Differential drug sensitivity patterns in myelodysplastic syndrome patients are recapitulated by ex vivo drug response profiling

A. Aleshin1, B. C. Medeiros1, S. Kamble1, D. Heiser2, M. Santaguida3, P. Quinzio2, P. L. Greenberg1;
(1) Stanford Univ., Stanford, CA, (2) Notable Labs, San Francisco, CA

ABSTRACT

Myelodysplastic syndromes (MDS) are a collection of clonal diseases of dysfunctional hematopoietic stem cells, characterized by ineffective hematopoiesis, cytopenia, and dysplasia. Limited conventional treatment options exist for these patients, with hypomethylating agents remaining the standard of care for higher-risk MDS patients. Drug sensitivity and resistance testing on myelodysplastic syndromes (MDS) samples should provide important functional information to guide actionable target and biomarker discovery.

METHODS

Blood or bone marrow samples were red blood cell lysed upon arrival, counted and resuspended at the appropriate concentration in proprietary serum free media with hypomethylating agents remaining the standard of care for higher-risk MDS patients. Drug sensitivity and resistance testing on myelodysplastic syndromes (MDS) samples should provide important functional information to guide actionable target and biomarker discovery.

RESULTS

Blood was treated with drugs in triplicate for 48 hours and measured by an Intellicyt iQue Plus flow cytometer. The samples were then plated in 384 well microtiter plates and treated with drugs in triplicate for 72 hours. The cells were then stained with appropriate antibodies and analyzed.

CONCLUSIONS

2. Demonstrate temporal evolution of ex vivo drug sensitivity which correlates with clinical responses.
3. Demonstrate utility of ex vivo approach to analysis of primary MDS PB and BM biopsies specimens.
4. Identify 3 distinct subgroups of MDS characterized by differential ex vivo responses to HDAC, PARP, and HMA agents.

REFERENCES