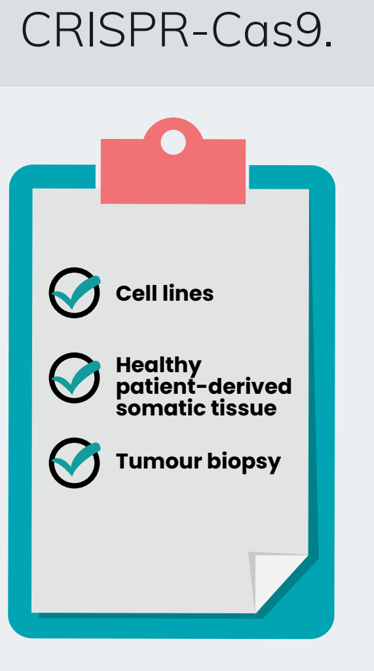
Sartorius' top tip:

Live-cell analysis techniques can be used to automatically and continuously acquire and assess the morphology, size, growth and health of organoids as they develop.

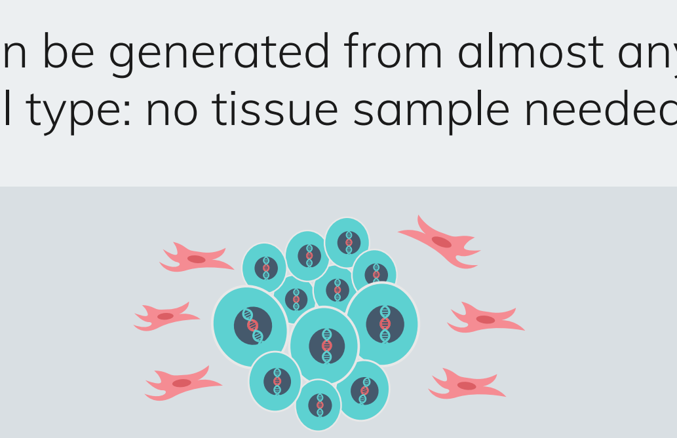


Can observe how an oncogenic mutation leads to the formation of a tumor, which is beneficial for the study of hereditary cancers.

Amenable to early manipulation by gene editing techniques such as CRISPR-Cas9.

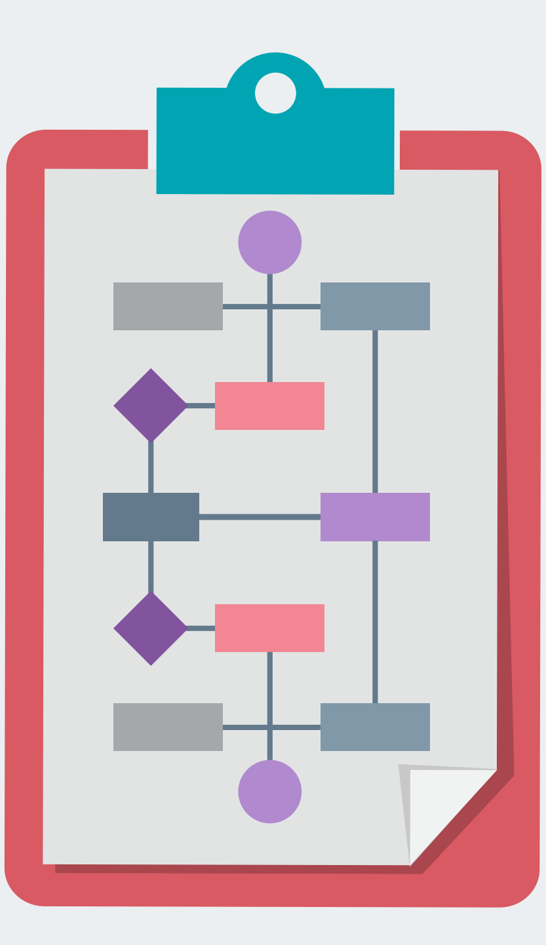


Can be generated from almost any cell type: no tissue sample needed.



Can generate iPSC-derived epithelial cells and obtain patient's mesenchymal stem cells to co-culture with the oncogene containing iPSCs to recapitulate the *in vivo* tumor microenvironment.

Cons



More complex procedure.

Time and cost increases due to complexity.

Sartorius' top tip:

Once fully developed, organoids must be extracted from their matrix quickly for further analysis, i.e. screening or characterization. Automated solutions for scanning, detection and gentle picking and transfer of individual organoids are available to help.

References

[1] Porter R, Murray G, McLean M. Current concepts in tumour-derived organoids. *Br. J. Cancer* 123(8), 1209-1218 (2020).
https://www.nature.com/articles/s41416-020-0993-5

[2] Turhan A, Whang J, Chaker D *et al.* iPSC-derived organoids as therapeutic models in regenerative medicine and oncology. *Front. Med.* 8, 728543 (2021).
https://www.frontiersin.org/articles/10.3389/fmed.2021.728543/full

[3] Abuwatfa W, Pitt W, Husseini. Scaffold-based 3D cell culture models in cancer research. *J. Biomed. Sci.* 31(1), 7 (2024).
https://jbiomedsci.biomedcentral.com/articles/10.1186/s12929-024-00994-y

[4] Hilion K, Mahe M. Redesigning hydrogel geometry for enhanced organoids. *Nat. Methods* 19(11), 1347–1348 (2022).
https://www.nature.com/articles/s41592-022-01656-3

[5] Fang Z, Li P, Du F, Shang L, Li L. The role of organoids in cancer research. *Exp. Hematol. Oncol.* 12(1), 69 (2023).
https://ehoonline.biomedcentral.com/articles/10.1186/s40164-023-00433-y