Ovarian cancer immunotherapy on-a-chip: a 3D preclinical model to test novel mi-RNA based therapies

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Ovarian cancer (OCa) is a highly aggressive tumor of women reproductive system. The immunosuppressant microenvironment is the main culprit of drug inefficacy and metastasis formation. Mounting evidences suggest that mi-RNAs are promising immunotherapy tools. miR-200c is a master regulator of OC-related genes that inhibits cancer growth and enhances tumor immunogenicity. Despite the countless novel molecules proposed as therapeutic tools, most drugs that overcome preclinical studies fail to succeed clinical trials. In this context, the development of human in vitro models that recapitulate the 3-dimensionality of tumor microenvironment (TME) is an urgent need that tissue engineering is trying to meet in order to bridge the gap between preclinical and clinical research. We hypothesise that an OCa tissue can be biofabricated to replicate in 3D the crosstalk of cancer and immune cells, and explore the role of miR-200c on cancer progression and metastasis initiation. We harnessed microfluidics technologies to create a functional ovarian cancer tissue in contact with a phantom vessel where immune cells can circulate. The model incorporates important physiological features of their interaction, among which immune cell infiltration and cancer cell invasion across a porous membrane that simulates the endothelial layer. We used live microscopy, viability assays and immunofluorescence on samples treated with miR-200c expression vector and untreated samples. Preliminary results showed that miR-200c hinders tumor growth, dysregulate actin organization, and reduces SOX2, a cancer stemness marker. Once included T-cells in the model, we observed that immunity activity was significantly higher in presence of miR200c, causing cancer cell death. The proposed platform offers a reliable surrogate of human OCa to reveal unclear molecular mechanisms regulating cancer progression and study immunotherapy treatments. Remarkably, the high potential of this study resides in the outstanding versatility of the model, suitable for disease studies, drug screening and delivery, and adaptable to other tumors.