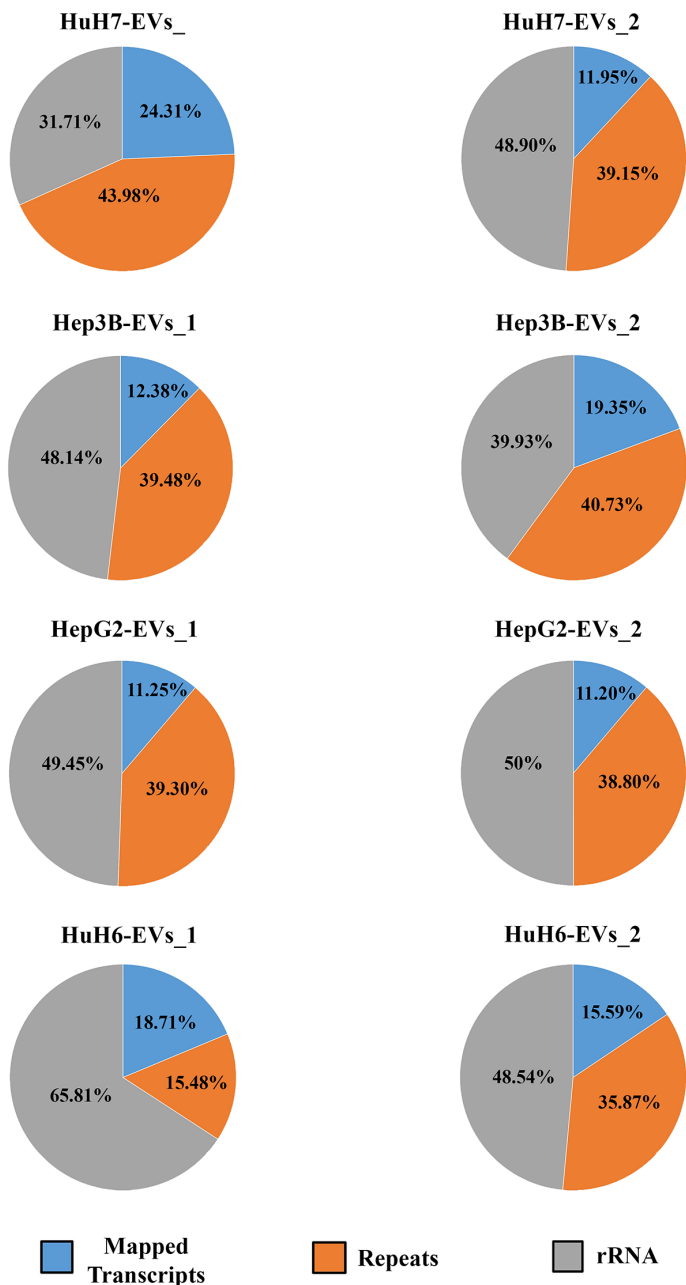


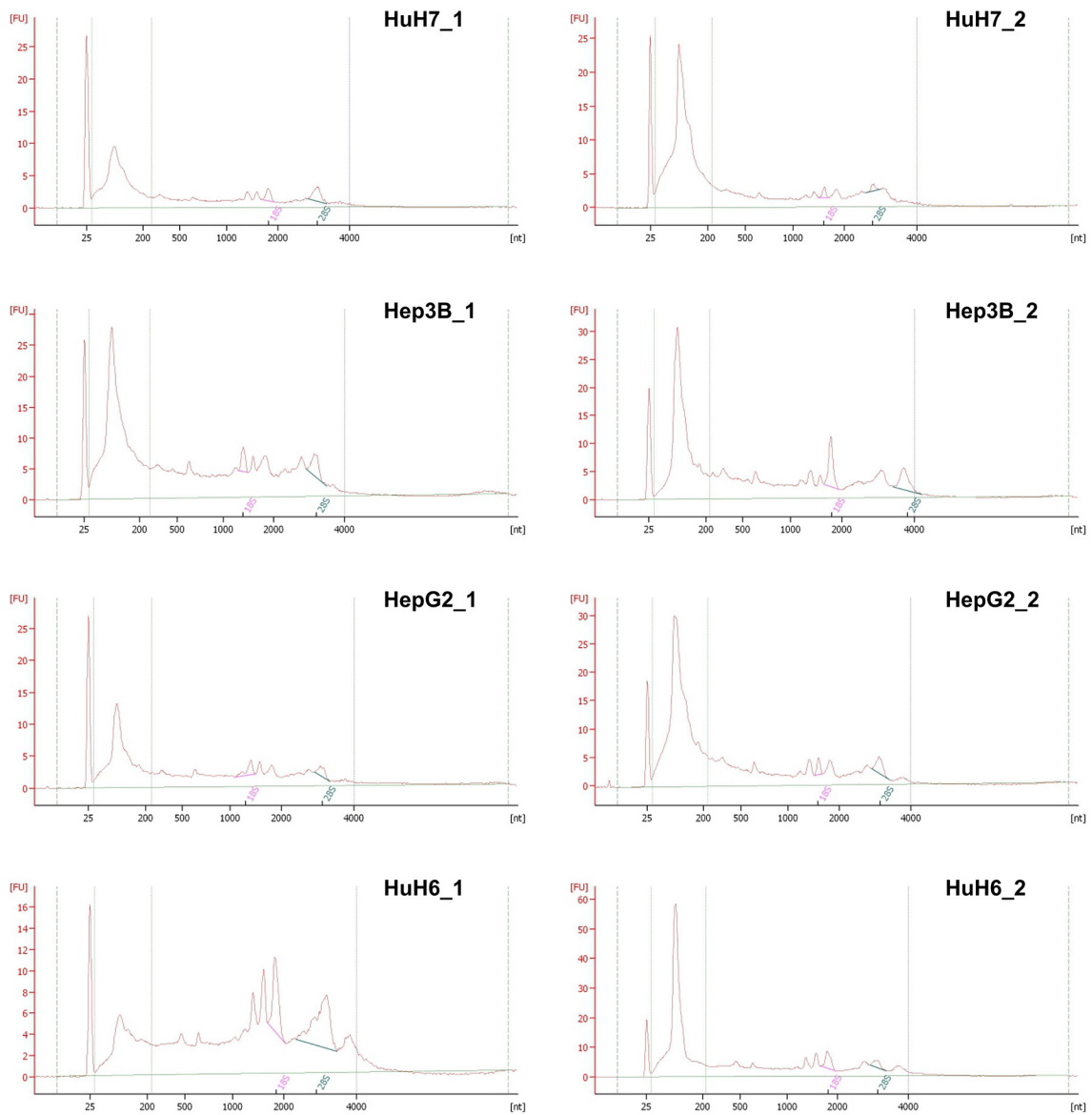
# RNA-seq reveals distinctive RNA profiles of small extracellular vesicles from different human liver cancer cell lines

## SUPPLEMENTARY MATERIALS

### Whole Transcriptome Analysis

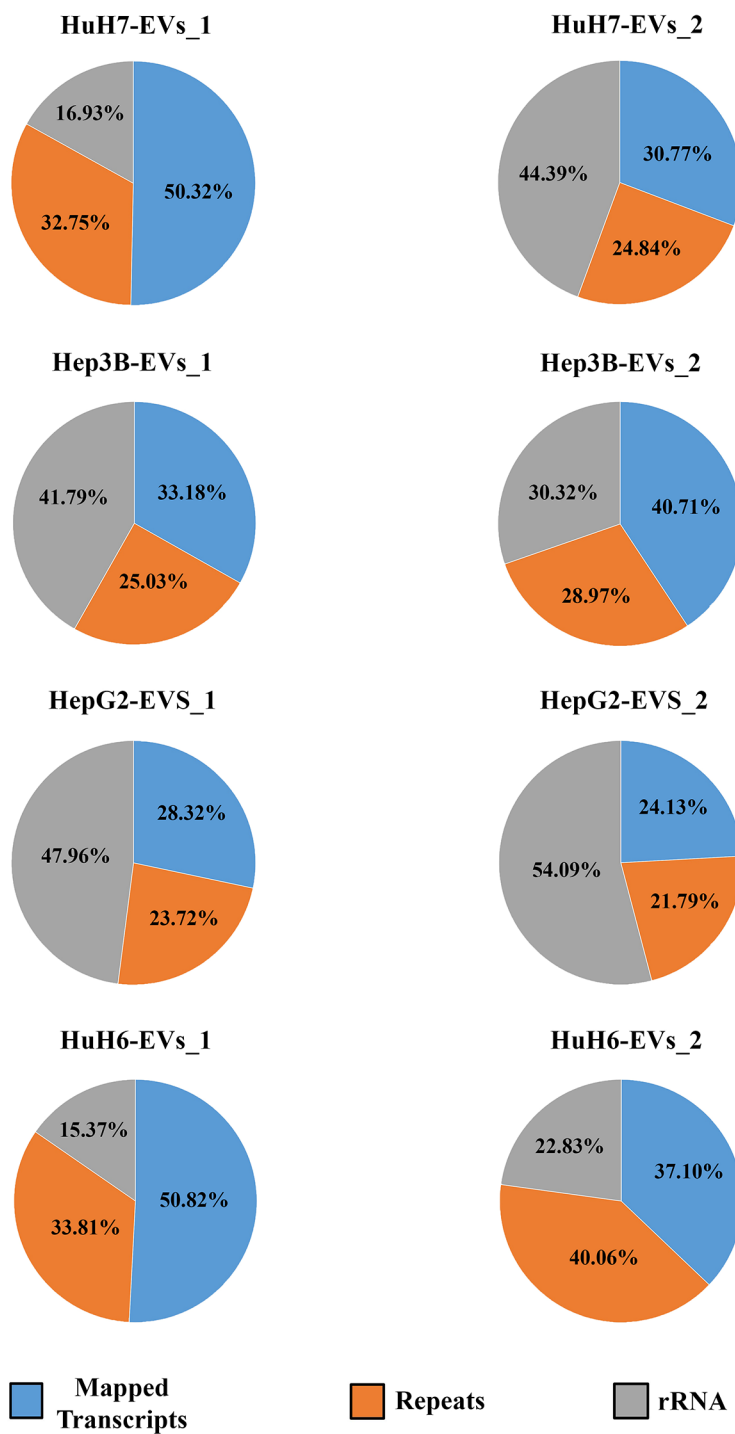


**Supplementary Figure 1: WTA library mapping statistics on the reference genome (hg38).** The WTA libraries, two duplicates for each LCC analyzed, have been used to identify coding and non-coding RNAs and snoRNAs.

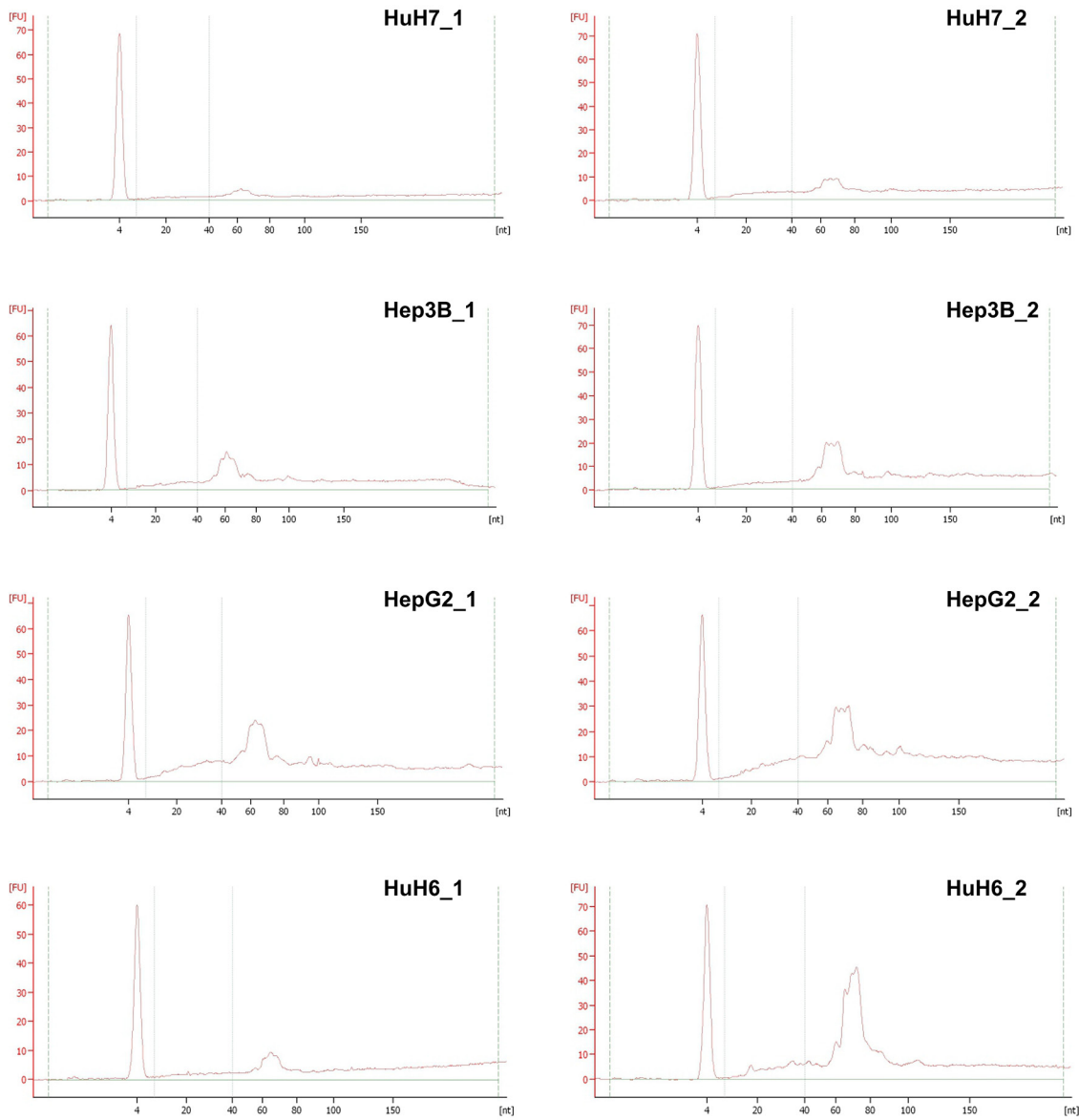


**Supplementary Figure 2: Size distribution of total RNA molecules contained in extracellular vesicles secreted from the 4 LCC. Two duplicates for each LCC are shown.**

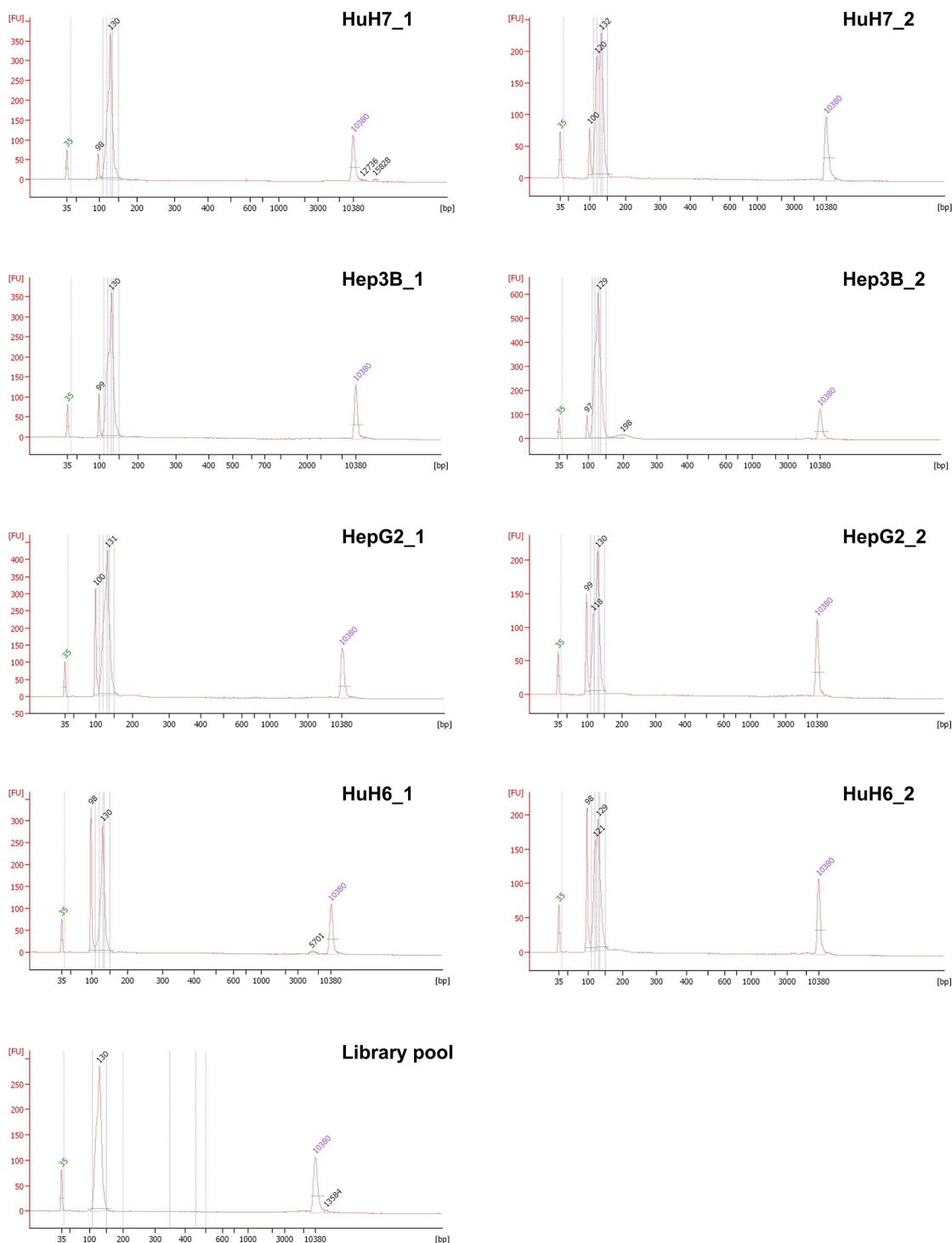
Small RNA



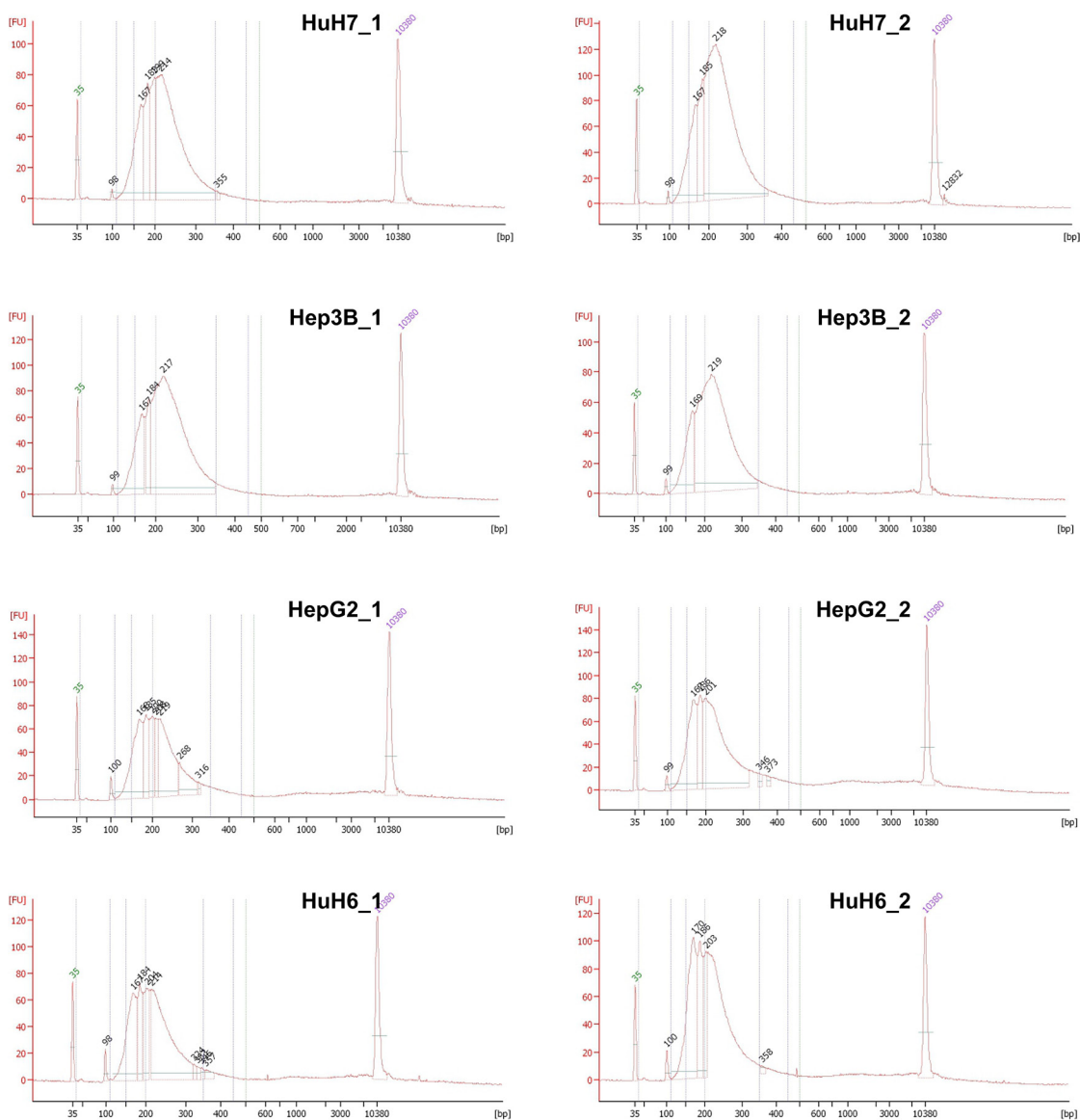
**Supplementary Figure 3: Small RNA library mapping statistics on the reference genome (hg38).** Small RNA libraries, two duplicates for each LCC analyzed, have been used to identify microRNAs and snoRNAs.



**Supplementary Figure 4: Size distribution of small RNA molecules contained in extracellular vesicles secreted from the 4 LCC. Two duplicates for each LCC are shown, as indicated.**



**Supplementary Figure 5: Size distribution of the small RNA libraries prepared from the total RNA contained in extracellular vesicles secreted from the 4 LCC.** Two duplicates for each LCC are shown, as indicated. 99-100 bp peak: “devil band”, formed by the excess adapter dimers; 118-130 bp peaks: bands containing the library inserts plus the adapters. Library pool: the 8 small RNA barcoded libraries were pooled and purified by gel electrophoresis to eliminate the devil band. The peaks at 35 bp and 10380 bp are size markers.



**Supplementary Figure 6: Size distribution of the WTA libraries prepared from the total RNA contained in extracellular vesicles secreted from the 4 LCC.** Two duplicates for each LCC are shown, as indicated. 99-100 bp peak: “devil band”, formed by the excess adapter dimers; 150-300 bp range: region containing the library inserts plus the adapters. The peaks at 35 bp and 10380 bp are size markers.

**Supplementary Table 1: Gene transcripts**

See Supplementary File 1

**Supplementary Table 2: miRNAs CPM**

See Supplementary File 2

**Supplementary Table 3A: isomiR CPM**

See Supplementary File 3A

**Supplementary Table 3B: 10 most expressed isomiRs**

See Supplementary File 3B

**Supplementary Table 4: miRNA-isomiR fraction**

Small RNA library	isomiR reads	Canonical miRNA reads	Total reads	miRNA fraction	isomiR fraction
HuH7-EVs_1	349646	151404	501050	0,70	0,30
HuH7-EVs_2	73628	25826	99454	0,74	0,26
Hep3B-EVs_1	252180	110761	362941	0,69	0,31
Hep3B-EVs_2	644988	229879	874867	0,74	0,26
HepG2-EVs_1	273205	101597	374802	0,73	0,27
HepG2-EVs_2	428603	144845	573448	0,75	0,25
HuH6-EVs_1	796749	313573	1110322	0,72	0,28
HuH6-EVs_2	1761404	697756	2459160	0,72	0,28

**Supplementary Table 5: snoRNAs**

See Supplementary File 4

**Supplementary Table 6: snoRNA**

See Supplementary File 5