

# Generation of human breast organoids using primary breast tissue

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## SCOPE OF THE METHOD

<b>The Method relates to</b>	Human health
<b>The Method is situated in</b>	Basic Research
<b>Type of method</b>	In vitro - Ex vivo
<b>This method makes use of</b>	Human derived cells / tissues / organs
<b>Specify the type of cells/tissues/organs</b>	Primary breast tissue

## DESCRIPTION

### Method keywords

Human breast organoids  
primary breast material  
branched morphology  
ECM composition

growth factor supplementation  
tumor initiation  
dynamic developmental stages

### **Scientific area keywords**

Developmental biology  
Oncology  
3D organoid models  
stem cell biology

### **Method description**

The protocol is aimed at developing primary human breast organoids that have a morphology similar to the one observed in the *in vivo* breast. This morphology encompasses a complex network organization composed of interconnected branches that terminate in TDLU-like structures. The organoids are derived from breast tissue reduction mammoplasties (tissue leftovers) by mechanical dissociation, followed by enzymatic digestion of the tissue to obtain small breast tissue fragments that are plated in hydrogels composed of different ECM proteins. By day 5 in culture, these organoids organize into a characteristic stick-shaped organoids. To mimic the menstrual cycle that occurs, on average, every 28 days, these cultures are supplemented with a different medium composition (after day 5) that includes ovarian hormones and other specific growth factors. By combining of the right ECM stiffness, close-to-physiological composition, and growth factor supplementation, breast organoids endowed with a complex morphology can be generated. This *in vitro* model will allow the study of several fundamental questions in the field of human breast biology and concomitantly, the reduction of animal usage.

### **Lab equipment**

### **Method status**

Still in development

History of use

Published in peer reviewed journal

## **PROS, CONS & FUTURE POTENTIAL**

### **Advantages**

- Organoids are derived from primary human breast material, thus these are not transformed (i.e. derived from cell lines that might carry other mutations due to extensive passages).
- They show a complex morphology similar to the *in vivo* human breast.
- The generation of these *in vitro* organoid structures is a relatively fast procedure.
- No need of special equipment.

### **Challenges**

- Healthy human breast tissue donation is a relatively challenging phenomenon.
- Additionally, this protocol is not high throughput and technically challenging.
- Cultures are lengthy (15-20 days).
- Primary material cannot be expanded indefinitely.

### **Modifications**

To increase organoid yield, we are currently experimenting with the following setups.

Primary breast cells have been:

- 1) grown in 2D settings to allow greater/faster expansion and
- 2) immortalized (aiming at the generation of organoids with these immortalized lines).

### **Future & Other applications**

The model can be used to study the impact of breast remodeling on tumor

predisposition. These dual concept of modulating the matrix composition/stiffness and supplementing with different media compositions a growth factor alternation may apply to induce branching also in organoid models of other branched organs.

## REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

### References

Jelena R. Linnemann, Haruko Miura, Lisa K. Meixner, Martin Irmeler, Uwe J. Kloos, Benjamin Hirschi, Harald S. Bartsch, Steffen Sass, Johannes Beckers, Fabian J. Theis, Christian Gabka, Karl Sotlar, Christina H. Scheel; Quantification of regenerative potential in primary human mammary epithelial cells. *Development* 15 September 2015; 142 (18): 3239–3251. doi: <https://doi.org/10.1242/dev.123554>

Sokol, E.S., Miller, D.H., Breggia, A. et al. Growth of human breast tissues from patient cells in 3D hydrogel scaffolds. *Breast Cancer Res* 18, 19 (2016). <https://doi.org/10.1186/s13058-016-0677-5>

### Associated documents

### Links

[Quantification of regenerative potential in primary human mammary epithelial ce...](#)  
[Growth of human breast tissues from patient cells in 3D hydrogel scaffolds](#)

## PARTNERS AND COLLABORATIONS

### Organisation

**Name of the organisation** Katholieke Universiteit Leuven (KUL)

**Department** Oncology

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