Exosomal RNA-profiling of lung pleural effusions identifies adenocarcinoma patients through elevated miR-200 and LCN2

Per Hydbring1, Luigi De Petris1, Eva Brandén3, Hirsh Koyi1, Metka Novak1, Lena Kanter1, Petra Häag1, James Hurley2, Vasisht Tadigotla2, Johan Skog2, Kristina Viktorsson1, Simon Ekman1 and Rolf Lewensohn1
1Department of Oncology-Pathology, Karolinska Institutet, 17176 Stockholm, Sweden
2Exosome Diagnostics Inc. Cambridge, MA 02139, USA
3Department of Respiratory Medicine, Gävle Hospital, Gävle, Sweden

Methods

• Systematic RNA profiling was carried out on exosomes, derived from 36 clinical pleural effusions, separated into 18 benign and 18 lung adenocarcinoma samples. Benign pleural effusion consisted of unspecific inflammation.

• The two groups were well balanced with respect to age (median = 72Y) and smoking history (ever smokers in circa 70% of cases). Profiling was conducted using TaqMan RT-qPCR arrays followed by statistical ranking of differentially expressed transcripts between the two groups.

Results

• Exosomal RNA profiling revealed a substantial, and significant (p<0.05), differential expression of 17 microRNAs and 71 mRNAs in pleural effusions from patients with lung adenocarcinoma.

• A few differentially expressed RNAs, including miR-200 family microRNAs, displayed excellent diagnostic power, calculated through ROC curves. The mRNA transcript encoding Lipocalin-2 (LCN2) displayed the strongest diagnostic power of all analyzed transcripts (AUC: 0.9916).

This study demonstrates the usage of exosomal RNA profiling from pleural effusions to define patients with lung adenocarcinoma and further highlights miR-200 microRNAs and LCN2 mRNA as diagnostic markers in lung cancer liquid biopsies.

Overview and Conclusions

Pleural effusion samples (18 benign and 18 malignant)

Isolation of Exosomal RNA (Qiagen exoRNeasy)

RT-qPCR miRNA (754 miRNAs)

RT-qPCR mRNA (624 mRNAs)

Filtering of results

Ranking of differentially expressed miRNAs and mRNAs (Mann-Whitney test)

In the next step, we plan to monitor disease in lung adenocarcinoma patients subjected to targeted therapies via exosomal miRNA/mRNA profiling. In addition of validating the impact of liquid biopsy RNA profiling in lung cancer patients, this will specifically highlight RNAs with potential to predict responders vs non-responders to targeted therapies.

Exosomal RNA-profiling of lung pleural effusions identifies adenocarcinoma patients through elevated miR-200 and LCN2

Per Hydbring
Assistant Professor, Department of Oncology-Pathology
Karolinska Biomics Center, Cancer Center
Karolinska, Z5:01, 17176 Stockholm
E-mail: per.hydbring@ki.se
Phone: +46709495528