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Suitability of circulating microRNAs as potential prognostic markers in colorectal cancer

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Colorectal cancer is one of the most common cancer types worldwide and accounts for 8% of all cancer-related deaths in the world. Due to screening programs and some risk factor reductions, incidence rates have been declining in industrial countries, but are still increasing in transitioning states. The early detection of both primary tumors and recurrences is essential to increase the probability of cure and improve clinical outcomes. Today's use of tumor stage and CEA levels as prognostic factors and tumor marker, respectively, is inadequate and does not reflect clinical heterogeneity among patients. New blood-based biomarkers with high sensitivity and specificity are desirable as a blood-based test is minimally invasive and markers in the plasma can be monitored over time. Circulating microRNAs are promising biomarkers as they are reproducibly quantifiable in the plasma and thought to be released into the bloodstream by tumor cells. Used as a diagnostic screening tool, they could easily be integrated into screening programs, possibly achieving wide acceptance in the population compared to invasive procedures such as colonoscopy. Providing information about tumor characteristics such as tumor stage or location, circulating miRNAs could become valuable prognostic biomarkers being able to predict clinically relevant outcomes, such as progression, recurrence and survival.

In this pilot study, nested in the ColoCare study, 17 different plasma microRNAs were quantified in 35 patients at three time points: pre-surgery, post-surgery (mean: 4 days) and six months post-surgery. Results demonstrate that even though the sample size was small, nine specific microRNAs were substantially decreased after surgical removal of the tumor (miR-92a, miR-18a, miR-320a, miR-106a, miR-16-2, miR-20a, miR-223, miR-143, miR-17). Analyses of all three time points, including the one six months after surgery, revealed significance for both a decrease between pre- and post-surgery and an increase back to pre-surgery levels at the 6 month time point for four different circulating microRNAs (miR-92a, miR-320a, miR-106a, miR-18).

These results underscore the thesis of active release of microRNAs into the circulation by tumor cells. Long-term information about tumor recurrence and survival, as well as controlled trials including a larger study population, validation samples or study tumor tissue of the same patients simultaneously are needed, however, to further validate this hypothesis. This study also suggests that clinicopathological parameters such as patients' age, stage of disease and location of the tumor affect the expression and/or release of tumor-related microRNAs into the circulation. As there is still only little known about the exact regulation of microRNAs and their specific roles in cancerogenesis, more time will past until circulating microRNAs will actually be used as diagnostic, prognostic or therapeutic biomarkers on a routine basis. Nevertheless, the potential of microRNAs as blood- based biomarkers is undoubted. In conclusion, this pilot study provides valuable information about the reactivity of microRNA profiles in the plasma towards surgical interventions as well as their long-term characteristics.