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Nanoparticles: A novel approach to drug development, targeting and therapeutic monitoring

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Statement of the Problem: Currently, for most cancers, diagnostic tests are too expensive and invasive; primarily detect late-stage cancers exhibit too many false negatives/positives to be reliably used. Traditional tissue biopsies provide limited value due to access and availability of samples. Further, cancers that have spread often differ from the primary and tumor cells change in response to treatment. Based on these heterogeneities, traditional biopsies can only provide a limited window into the dynamic genetic and translational changes occurring in tumors, resulting in an ineffective view of tumor progression and metastasis.

Methodology & Theoretical Orientation: Liquid biopsies, or blood-sample tests can generate actionable information by analyzing circulating components released from the tumor. The most common version of the liquid biopsy comprises either circulating tumor cells (CTC) or fragments of tumor cell-derived DNA (cell-free DNA or cfDNA). Since CTCs are markers of metastatic disease, they have limited application for initial diagnosis or identification of early stage disease. cfDNA is generated from necrosis and apoptosis and are thus the product of cell death, from both normal and tumor cells. Analysis of cfDNA provides limited information about tumor cells not affected by specific therapies. In contrast, using our proprietary technology, it is now possible to enrich for circulating exosomes (50-200 nm vesicles), released specifically by tumor cells.

Findings: From these cancer specific exosomes, the transcriptome and proteome of the tumor cells can be defined. By detecting and quantifying genomic alterations reflected in tumor exosomes, these can provide real-time information on tumor progression, therapeutic targets and treatment effectiveness. We have developed an IVD cancer platform based on our discovery and characterization of exosomes derived from biofluids, including blood, saliva, cerebrospinal fluid and urine. These exosomes mirror protein and RNA components present in the tumor cell that released them.

Conclusion & Significance: Analysis of proteins and RNA cargoes of exosomes derived specifically from the tumor provides critical information in identifying and monitoring tumor type and stage, as well as predicting and monitoring responses to therapy and targets for therapy.

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