In vitro functional interrogation of viable circulating tumor associated cells (C-TACs) for evaluating platin resistance


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Background: Platinas are used extensively to treat Solid Organ Cancers like Ovarian, Breast, Colorectal, Lung, Pancreatic and Bladder Cancer. Eventually however, most cancer patients develop resistance to these treatments. As presently, no assay is available to non-invasively determine the onset of resistance to platinum drugs, the lethal evolution is usually silent. We show that apoptosis resistant Circulating Tumor Associated Cells (C-TACs) can be isolated and functionally interrogated in vitro to determine response / resistance to Platins in real time by chemo-sensitivity.

Methods: We evaluated the chemo-sensitivity / resistance profile of C-TACs obtained from 256 patients with confirmed diagnosis of Breast, Ovarian, Colorectal, Pancreatic, or Lung cancer; 207 (80.8%) patients were refractory to Platins, 49 (19.2%) were treatment naïve and 36 (14.0%) of C-TAC samples were compared with corresponding Tumor Derived Cells (TDCs).

Results: Out of 256 samples of venous blood examined, more than 5000 C-TACs could be harvested in 244 (95.0%) samples. 182 (88.0%) samples from the refractory cohort showed chemo resistance to Platins, 16 (34.0%) of samples from treatment naïve samples showed Platin resistance and 29 (85.2%) concurrently analyzed C-TAC samples showed chemo resistance to Platins corresponding to identical resistance in TDCs.

Conclusions: Functional interrogation of C-TACs by in vitro chemo-sensitivity analysis provides an accurate non-invasive method to determine Platin resistance in solid organ cancers.

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