MODELING BREAST CANCER PROGRESSION AND DRUG RESPONSIVENESS ON A BIOMIMETIC SCAFFOLD

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Abstract

Engineered *in vitro* models have lead to new insight into the pathogenesis, the prognosis and the treatment of human diseases. This is particularly noticeable in the field of oncology, where the behavior of cancer cells is a function of the environmental context where tumors arise and develop. For this reason a number of 3D systems mimicking specific physico-chemical or biological elements of the tumor microenvironment have been developed, and are becoming increasingly attractive to cancer research. Here we developed a biomimetic 3D cancer model based on macroporous type I collagen scaffolds **(Figure 1 a-d)** and studied within this system cell lines of two breast tumor subtypes that have opposite clinical outcomes: MCF-7 that belong to the luminal A subtype often connected to indolent disease and a better prognosis, and high-grade aggressive basal-like MDA-MB-231. We investigated their growth dynamics, molecular phenotypes and drug responsiveness performing multiple comparisons with standard monolayer cultures, animal models and patient samples. We demonstrated that breast cancer cells within this system: i) display *in vivo*-like growth dynamics **(Figure 1e)**, ii) activated pathological hypoxic and glycolitic states, iii)

showed increased drug resistance **(Figure 1f)**; iv) display a molecular profile closely matching that of *in vivo* tumors. Through a time-dependent investigation of these phenotypes and behavior we provided a comprehensive description of the mechanisms and signals that contribute to the tumor evolution and to the emergence of drug resistance. This system may provides a key enabling technology for disease progression modeling, biomarker detection, tumor invasiveness assay and drug efficacy screenings.

Figure 1