Development of a Standardized Drug-Testing Platform Using Human Primary Tumor Samples


Abstract:
In the past few years, various groups have demonstrated the role of tumor heterogeneity and the impacts of drug resistance in solid tumor and hematopoietic malignancies. A major limitation of the current drug testing platform is that it relies on limited human primary cell line samples, which are not representative of the entire population. To address this, we have developed a standardized drug-testing platform that is available to the research community. An array of different in vitro (i.e. 2D and 3D) cell culture models was developed for human primary solid tumors (similar platform was developed for blood/bone marrow malignancies), as well as high throughput screening (HTS) methods to identify drug response profiles. The platform utilizes primary tumor cell lines, isolated from human primary solid tumors, and is designed to identify drug response profiles, drug resistance, drug interaction, drug combination, and drug targets. The platform, which is currently being explored with our human primary samples, both human primary cells, both human primary and hematopoietic malignancies.

Characterization of dissociated solid tumor cells

Flow Cytometric Analysis of 25 Post-thawed Human Primary Solid Tumor Specimens

Examples of in vitro compound testing

6-Day Viability & Flow Cytometric Study

Summary:
- We developed an optimized, standardized platform for ordering, collecting, shipping, processing, cryopreserving and analyzing human primary solid tumors (similar platform was developed for blood/bone marrow malignancies... not shown).
- Tested human primary solid tumors contain 10-80% EpCAM+ epithelial cells, 1-30% hematopoietic cells, 0-20% endothelial cells and 0.1-12% putative cancer stem cells.
- The post-thaw viability of dissociated solid tumor cells is typically >70%.
- Most tested human primary solid tumor cells remain viable for 6 days in culture and some samples show signs of proliferation.
- 3 of 8 tested patient samples demonstrated altered proliferation when cells were plated on tissue culture treated plastic compared to Matrigel coated plates; this change in cell growth was most evident from day 4-6.
- The percentage of EpCAM+ cells on tested lung and ovarian cancer specimens decreases by 0-20% following 6 days in culture.
- Cells cultured for 4 days and treated with staurosporine for 3 days, show similar drug responses when cells are plated on tissue culture treated plastic or Matrigel coated plates. When the same study was carried out with cells embedded in Matrigel (3D assay), 2 of 3 samples showed slight drug resistance at higher doses while 1 of 3 samples showed complete drug resistance at all doses.