Development and characterization of breast cancer organoids as a platform for boosting the preclinical development of novel pharmacological approaches

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Organoids represent in vitro organ-like structures that faithfully recapitulate many features of the corresponding in vivo tissue. In the last years, major progress has been accomplished in establishing three-dimensional culture systems toward stem cell-derived organoids. These amazing organoid constructs bridge the conventional in vitro and in vivo models, providing an outstanding opportunity to investigate the complexities of cancer diseases, ranging from their pathogenesis to the prevention, therapy, or even future organ replacement strategies (1). In this work, we set up an in vitro protocol to develop breast cancer organoids, starting from spontaneous canine breast cancers (CBCO) that represent an attractive model sharing many features with human breast cancers, including subtype classification, genetic profiles, key histological features, and prognostic factors (2,3). The protocol was then optimized for the development of human breast cancer organoids (HBCO) from patient specimens. Both CBCO and HBCO were analyzed monitoring their growth over time and characterized with specific markers such as CD44, CD326, integrin beta 4/CD104 and fibroblast activation protein alpha (FAP) using flow cytometry. In particular, patient derived organoids showed cell types positive to CD44, CD326 and integrin beta 4/CD104, while any positivity to the FAP marker was observed. Furthermore, other specific breast cancer features such as expression of ESR1, PGR, ERBB2, EGFR genes were compared between HBCO and the related patient

tissue specimen by Real-Time PCR. We present in this work the development of a robust 3D in vitro preclinical model of breast cancer for translational research, where organoids from breast cancer tissues can be propagated in vitro, characterized to resemble the features of original tissue, and finally used as a platform for evaluating novel pharmacological approaches.

References

1) 10.3389/fbioe.2021.745943

2) 10.1038/s41598-022-21706-2

3) 10.4048/jbc.2023.26

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