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Title

Real-time Non-Invasive Chemoresistance Profiling of Circulating Tumor Associated Cells in Breast Cancers to Determine Resistance towards Mitotic Inhibitors

Authors

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Abstract:

Background:

Paclitaxel, Docetaxel and Vinorelbine exert anti-tumor activity by interfering with microtubule dynamics, leading to mitotic arrest. Though these agents are commonly used in treatment of breast cancers, therapy failures are noted due to innate and acquired chemoresistance. Real-time monitoring of chemoresistance towards such treatment agents is an unmet clinical need since conventional methods for chemoresistance profiling (CRP) necessitate invasive biopsies to obtain viable tumor tissue. We evaluated the utility of peripheral blood Circulating Tumor Associated Cells (C-TACs) for real-time non-invasive CRP in breast cancers.

Materials and Methods:

We obtained 15 mL peripheral blood from 1034 known cases of breast cancers, among whom 353 were therapy naïve and 681 were pretreated. Viable C-TACs were enriched and harvested from PBMCs using an epigenetically active media that selectively kills normal cells and simultaneously confers survival benefit on apoptosis-resistant cells of tumorigenic origin. Surviving cells (C-TACs) confirmed by immunostaining (EPCAM+, CK+, CD45±, GCDFP+). Viable C-TACs were seeded into multi-well plates and treated with Paclitaxel, Docetaxel or Vinorelbine. Surviving C-TAC fraction was measured to determine % cell-death and chemoresistance.

Results:

Innate resistance towards Docetaxel, Paclitaxel and Vinorelbine was observed in 42%, 59% and 56% of samples respectively in therapy naïve patients' samples. Acquired resistance towards Docetaxel, Paclitaxel and Vinorelbine was observed in 78%, 72% and 66% of pretreated patients' samples.

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Conclusion:

Our study demonstrates the feasibility of CRR profiling of C-TACs in therapy naïve and pretreated patients. Adoption of C-TAC - CRR profiling can non-invasively provide real time oversight towards treatment selection, monitoring of drug resistance and timely therapeutic course correction.