Generation of human breast organoids using primary breast tissue

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Organisation

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SCOPE OF THE METHOD

The Method relates to	Human health
The Method is situated in	Basic Research
Type of method	In vitro - Ex vivo
Specify the type of cells/tissues/organs	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.

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

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