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Three-dimensional tissue culture based on magnetic cell levitation

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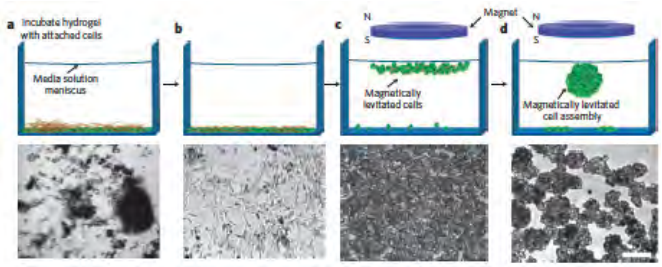
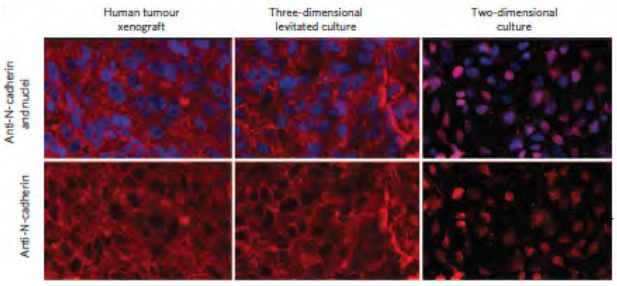
Abstract: Cell culture is an essential tool in drug discovery, tissue engineering and stem cell research. Conventional tissue culture produces two-dimensional cell growth with gene expression, signalling and morphology that can be different from those found in vivo, and this compromises its clinical relevance. Here, we report a three-dimensional tissue culture based on magnetic levitation of cells in the presence of a hydrogel consisting of gold, magnetic iron oxide nanoparticles and filamentous bacteriophage. By spatially controlling the magnetic field, the geometry of the cell mass can be manipulated, and multicellular clustering of different cell types in co-culture can be achieved.



Schematic of magnetic levitation. Cells are incubated with the nanoparticles overnight (a), to which they bind (b). The next day, the cells are detached from their substrate and levitated by applying a magnetic force above the plate (c). Over time, the cells aggregate, interact, and proliferate to form larger 3D cultures. Micrographs (bottom row) show progression of cells from monolayer to 3D magnetically levitated culture within 12 hours after levitation. Scale bar = 30 μm.



2D v. 3D culture: Immunohistochemistry of a tumor xenograft (left), and 3D magnetically levitated cultures (center) and 2D cultures (right) of human glioblastomas for N-cadherin (red). Note the similarity in structure and stain intensity between the 3D culture and the explant, but not with the 2D culture. Scale bar = 10 μm.

Magnetically levitated human glioblastoma cells showed similar protein expression profiles to those observed in human tumour xenografts. Taken together, these results indicate that levitated three-dimensional culture with magnetized phage-based hydrogels more closely recapitulates in vivo protein expression and may be more feasible for long-term multicellular studies.

- **Magnetic levitation can be used to rapidly create 3D cultures**
- **Magnetically levitated 3D cultures approximate *in vivo* cell-cell and cell-ECM interactions and organization**