PS08.10

Monitoring the potential role of circulating miR-181b-5p in minimal residual disease in paediatric acute lymphoblastic leukaemia

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Background: Circulating microRNAs are promising biomarkers as they can be found in a variety of body fluids and can be non-invasively or minimally invasively obtained. The profile of circulating microRNAs reflects the presence of malignant and non-malignant diseases. Recently, plasma miR-181b-5p was found to be upregulated in acute myeloid leukaemia patients. In addition, it was associated with shorter overall survival. The aim of our study was to determine the relative expression pattern of plasma miR-181b-5p through paediatric acute lymphoblastic leukaemia (ALL) treatment to evaluate its possible role in minimal residual disease (MRD) detection.
Methods: Peripheral blood was obtained from 11 paediatric pre-B ALL patients with normal karyotype at four different time points of their treatment: on day 1 at diagnosis, and on days 8, 15 and 33. The preparation of platelet-free plasma from blood samples was carried out within 2 h of sampling. Cell-free total RNA was purified using the miRNeasy Serum/Plasma Kit (Qiagen). Quantitative RT-PCR was performed to detect the relative expression of miR-181b-5p using the Taqman Advanced miRNA assays.
Results: The relative expression level of miR-181b-5p was significantly reduced on days 8, 15 and 33 compared to that on day 1 ($p = 0.006$, $p = 0.047$ and $p = 0.009$ respectively). The fold change between day 1 and day 8 and between day 1 and day 15 correlated significantly with the flow cytometry-based MRD values of ALL patients on day 15 ($r = 0.982$, $p = 0.00009$ and $r = 0.956$, $p = 0.003$ (Pearson)).
Summary/Conclusion: Growing evidence suggests that miR-181b affects several types of malignancies, including leukaemia. Based on our results, the measurement of plasma miR-181b-5p expression may have relevance in the development of a less invasive MRD monitoring in paediatric ALL.
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PS08.11

Serum exosomal microRNAs as non-invasive biomarkers for human hepatocellular carcinoma

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Background: Although considerable progress has been made in the treatment of hepatocellular carcinoma (HCC), early detection is still highly considered the key to improved survival. Recently, cancer cell-derived extracellular vesicles have been known to contain various intracellular biomolecules including microRNAs (miRNAs). The aim of this study was to evaluate whether exosomal miRNAs can serve as a serum-based biomarker in HCC.
Methods: Expression of six miRNAs (miRNA-24, -130a, -182, -203, -373 and -423) was analysed in the exosome samples. We also investigated expression status of the six miRNAs in matched HCC tissues and corresponding normal liver tissues.
Results: We observed that serum exosomal miRNA-203 ($P < 0.05$) and miRNA-373 ($P < 0.05$) were significantly up-regulated in advanced HCC patients. More interestingly, high serum exosomal miRNA-203 and miRNA-373 was associated with HCC progression ($P < 0.01$) as well as prognosis ($P < 0.05$) of HCC patients.
Summary/Conclusion: We provided the novel evidence for usefulness of serum circulating exosomal miR-203 and miR-373 expressions as strong potential biomarkers for predicting prognosis and metastasis of HCC patients.

PS08.12

Extracellular small non-coding RNAs as promising biomarkers for early cancer detection

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Background: Extracellular small non-coding RNAs, such as microRNAs, isoforms of microRNAs (isomiRs) and tRNA-derived fragments (tRFs) are known to regulate expression of genes involved in cell metabolism, and are released into body fluid from various cells with extracellular vesicles including exosomes. In this study, we focused on isomiRs and tRFs as novel cancer biomarkers and characterized their expression profiles to find those expressed specifically in serum from cancer patients.
Methods: Serum samples were collected from the patients who provided written informed consent to participate in the study (approved by IRB of Hiroshima University). Cells were cultured in DMEM with FBS and the supernatant were collected after 1-day culture without FBS. Small RNAs were purified from serum and cell culture supernatant by using miRNeasy Mini Kit (Qiagen). Extracellular vesicles (EVs), including exosomes, were isolated by using Total Exosome Isolation kit (Thermo Fisher Scientific). Size and amounts of EVs were measured by qNano (IZON). Next generation sequencing (NGS) was performed by using Ion S5 (Thermo Fisher Scientific). The data were analysed by using CLC Genomics and JMP, and sequences of small RNAs (15–55 nt) found to differ between cancer patients and healthy individuals were considered candidate biomarkers.
Results: We identified several isomiRs and tRFs expressed specifically in serum from cancer patients. Some of them were expressed at higher levels and performed better as biomarkers than microRNAs. The expression profiles of some isomiRs and tRFs in cancer serum samples were demonstrated to correlate with extracellular RNA profiles in EVs released from cultured cancer cell lines. The combined use of isomiR and tRF levels allowed us to detect early-stage pancreatic cancer.
Summary/Conclusion: Our results suggest that isomiR and tRF forms of extracellular small non-coding RNAs in serum are useful biomarkers for NGS-based detection of early cancers.

PS08.13

Exosomal miR-486-5p, miR-181a-5p and miR-30d-5p from hypoxic tumour cells are candidate circulating markers of high-risk rectal cancer

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Background: Tumour hypoxia (oxygenation deficiency) contributes significantly to treatment resistance and metastasis in locally advanced rectal cancer (LARC). Exosomes play a central role in the aggravated