In vitro Chemo Resistance Profiles of Circulating Glial Cells Replicate Chemo Characteristics of Tumor Tissue

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Conflict of Interest :
Datar Cancer Genetics offers commercial services in the area of Oncology.

BACKGROUND

Poor survival in high-grade glioma patients is due to onset of resistance towards the limited systemic treatment option. Apart from MGMT promoter methylation for Temozolomide, there are no biomarkers for prediction of drug resistance. In vitro chemoresistance profiling (CRP) of viable tumor cells can convey potential efficacy of treatment agents. However, biopsies to obtain viable tumor cells are associated with risks of morbidity and mortality. CRP of Circulating Glial Cells (CGCs) from peripheral blood is restricted by low yield.

APPROACH

We obtained 15 mL peripheral blood from patients (n = 9) with Glioblastoma. In 2 patients, viable tumor cells were available from a recent biopsy. CGCs were harvested from peripheral blood using an epigenetically active process that induces lethality in normal cells (with functional apoptotic machinery) and confers survival privilege on apoptosis resistant cells of tumorigenic origin. CRP of viable CGCs and TDCs was performed against a panel of cytotoxic anticancer agents including Temozolomide.

DEMOGRAPHICS OF STUDY COHORT

Gender	#
Male	6
Female	3
Total	9

Age	(Years)
Minimum	35
Maximum	76
Median	55

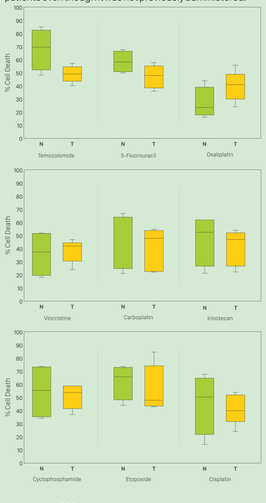
Therapy	Number
Naïve	2
Pretreated	7

Prior Therapies	Number
Systemic	5
Surgery	7
Radiation	4

Systemic Agents	Number
Temozolomide	5
Irinotecan	1
Other	-

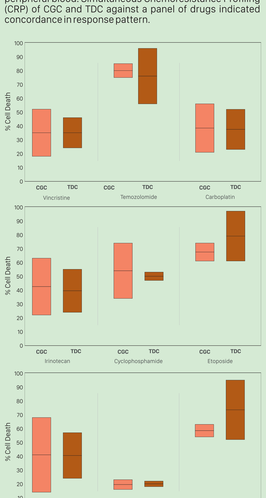
CGCs CONVEY INNATE AND ACQUIRED CHEMORESISTANCE

Differential CRP of CGCs from therapy naïve and pretreated cases indicated a clear acquired resistance to Temozolomide, which had been administered to patients previously. Lower sensitivity was also observed towards 5-fluorouracil in pretreated patients even though it was not previously administered. On the other hand, higher sensitivity towards Oxaliplatin was observed in pretreated patients even though it was not previously administered.



CHEMOCONCORDANCE BETWEEN CGCs and TDCs

In 2 patients, viable tumor derived cells (TDCs) were obtained from freshly biopsied tumor tissue and viable CGCs were obtained from simultaneously collected peripheral blood. Simultaneous Chemoresistance Profiling (CRP) of CGC and TDC against a panel of drugs indicated concordance in response pattern.



FINDINGS

- Sufficient viable CGCs could be obtained from all patients to perform CRP.
- CGCs detected resistance towards Temozolomide in pretreated patients.
- CRP of CGCs was concordant with that of TDCs.

CONCLUSION

In vitro chemoresistance profiling (CRP) of Circulating Glial Cells is a viable approach for monitoring in CNS malignancies. The non-invasive nature of the approach permits real time monitoring which can effect immediate therapeutic course correction.