

## Impact of tumor microenvironment on miRNAs expression

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The tumour microenvironment (TME) and miRNAs play an important role in cancer progression, invasion, metastasis, and drug resistance. The relationship between TME and miRNA's expression are still not fully understood. The aim of the present study was to assess the impact of co-culture and matrix property on miRNA expression and drug sensitivity. In this study, a tumour model was created by co-culturing breast cancer cells (MCF-7) and human foreskin fibroblasts (HFF-1) in a matrix with or without a cell adhesion motif Arg-Gly-Asp condition. These cells were bioprinted and grown, the tumor spheroids were then treated with doxorubicin to investigate their response to anticancer drug treatment. From the extracted exosomes, we detected 1,646 out of 2,632 well-known miRNAs. The adhesive motifs in the extracellular matrix (ECM) mimics and the cellular composition of tumour spheroids significantly influenced the types and expression levels of miRNA. The identified miRNAs can serve as effective biomarkers targeting mRNAs, thereby affecting protein expression. These results represent significant advancements in understanding the relationship between TME and miRNAs expression. The findings also provide insights into the mechanisms behind drug sensitivity in the context of co-culture and matrix properties. In conclusion, the study sheds light on the intricate interplay between the tumour microenvironment (TME), miRNAs expression, and drug sensitivity, providing valuable information for future cancer research and potential therapeutic interventions.

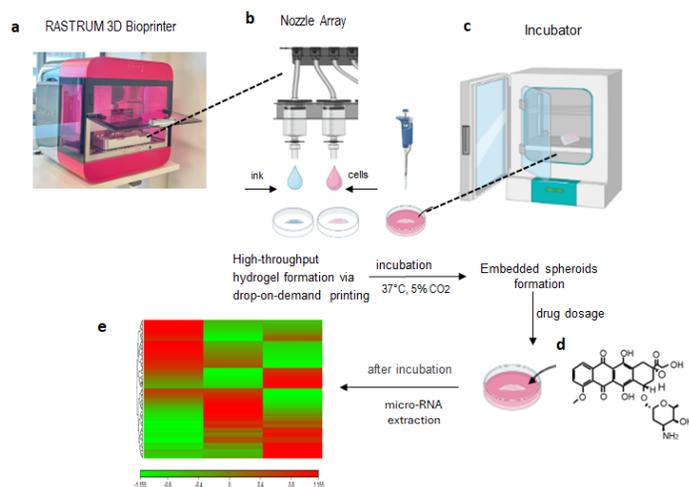


Figure 1. Schematics of embedded spheroids formation and miRNA extraction. a. RASTRUM 3D bioprinter. b. blue bioink drop and pink activator drop contained cells. c. incubation the cell dish. d. drug dosage the spheroids. e. micro-RNA extraction and analysis.