Surgical resection is rarely an option for small cell lung cancer (SCLC) patients as the majority present with extensive disease at diagnosis. This scarcity of patient samples suitable for research presents a significant road block for the development of SCLC targeted therapeutics. To address the problem of tissue scarcity, we have developed a method for the isolation and expansion of cancer stem cells (CSC) and circulating tumor cells (CTC) from primary tissues and blood of SCLC patients using the 3DKUBE® perfusion microbioreactor. We have established a label-free, combined chemical and functional selection method for the isolation that does not rely upon the bias imposed by marker-based selection. These cells will be utilized to generate 3D microtumors to accurately predict SCLC drug response in vitro, a determination that is not accurately performed in conventional 2D cell culture and is inhibited by both cost and time in patient-derived xenografts (PDX).

**Methods**

**In vitro 3D CSC Expansion**

**CSC Validation**

**EV3D Drug Response Profiling**

**Conclusions**

- KIYATEC’s CSC media is optimized to enhance spheroid formation, growth and metabolism in SCLC cell lines, PDX and patient samples.
- Label-free selection method avoids inherent bias of marker-based CSC identification and selection protocols.
- KIYATEC 3DKUBE® expanded CSCs maintain drug resistance, clonogenicity and canonical CSC marker expression.
- Ex-vivo expansion of SCLC CSC provides more accurate drug predictions compared to 2D cultured SCLC cell lines and cost-savings compared PDX samples.
- The design and use of the 3DKUBE® is covered by patents 8,865,460 and 9,575,055.
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