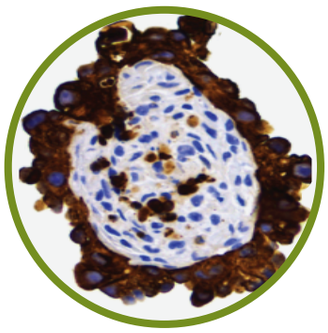
insphero
Biomimetic Microtissue Technology

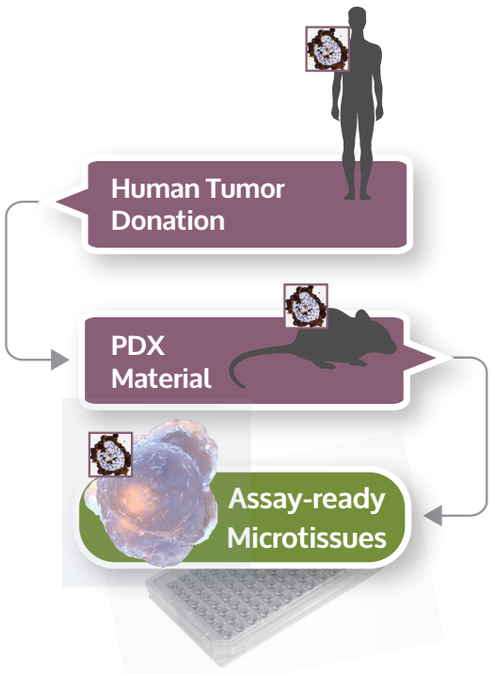


Cytokeratin staining of PDX-derived tumor model of Lung Adenocarcinoma LXFA 1647 in co-culture with NhDF

3D InSight™ **PDX Microtissues**

3D InSight™ Tumor Microtissues from Patient-Derived Xenografts (PDX) are custom assay-ready 3D *in vitro* tumor models engineered to reflect complex tumor biology without the use of artificial matrices. Ideal for early stage cancer drug efficacy testing and screening appliciations, these advanced cancer models help bridge the gap between preclinical animal studies and translation of outcome into clinical applications, and enable oncologists to quickly identify the most promising mouse PDX models for subsequent *in vivo* testing.

- **Screen and profile drug candidates** using cost-effective PDX-derived, 3D *in vitro* tumor models that recapitulate the heterogeneity of tumor microenvironments (Figure 1).
- **Conduct assays for biomarker discovery and disease-oriented drug development** using relevant 3D models chosen for genetic alteration or tumor type.
- **Preselect agents of interest for further preclinical development** with a oncology drug discovery tool designed to reduce research costs and optimize human tumor material.



An *in vitro* 3D model with *in vivo-like* heterogeneity

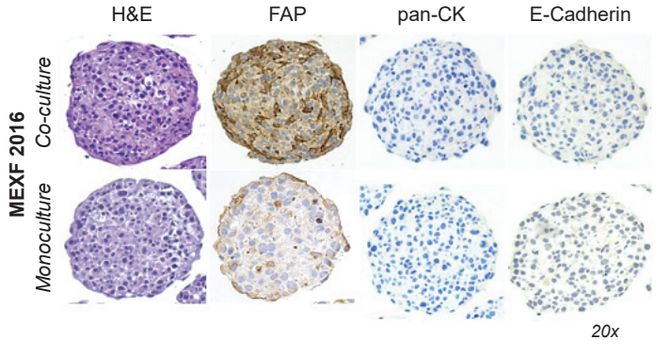


Figure 1. 3D InSight™ Tumor Microtissue from Melanoma PDX. *IHC markers: pan-CK and E-Cadherin (epithelial cells), FAP (fibroblasts). PDX cell suspension from MEXF 2106 generated spheroids either with (top, co-culture panel) or without additional fibroblasts (bottom, monoculture panel). Co-cultures show an heterogenous distribution of fibroblasts and melanoma tumor cells within the entire cell structure.*

Amplify the power of PDX models **www.insphero.com/services**

PDX-derived 3D InSight™ Tumor Microtissue Characterization Data

Our PDX-derived tumor models can be used to screen cytotoxic drugs or targeted cancer therapies as single agents or as combinatorial drugs regimens. MIcrotissues are validated through correlations with parental tumors for histological features retainment and corroborating drug response with *in vivo* data (Figure 2). To evaluate the impact of molecular targeted drugs on cell proliferation, PDX-derived 3D microtissues were exposed to Vemurafenib which was assayed at a range of nine drug concentrations with 2-fold dilution series over 10 days (Figure 3).

Histological correlation: *in vivo* to *in vitro*

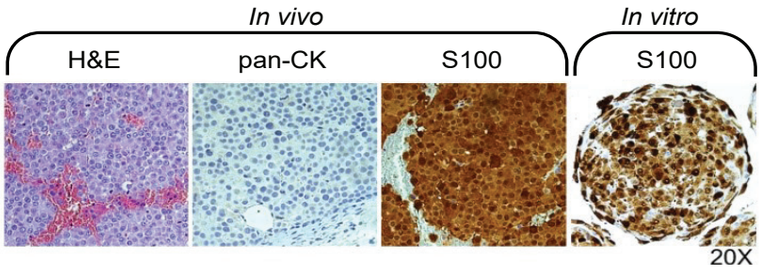


Figure 2: Histological correlation of in vivo and ex vivo tumors. *Immunohistochemistry assessment of 3D microtumors confirmed the resemblance with their respective PDX tumor models. Here,* in vitro *and* in vivo *models are negative for all epithelial markers and positive for the melanoma-specific marker S100.*

Drug sensitivity testing: *in vitro* versus *in vivo*

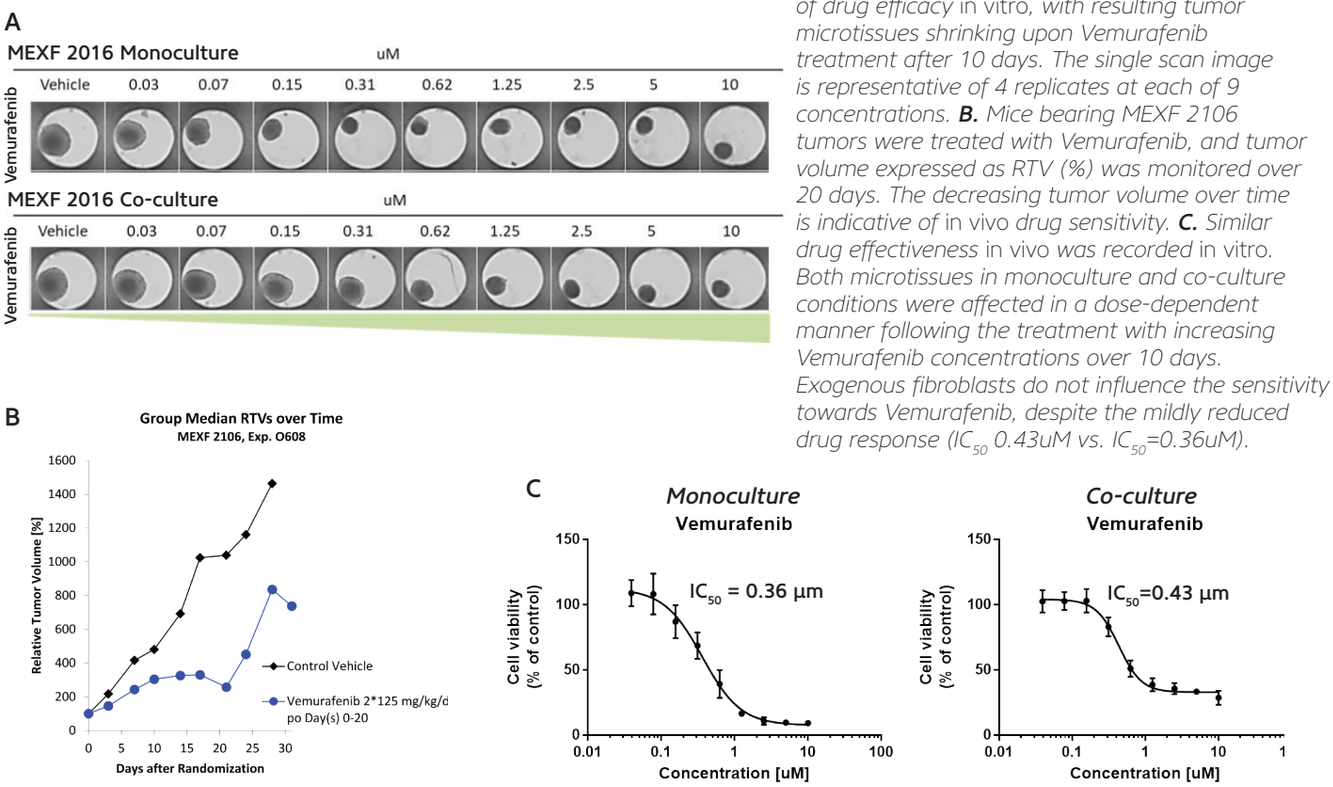


Figure 3: Drug Sensitivity Testing. A. *Visualization of drug efficacy* in vitro, *with resulting tumor microtissues shrinking upon Vemurafenib treatment after 10 days. The single scan image is representative of 4 replicates at each of 9 concentrations.* ***B.*** *Mice bearing MEXF 2106 tumors were treated with Vemurafenib, and tumor volume expressed as RTV (%) was monitored over 20 days. The decreasing tumor volume over time is indicative of* in vivo *drug sensitivity.* ***C.*** *Similar drug effectiveness* in vivo *was recorded* in vitro. *Both microtissues in monoculture and co-culture conditions were affected in a dose-dependent manner following the treatment with increasing Vemurafenib concentrations over 10 days. Exogenous fibroblasts do not influence the sensitivity towards Vemurafenib, despite the mildly reduced drug response (IC_{50} 0.43uM vs. IC_{50}=0.36uM).*

Visit insphero.com to learn more about our oncology drug discovery platform and custom tumor model development service.

Catalog #	Description
SP-01-046-01	3D InSight™ Custom PDX Tumor Microtissue Development (1 model)

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