**Supplementary File S2**

**Supplementary File S2: Description of results on differential tests of miRNAs and methylation.**

As a result, 16 miRNAs were found up-regulated in aggressive subtype S1 and 7 were found down-regulated after the filtering criteria mentioned in Methods section **(**Supplementary Figure S2A**)**. miR-200a, miR-200b, miR-200c, miR-141, and miR-429 (members of hsa-200 family) stand out as being up-regulated in aggressive S1 subtype. Interestingly, upregulation of miR-200 was reported to be associated with high risk in glioblastoma patients with poor survival (1). Among the miRNAs that are overexpressed in S1, miR-34c and miR-183 have been found upregulated in cluster S1 in our study and have been reported to be potentially associated with HCC in the other studies (2,3).

55 genes had averaged M value difference greater than 1 and adjusted p-value <0.05 (Supplementary Figure S2B). Interestingly, multiple small nucleolar RNA family genes (*SNORD22*, *SNORD44*, *SNORD77*, *SNORD78*, *SNORD79*, *SNORD80* and *SNORD87*) have been found hypomethylated in aggressive subtype S1, along with *GLRX*, *EID3*, *TMEFF1* and *CYBA*. *SNORD44* has been identified as the housekeeping gene in colon cell line HCT-116 (4). Over expression of *SNORD78* is reported to be associated with poor prognosis in HCC (5). 44 genes were hypermethylated in S1 subtype. Among them, the ones with high averaged difference include *RAPGEF2*, *OR9I1*, *KRTAP2-2*, *SERPINC1*, *OR9Q1*, *ZNF366* and *TREML4*. *RAPGEF2* (Rap Guanine Nucleotide Exchange Factor 2) is instrumental in RAS activation (6), though no direct evidence of its methylation was previously reported in HCC. *SERPINC1* was reported to be downregulated in the HCC and was among the gene signatures that discriminates high-risk group from the low-risk group (7).

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