The analysis of circulating tumor cells (CTCs) and circulating nucleic acids (in particular ctDNA) in blood may provide clinically relevant information as “liquid biopsy” and provide new insights into tumor biology. Although the studies have been performed on patients with carcinomas, CTCs have been also detected in the peripheral blood of patients with primary brain tumors (glioblastomas) despite the blood-brain barrier (Mueller et al., Science Transl. Med., 2014). Sensitive methods have been developed to detect CTCs and ctDNA in the peripheral blood (Alix-Panabieres & Pantel, Nature Rev Cancer 2014; Bardelli & Pantel, Cancer Cell 2017). CTC and ctDNA enumeration and characterization with certified systems provides reliable information on prognosis and may serve as liquid biopsy 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 CTCs and ctDNA 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. Functional characterization of CTCs using specialized in vitro and in vivo test systems has started, which might provide novel insights into the biology of metastatic tumor cells and serve as models for drug testing. New blood-based biomarkers currently validated in clinical trials include miRNAs, exosomes and tumor-educated platelets.