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Microfabricated Tepui: probing into cancer invasion, metastasis and evolution in a 3D environment[1]

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Cancer metastasis and chemotherapeutic resistance are the major reasons why cancer remains recalcitrant to long-term therapy. We are interested to know: 1. How cancer cells invade tissues and metastasize in a 3D spatial environment? 2. How cancer cells evolve resistance to chemotherapeutic therapy? Answering these fundamental questions will require spatially propagating cancer cells in a 3D *in vitro* micro environment with dynamically controlled chemical stress. Here we attempt to realize this micro environment with a three-dimentional topology on a micro-chip which consist of isolated highlands (Tepui) and deep lower lands. Cancer cells are patterned in the lower lands and their spatial invasion to the mesas of Tepui is observed continuously with a microscope. Experiments have demonstrated that the cell invasion potential is time dependent, which is not only determined by cell motility, but also cell number and spatial stress. Quantitative analysis shows that the invasion rate fits logistic equation. Further more, we have also imbedded collagen based Extracellular Matrix (ECM) inside these structures and established a robust chemical gradient in a vertical space. With merit of real-time confocal imaging, cell propagation, metastasis and evolution in the 3D environment are studied with time as a model for cell behavior inside tissues.

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