LICENSING OPPORTUNITY

Diagnostic for Predicting Response to Therapies in Multiple Myeloma

Multiple Myeloma (MM) is an incurable but treatable cancer, where patients are prescribed a combination of drugs in response to successive relapses. Our novel digital imaging algorithm diagnostic uses continuous live brightfield microscopy to assess patient derived MM cells' response to therapeutic agents in varying combinations and concentrations at multiple time points to support physician's choice of therapy to produce the longest duration of remission.

COMMERCIAL OPPORTUNITY

- NIH's SEER reported ***32,720*** new cases, ***12,830*** deaths and ***141,000*** individuals living with Multiple Myeloma (MM) in the US in 2020. In the current standard of care, clinicians have seven drugs, and nine possible 3-4-drug combination regimens, to choose from in the first round of treatment. Based on overall progression free survival in MM, the average patient relapses once every two years, upon which a bone marrow biopsy is requested along with diagnostic and prognostic tests. Upon relapse, the number of drugs rises to sixteen, and therapeutic options continue to increase for relapsed patients who are sent to clinical trials. Effective treatment regimens may result in superior clinical outcomes because ineffective therapies may allow tumors to grow and evolve, as well as burdening the patients with unnecessary toxicities and financial cost of ineffective drugs. Unfortunately, there are no predictive tests available for choice of therapy in MM.

- The market for drug response diagnostics is attractive as evidenced by the products offered by Foundation Medicine and Quest Diagnostics.

- Moffitt's technology can test between 32 and 127 drugs/combinations over a range of concentrations from a standard of care biopsy, with results generated in under a week to predict therapeutic agent(s) (or combination) to maximize disease remission. Additionally, this technology has been used, in collaboration with partners in Pharmaceutical Industry, to conduct ***virtual*** clinical trials, where patient-derived samples were screened with experimental drugs, in order to assess clinical efficacy, as well as identify biomarkers for response. When validated in an observational predictive clinical study from 23 patients, it predicted treatment responses and accurately classified them as per International Myeloma Working Group (IMWG) response stratification.

TECHNOLOGY

Multiple Myeloma patient bone marrow aspirates were used to reconstruct the tumor and bone marrow microenvironment (primary MM cells, and stroma, and extracellular matrix and patient-derived growth factors) in 384- or 1,536 multi-well plates. Between 32 and 127 drug combinations, respectively, were tested in replicates at five different concentrations, covering the physiologically prescribed doses of each drug. A novel, dye-free and non-destructive, digital imaging analysis algorithm continuously tracked changes in cell viability (based on membrane motion of live MM cells) for up to 144 hours, with bright field images of each well taken at 30-minute intervals. Additionally, the algorithm captures the two-way synergistic effect in two-drug combinations to estimate a clinical response, as reported in a retrospective study in 203 MM patients. When validated in an observational predictive clinical study, the algorithm predicted treatment responses for 23 patients from the *ex vivo* AUC values and accurately categorized them into three groups: Very good partial response or complete response (VGPR/CR), Minimal or partial response (MR/PR), and stable or progressive disease (SD/PD). The AUC of the combination therapy was found to be an excellent classifier between CR/VGPR and MR/PR/SD/PD (area under the ROC = 0.9804, p-value= 0.0006).

PUBLICATION/PATENT

PCT applications were filed for Drs. Ariosto Silva, *et al.* 2013 & 2019
Khin et al., *Cancer Res 2014*; Silva et al., *Cancer Res 2017*; Sudalagunta et al., *EBioMedicine 2020*

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