PRESS RELEASE
Tuesday, March 21, 2017

Three KIYATEC abstracts accepted for poster presentations during 2017 AACR Conference in Washington D.C.

KIYATEC, a private company prioritizing accurate ex vivo prediction of patients' response to drug treatment, received acceptance of three posters for presentations during the upcoming AACR conference.

GREENVILLE, South Carolina, March 21, 2017– KIYATEC Inc. is pleased to announce that three abstracts have been accepted by the committee at the American Association for Cancer Research (www.aacr.org). KIYATEC scientific and business development staff will be in attendance at the conference. In addition to the poster presentations, also **KIYATEC will be exhibiting at Booth 1556**. Stop by to learn more about our 10+ years of 3D cell culture experience and the latest 3D co-culture model development projects focused on immuno-oncology applications.

Abstract #1923: Paired isolation and expansion of CSC and CTC from primary small cell lung cancer patient tissue and blood using the 3DKUBE® bioreactor platform
Monday Apr 13, 2017 8:00 AM - 12:00 PM
Location: Section 41 / Poster 24
Session Title: Normal and Neoplastic Stem Cells
Authors: Melissa Millard1, Alina Lotstein1, Lillia Holmes1, David Schammel2, Ki Chung3, Jeff Edenfield3, Hal E. Crosswell1, Tessa DesRochers1. 1KIYATEC, Inc., Greenville, SC; 2Pathology Consultants, Greenville, SC; 3GHS, Greenville, SC

Abstract: 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 of CSCs from SCLC samples, solid tumor as well as blood, that does not rely upon the bias imposed by marker-based selection. Cells enriched in this manner were further purified and expanded under optimized conditions (growth factors, ECM, scaffolding and oxygen tension) within the 3DKUBE™ perfusion microbioreactor. These isolated and expanded CSCs have maintained resistance to cisplatin and etoposide, stabilized the expression of traditional CSC markers, and been validated in vitro through serial spheroid formation assays. These CSCs are currently being characterized and compared to parental tissue through correlative genomic and phenomic analysis and validated through in vivo tumorigenesis models. 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)

Abstract #4834: 3D modeling of immune cell interactions in breast cancer and prediction of immunotherapy response

Tuesday, Apr 4, 2017, 1:00 PM - 5:00 PM
Location: Section 39 / Poster 24
Session Title: Cell Culture and Animal Models of Cancer 5
Authors: Qi Guo1, Stephen Shuford1, Brian McKinley2, Mary Rippon2, Wendy Cornett2, Mark O'Rourke2, David Schammel3, Jeff Edenfield2, David L. Kaplan4, Hal E. Crosswell1, Teresa Desrochers1. 1KIYATEC, Inc., Greenville, SC; 2GHS, Greenville, SC; 3Upstate Pathology, Greenville, SC; 4Tufts University, Boston, MA

Abstract: While breast cancer has an overall 5-year survival rate of 89%, the rate for patients with stage 4 metastatic disease is only 26%. Immunotherapies have the potential to improve the prognosis for these patients while also providing better treatment options for all breast cancer patients since they have fewer side effects enabling longer treatment times and the use of combination therapies and reduced chances of developing resistance. Currently these treatments are tested in standard 2D cell cultures that are inaccurate in mimicking in vivo drug response or animal models where the immune system differs from humans in numerous ways including T-cell subsets, cytokine receptors, and costimulatory molecule expression. We have developed 3D models of human breast cancer that span the subtypes, ER+, HER2+, and triple negative, incorporate numerous stromal cell types, fibroblasts and adipocytes, and include different immune cells, macrophages and T-cells under either static or perfusion culture systems. These models have been used to examine how tumor cells influence macrophage differentiation using undifferentiated peripheral blood mononuclear cells (PBMCs), how M1 and M2 macrophages influence tumor cell survival and proliferation, how the combination of these cell types influence cytokine secretion, and how the microenvironment affects macrophage invasion. We have also used these complex models to examine response of tumor cells and T-cells to checkpoint inhibitors through standard viability assays and flow cytometry. These models have several potential uses which include the ability to quickly answer whether a particular immunotherapy agent is effective for that particular patient-specific manner and to screen potential novel immunotherapeutic candidates and/or combinations prior to clinical use.

Abstract #4837: Development of an in vitro 3D glioblastoma model system for patient-specific drug response profiling

Tuesday, Apr 4, 2017, 1:00 PM - 5:00 PM
Location: Section 39 / Poster 27
Session Title: Cell Culture and Animal Models of Cancer 5
Authors: Teresa DesRochers1, Ashley Clark1, Lauren O'Donnell1, Qi Guo1, Lillia Holmes1, Lacey Dobrolecki2, Michael Lewis2, David Schammel3, Jeff Edenfield4, Charles Kanos4, Fred Nelson4, Steve Gardner4, Michael Lynn4, Philip Hodge4, Christopher Corless5, Paul Clark6, Hal E. Crosswell1, John Kuo6. 1KIYATEC, Inc., Greenville, SC; 2StemMed Inc, Houston, TX; 3Upstate Pathology, Greenville, SC; 4GHS, Greenville, SC; 5OHSU, Portland, OR; 6U. Wisconsin, Madison, WI

Abstract: Glioblastoma (GBM) has a median survival of less than 2 years due to intra-tumoral and inter-patient heterogeneity, diffuse infiltration of adjacent brain tissue, and absence of effective therapies. Development of more efficacious therapies will require better GBM models for the testing and identification of novel agents; traditional 2D cell culture lacks biologic and clinical fidelity and orthotopic xenograft models are costly, low throughput, and time consuming. We have developed a complex, patient-specific 3D cultured GBM model to assay drug response that combines high-throughput drug response determination with neurosphere formation and next-generation sequencing (NGS). Neurosphere formation and the

presence/quality of glioblastoma stem cells (GSCs) has been validate through limited dilution growth in vivo. Our 3D model system has been validated against the primary patient GBM tissue and/or patient-derived xenografts (PDX) and consists of histology, epigenetic and mRNA expression analysis, and comparison of in vivo drug response. This strategy enabled examination of MGMT methylation in relation to temozolomide response, and possible actionable genetic mutations with candidate targeted therapies. Using our 3D model, we have observed EGFR-amplified GBM sensitivity to the EGFR inhibitor afatanib, and PTEN mutant GBM sensitivity to dual PI3K/mTOR inhibitor dactolisib. These data suggest validation of clinical and molecular correlation with this new in vitro, patient-derived 3D GBM model for drug response profiling. Our data supports the further development and use of complex 3D models, neurosphere formation, and NGS profiling for patient-specific GBM analysis. This model system is currently being considered for preclinical assessment of novel therapies and may be a useful adjunct in future precision medicine applications to improve patient outcomes.

About KIYATEC Inc.

KIYATEC prioritizes accurate ex vivo prediction of patients' response to drug treatment, with a focus on data correlation to human clinical outcomes. The company creates and utilizes live phenotypic 3D cell-based models for drug response profiling and applies them to generate information relevant to preclinical testing, clinical trials and clinical diagnostics applications. By accurately predicting patient drug response without ever exposing actual patients to drugs, KIYATEC will create informed drug selection that minimizes clinical trials' failures and maximizes patient outcomes in the clinic. For more information, please visit www.kiyatec.com or follow KIYATEC on Twitter (@KIYATEC).