Liquid Biopsy: Clinical Applications and Current Challenges

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The analysis of circulating tumor cells (CTCs) in blood may provide clinically relevant information as "liquid biopsy" (Alix-Panabieres & Pantel, Nature Rev Cancer 2014) and provide new insights into tumor biology (Lu et al., Cancer Cell, 2011; LeBleu et al., Nat. Cell Biol., 2014; Mueller et al., Science TM, 2014; Werner et al., Cancer Discovery, 2015).
Besides CTCs the molecular analysis of ctDNA provides important complementary information as "liquid biopsy" (Pantel & Alix-Panabieres, Cancer Res., 2013; Pantel et al., Nature Med. 2013; Heitzer et al., Genome Med. 2013; Schwarzenbach et al., Nature Rev. Clin. Oncol., 2014, Joosse & Pantel, Cancer Cell 2015; Bardelli & Pantel, Cancer Cell 2017). Moreover, circulating microRNAs, extracellular vesicles and tumor-educated platelets are also interesting new members of the "Liquid Biopsy family" with potential clinical relevance in the future.
Recently, exosomes have received great interest because they act as biomarker with important functional properties for tumor progression. E.g., the integrin composition of exosomes can determine the organ site of metastases (Hoshino, Pantel, Lyden et al., Nature, 2015) and microRNAs in exosomes can impact the biology of the recipient cells (Anfossi et al., Nature. Rev. Clin. Oncol. 2018). Detection of these miRNAs can contribute to early detection of cancer (Meng et al., Oncotarget, 2016).
Liquid biopsy analyses with validated platforms provides reliable information on prognosis and may serve to identify therapeutic targets or mechanisms of resistance on metastatic cells. Metastatic cells might have unique characteristics that can differ from the bulk of cancer cells in the primary tumor currently used for stratification of patients to systemic therapy. Moreover, monitoring of blood samples before, during and after systemic therapy (e.g., chemotherapy, hormonal therapy, antibody therapy) might provide unique information for the future clinical management of the individual cancer patient and might serve as surrogate marker for response to therapy.
In conclusion, liquid biopsies can be used to improve the management of individual cancer patients and contribute to the vision of personalized medicine (Alix-Panabieres & Pantel, Cancer Discovery, 2016; Bardelli & Pantel, Cancer Cell 2017). Validation of liquid biopsy assays is essential and is currently being performed by the EU/IMI consortium CANCER-ID (www.cancer-id.eu).