An Extracellular Matrix-like hydroscaffold for 3D cell culture to bring the gap between in vitro & in vivo: focus on cancer models

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In oncology, 97% of drug candidates fail in clinical trials, pointing a lack of relevance of preclinical models. Indeed, human *in vitro* models don't take into account the microenvironment, in particular the Extracellular Matrix (ECM), although it is modified in tumors and strongly linked to cancer initiation, progression, propagation, and drug resistance.

BIOMIMESYS® is a hyaluronic acid-based matrix bio-functionalized with structural and adhesion molecules of ECM, providing a relevant microenvironment for *in vitro* 3D cell culture. This ECM-like hydroscaffold combines the advantages of solid scaffolds (porosity, structure) and hydrogels (cell-matrix interactions). It is chemically defined and ready-to-used in multi-well plates, thus it can be used for High Content Screening (HCS). Moreover, its composition and stiffness can be modified to reproduce the organ-specificity of the ECM, or to mimic a pathological microenvironment like in cancer.

Cancer cells can be advantageously grown in BIOMIMESYS® for several weeks. The EC50 curve of cancer cells exposed to an anti-cancerous drug showed a closer *in vitro/in vivo* correlation in BIOMIMESYS® than in 2D*.* We also demonstrated that BIOMIMESYS® allows to reproduce *in vitro* the behavior of cancerous cells *in vivo*, like mutation effects and metastasis propagation. These results showed that the matricial microenvironment modifies the behavior of cancerous cells *in vitro* and should be considered carefully in drug discovery. This hydroscaffold offers a good predictability and is adapted to HCS; it represents a powerful tool to better select drug candidates and to increase the success rate in clinical trials.