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## **Integrated analysis of somatic mutations and focal copy-number changes identifies key genes and pathways in hepatocellular carcinoma.**

Cécile Guichard, Giuliana Amaddeo, Sandrine Imbeaud, Yannick Ladeiro, Laura Pelletier, Ichrafe Ben Maad, Julien Calderaro, Paulette Bioulac-Sage, Mélanie Letexier, Françoise Degos, et al.

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Cécile Guichard, Giuliana Amaddeo, Sandrine Imbeaud, Yannick Ladeiro, Laura Pelletier, et al.. Integrated analysis of somatic mutations and focal copy-number changes identifies key genes and pathways in hepatocellular carcinoma.. *Nature Genetics*, 2012, 44 (6), pp.694-8. 10.1038/ng.2256 . inserm-00719917

**HAL Id: inserm-00719917**

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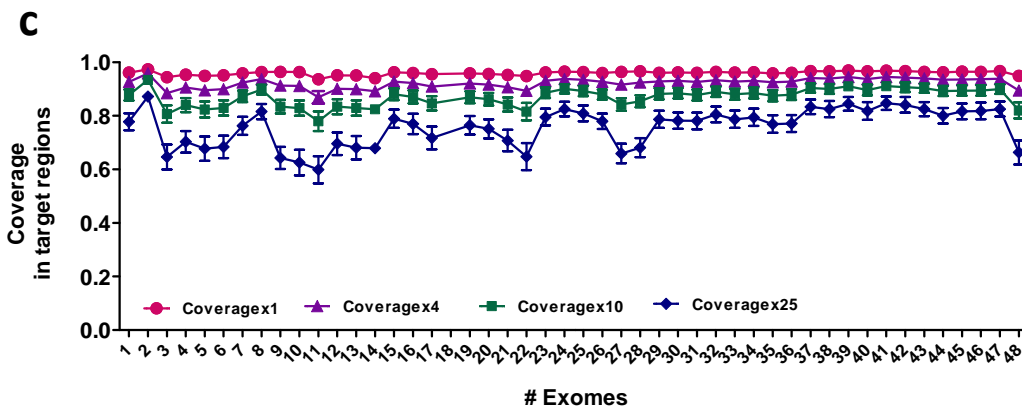
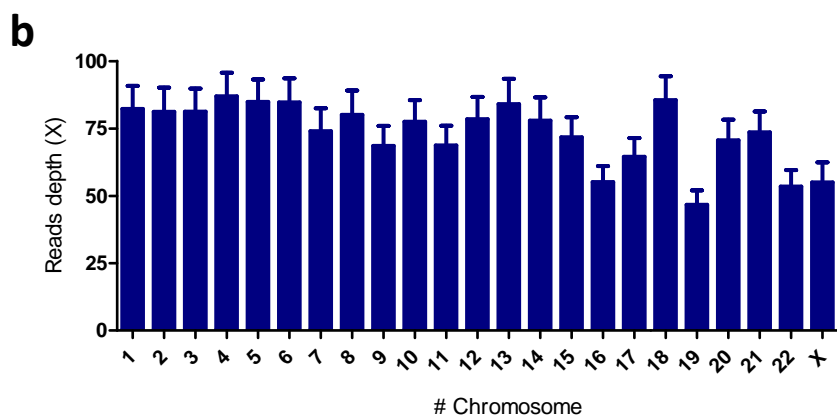
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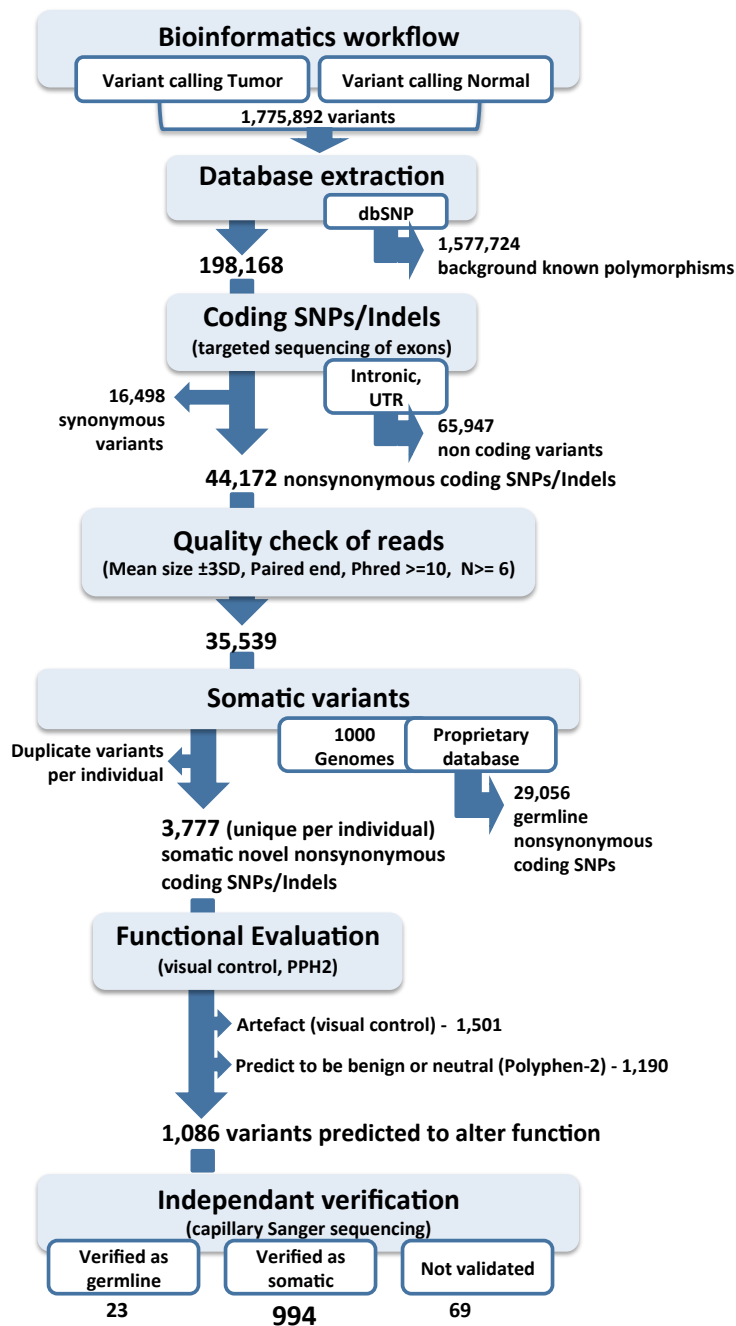
**a**

|                              |         |
|------------------------------|---------|
| Final target bases           | 46.2 Mb |
| Target bases covered         | 43.3 Mb |
| Percent target bases covered | 93.81%  |
|                              |         |
| Average depth                | 73.3    |
| Median depth                 | 70      |
|                              |         |
| Coverage at 25x              | 75.9%   |
| Coverage at 10x              | 87.0%   |
| Coverage at 4x               | 92.3%   |
| Coverage at 1x               | 96.0%   |



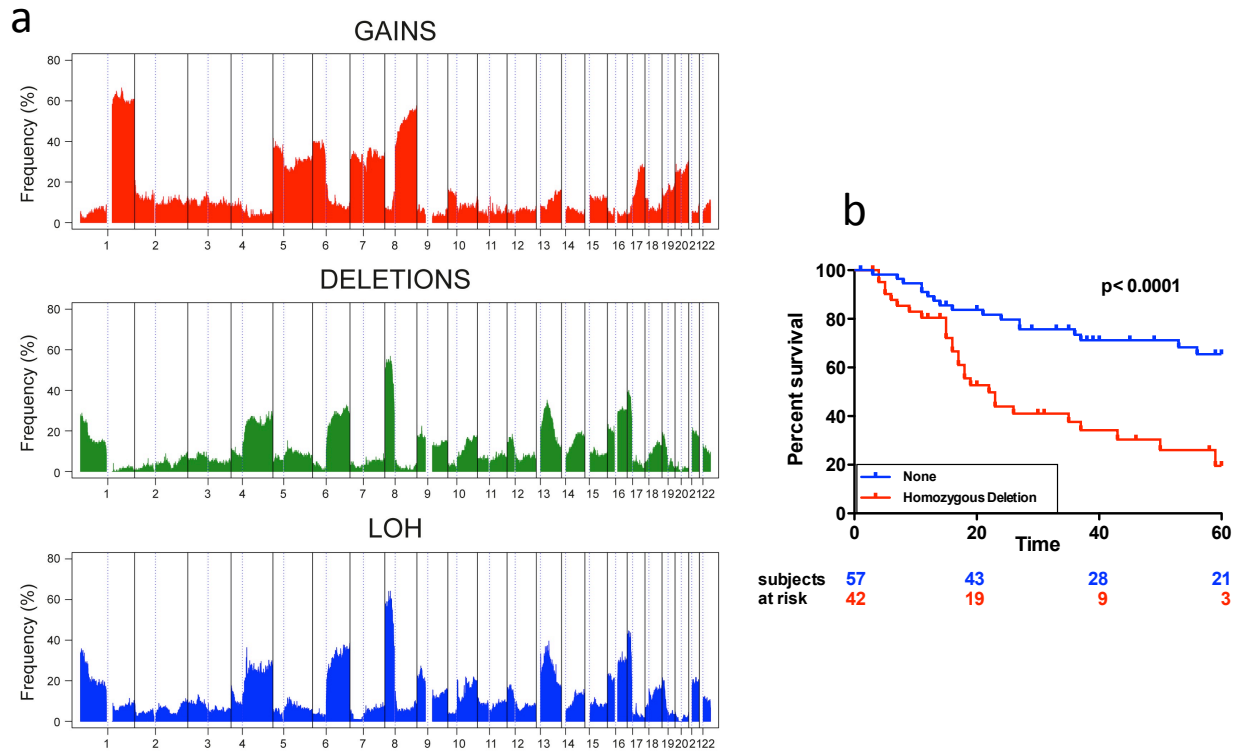
### Supplementary Figure 1. Statistics of mapping of sequencing reads

**a**, summary statistics for whole-exome sequence reads of 24 HCC with their non tumor liver tissues. **b**, mean depth (with 95% IC) of reads on each chromosome, **c**, cumulative fraction of coding bases covered in captured regions. A 1-fold, 4-fold, 10-fold and 25-fold coverage were considered (mean with 95% IC) per exome (numbered #1-48).

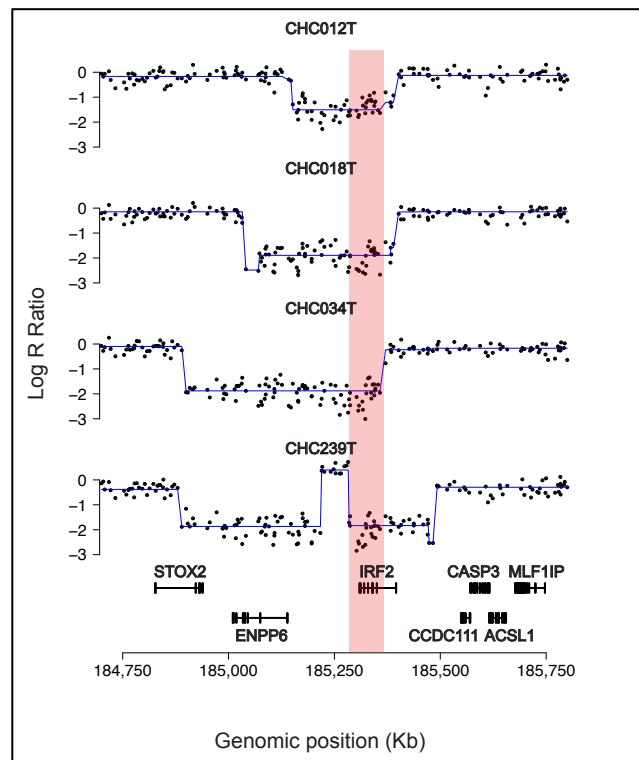
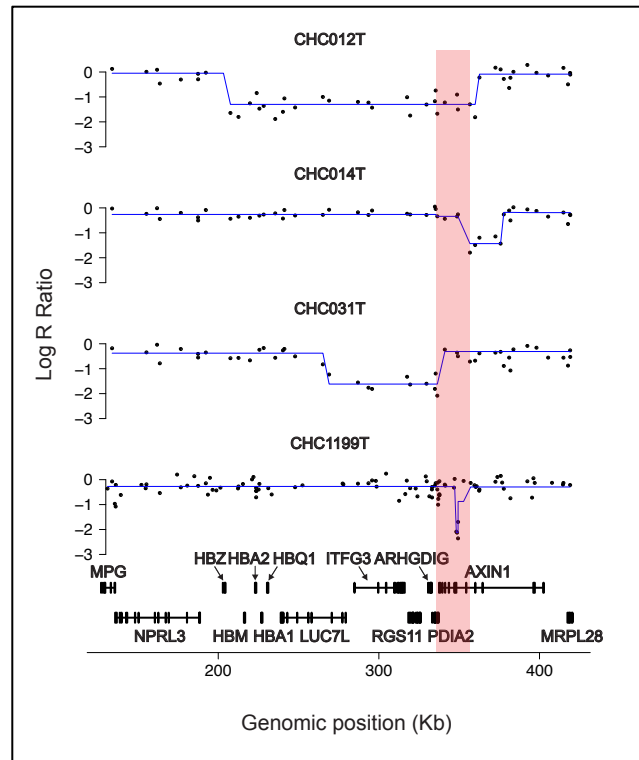
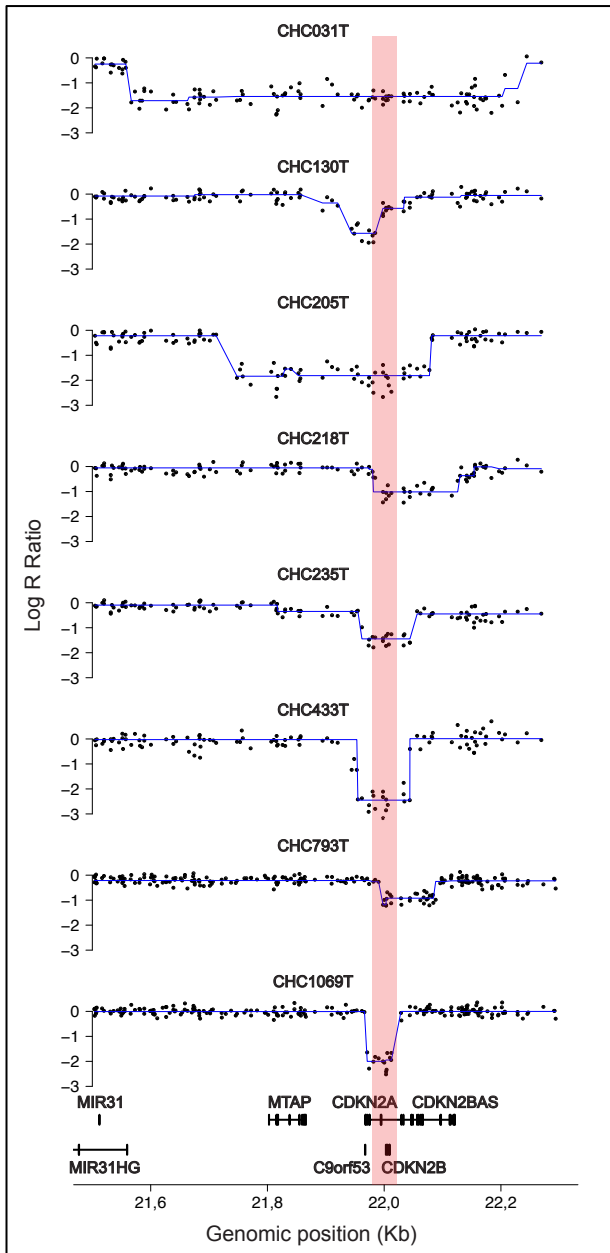


**Supplementary Figure 2. Whole-exome sequencing analysis flowchart.**

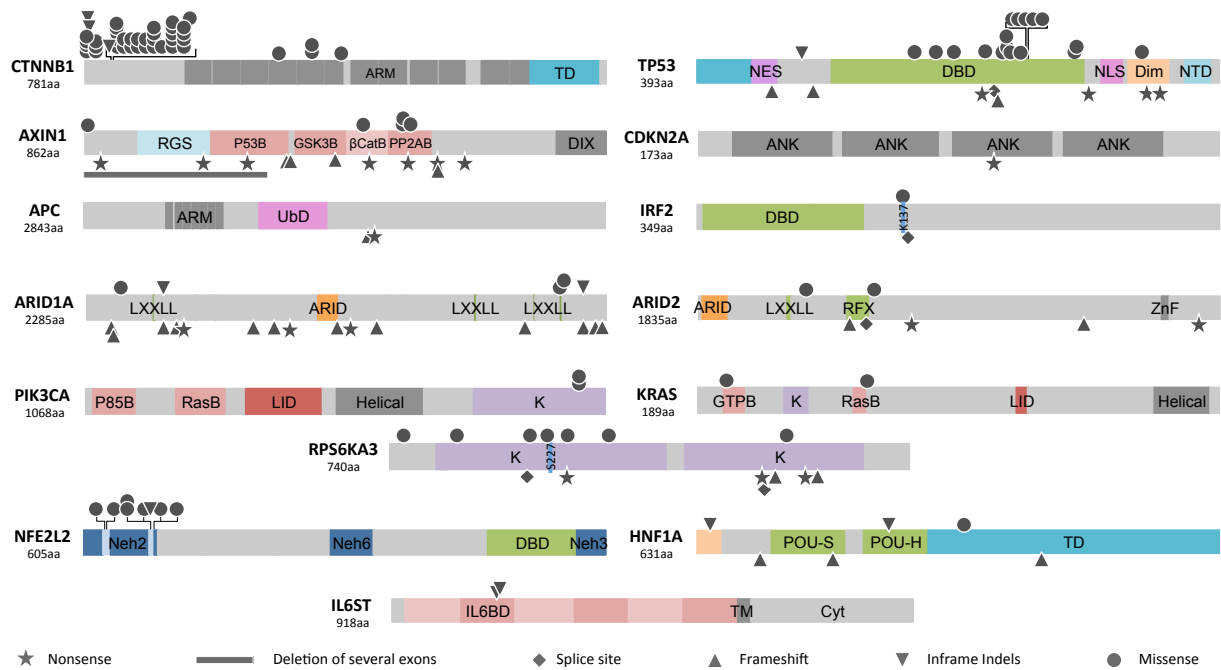
Extraction of functionally somatic gene mutations for 24 HCC. Boxes refer to major bioinformatics steps; arrows indicate the number of variants obtained or removed from subsequent analysis. Variants were filtered for their coding localization, annotation in dbSNP31 or 1000 genomes, somatic and functionally impairment. The per-base and reads quality scores were used to filter false positive gene mutation events.



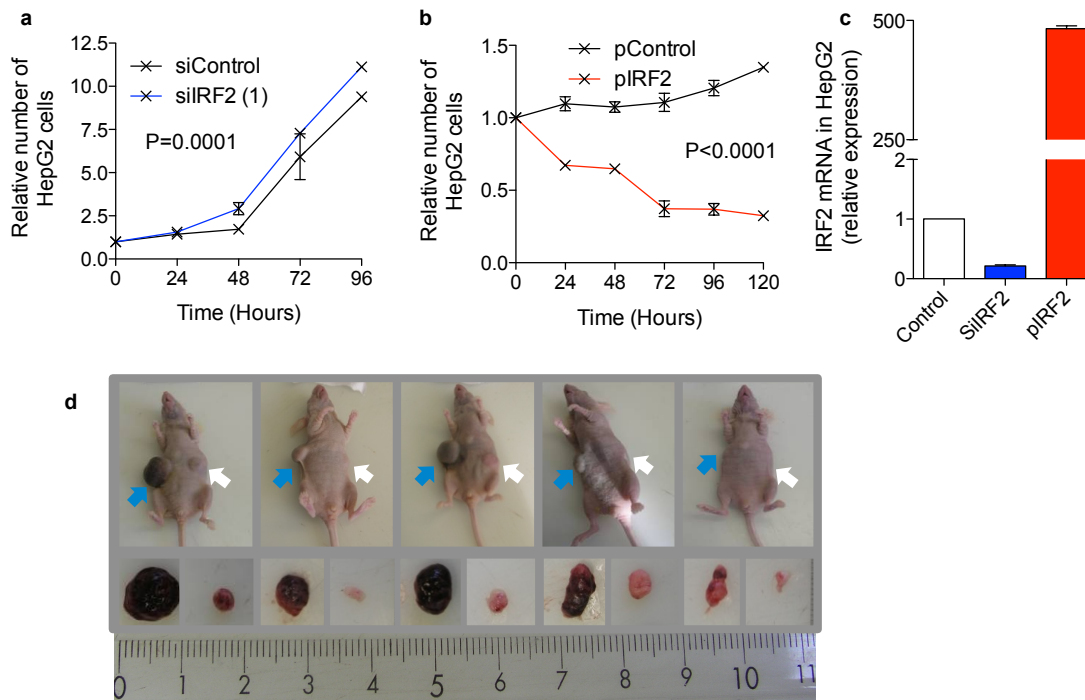
**Supplementary Figure 3.** Genome-wide copy number changes and recurrent homozygous deletions in HCC. **a**, Frequency of gains, deletions, and losses of heterozygosity (LOH) along the genome in a series of 125 HCC. **b**, Kaplan-Meier analysis comparing survival of cases presenting homozygous deletions ( $n=42$ ) versus those without local losses ( $n=57$ ). Univariate Cox P-value for risk index is included. Only patients with curative (R0) resection were included in survival analysis.



**Supplementary Figure 4.** Recurrent homozygous deletions at *CDKN2A/B*, *AXIN1* and *IRF2* loci. Raw log R ratios are represented as black dots, and smoothed log R ratios as blue lines. The minimal region of loss is indicated in red for each region.



**Supplementary Figure 5.** Somatic mutation spectra in 125 HCC. Inactivating and activating mutations are shown above and below the core protein, respectively. Functional domains are colored boxes. ANK: Ankyrin repeat, ARM: Armadillo repeat, βCatB: βCatenin binding Domain, Cyt: Cytosolic Domain, DBD: DNA Binding domain, Dim: Dimerization Domain, GSK3B: GSK3 Binding Domain, GTPB: GTP binding Domain, IL6BD: IL6 Binding Domain, K: Kinase domain, LID: Lipid interaction domain, Neh: Nrf2-ECH Homology Domain, NES: Nuclear Export Signal, NLS: Nuclear Localization Signal, NTD: Negative Transactivation Domain, P53B: P53 Binding Domain, P85B: P85 Binding Domain, PP2AB: PP2A Binding Domain, RasB: Ras Binding Domain, RGS: regulator of G-protein signalling, TD: Transactivation domain, TM: Transmembrane domain, UbD: Ubiquitinated domain.



**Supplementary Figure 6. IRF2 as a new tumor suppressor gene in HCC controlling p53 pathway**

**a**, Effect of *in vitro* IRF2 silencing in HepG2 hepatoblastoma cell line: increased cell proliferation with IRF2 siRNA (SiIRF2) when compared to control siRNA (triplicates, mean±SD, regression analysis). **b**, IRF2 overexpression in HepG2 cell line by transfection of a plasmid containing the coding sequence of IRF2 (pIRF2) induced dramatic cell death when compared to HepG2 transfected with an empty plasmid (pControl; triplicates, mean±SD, regression analysis) **c**. Relative mRNA expression was quantified by qRT-PCR ( $n=3$ ; mean ± SD). **d**. Xenograft model in CD1 nude mice injected in right flank with HepaRG stably transfected with ShIRF2(1) (blue arrow) and in left flank with HepaRG stably transfected with ShControl (white arrow). Respective subcutaneous tumors after 4 weeks of cell injection are displayed below.

**Supplementary Table 1: Clinical, histological and molecular data of HCC**

|                                      | <b>24 HCC (Exome sequencing)</b>                       | <b>125 HCC (series of validation)</b>                   |
|--------------------------------------|--|---|
| <b>Age</b>                           |  |   |
| < 60 years                           | 3 (12.5%)  | 46 (37%)  |
| ≥ 60 years                           | 21 (87.5%)   | 79 (63%)  |
| <b>Gender</b>                        |  |   |
| Male                                 | 20 (83%)   | 100 (80%)   |
| Female                               | 4 (17%)  | 25 (20%)  |
| <b>Etiology<sup>(*)</sup></b>        |  |   |
| HCV                                  | 4 (17%)  | 24 (19%)  |
| HBV                                  | 1 (4%)   | 35 (28%)  |
| Alcohol                              | 12 (50%)   | 43 (34%)  |
| NASH                                 | 2 (8%)   | 5 (4%)  |
| Hemochromatosis                      | 0 (0%)   | 6 (5%)  |
| Other                                | 7 (29%)  | 26 (21%)  |
|                                      | <sup>(*)</sup> including 2 cases with ≥ 2 risk factors | <sup>(*)</sup> including 14 cases with ≥ 2 risk factors |
| <b>Tumor size ( n=124)</b>           |  |   |
| ≤ 50 mm                              | 12 (50%)   | 56 (45%)  |
| > 50 mm                              | 12 (50%)   | 68 (55%)  |
| <b>Tumor features</b>                |  |   |
| Unique nodule (n=124)                | 18 (75%)   | 94 (76%)  |
| Satellites nodules (n=124)           | 9 (38%)  | 59 (48%)  |
| Vascular invasion (n=122)            | 11 (46%)   | 61 (50%)  |
| <b>Differentiation ( n=120)</b>      |  |   |
| Edmonson I-II                        | 11 (48%)   | 60 (50%)  |
| Edmonson III-IV                      | 12 (52%)   | 60 (50%)  |
| <b>Non tumor liver ( n=124)</b>      |  |   |
| Metavir score F0-F1                  | 9 (37%)  | 45 (36%)  |
| Metavir score F2-F3                  | 7 (29%)  | 33 (27%)  |
| Metavir score F4                     | 8 (33%)  | 46 (37%)  |
| <b>Apha Focto Protein (n=108)</b>    |  |   |
| ≥ 24 ng/ml                           | 7 (37%)  | 52 (48%)  |
| <b>Mutations</b>                     |  |   |
| <i>TP53</i>                          | 3 (13%)  | 26 (21%)  |
| <i>CTNNB1</i>                        | 11 (46%)   | 41 (33%)  |
| <i>AXIN1</i>                         | 5 (21%)  | 19 (15%)  |
| <i>CDKN2A</i>                        | 2 (8%)   | 9 (7%)  |
| <i>KRAS</i>                          | 0 (0%)   | 2 (1.6%)  |
| <i>ARID2</i>                         | 2 (8%)   | 7 (5.6%)  |
| <b>Transcriptome Groups ( n=123)</b> |  |   |
| G1                                   | 1 (4%)   | 15 (12%)  |
| G2                                   | 0 (0%)   | 13 (11%)  |
| G3                                   | 4 (17%)  | 19 (16%)  |
| G4                                   | 8 (33%)  | 38 (30%)  |
| G5                                   | 7 (29%)  | 25 (20%)  |
| G6                                   | 4 (17%)  | 13 (11%)  |



Supplementary Table 2: Clinical, histological and molecular data of HCC

| ID       | Age (year) | Gender | Etiology | Tumor size (mm) | Microscopic Vascular Invasion | BCLC | Edmonson | META VIR | AFP (ng/ml) | Transcriptome subgroups | Ploidy | FAA  | PFS time | PFS status | OS time | OS status |
|----------|------------|--------|----------|-----------------|-------------------------------|------|----------|----------|-------------|-------------------------|--------|------|----------|------------|---------|-----------|
| CHC008T  | 73         | F      | HBV      | 20              | no                            | 0    | I-II     | F4       | ≥24         | G4                      | 2      | 0    | 1        | 1          | 7       | 1         |
| CHC012T  | 35         | M      | HBV      | 80              | yes                           | A    |          | F4       | ≥24         | G1                      | 3      | 0.63 | 8        | 1          | 15      | 1         |
| CHC013T  | 62         | M      | HCV      | 30              | yes                           | A    | I-II     | F4       | ≥24         | G5                      | 2      | 0.16 | 6        | 1          | 15      | 1         |
| CHC014T  | 29         | M      | HBV      | 130             | yes                           | A    | III-IV   | F2-F3    | ≥24         | G3                      | 3      | 0.74 | 3        | 1          | 5       | 1         |
| CHC018T  | 34         | F      | HBV      | 170             | yes                           | A    | III-IV   | F2-F3    | ≥24         | G1                      | 3      | 0.34 | 14       | 1          | 35      | 1         |
| CHC028T  | 63         | M      | HCV      | 30              | yes                           | A    | III-IV   | F4       | <24         | G6                      | 3      | 0.61 | 40       | 1          | 60      | 0         |
| CHC031T  | 67         | M      | AL       | 16              | no                            | 0    | I-II     | F4       | <24         | G5                      | 3      | 0.76 | 15       | 1          | 26      | 1         |
| CHC032T  | 59         | M      | HBV      | 25              | no                            | B    | I-II     | F4       | ≥24         | -                       | 2      | 0    | NE       | NE         | NE      | NE        |
| CHC033T  | 38         | M      | HBV      | 250             | yes                           | C    | III-IV   | F2-F3    | ≥24         | -                       | 2      | 0.32 | NE       | NE         | NE      | NE        |
| CHC034T  | 55         | M      | HBV      | 170             | yes                           | A    | III-IV   | F2-F3    | ≥24         | G2                      | 3      | 0.63 | 12       | 1          | 23      | 1         |
| CHC037T  | 50         | M      | Other    | 120             | no                            | A    | I-II     | F0-F1    | <24         | G4                      | 2      | 0.47 | 60       | 0          | 60      | 0         |
| CHC043T  | 55         | M      | HBV      | 50              | no                            | A    | III-IV   | F2-F3    | ≥24         | G3                      | 4      | 0.82 | 58       | 0          | 58      | 0         |
| CHC046T  | 61         | F      | HBV      | 65              | yes                           | C    | III-IV   | F4       | ≥24         | G3                      | 3      | 0.74 | 12       | 0          | 12      | 0         |
| CHC051T  | 68         | F      | HCV      | 60              | no                            | A    |          | F4       | ≥24         | G6                      | 2      | 0.13 | 32       | 1          | 53      | 1         |
| CHC059T  | 40         | M      | AL       | 80              | yes                           | C    | III-IV   | F0-F1    | ≥24         | G6                      | 2      | 0.05 | 16       | 1          | 16      | 1         |
| CHC060T  | 68         | M      | AL       | 28              | yes                           | C    | III-IV   | F4       | <24         | G1                      | 2      | 0    | 21       | 1          | 27      | 1         |
| CHC081T  | 75         | F      | HBV      | 90              | no                            | A    | I-II     | F4       | ≥24         | G4                      | 2      | 0.11 | NE       | NE         | NE      | NE        |
| CHC097T  | 56         | M      | Other    | 70              | yes                           | B    | I-II     | F0-F1    | <24         | G5                      | 2      | 0.16 | 13       | 1          | 37      | 1         |
| CHC100T  | 68         | M      | HCV AL   | 20              | yes                           | A    | III-IV   | F4       |             | G2                      | 4      | 0.42 | NE       | NE         | NE      | NE        |
| CHC1035T | 68         | M      | HBV AL   | 75              | no                            | A    | I-II     | F2-F3    | <24         | G5                      | 2      | 0.3  | 10       | 1          | 30      | 0         |
| CHC1040T | 72         | M      | AL       | 160             | yes                           | A    | III-IV   | F2-F3    | ≥24         | G4                      | 2      | 0.3  | 33       | 1          | 35      | 0         |
| CHC1041T | 68         | M      | Other    | 10              | no                            | 0    | I-II     | F0-F1    | <24         | G6                      | 2      | 0.2  | 35       | 0          | 35      | 0         |
| CHC1044T | 78         | M      | AL       | 16              | yes                           | 0    | III-IV   | F2-F3    | ≥24         | G1                      | 2      | 0.15 | 33       | 0          | 33      | 0         |
| CHC1052T | 75         | M      | AL       | 130             | yes                           | A    | III-IV   | F2-F3    | <24         | G4                      | 3      | 0.52 | 1        | 0          | 1       | 0         |
| CHC1053T | 73         | M      | AL       | 35              | yes                           | A    | III-IV   | F4       | ≥24         | G4                      | 2      | 0.15 | 19       | 1          | 19      | 1         |
| CHC1055T | 67         | M      | AL       | 200             | yes                           | B    | III-IV   | F2-F3    | ≥24         | G3                      | 2      | 0.15 | 6        | 1          | 6       | 1         |
| CHC1060T | 66         | M      | NASH     | 30              | no                            | A    | III-IV   | F4       |             | G4                      | 2      | 0    | 29       | 0          | 29      | 0         |
| CHC1061T | 79         | F      | Other    | 150             | yes                           | A    | I-II     | F0-F1    | <24         | G4                      | 4      | 0.28 | 13       | 1          | 39      | 0         |
| CHC1062T | 65         | M      | HM       | 30              | yes                           | A    | I-II     | F2-F3    | ≥24         | G2                      | 2      | 0    | 36       | 0          | 36      | 0         |
| CHC1065T | 77         | M      | Other    | 35              | yes                           | C    | I-II     | F0-F1    | <24         | G4                      | 2      | 0.12 | 22       | 1          | 40      | 0         |
| CHC1069T | 77         | M      | AL       | 50              | yes                           | A    | III-IV   | F2-F3    | <24         | G5                      | 2      | 0.28 | 3        | 0          | 3       | 0         |
| CHC1146T | 59         | M      | AL       | 170             | yes                           | C    | III-IV   | F0-F1    | ≥24         | G3                      | 2      | 0.25 | 16       | 1          | 18      | 1         |
| CHC1154T | 43         | M      | HBV      | 130             | yes                           | A    | I-II     | F2-F3    | ≥24         | G6                      | 3      | 0.45 | 60       | 0          | 60      | 0         |
| CHC115T  | 59         | M      | NASH     | 70              | yes                           | A    | I-II     | F0-F1    | <24         | G5                      | 4      | 0.11 | 24       | 1          | 60      | 0         |
| CHC1162T | 59         | M      | AL       | 55              |                               | B    | I-II     | F4       | <24         | G4                      | 2      | 0    | 60       | 0          | 60      | 0         |
| CHC1185T | 52         | M      | HBV      | 30              | no                            | A    | III-IV   | F4       | ≥24         | G1                      | 2      | 0.18 | 60       | 0          | 60      | 0         |
| CHC1190T | 68         | F      | HCV AL   | 22              | yes                           | A    | I-II     | F2-F3    | ≥24         | G4                      | 2      | 0    | 27       | 1          | 60      | 0         |
| CHC1192T | 40         | M      | HBV      | 70              | yes                           | A    | III-IV   | F4       | ≥24         | G2                      | 4      | 0.48 | 9        | 1          | 18      | 1         |
| CHC1196T | 26         | M      | HBV      | 90              | yes                           | A    | III-IV   | F2-F3    | ≥24         | G1                      | 2      | 0.13 | 3        | 1          | 11      | 1         |
| CHC1199T | 62         | M      | Other    | 140             | yes                           | C    | I-II     | F0-F1    | <24         | G2                      | 2      | 0.35 | 20       | 1          | 43      | 1         |
| CHC1201T | 72         | M      | AL       | 60              | no                            | A    | I-II     | F4       | <24         | G4                      | 3      | 0.45 | 30       | 1          | 60      | 0         |
| CHC121T  | 66         | M      | AL       | 120             | no                            | A    | I-II     | F0-F1    | <24         | G5                      | 2      | 0.18 | 60       | 0          | 60      | 0         |
| CHC123T  | 42         | M      | HBV      |                 |                               | 0    |          | F0-F1    |             | G4                      | 2      | 0.34 | 4        | 1          | 4       | 1         |
| CHC126T  | 68         | F      | HCV      | 70              | no                            | A    |          | F4       | ≥24         | G3                      | 3      | 0.61 | 60       | 0          | 60      | 0         |
| CHC129T  | 61         | F      | Other    | 130             | yes                           | A    | I-II     | F0-F1    | ≥24         | G5                      | 2      | 0.21 | 4        | 1          | 4       | 1         |
| CHC130T  | 60         | M      | Other    | 180             | no                            | A    | I-II     | F0-F1    | <24         | G5                      | 2      | 0.29 | 20       | 1          | 31      | 0         |
| CHC137T  | 71         | M      | HBV      | 35              | no                            | A    | III-IV   | F2-F3    | ≥24         | G5                      | 3      | 0.61 | 60       | 0          | 60      | 0         |
| CHC141T  | 67         | F      | Other    | 35              | yes                           | A    | III-IV   | F0-F1    | ≥24         | G1                      | 4      | 0.24 | 60       | 0          | 60      | 0         |
| CHC152T  | 64         | M      | HBV      | 30              | no                            | C    |          | F4       | <24         | G6                      | 2      | 0.11 | NE       | NE         | NE      | NE        |
| CHC154T  | 67         | F      | Other    | 90              | no                            | A    | I-II     | F0-F1    | <24         | G4                      | 2      | 0.11 | 16       | 1          | 49      | 0         |
| CHC155T  | 62         | M      | AL       | 35              | no                            | A    | I-II     | F4       | <24         | G4                      | 2      | 0.03 | 16       | 1          | 20      | 0         |
| CHC158T  | 65         | M      | HBV AL   | 25              | no                            | A    | I-II     | F4       | <24         | G4                      | 2      | 0.24 | 20       | 0          | 20      | 0         |
| CHC164T  | 65         | M      | Other    | 100             | no                            | B    | I-II     | F0-F1    | <24         | G5                      | 2      | 0.32 | 36       | 1          | 36      | 1         |
| CHC168T  | 67         | M      | AL       | 100             | yes                           | A    | I-II     | F4       | ≥24         | G6                      | 2      | 0.24 | 3        | 1          | 3       | 1         |
| CHC191T  | 71         | M      | AL       | 110             | yes                           | C    | I-II     | F0-F1    | <24         | G4                      | 2      | 0.13 | 11       | 1          | 11      | 1         |
| CHC195T  | 71         | M      | AL       | 70              | no                            | A    | I-II     | F0-F1    | <24         | G4                      | 2      | 0.32 | 60       | 0          | 60      | 0         |
| CHC196T  | 33         | M      | Other    | 100             | no                            | A    | I-II     | F0-F1    | <24         | G4                      | 2      | 0    | 60       | 0          | 60      | 0         |
| CHC197T  | 73         | M      | AL       | 130             | yes                           | B    | III-IV   | F2-F3    | ≥24         | G6                      | 2      | 0.39 | 36       | 1          | 60      | 0         |
| CHC203T  | 45         | M      | AL       | 50              | no                            | A    | I-II     | F4       | ≥24         | G4                      | 2      | 0.21 | 15       | 0          | 15      | 0         |
| CHC205T  | 45         | M      | AL       | 100             | no                            | A    | III-IV   | F0-F1    | ≥24         | G3                      | 3      | 0.61 | 2        | 1          | 9       | 1         |
| CHC206T  | 63         | M      | HBV      | 40              | no                            | B    | III-IV   | F4       | <24         | G4                      | 2      | 0    | NE       | NE         | NE      | NE        |
| CHC208T  | 79         | M      | HCV AL   | 45              | yes                           | A    | III-IV   | F2-F3    | ≥24         | G3                      | 2      | 0.37 | 6        | 1          | 17      | 1         |
| CHC210T  | 58         | M      | HCV      | 50              | no                            | B    | III-IV   | F4       |             | G4                      | 2      | 0.24 | NE       | NE         | NE      | NE        |
| CHC211T  | 68         | M      | AL       | 80              | yes                           | C    | I-II     | F0-F1    | <24         | G4                      | 2      | 0.21 | 12       | 1          | 12      | 1         |
| CHC218T  | 69         | M      | Other    | 130             | yes                           | C    | III-IV   | F0-F1    | ≥24         | G4                      | 2      | 0.26 | NE       | NE         | NE      | NE        |
| CHC226T  | 42         | M      | HBV      | 190             | yes                           | C    | I-II     | F2-F3    |             | G3                      | 2      | 0.42 | NE       | NE         | NE      | NE        |
| CHC228T  | 48         | M      | Other    | 145             | yes                           | C    | III-IV   | F0-F1    | ≥24         | G1                      | 3      | 0.37 | 4        | 1          | 14      | 1         |
| CHC229T  | 64         | F      | HCV      | 55              | yes                           | A    | III-IV   | F4       | <24         | G3                      | 2      | 0.24 | NE       | NE         | NE      | NE        |
| CHC230T  | 70         | M      | Other    | 160             | no                            | A    | I-II     | F0-F1    | <24         | G5                      | 2      | 0.24 | 60       | 0          | 60      | 0         |
| CHC235T  | 66         | F      | HCV      | 30              | no                            | A    | I-II     | F4       | ≥24         | G1                      | 2      | 0.42 | 46       | 0          | 46      | 0         |
| CHC237T  | 26         | F      | HBV      | 125             | no                            | B    | III-IV   | F0-F1    | <24         | G1                      | 2      | 0.24 | 11       | 0          | 11      | 0         |
| CHC239T  | 21         | F      | HBV      | 100             | yes                           | A    | I-II     | F2-F3    | <24         | G2                      | 2      | 0.32 | 12       | 0          | 12      | 0         |
| CHC241T  | 59         | M      | HBV      | 30              | no                            | A    | III-IV   | F2-F3    | <24         | G4                      | 2      | 0.29 | 60       | 0          | 60      | 0         |
| CHC242T  | 69         | M      | Other    | 150             | no                            | A    | I-II     | F0-F1    | <24         | G6                      | 2      | 0.13 | 49       | 1          | 59      | 1         |
| CHC245T  | 62         | M      | HBV      | 3               | no                            | 0    | I-II     | F4       | <24         | G2                      | 2      | 0.34 | 9        | 1          | 13      | 1         |
| CHC250T  | 34         | M      | HBV HCV  | 70              | no                            | C    | I-II     | F4       | ≥24         | G1                      | 2      | 0.32 | NE       | NE         | NE      | NE        |

Supplementary Table 2: Clinical, histological and molecular data of HCC

| ID      | Age (year) | Gender | Etiology | Tumor size (mm) | Microscopic Vascular Invasion | BCLC | Edmonson | META VIR | AFP (ng/ml) | Transcriptome subgroups | Ploidy | FAA  | PFS time | PFS status | OS time | OS status |
|---------|------------|--------|----------|-----------------|-------------------------------|------|----------|----------|-------------|-------------------------|--------|------|----------|------------|---------|-----------|
| CHC252T | 57         | M      | HBV HCV  | 17              | no                            | 0    | I-II     | F2-F3    | ≥24         | G1                      | 3      | 0.55 | 33       | 1          | 60      | 0         |
| CHC253T | 66         | M      | Other    | 80              | yes                           | C    | III-IV   | F4       | <24         | G3                      | 2      | 0.03 | NE       | NE         | NE      | NE        |
| CHC254T | 62         | M      | HBV HCV  | 80              | yes                           | C    | III-IV   | F4       | <24         | G3                      | 4      | 0.53 | 8        | 1          | 14      | 0         |
| CHC258T | 56         | M      | Other    | 100             | no                            | A    | I-II     | F0-F1    |             | G5                      | 2      | 0.21 | 60       | 0          | 60      | 0         |
| CHC301T | 77         | M      | NASH     | 45              | no                            | B    | I-II     | F2-F3    | <24         | G3                      | 2      | 0.21 | 44       | 1          | 50      | 1         |
| CHC302T | 72         | M      | HCV      | 45              | no                            | A    | I-II     | F2-F3    |             | G5                      | 2      | 0.13 | 60       | 0          | 60      | 0         |
| CHC303T | 73         | M      | AL       | 90              | yes                           | A    | III-IV   | F4       | ≥24         | G5                      | 2      | 0.18 | NE       | NE         | NE      | NE        |
| CHC304T | 77         | M      | AL       | 180             | yes                           | C    | III-IV   | F0-F1    | ≥24         | G3                      | 3      | 0.71 | 6        | 1          | 22      | 1         |
| CHC306T | 67         | M      | HCV      | 20              | no                            | 0    | I-II     | F4       |             | G4                      | 2      | 0.13 | NE       | NE         | NE      | NE        |
| CHC307T | 53         | M      | AL       | 30              | yes                           | A    | III-IV   | F4       |             | G4                      | 2      | 0.16 | NE       | NE         | NE      | NE        |
| CHC309T | 69         | F      | HCV      | 20              | yes                           | 0    | III-IV   | F2-F3    |             | G2                      | 2      | 0.18 | NE       | NE         | NE      | NE        |
| CHC313T | 43         | F      | HCV      | 130             | yes                           | A    | III-IV   | F2-F3    | ≥24         | G4                      | 2      | 0.21 | 4        | 1          | 11      | 1         |
| CHC314T | 71         | M      | HCV AL   | 45              | no                            | A    | I-II     | F2-F3    | <24         | G4                      | 2      | 0.21 | 59       | 0          | 59      | 0         |
| CHC317T | 68         | F      | HCV      | 15              | no                            | A    | III-IV   | F4       |             | G5                      | 2      | 0.11 | NE       | NE         | NE      | NE        |
| CHC320T | 64         | M      | HCV AL   | 35              | no                            | B    | III-IV   | F4       |             | G6                      | 2      | 0.02 | NE       | NE         | NE      | NE        |
| CHC322T | 73         | M      | AL       | 40              | no                            | A    | III-IV   | F4       | <24         | G4                      | 3      | 0.58 | 21       | 1          | 21      | 1         |
| CHC326T | 48         | M      | HBV      | 18              | no                            | A    | I-II     | F4       |             | G4                      | 2      | 0.03 | NE       | NE         | NE      | NE        |
| CHC327T | 62         | M      | HCV      | 25              | no                            | A    | I-II     | F4       |             | G1                      | 2      | 0.13 | NE       | NE         | NE      | NE        |
| CHC333T | 72         | M      | AL       | 42              | no                            | A    | I-II     | F2-F3    | <24         | G5                      | 2      | 0.29 | NE       | NE         | NE      | NE        |
| CHC335T | 68         | M      | HBV      | 160             | yes                           | A    | I-II     | F2-F3    | ≥24         | G6                      | 2      | 0.05 | 59       | 0          | 59      | 0         |
| CHC339T | 26         | F      | HBV      | 100             | yes                           | C    | I-II     | F2-F3    | ≥24         | G2                      | 3      | 0.55 | 34       | 1          | 56      | 1         |
| CHC361T | 67         | F      | Other    | 60              | no                            | A    | I-II     | F0-F1    | <24         | G5                      | 2      | 0.03 | 60       | 0          | 60      | 0         |
| CHC398T | 50         | M      | HBV      | 40              | no                            | 0    | I-II     |          |             | G2                      | 2      | 0.21 | NE       | NE         | NE      | NE        |
| CHC399T | 67         | M      | HM       | 30              | no                            | A    | I-II     | F2-F3    | <24         | G6                      | 2      | 0.18 | 26       | 1          | 37      | 0         |
| CHC402T | 27         | M      | HBV HCV  | 65              | no                            | B    | I-II     | F4       | ≥24         | G2                      | 2      | 0.34 | 11       | 1          | 16      | 1         |
| CHC405T | 77         | M      | HM       | 43              | no                            | A    | I-II     | F0-F1    | <24         | G4                      | 2      | 0.05 | 38       | 0          | 38      | 0         |
| CHC429T | 61         | F      | Other    | 45              | yes                           | A    | III-IV   | F0-F1    | ≥24         | G5                      | 2      | 0.08 | 23       | 1          | 60      | 0         |
| CHC430T | 50         | M      | HCV      | 60              | yes                           | B    | III-IV   | F4       | <24         | G5                      | 2      | 0.05 | 8        | 1          | 8       | 1         |
| CHC433T | 69         | M      | AL       | 180             | yes                           | A    | I-II     | F0-F1    | <24         | G5                      | 2      | 0.34 | 11       | 1          | 15      | 1         |
| CHC434T | 71         | F      | Other    | 80              | no                            | A    | III-IV   | F0-F1    | ≥24         | G1                      | 4      | 0.5  | 26       | 1          | 60      | 0         |
| CHC437T | 59         | M      | AL       | 50              | no                            | A    | I-II     | F4       |             | G5                      | 2      | 0.18 | 13       | 1          | 24      | 1         |
| CHC438T | 75         | M      | Other    | 185             | no                            | A    | III-IV   | F0-F1    | <24         | G2                      | 2      | 0.32 | NE       | NE         | NE      | NE        |
| CHC441T | 77         | M      | HM       | 40              | no                            | A    | III-IV   | F0-F1    |             | G3                      | 2      | 0.18 | 6        | 1          | 7       | 1         |
| CHC445T | 55         | M      | HCV AL   | 14              | no                            | 0    | I-II     | F4       | ≥24         | G4                      | 2      | 0.03 | 13       | 0          | 13      | 0         |
| CHC465T | 42         | F      | Other    | 100             |                               | A    | I-II     | F0-F1    | <24         | G4                      | 2      | 0.08 | 60       | 0          | 60      | 0         |
| CHC469T | 32         | F      | Other    | 135             | yes                           | C    | III-IV   | F0-F1    | <24         | G6                      | 2      | 0.34 | 12       | 1          | 23      | 1         |
| CHC609T | 60         | M      | HBV AL   | 50              | yes                           | B    | III-IV   | F2-F3    | <24         | G5                      | 2      | 0.45 | 18       | 1          | 50      | 0         |
| CHC614T | 60         | M      | NASH     | 30              | yes                           | A    | III-IV   | F2-F3    | <24         | G5                      | 2      | 0.1  | 12       | 0          | 12      | 0         |
| CHC715T | 46         | M      | NASH AL  | 40              | yes                           | B    | III-IV   | F0-F1    | <24         | G4                      | 2      | 0.13 | NE       | NE         | NE      | NE        |
| CHC725T | 59         | M      | HBV      | 27              | no                            | A    | III-IV   | F4       | <24         | G2                      | 2      | 0.18 | NE       | NE         | NE      | NE        |
| CHC793T | 61         | M      | HM       | 80              | yes                           | A    | III-IV   | F0-F1    | ≥24         | G3                      | 2      | 0.35 | 20       | 1          | 37      | 1         |
| CHC794T | 72         | M      | HM       | 160             | yes                           | C    | III-IV   | F0-F1    | ≥24         | G3                      | 3      | 0.53 | 1        | 1          | 5       | 1         |
| CHC798T | 72         | M      | AL       | 95              | no                            | A    | I-II     | F0-F1    | <24         | G4                      | 2      | 0.18 | 16       | 0          | 16      | 0         |
| CHC882T | 54         | M      | AL       | 40              | no                            | A    | III-IV   | F0-F1    | <24         | G3                      | 2      | 0.21 | NE       | NE         | NE      | NE        |
| CHC891T | 72         | F      | Other    | 45              | yes                           | A    | III-IV   | F4       | ≥24         | G1                      | 2      | 0.25 | 7        | 1          | 16      | 1         |
| CHC909T | 69         | M      | Other    | 210             | yes                           | C    | III-IV   | F0-F1    | ≥24         | G3                      | 2      | 0.32 | 37       | 0          | 37      | 0         |
| CHC918T | 82         | M      | AL       | 95              | no                            | A    | I-II     | F0-F1    | <24         | G4                      | 2      | 0.13 | 45       | 0          | 45      | 0         |
| CHC961T | 57         | M      | AL       | 190             | yes                           | B    | III-IV   | F0-F1    | <24         | G5                      | 2      | 0.26 | 7        | 1          | 17      | 1         |
| CHC983T | 53         | M      | AL       | 50              | no                            | B    | III-IV   | F4       | <24         | G4                      | 2      | 0.05 | 6        | 1          | 27      | 1         |

AL= Alcohol intake; HM= Hemochromatosis

NE= patients non evaluable for survival (including transplantation, non curative resection)

**Supplementary Table 3. List of all somatic mutations identified in the exome sequencing of 24 HCC**

| HCC-ID   | Ensembl Gene ID | Gene symbol | Chromosome | Nucleotide (genomic position hg19) | Amino Acid             | Mutation Type |
|----------|-----------------|-------------|------------|------------------------------------|------------------------|---------------|
| CHC433T  | ENSG00000168036 | CTNNB1      | 3          | g.41266098A>G                      | p.Asp32Gly             | missense      |
| CHC1041T | ENSG00000168036 | CTNNB1      | 3          | g.41266098A>T                      | p.Asp32Val             | missense      |
| CHC051T  | ENSG00000168036 | CTNNB1      | 3          | g.41266100T>C                      | p.Ser33Pro             | missense      |
| CHC429T  | ENSG00000168036 | CTNNB1      | 3          | g.41266101C>G                      | p.Ser33Cys             | missense      |
| CHC301T  | ENSG00000168036 | CTNNB1      | 3          | g.41266107T>G                      | p.Ile35Ser             | missense      |
| CHC320T  | ENSG00000168036 | CTNNB1      | 3          | g.41266113C>G                      | p.Ser37Cys             | missense      |
| CHC614T  | ENSG00000168036 | CTNNB1      | 3          | g.41266125C>A                      | p.Thr41Asn             | missense      |
| CHC1052T | ENSG00000168036 | CTNNB1      | 3          | g.41266128_41266129insCAGCTC       | p.Thr42_Ala43insSerSer | insertion     |
| CHC121T  | ENSG00000168036 | CTNNB1      | 3          | g.41266136T>G                      | p.Ser45Ala             | missense      |
| CHC302T  | ENSG00000168036 | CTNNB1      | 3          | g.41266137C>A                      | p.Ser45Tyr             | missense      |
| CHC197T  | ENSG00000168036 | CTNNB1      | 3          | g.41266137C>T                      | p.Ser45Phe             | missense      |
| CHC434T  | ENSG00000103126 | AXIN1       | 16         | g.347772G>T                        | p.Tyr578X              | nonsense      |
| CHC1065T | ENSG00000103126 | AXIN1       | 16         | g.354326_354327insA                | p.Glu411ValfsX13       | insertion     |
| CHC1053T | ENSG00000103126 | AXIN1       | 16         | g.354381_354406del                 | p.Glu384AspfsX31       | deletion      |
| CHC306T  | ENSG00000103126 | AXIN1       | 16         | g.364602del                        | p.Asp320GlufsX94       | deletion      |
| CHC306T  | ENSG00000103126 | AXIN1       | 16         | g.396233C>A                        | p.Gly265X              | nonsense      |
| CHC1053T | ENSG00000177189 | RPS6KA3     | X          | g.20181154A>C                      | p.Leu590X              | nonsense      |
| CHC258T  | ENSG00000177189 | RPS6KA3     | X          | g.20194611C>A                      | p.Gly314X              | nonsense      |
| CHC1053T | ENSG00000177189 | RPS6KA3     | X          | g.20205972C>T                      | p.Asp250Asn            | missense      |
| CHC434T  | ENSG00000177189 | RPS6KA3     | X          | g.20206044A>T                      | p.Tyr226Asn            | missense      |
| CHC429T  | ENSG00000177189 | RPS6KA3     | X          | g.20222175T>C                      | p.Tyr97Cys             | missense      |
| CHC155T  | ENSG00000117713 | ARID1A      | 1          | g.27056173_27056174insT            | p.Met390IlefsX10       | insertion     |
| CHC205T  | ENSG00000117713 | ARID1A      | 1          | g.27099938_27099962del             | p.Gly1274GlufsX7       | deletion      |
| CHC205T  | ENSG00000117713 | ARID1A      | 1          | g.27099964T>G                      | p.Tyr1281X             | nonsense      |
| CHC320T  | ENSG00000117713 | ARID1A      | 1          | g.27106640T>A                      | p.Val2084Asp           | missense      |
| CHC121T  | ENSG00000164796 | CSMD3       | 8          | g.113318267C>A                     | p.Trp2680Cys           | missense      |
| CHC121T  | ENSG00000164796 | CSMD3       | 8          | g.113318310G>A                     | p.Ser2666Phe           | missense      |
| CHC051T  | ENSG00000164796 | CSMD3       | 8          | g.113364712T>G                     | p.Lys2063Thr           | missense      |
| CHC307T  | ENSG00000164796 | CSMD3       | 8          | g.114031312del                     | p.Phe338LeuX11         | deletion      |
| CHC1035T | ENSG00000163638 | ADAMTS9     | 3          | g.64527575G>T                      | p.Ser1712Arg           | missense      |
| CHC301T  | ENSG00000163638 | ADAMTS9     | 3          | g.64627650C>A                      | p.Cys577Phe            | missense      |
| CHC301T  | ENSG00000163638 | ADAMTS9     | 3          | g.64640135C>A                      | splicing               | intron        |
| CHC1065T | ENSG00000163631 | ALB         | 4          | g.74274500_74274501del             | p.Asn154X              | deletion      |
| CHC614T  | ENSG00000163631 | ALB         | 4          | g.74277791_74277801del             | p.Val265MetfsX8        | deletion      |
| CHC258T  | ENSG00000163631 | ALB         | 4          | g.74284018_74284020del             | p.Lys549del            | deletion      |
| CHC205T  | ENSG00000084674 | APOB        | 2          | g.21239482_21239483insATAA         | p.Asn1054IlefsX11      | insertion     |
| CHC302T  | ENSG00000084674 | APOB        | 2          | g.21251397A>G                      | p.Leu544Pro            | missense      |
| CHC1041T | ENSG00000084674 | APOB        | 2          | g.21252826del                      | p.Glu472AsnfsX16       | deletion      |
| CHC307T  | ENSG00000183117 | CSMD1       | 8          | g.3205676A>T                       | p.Cys1104X             | nonsense      |
| CHC155T  | ENSG00000165323 | FAT3        | 11         | g.92085687G>T                      | p.Asp137Tyr            | missense      |
| CHC301T  | ENSG00000165323 | FAT3        | 11         | g.92086194G>A                      | p.Gly306Arg            | missense      |
| CHC155T  | ENSG00000165323 | FAT3        | 11         | g.92620270G>T                      | p.Asp4348Tyr           | missense      |
| CHC614T  | ENSG00000116044 | NFE2L2      | 2          | g.178098800T>G                     | p.Glu82Gly             | missense      |
| CHC1041T | ENSG00000116044 | NFE2L2      | 2          | g.178098807T>G                     | p.Thr80Pro             | missense      |
| CHC205T  | ENSG00000116044 | NFE2L2      | 2          | g.178098959T>C                     | p.Asp29Gly             | missense      |
| CHC433T  | ENSG00000156709 | AIFM1       | X          | g.129267388T>A                     | p.Arg450Trp            | missense      |
| CHC429T  | ENSG00000156709 | AIFM1       | X          | g.129271128A>G                     | p.Phe334Leu            | missense      |
| CHC429T  | ENSG00000163286 | ALPPL2      | 2          | g.233273095G>A                     | p.Trp256X              | nonsense      |
| CHC429T  | ENSG00000189079 | ARID2       | 12         | g.46244040G>T                      | p.Glu712X              | nonsense      |
| CHC301T  | ENSG00000138175 | ARL3        | 10         | g.104436683C>A                     | p.Val173Phe            | missense      |
| CHC121T  | ENSG00000198960 | ARMCX6      | X          | g.100871207C>A                     | p.Gly135Val            | missense      |
| CHC121T  | ENSG00000198960 | ARMCX6      | X          | g.100871208C>A                     | p.Gly135X              | nonsense      |
| CHC433T  | ENSG00000112249 | ASCC3       | 6          | g.101110274T>C                     | p.Thr809Ala            | missense      |
| CHC433T  | ENSG00000118322 | ATP10B      | 5          | g.160047869C>A                     | p.Ser634Ile            | missense      |
| CHC301T  | ENSG00000118322 | ATP10B      | 5          | g.160061403G>A                     | p.Arg447Cys            | missense      |
| CHC614T  | ENSG00000105726 | ATP13A1     | 19         | g.19758027A>G                      | p.Tyr1006His           | missense      |
| CHC155T  | ENSG00000105726 | ATP13A1     | 19         | g.19758063T>C                      | p.Asn994Asp            | missense      |
| CHC433T  | ENSG00000187527 | ATP13A5     | 3          | g.193029609G>A                     | p.Pro814Leu            | missense      |
| CHC1035T | ENSG00000187527 | ATP13A5     | 3          | g.193036884G>C                     | p.Phe643Leu            | missense      |
| CHC429T  | ENSG00000197299 | BLM         | 15         | g.91290711C>T                      | p.Pro30Leu             | missense      |
| CHC302T  | ENSG00000197299 | BLM         | 15         | g.91304159A>G                      | p.Tyr519Cys            | missense      |
| CHC322T  | ENSG00000182326 | C1S         | 12         | g.7173239dup                       | p.Trp283LeufsX14       | duplication   |
| CHC301T  | ENSG00000182326 | C1S         | 12         | g.7169912G>A                       | p.Gly47Arg             | missense      |
| CHC429T  | ENSG00000153132 | CLGN        | 4          | g.141317095C>T                     | p.Ala343Thr            | missense      |
| CHC302T  | ENSG00000153132 | CLGN        | 4          | g.141334123T>A                     | p.Glu37Val             | missense      |
| CHC302T  | ENSG00000176566 | DCAF4L2     | 8          | g.88885884C>A                      | p.Gly106Cys            | missense      |
| CHC1035T | ENSG00000176566 | DCAF4L2     | 8          | g.88886169C>A                      | p.Glu11X               | nonsense      |
| CHC322T  | ENSG00000198947 | DMD         | X          | g.31514964G>A                      | p.Arg2830Trp           | missense      |
| CHC301T  | ENSG00000198947 | DMD         | X          | g.32834622C>G                      | p.Asp165His            | missense      |
| CHC155T  | ENSG00000124721 | DNAH8       | 6          | g.38793962C>A                      | p.Ala1076Asp           | missense      |
| CHC434T  | ENSG00000124721 | DNAH8       | 6          | g.38795966_38795975del             | p.Tyr1147X             | deletion      |
| CHC1055T | ENSG00000130158 | DOCK6       | 19         | g.11348904C>T                      | p.Val574Met            | missense      |
| CHC302T  | ENSG00000130158 | DOCK6       | 19         | g.11354495C>A                      | p.Glu363X              | nonsense      |
| CHC320T  | ENSG00000171560 | FGA         | 4          | g.155505794_155505795del           | p.Gly695PhefsX6        | deletion      |
| CHC302T  | ENSG00000171560 | FGA         | 4          | g.155510662C>A                     | p.Gly36Val             | missense      |
| CHC1055T | ENSG00000110422 | FIGLN2      | 12         | g.52216187G>A                      | p.Thr41le              | missense      |
| CHC1053T | ENSG00000110422 | HIPK3       | 11         | g.33309053T>G                      | p.Tyr365Asp            | missense      |
| CHC320T  | ENSG00000110422 | HIPK3       | 11         | g.33373152A>G                      | splicing               | intron        |
| CHC1061T | ENSG00000135100 | HNF1A       | 12         | g.121426648_121426651del           | p.Arg114TrpfsX40       | deletion      |
| CHC155T  | ENSG00000135100 | HNF1A       | 12         | g.121437143C>T                     | p.Thr525Ile            | missense      |
| CHC1061T | ENSG00000086758 | HUWE1       | X          | g.53581856G>C                      | p.Tyr2744X             | nonsense      |
| CHC429T  | ENSG00000086758 | HUWE1       | X          | g.53644075G>C                      | p.Pro605Ala            | missense      |
| CHC429T  | ENSG00000102313 | ITIH5L      | X          | g.54776357C>A                      | p.Gly1305Cys           | missense      |
| CHC433T  | ENSG00000102313 | ITIH5L      | X          | g.54815056T>A                      | p.Arg215Trp            | missense      |
| CHC301T  | ENSG00000198399 | ITSN2       | 2          | g.24477267_24477268insA            | p.Lys974AsnfsX33       | insertion     |
| CHC1041T | ENSG00000198399 | ITSN2       | 2          | g.24533166A>C                      | p.Leu214Val            | missense      |
| CHC1055T | ENSG00000138688 | KIAA1109    | 4          | g.123140664G>T                     | p.Arg806Leu            | missense      |
| CHC1061T | ENSG00000138688 | KIAA1109    | 4          | g.123188092G>C                     | p.Arg2491Thr           | missense      |
| CHC320T  | ENSG00000122778 | KIAA1549    | 7          | g.138524987G>T                     | p.Ala1780Asp           | missense      |
| CHC1052T | ENSG00000122778 | KIAA1549    | 7          | g.138566137C>T                     | p.Gly1359Glu           | missense      |
| CHC614T  | ENSG00000161850 | KRT82       | 12         | g.52797639G>T                      | p.Gln156Lys            | missense      |
| CHC429T  | ENSG00000135443 | KRT85       | 12         | g.52760844C>T                      | p.Ala116Thr            | missense      |
| CHC1052T | ENSG00000161813 | LARP4       | 12         | g.50869451C>G                      | p.Ser660Cys            | missense      |
| CHC433T  | ENSG00000168702 | LRP1B       | 2          | g.141200113C>G                     | p.Glu3458Asp           | missense      |
| CHC433T  | ENSG00000151276 | MAG11       | 3          | g.65367726C>A                      | p.Val843Leu            | missense      |
| CHC1052T | ENSG00000166603 | MC4R        | 18         | g.58038652T>G                      | p.Lys311Gln            | missense      |

**Supplementary Table 3. List of all somatic mutations identified in the exome sequencing of 24 HCC**

| HCC-ID   | Ensembl Gene ID | Gene symbol | Chromosome | Nucleotide (genomic position hg19) | Amino Acid           | Mutation Type |
|----------|-----------------|-------------|------------|------------------------------------|----------------------|---------------|
| CHC197T  | ENSG00000166603 | MC4R        | 18         | g.58039311A>T                      | p.Met91Lys           | missense      |
| CHC121T  | ENSG00000175471 | MCTP1       | 5          | g.94275805C>T                      | p.Gly386Arg          | missense      |
| CHC155T  | ENSG00000175471 | MCTP1       | 5          | g.94353071C>G                      | p.Gly280Arg          | missense      |
| CHC1052T | ENSG00000168404 | MLKL        | 16         | g.74708973del                      | p.Lys422AsnfsX5      | deletion      |
| CHC1052T | ENSG00000168404 | MLKL        | 16         | g.74708974T>A                      | p.Lys422Met          | missense      |
| CHC1065T | ENSG00000166670 | MMP10       | 11         | g.102645969A>G                     | p.Leu339Ser          | missense      |
| CHC121T  | ENSG00000166670 | MMP10       | 11         | g.102650238del                     | p.Tyr115SerfsX4      | deletion      |
| CHC155T  | ENSG00000181143 | MUC16       | 19         | g.9008346C>T                       | splicing             | intron        |
| CHC322T  | ENSG00000181143 | MUC16       | 19         | g.9090101del                       | p.Leu572X            | deletion      |
| CHC429T  | ENSG00000154654 | NCAM2       | 21         | g.22656588G>A                      | p.Val69Met           | missense      |
| CHC301T  | ENSG00000154654 | NCAM2       | 21         | g.22881300A>C                      | p.Thr736Pro          | missense      |
| CHC1061T | ENSG00000100968 | NFATC4      | 14         | g.24841806del                      | p.Lys516SerfsX3      | deletion      |
| CHC155T  | ENSG00000100968 | NFATC4      | 14         | g.24843538G>A                      | p.Arg643His          | missense      |
| CHC1061T | ENSG00000155561 | NUP205      | 7          | g.135279433C>G                     | p.Pro657Ala          | missense      |
| CHC429T  | ENSG00000155561 | NUP205      | 7          | g.135287699A>G                     | p.Asn887Asp          | missense      |
| CHC155T  | ENSG00000186117 | OR5L1       | 11         | g.55579487C>T                      | p.Pro182Leu          | missense      |
| CHC1052T | ENSG00000186117 | OR5L1       | 11         | g.55579674C>A                      | p.His244Gln          | missense      |
| CHC1052T | ENSG00000125879 | OTOR        | 20         | g.16729554C>T                      | p.Pro53Leu           | missense      |
| CHC433T  | ENSG00000125879 | OTOR        | 20         | g.16729567C>G                      | p.Phe57Leu           | missense      |
| CHC434T  | ENSG00000116117 | PARD3B      | 2          | g.205983655C>A                     | p.Leu231Ile          | missense      |
| CHC301T  | ENSG00000116117 | PARD3B      | 2          | g.205989162G>T                     | p.Arg426Leu          | missense      |
| CHC429T  | ENSG00000102290 | PCDH11X     | X          | g.91456373G>A                      | splicing             | intron        |
| CHC429T  | ENSG00000102290 | PCDH11X     | X          | g.91873287C>A                      | p.Thr1131Asn         | missense      |
| CHC121T  | ENSG00000197991 | PCDH20      | 13         | g.61986389C>A                      | p.Gly615Trp          | missense      |
| CHC614T  | ENSG00000197991 | PCDH20      | 13         | g.61989221G>C                      | p.Pro24Gln           | missense      |
| CHC429T  | ENSG00000187372 | PCDHB13     | 5          | g.140594857G>T                     | p.Glu388X            | nonsense      |
| CHC155T  | ENSG00000187372 | PCDHB13     | 5          | g.140595883G>T                     | p.Gly730Cys          | missense      |
| CHC1052T | ENSG00000099139 | PCSK5       | 9          | g.78794565C>A                      | p.His652Asn          | missense      |
| CHC1041T | ENSG00000099139 | PCSK5       | 9          | g.78953327T>C                      | p.Cys1617Arg         | missense      |
| CHC1041T | ENSG00000174840 | PDE12       | 3          | g.57542299C>T                      | p.Arg65Cys           | missense      |
| CHC433T  | ENSG00000174840 | PDE12       | 3          | g.57545728A>T                      | p.Lys609Asn          | missense      |
| CHC1035T | ENSG00000134853 | PDGFRA      | 4          | g.55152023C>A                      | p.Leu819Met          | missense      |
| CHC205T  | ENSG00000134853 | PDGFRA      | 4          | g.55156639_55156647del             | p.Ala1014_Ser1016del | deletion      |
| CHC051T  | ENSG00000130024 | PHF10       | 6          | g.170115879_170115880insA          | p.Lys206AsnfsX6      | insertion     |
| CHC1041T | ENSG00000105851 | PIK3CG      | 7          | g.106508490G>A                     | p.Val162Ile          | missense      |
| CHC434T  | ENSG00000105851 | PIK3CG      | 7          | g.106520043C>A                     | p.Ser824X            | nonsense      |
| CHC301T  | ENSG00000101333 | PLCB4       | 20         | g.9370557T>C                       | p.Phe397Ser          | missense      |
| CHC429T  | ENSG00000101333 | PLCB4       | 20         | g.9424651A>T                       | p.Arg918Trp          | missense      |
| CHC197T  | ENSG00000046889 | PREX2       | 8          | g.68965367G>C                      | p.Gly327Arg          | missense      |
| CHC433T  | ENSG00000046889 | PREX2       | 8          | g.69104724C>T                      | p.Ala1523Val         | missense      |
| CHC429T  | ENSG00000101292 | PROKR2      | 20         | g.5283292del                       | p.Ile184LeufX56      | deletion      |
| CHC205T  | ENSG00000101292 | PROKR2      | 20         | g.5294732A>G                       | p.Leu95Pro           | missense      |
| CHC434T  | ENSG00000153707 | PTPRD       | 9          | g.8521544G>A                       | p.Arg232Cys          | missense      |
| CHC434T  | ENSG00000134597 | RBMX2       | X          | g.129543262C>T                     | p.Arg69Trp           | missense      |
| CHC1041T | ENSG00000134597 | RBMX2       | X          | g.129546368A>G                     | p.Lys172Arg          | missense      |
| CHC1061T | ENSG00000079841 | RIMS1       | 6          | g.72967838G>T                      | p.Arg927Ser          | missense      |
| CHC1041T | ENSG00000079841 | RIMS1       | 6          | g.73100381del                      | p.Arg1483SerfsX21    | deletion      |
| CHC434T  | ENSG00000241343 | RPL36A      | X          | g.100646036T>C                     | splicing             | intron        |
| CHC197T  | ENSG00000241343 | RPL36A      | X          | g.100646511dup                     | p.Thr60AspfsX19      | duplication   |
| CHC301T  | ENSG00000198626 | RYR2        | 1          | g.237811777G>A                     | p.Gly2459Glu         | missense      |
| CHC1035T | ENSG00000198626 | RYR2        | 1          | g.237936853G>T                     | p.Gly3894Trp         | missense      |
| CHC301T  | ENSG00000156398 | SFXN2       | 10         | g.104491503T>G                     | p.Val206Gly          | missense      |
| CHC614T  | ENSG00000127616 | SMARCA4     | 19         | g.11141554C>A                      | p.Asp1177Glu         | missense      |
| CHC306T  | ENSG00000163554 | SPTA1       | 1          | g.158624466G>C                     | p.Arg991Gly          | missense      |
| CHC155T  | ENSG00000163554 | SPTA1       | 1          | g.158636156T>G                     | p.Asn724His          | missense      |
| CHC1061T | ENSG00000133138 | TBC1D8B     | X          | g.106066520_106066521insA          | p.Glu218ArgfsX21     | insertion     |
| CHC306T  | ENSG00000133138 | TBC1D8B     | X          | g.106069360C>T                     | p.Pro310Ser          | missense      |
| CHC302T  | ENSG00000198586 | TLK1        | 2          | g.171863026T>G                     | p.Asn576His          | missense      |
| CHC302T  | ENSG00000198586 | TLK1        | 2          | g.171863367T>C                     | p.Glu514Gly          | missense      |
| CHC051T  | ENSG00000158882 | TOMM40L     | 1          | g.161197755A>C                     | p.Asn154His          | missense      |
| CHC1052T | ENSG00000158882 | TOMM40L     | 1          | g.161197758_161197762del           | p.Leu157TrpfsX69     | deletion      |
| CHC1061T | ENSG00000141510 | TP53        | 17         | g.7574017C>A                       | p.Arg337Leu          | missense      |
| CHC1055T | ENSG00000141510 | TP53        | 17         | g.7579520_7579521ins17             | p.Glu56AlafsX73      | insertion     |
| CHC205T  | ENSG00000042781 | USH2A       | 1          | g.216073468C>T                     | p.Gly2515Arg         | missense      |
| CHC614T  | ENSG00000042781 | USH2A       | 1          | g.216595640C>A                     | p.Leu13Phe           | missense      |
| CHC433T  | ENSG00000126870 | WDR60       | 7          | g.158679710A>T                     | splicing             | intron        |
| CHC1052T | ENSG00000126870 | WDR60       | 7          | g.158718881G>C                     | p.Gly754Val          | missense      |
| CHC320T  | ENSG00000140836 | ZFXH3       | 16         | g.72992468G>C                      | p.Ser526X            | nonsense      |
| CHC322T  | ENSG00000183579 | ZNRF3       | 22         | g.29444461T>A                      | p.Cys233Ser          | missense      |
| CHC1041T | ENSG00000183579 | ZNRF3       | 22         | g.29445379G>T                      | p.Glu304X            | nonsense      |
| CHC1052T | ENSG00000166535 | A2ML1       | 12         | g.8990935G>A                       | p.Asp287Asn          | missense      |
| CHC1041T | ENSG00000167972 | ABCA3       | 16         | g.2369582C>G                       | p.Lys291Asn          | missense      |
| CHC1052T | ENSG00000140798 | ABCC12      | 16         | g.48172207T>A                      | p.Glu304Val          | missense      |
| CHC433T  | ENSG00000117528 | ABCD3       | 1          | g.94982631A>T                      | p.Arg642Ser          | missense      |
| CHC253T  | ENSG00000138075 | ABCG5       | 2          | g.44052030_44052032del             | p.Tyr301del          | deletion      |
| CHC205T  | ENSG00000100997 | ABHD12      | 20         | g.25304040T>G                      | p.Lys115Gln          | missense      |
| CHC205T  | ENSG00000111198 | ABHD5       | 3          | g.43743764G>A                      | p.Trp64X             | nonsense      |
| CHC205T  | ENSG00000138443 | AB12        | 2          | g.204231700T>G                     | p.Leu73Arg           | missense      |
| CHC433T  | ENSG00000072778 | ACADVL      | 17         | g.7128403C>T                       | p.Pro652Leu          | missense      |
| CHC429T  | ENSG00000157766 | ACAN        | 15         | g.89398140C>A                      | p.Pro775His          | missense      |
| CHC306T  | ENSG00000111058 | ACSS3       | 12         | g.81647408C>G                      | p.Arg652Gly          | missense      |
| CHC429T  | ENSG00000117148 | ACTL8       | 1          | g.18022124T>C                      | p.Ser12Pro           | missense      |
| CHC1061T | ENSG00000123612 | ACVR1C      | 2          | g.158412680C>A                     | p.Glu157X            | nonsense      |
| CHC197T  | ENSG00000073670 | ADAM11      | 17         | g.42852104A>G                      | p.Met403Val          | missense      |
| CHC433T  | ENSG00000148848 | ADAM12      | 10         | g.127724804G>A                     | p.Arg817X            | nonsense      |
| CHC1035T | ENSG00000008277 | ADAM22      | 7          | g.87763647G>T                      | p.Gly361Trp          | missense      |
| CHC433T  | ENSG00000114948 | ADAM23      | 2          | g.207345992G>A                     | p.Ala157Thr          | missense      |
| CHC155T  | ENSG00000151388 | ADAMTS12    | 5          | g.33684073G>A                      | p.Ser241Phe          | missense      |
| CHC301T  | ENSG00000173157 | ADAMTS20    | 12         | g.43862407G>A                      | p.His407Tyr          | missense      |
| CHC121T  | ENSG00000178031 | ADAMTSL1    | 9          | g.18574050A>G                      | p.Asp87Gly           | missense      |
| CHC155T  | ENSG00000078549 | ADCYAP1R1   | 7          | g.31125052T>C                      | p.Ser222Pro          | missense      |
| CHC429T  | ENSG00000198099 | ADH4        | 4          | g.100057768T>C                     | p.Tyr144Cys          | missense      |
| CHC434T  | ENSG00000173020 | ADRBK1      | 11         | g.67046728_67046730del             | p.Val83del           | deletion      |
| CHC320T  | ENSG00000169129 | AFAP112     | 10         | g.116073668C>A                     | p.Gly252Cys          | missense      |
| CHC320T  | ENSG00000172493 | AFF1        | 4          | g.88035557_88035582del             | p.Trp525CysfsX19     | deletion      |
| CHC434T  | ENSG00000155966 | AFF2        | X          | g.148037388C>A                     | p.Pro605Thr          | missense      |

**Supplementary Table 3. List of all somatic mutations identified in the exome sequencing of 24 HCC**

| HCC-ID   | Ensembl Gene ID | Gene symbol | Chromosome | Nucleotide (genomic position hg19) | Amino Acid               | Mutation Type |
|----------|-----------------|-------------|------------|------------------------------------|--------------------------|---------------|
| CHC1052T | ENSG00000133612 | AGAP3       | 7          | g.150839673G>T                     | p.Trp742Leu              | missense      |
| CHC121T  | ENSG00000166748 | AGBL1       | 15         | g.86791013G>T                      | p.Gly167Val              | missense      |
| CHC1053T | ENSG00000173744 | AGFG1       | 2          | g.228389633_228389634insT          | indels                   | insertion     |
| CHC1041T | ENSG00000164252 | AGGF1       | 5          | g.76326802G>A                      | splicing                 | intron        |
| CHC433T  | ENSG00000153207 | AHCTF1      | 1          | g.247070852C>A                     | splicing                 | intron        |
| CHC051T  | ENSG00000106305 | AIMP2       | 7          | g.6057645T>G                       | p.Tyr181X                | nonsense      |
| CHC306T  | ENSG00000129221 | AIPL1       | 17         | g.6330331T>A                       | p.Asn171Ile              | missense      |
| CHC302T  | ENSG00000108599 | AKAP10      | 17         | g.19812566_19812583del             | p.Glu632_Lys637del       | deletion      |
| CHC1061T | ENSG00000023330 | ALAS1       | 3          | g.52240628G>T                      | p.Met342Ile              | missense      |
| CHC155T  | ENSG00000136872 | ALDOB       | 9          | g.104184093_104184113del           | p.Phe358X                | deletion      |
| CHC302T  | ENSG00000091542 | ALKBH5      | 17         | g.18111543C>G                      | p.Leu340Val              | missense      |
| CHC1053T | ENSG00000178038 | ALS2CL      | 3          | g.46730893T>C                      | p.Glu13Gly               | missense      |
| CHC434T  | ENSG00000243480 | AMY2A       | 1          | g.104160220G>A                     | p.Gly53Glu               | missense      |
| CHC1055T | ENSG00000145362 | ANK2        | 4          | g.114290867G>A                     | p.Ser3839Asn             | missense      |
| CHC322T  | ENSG00000151150 | ANK3        | 10         | g.61830119C>A                      | p.Gly3507Val             | missense      |
| CHC301T  | ENSG00000151687 | ANKAR       | 2          | g.190608051del                     | p.Asn1287LysfsX7         | deletion      |
| CHC301T  | ENSG00000166839 | ANKDD1A     | 15         | g.65242180G>C                      | p.Arg490Ser              | missense      |
| CHC320T  | ENSG00000185722 | ANKFY1      | 17         | g.4071195C>T                       | p.Gly1131Arg             | missense      |
| CHC302T  | ENSG00000170209 | ANKK1       | 11         | g.113264433C>T                     | p.Pro139Leu              | missense      |
| CHC433T  | ENSG00000168876 | ANKRD49     | 11         | g.2075dup                          | p.Ile37AsnfsX14          | duplication   |
| CHC302T  | ENSG00000166825 | ANPEP       | 15         | g.90349277T>G                      | p.Ser180Arg              | missense      |
| CHC301T  | ENSG00000104537 | ANXA13      | 8          | g.124748094_124748103del           | p.Leu11AlafsX51          | deletion      |
| CHC1065T | ENSG00000034053 | APBA2       | 15         | g.29398928G>A                      | p.Arg608His              | missense      |
| CHC205T  | ENSG00000134982 | APC         | 5          | g.152789_152790insT                | p.Glu1573X               | insertion     |
| CHC301T  | ENSG00000169621 | APLF        | 2          | g.68729883T>G                      | p.Phe63Leu               | missense      |
| CHC1053T | ENSG00000157500 | APPL1       | 3          | g.57294005G>A                      | p.Arg539His              | missense      |
| CHC302T  | ENSG00000198931 | APRT        | 16         | g.88876116T>C                      | p.Gln178Arg              | missense      |
| CHC051T  | ENSG00000078061 | ARAF        | X          | g.47424300T>A                      | splicing                 | intron        |
| CHC1053T | ENSG00000047365 | ARAP2       | 4          | g.36179625C>A                      | p.Glu561X                | nonsense      |
| CHC614T  | ENSG00000132254 | ARFIP2      | 11         | g.6499281C>G                       | p.Glu229Gln              | missense      |
| CHC302T  | ENSG00000071205 | ARHGAP10    | 4          | g.148887833T>A                     | p.Val20Asp               | missense      |
| CHC1055T | ENSG00000075884 | ARHGAP15    | 2          | g.143913066A>T                     | p.Lys3X                  | nonsense      |
| CHC434T  | ENSG00000074964 | ARHGEF10L   | 1          | g.18021773C>T                      | p.Thr1102Ile             | missense      |
| CHC307T  | ENSG00000129675 | ARHGEF6     | X          | g.135764990C>T                     | p.Arg469Gln              | missense      |
| CHC1035T | ENSG00000140691 | ARMC5       | 16         | g.31477529A>T                      | p.Gln709His              | missense      |
| CHC614T  | ENSG00000105676 | ARMC6       | 19         | g.19168330_19168331del             | p.Ala467ProfsX3          | deletion      |
| CHC320T  | ENSG00000241685 | ARPC1A      | 7          | g.98942059T>A                      | p.Ser105Thr              | missense      |
| CHC433T  | ENSG00000130429 | ARPC1B      | 7          | g.98984368G>C                      | p.Trp42Ser               | missense      |
| CHC121T  | ENSG00000141480 | ARRB2       | 17         | g.4623914A>G                       | p.Asn372Ser              | missense      |
| CHC205T  | ENSG00000197070 | ARRDC1      | 9          | g.140508854A>G                     | p.Gln241Arg              | missense      |
| CHC258T  | ENSG00000111339 | ART4        | 12         | g.14993469C>T                      | p.Val25Ile               | missense      |
| CHC121T  | ENSG00000161664 | ASB16       | 17         | g.42248221T>C                      | p.Trp22Arg               | missense      |
| CHC197T  | ENSG00000138303 | ASCC1       | 10         | g.73956664G>A                      | p.Pro160Ser              | missense      |
| CHC302T  | ENSG00000066279 | ASPM        | 1          | g.197073328_197073334del           | p.Ile1683CysfsX7         | deletion      |
| CHC434T  | ENSG00000171681 | ATF7IP      | 12         | g.14577104dup                      | p.Ala86SerfsX13          | duplication   |
| CHC1041T | ENSG00000145246 | ATP10D      | 4          | g.47578814T>C                      | p.Tyr1131His             | missense      |
| CHC1053T | ENSG00000058063 | ATP11B      | 3          | g.182576989C>G                     | p.Leu348Val              | missense      |
| CHC121T  | ENSG00000105409 | ATP1A3      | 19         | g.42474375A>C                      | p.Val835Gly              | missense      |
| CHC197T  | ENSG00000175054 | ATR         | 3          | g.142254963T>C                     | p.Gln1269Arg             | missense      |
| CHC433T  | ENSG00000107518 | ATRNL1      | 10         | g.117045852C>A                     | p.Thr787Lys              | missense      |
| CHC1035T | ENSG00000167080 | B4GALNT2    | 17         | g.47241521C>T                      | p.Leu340Phe              | missense      |
| CHC306T  | ENSG00000182272 | B4GALNT4    | 11         | g.379985G>T                        | p.Val870Leu              | missense      |
| CHC1035T | ENSG00000151929 | BAG3        | 10         | g.121436548del                     | p.Glu495AsnfsX71         | deletion      |
| CHC434T  | ENSG00000156735 | BAG4        | 8          | g.38068002_38068004del             | p.Gly456del              | deletion      |
| CHC433T  | ENSG00000121753 | BAI2        | 1          | g.32207570T>A                      | splicing                 | intron        |
| CHC155T  | ENSG00000153064 | BANK1       | 4          | g.102951260T>A                     | p.Phe580Ile              | missense      |
| CHC1052T | ENSG00000138376 | BARD1       | 2          | g.215595141T>A                     | p.Glu665Asp              | missense      |
| CHC1052T | ENSG00000168062 | BATF2       | 11         | g.64764386T>G                      | p.Met1?                  | missense      |
| CHC320T  | ENSG00000099968 | BCL2L13     | 22         | g.18171818C>T                      | p.Ser99Leu               | missense      |
| CHC1055T | ENSG00000188761 | BCL2L15     | 1          | g.114423749C>T                     | p.Ser163Asn              | missense      |
| CHC429T  | ENSG00000085185 | BCORL1      | X          | g.129185928T>C                     | p.Met1597Thr             | missense      |
| CHC1061T | ENSG00000177324 | BEND2       | X          | g.18189238C>T                      | p.Ala690Thr              | missense      |
| CHC306T  | ENSG00000110330 | BIRC2       | 11         | g.102248780A>G                     | p.Met575Val              | missense      |
| CHC614T  | ENSG00000164713 | BRI3        | 7          | g.97920464T>A                      | p.Phe96Tyr               | missense      |
| CHC1052T | ENSG00000136492 | BRIP1       | 17         | g.59853896G>A                      | p.Pro655Ser              | missense      |
| CHC301T  | ENSG00000185658 | BRWD1       | 21         | g.40571534T>C                      | p.Tyr1603Cys             | missense      |
| CHC429T  | ENSG00000156970 | BUB1B       | 15         | g.40462740A>G                      | p.Tyr81Cys               | missense      |
| CHC433T  | ENSG00000005379 | BZRAP1      | 17         | g.56381753C>A                      | p.Arg1851Met             | missense      |
| CHC1053T | ENSG00000125730 | C3          | 19         | g.6677998C>A                       | p.Glu1629Asp             | missense      |
| CHC433T  | ENSG00000039537 | C6          | 5          | g.41195946C>A                      | p.Val179Ile              | missense      |
| CHC1061T | ENSG00000021852 | C8B         | 1          | g.57399085G>A                      | p.Ala492Val              | missense      |
| CHC1052T | ENSG00000074410 | CA12        | 15         | g.63631039C>T                      | p.Val285Ile              | missense      |
| CHC433T  | ENSG00000100346 | CACNA1I     | 22         | g.40060921C>A                      | p.Pro1282Thr             | missense      |
| CHC258T  | ENSG00000151062 | CACNA2D4    | 12         | g.1994175T>A                       | p.Glu379Val              | missense      |
| CHC320T  | ENSG00000067191 | CACNB1      | 17         | g.37342283G>A                      | p.Gln235X                | nonsense      |
| CHC301T  | ENSG00000185933 | CALHM1      | 10         | g.105215429G>A                     | p.Gln211X                | nonsense      |
| CHC429T  | ENSG00000110931 | CAMKK2      | 12         | g.121701718C>A                     | p.Arg217Leu              | missense      |
| CHC155T  | ENSG00000118200 | CAMSAP1L1   | 1          | g.200818972del                     | p.Asp1025GlufsX6         | deletion      |
| CHC433T  | ENSG00000132357 | CARD6       | 5          | g.40852644G>T                      | p.Ala404Ser              | missense      |
| CHC1041T | ENSG00000118307 | CASC1       | 12         | g.25264860A>G                      | p.Met542Thr              | missense      |
| CHC322T  | ENSG00000147044 | CASK        | X          | g.41383287C>T                      | p.Ala836Thr              | missense      |
| CHC1065T | ENSG00000118412 | CASP8AP2    | 6          | g.90630324del                      | p.Phe725LeufsX24         | deletion      |
| CHC051T  | ENSG00000175294 | CATSPER1    | 11         | g.65788574T>G                      | p.Thr592Pro              | missense      |
| CHC429T  | ENSG00000133962 | CATSPERB    | 14         | g.92171042G>A                      | p.Pro157Leu              | missense      |
| CHC433T  | ENSG00000163001 | CCDC104     | 2          | g.55771377G>T                      | p.Glu267X                | nonsense      |
| CHC1035T | ENSG00000181378 | CCDC108     | 2          | g.219888039G>A                     | p.Arg904Cys              | missense      |
| CHC258T  | ENSG00000180347 | CCDC129     | 7          | g.31622786C>A                      | p.Asp403Glu              | missense      |
| CHC1041T | ENSG00000244607 | CCDC13      | 3          | g.42798632del                      | p.Lys99SerfsX3           | deletion      |
| CHC1035T | ENSG00000162592 | CCDC27      | 1          | g.3670785C>A                       | p.Ala141Asp              | missense      |
| CHC614T  | ENSG00000135127 | CCDC64      | 12         | g.120530841A>G                     | p.Asp533Gly              | missense      |
| CHC1041T | ENSG00000120647 | CCDC77      | 12         | g.542363_542364insGGGAGA           | p.Gly233_Glu234insArgGly | insertion     |
| CHC1052T | ENSG00000110104 | CCDC86      | 11         | g.60609901T>C                      | p.Ser102Pro              | missense      |
| CHC320T  | ENSG00000185972 | CCIN        | 9          | g.36169747A>G                      | p.Asp83Gly               | missense      |
| CHC121T  | ENSG00000167236 | CCL23       | 17         | g.34344913G>T                      | p.Leu8Ile                | missense      |
| CHC258T  | ENSG00000121807 | CCR2        | 3          | g.46399680G>T                      | p.Cys221Phe              | missense      |
| CHC1061T | ENSG00000198445 | CCT8L2      | 22         | g.17072407C>G                      | p.Gly345Ala              | missense      |

**Supplementary Table 3. List of all somatic mutations identified in the exome sequencing of 24 HCC**

| HCC-ID   | Ensembl Gene ID | Gene symbol | Chromosome | Nucleotide (genomic position hg19) | Amino Acid         | Mutation Type |
|----------|-----------------|-------------|------------|------------------------------------|--------------------|---------------|
| CHC155T  | ENSG00000156535 | CD109       | 6          | g.74502461T>G                      | p.Tyr938X          | nonsense      |
| CHC1061T | ENSG00000134061 | CD180       | 5          | g.66479290T>C                      | p.Asn461Asp        | missense      |
| CHC429T  | ENSG00000174807 | CD248       | 11         | g.66083264G>A                      | p.Pro141Leu        | missense      |
| CHC614T  | ENSG00000153283 | CD96        | 3          | g.111356926A>T                     | p.Asp479Val        | missense      |
| CHC1053T | ENSG00000130177 | CD16        | 13         | g.115012466A>G                     | p.Arg320Gly        | missense      |
| CHC051T  | ENSG00000198752 | CDC42BPB    | 14         | g.103405957T>C                     | p.Asp1606Ala       | missense      |
| CHC1065T | ENSG00000140945 | CDH13       | 16         | g.82892035C>G                      | p.Ile38Met         | missense      |
| CHC051T  | ENSG00000179242 | CDH4        | 20         | g.60427891G>A                      | p.Asp272Asn        | missense      |
| CHC429T  | ENSG00000150394 | CDH8        | 16         | g.61855012 A>G                     | p.Tyr281His        | missense      |
| CHC1061T | ENSG00000163624 | CDS1        | 4          | g.85530581G>T                      | splicing           | intron        |
| CHC322T  | ENSG00000093072 | CECR1       | 22         | g.17690270T>A                      | p.Asn100Tyr        | missense      |
| CHC320T  | ENSG00000069998 | CECR5       | 22         | g.17622117A>T                      | p.Leu193His        | missense      |
| CHC1053T | ENSG00000198707 | CEP290      | 12         | g.88483000A>C                      | p.Leu1280Val       | missense      |
| CHC121T  | ENSG00000172831 | CES2        | 16         | g.66974180A>G                      | p.Asp224Gly        | missense      |
| CHC429T  | ENSG00000172824 | CES4A       | 16         | g.67035302G>A                      | p.Gly210Arg        | missense      |
| CHC258T  | ENSG00000134389 | CFHR5       | 1          | g.196953165G>A                     | p.Val110Ile        | missense      |
| CHC155T  | ENSG00000170004 | CHD3        | 17         | g.78120706C>G                      | p.Pro1834Ala       | missense      |
| CHC258T  | ENSG00000111642 | CHD4        | 12         | g.6701868C>T                       | p.Arg923Lys        | missense      |
| CHC302T  | ENSG00000188419 | CHM         | X          | g.85236743G>A                      | p.Gln63X           | nonsense      |
| CHC1061T | ENSG00000110172 | CHORDC1     | 11         | g.89948386A>T                      | p.Cys43Ser         | missense      |
| CHC1065T | ENSG00000124302 | CHST8       | 19         | g.34263921G>T                      | p.Asp410Tyr        | missense      |
| CHC301T  | ENSG00000127586 | CHTF18      | 16         | g.846056A>G                        | p.Gln812Arg        | missense      |
| CHC307T  | ENSG00000148337 | CIZ1        | 9          | g.130943033C>T                     | p.Glu217Lys        | missense      |
| CHC121T  | ENSG00000016602 | CLCA4       | 1          | g.87045737G>T                      | p.Lys823Asn        | missense      |
| CHC301T  | ENSG00000013297 | CLDN11      | 3          | g.170140971G>A                     | p.Ala83Thr         | missense      |
| CHC306T  | ENSG00000130779 | CLIP1       | 12         | g.122837329C>T                     | p.Val438Ile        | missense      |
| CHC322T  | ENSG00000079101 | CLUL1       | 18         | g.633333C>T                        | p.Pro298Ser        | missense      |
| CHC1061T | ENSG00000070729 | CNGB1       | 16         | g.57991268G>T                      | p.Pro284His        | missense      |
| CHC155T  | ENSG00000118432 | CNR1        | 6          | g.88854357C>G                      | p.Asp213His        | missense      |
| CHC1041T | ENSG00000082438 | COBLL1      | 2          | g.165584689_165584695del           | p.Val149LufsX10    | deletion      |
| CHC121T  | ENSG00000204248 | COL11A2     | 6          | g.33156861C>A                      | p.Gly113Cys        | missense      |
| CHC121T  | ENSG00000117999 | COL12A1     | 6          | g.75827230C>A                      | p.Val2463Phe       | missense      |
| CHC1035T | ENSG00000108821 | COL1A1      | 17         | g.48266608C>T                      | p.Gly953Val        | missense      |
| CHC155T  | ENSG00000171502 | COL24A1     | 1          | g.86524808C>A                      | p.Arg601Met        | missense      |
| CHC322T  | ENSG00000134871 | COL4A2      | 13         | g.111086756_111086757del           | p.Gly232ThrsX7     | deletion      |
| CHC433T  | ENSG00000130635 | COL5A1      | 9          | g.137648663A>T                     | p.Lys627Met        | missense      |
| CHC302T  | ENSG00000173163 | COMMD1      | 2          | g.62362984_62363004del             | p.Leu161_Lys167del | deletion      |
| CHC433T  | ENSG00000111652 | COP57A      | 12         | g.6840174G>T                       | p.Gly266Val        | missense      |
| CHC614T  | ENSG00000166260 | COX11       | 17         | g.53040247_53040248dup             | p.Pro227IlefsX6    | insertion     |
| CHC1065T | ENSG00000080618 | CPB2        | 13         | g.46632373G>C                      | p.Gln314Glu        | missense      |
| CHC429T  | ENSG00000214575 | CPEB1       | 15         | g.83226697C>T                      | p.Gly140Glu        | missense      |
| CHC433T  | ENSG00000196353 | CPNE4       | 3          | g.131274372C>A                     | p.Gly362Val        | missense      |
| CHC320T  | ENSG00000124772 | CPNE5       | 6          | g.36716015T>A                      | p.Asp334Val        | missense      |
| CHC121T  | ENSG00000100884 | CPNE6       | 14         | g.24546576G>A                      | p.Val505Met        | missense      |
| CHC121T  | ENSG00000150938 | CRIM1       | 2          | g.36764602C>A                      | p.Gln846Lys        | missense      |
| CHC197T  | ENSG00000213923 | CSNK1E      | 22         | g.38694910G>T                      | p.Arg256Ser        | missense      |
| CHC121T  | ENSG00000173546 | CSPG4       | 5          | g.75970125C>A                      | p.Asp1685Tyr       | missense      |
| CHC1052T | ENSG00000198561 | CTNND1      | 11         | g.57571197G>A                      | p.Glu509Lys        | missense      |
| CHC434T  | ENSG00000169862 | CTNND2      | 5          | g.10973648C>T                      | p.Asp1199Asn       | missense      |
| CHC1035T | ENSG00000107611 | CUBN        | 10         | g.16957911G>T                      | p.His2373Gln       | missense      |
| CHC433T  | ENSG00000055130 | CUL1        | 7          | g.148481130A>T                     | p.Glu420Val        | missense      |
| CHC197T  | ENSG00000165510 | CWC22       | 2          | g.180815577T>C                     | p.Thr632Ala        | missense      |
| CHC322T  | ENSG00000095485 | CWF19L1     | 10         | g.102016204C>T                     | p.Gly107Arg        | missense      |
| CHC051T  | ENSG00000138755 | CXCL9       | 4          | g.76926006C>A                      | p.Asp78Tyr         | missense      |
| CHC433T  | ENSG00000167740 | CYB5D2      | 17         | g.4058127del                       | p.Gly184AlafsX13   | deletion      |
| CHC306T  | ENSG00000071967 | CYBRD1      | 2          | g.172409907C>T                     | p.Arg152X          | nonsense      |
| CHC121T  | ENSG00000130649 | CYP2E1      | 10         | g.135347282T>A                     | p.Leu283X          | nonsense      |
| CHC197T  | ENSG00000197446 | CYP2F1      | 19         | g.41628015T>C                      | p.Cys267Arg        | missense      |
| CHC197T  | ENSG00000134780 | DAGLA       | 11         | g.61490434T>C                      | splicing           | intron        |
| CHC121T  | ENSG00000196730 | DAPK1       | 9          | g.90321432A>G                      | p.Gln1149Arg       | missense      |
| CHC302T  | ENSG00000070190 | DAPP1       | 4          | g.100756805C>A                     | p.His43Asn         | missense      |
| CHC301T  | ENSG00000078725 | DBC1        | 9          | g.121976292C>T                     | p.Cys276Tyr        | missense      |
| CHC205T  | ENSG00000170959 | DCDC5       | 11         | g.30902810T>A                      | p.Arg814X          | nonsense      |
| CHC205T  | ENSG00000166341 | DCHS1       | 11         | g.6654847G>A                       | p.Arg751Trp        | missense      |
| CHC306T  | ENSG00000118655 | DCLRE1B     | 1          | g.114453990G>T                     | p.Arg259Leu        | missense      |
| CHC205T  | ENSG00000080166 | DCY1        | 13         | g.95114433A>G                      | p.Tyr292His        | missense      |
| CHC121T  | ENSG00000170967 | DDI1        | 11         | g.103908358C>A                     | p.Gln270Lys        | missense      |
| CHC429T  | ENSG00000165359 | DDX26B      | X          | g.134715453G>T                     | p.Arg826Ser        | missense      |
| CHC320T  | ENSG00000067048 | DDX3Y       | Y          | g.15028344T>C                      | p.Val494Ala        | missense      |
| CHC1041T | ENSG00000107625 | DDX50       | 10         | g.70673842_70673843insT            | p.Ser326PhefsX21   | insertion     |
| CHC434T  | ENSG00000176782 | DEFB104A    | 8          | g.7698598C>T                       | p.Thr34Ile         | missense      |
| CHC1061T | ENSG00000119522 | DENND1A     | 9          | g.126144679C>T                     | p.Glu688Lys        | missense      |
| CHC1065T | ENSG00000137145 | DENND4C     | 9          | g.19300207C>G                      | p.Leu161Val        | missense      |
| CHC1052T | ENSG00000095397 | DFNB31      | 9          | g.117266498G>A                     | p.Ser195Phe        | missense      |
| CHC306T  | ENSG00000136267 | DGKB        | 7          | g.14378298A>C                      | p.Leu656Arg        | missense      |
| CHC429T  | ENSG00000116133 | DHCR24      | 1          | g.55341714G>C                      | p.Arg132Gly        | missense      |
| CHC121T  | ENSG00000181192 | DHTKD1      | 10         | g.12126663G>T                      | p.Trp145Cys        | missense      |
| CHC433T  | ENSG00000139734 | DIAPH3      | 13         | g.60435576A>T                      | p.Val901Glu        | missense      |
| CHC155T  | ENSG00000006677 | DLX6        | 7          | g.96639195G>T                      | p.Gly240Cys        | missense      |
| CHC301T  | ENSG00000197653 | DNAH10      | 12         | g.124305236dup                     | p.Glu1253ArgfsX20  | duplication   |
| CHC320T  | ENSG00000183914 | DNAH2       | 17         | g.7660536G>A                       | p.Val678Ile        | missense      |
| CHC306T  | ENSG00000158486 | DNAH3       | 16         | g.20996748C>T                      | p.Gly2439Glu       | missense      |
| CHC155T  | ENSG00000039139 | DNAH5       | 5          | g.13811834T>A                      | p.Leu2443Phe       | missense      |
| CHC1035T | ENSG00000118997 | DNAH7       | 2          | g.196651884C>A                     | p.Lys3576Asn       | missense      |
| CHC433T  | ENSG00000118997 | DNAH7       | 2          | g.196723366_196723367insAG         | p.Glu2633AspfsX4   | insertion     |
| CHC121T  | ENSG00000007174 | DNAH9       | 17         | g.11726297C>A                      | p.Cys3064X         | nonsense      |
| CHC155T  | ENSG00000171595 | DNAI2       | 17         | g.72278000G>T                      | p.Gly15Val         | missense      |
| CHC1065T | ENSG00000178401 | DNAJC22     | 12         | g.49742950_49742953del             | p.Ser100ProfX16    | deletion      |
| CHC433T  | ENSG00000187957 | DNER        | 2          | g.230253046A>T                     | p.Leu597Gln        | missense      |
| CHC429T  | ENSG00000088538 | DOCK3       | 3          | g.51395492G>A                      | p.Arg1623Gln       | missense      |
| CHC434T  | ENSG00000115325 | DOK1        | 2          | g.74784185G>A                      | p.Gly464Arg        | missense      |
| CHC429T  | ENSG00000159147 | DONSON      | 21         | g.34955900A>C                      | p.Tyr286X          | nonsense      |
| CHC051T  | ENSG00000175497 | DPP10       | 2          | g.116598368T>C                     | p.Leu746Pro        | missense      |
| CHC301T  | ENSG00000113657 | DPYSL3      | 5          | g.146795328A>G                     | p.Ile255Thr        | missense      |
| CHC1053T | ENSG00000175065 | DSG4        | 18         | g.2899333G>C                       | p.Glu985Asp        | missense      |
| CHC205T  | ENSG00000096696 | DSP         | 6          | g.7580297_7580301del               | p.Glu1292ArgfsX11  | deletion      |

**Supplementary Table 3. List of all somatic mutations identified in the exome sequencing of 24 HCC**

| HCC-ID   | Ensembl Gene ID | Gene symbol | Chromosome | Nucleotide (genomic position hg19) | Amino Acid           | Mutation Type |
|----------|-----------------|-------------|------------|------------------------------------|----------------------|---------------|
| CHC429T  | ENSG00000135144 | DTX1        | 12         | g.113532598G>A                     | p.Cys411Tyr          | missense      |
| CHC121T  | ENSG00000120129 | DUSP1       | 5          | g.172195846G>T                     | p.Phe341Leu          | missense      |
| CHC429T  | ENSG00000187240 | DYNC2H1     | 11         | g.103270517_103270518insA          | p.Ala4102AspfsX63    | insertion     |
| CHC121T  | ENSG00000106823 | ECM2        | 9          | g.95256390G>C                      | p.Ser636X            | nonsense      |
| CHC433T  | ENSG00000134109 | EDEM1       | 3          | g.5241287A>T                       | p.Asn198Ile          | missense      |
| CHC1052T | ENSG00000130038 | EFCAB4B     | 12         | g.3763565G>T                       | p.Leu287Met          | missense      |
| CHC205T  | ENSG00000126070 | EIF2C3      | 1          | g.36475119C>A                      | p.Thr358Lys          | missense      |
| CHC051T  | ENSG00000104131 | EIF3J       | 15         | g.44843655del                      | p.Ile77X             | deletion      |
| CHC320T  | ENSG00000162374 | ELAVL4      | 1          | g.50661248T>A                      | p.Val192Glu          | missense      |
| CHC302T  | ENSG00000102034 | ELF4        | X          | g.129205085C>A                     | p.Val247Leu          | missense      |
| CHC197T  | ENSG00000110675 | ELMOD1      | 11         | g.107506390C>A                     | p.Leu107Met          | missense      |
| CHC121T  | ENSG00000132205 | EMILIN2     | 18         | g.2892076A>G                       | p.Arg651Gly          | missense      |
| CHC1055T | ENSG00000100393 | EP300       | 22         | g.41525894T>G                      | p.Val390Gly          | missense      |
| CHC434T  | ENSG00000116016 | EPAS1       | 2          | g.46597022A>T                      | p.Glu279Val          | missense      |
| CHC306T  | ENSG00000119888 | EPCAM       | 2          | g.47600959G>A                      | p.Cys66Tyr           | missense      |
| CHC121T  | ENSG00000044524 | EPHA3       | 3          | g.89448579del                      | p.Ala515LeufsX30     | deletion      |
| CHC1052T | ENSG00000116106 | EPHA4       | 2          | g.222428753C>T                     | p.Gly174Glu          | missense      |
| CHC051T  | ENSG00000145242 | EPHA5       | 4          | g.66233102C>A                      | p.Glu633X            | nonsense      |
| CHC301T  | ENSG00000080224 | EPHA6       | 3          | g.96706224C>G                      | p.Tyr167X            | nonsense      |
| CHC429T  | ENSG00000178567 | EPM2AIP1    | 3          | g.37033992C>T                      | p.Val193Ile          | missense      |
| CHC1035T | ENSG00000121053 | EPX         | 17         | g.56274527C>A                      | p.Asp343Glu          | missense      |
| CHC121T  | ENSG00000178607 | ERN1        | 17         | g.62121362G>A                      | p.Pro974Ser          | missense      |
| CHC1052T | ENSG00000196482 | ESRRG       | 1          | g.216692704del                     | p.Ile308PhefsX2      | deletion      |
| CHC051T  | ENSG00000126860 | EVI2A       | 17         | g.29645740A>G                      | p.Ser98Pro           | missense      |
| CHC121T  | ENSG00000116903 | EXOC8       | 1          | g.231473409A>T                     | p.Val28Glu           | missense      |
| CHC433T  | ENSG00000110723 | EXPH5       | 11         | g.108382711A>C                     | p.Leu1175Val         | missense      |
| CHC051T  | ENSG00000106462 | EZH2        | 7          | g.148507430T>C                     | p.Asn675Ser          | missense      |
| CHC429T  | ENSG00000143278 | F13B        | 1          | g.197021884C>T                     | p.Gly479Arg          | missense      |
| CHC433T  | ENSG00000177096 | FAM109B     | 22         | g.42473985T>A                      | p.Trp230Arg          | missense      |
| CHC301T  | ENSG00000135842 | FAM129A     | 1          | g.184801036C>A                     | p.Arg221Gln          | missense      |
| CHC197T  | ENSG00000167483 | FAM129C     | 19         | g.17653000G>A                      | p.Arg440His          | missense      |
| CHC301T  | ENSG00000141699 | FAM134C     | 17         | g.40734153G>A                      | p.Ser360Phe          | missense      |
| CHC121T  | ENSG00000051009 | FAM160A2    | 11         | g.6239185G>A                       | p.Pro558Leu          | missense      |
| CHC197T  | ENSG00000184305 | FAM190A     | 4          | g.91230195G>T                      | p.Ala254Ser          | missense      |
| CHC1052T | ENSG00000174016 | FAM46D      | X          | g.79698174G>T                      | p.Val46Phe           | missense      |
| CHC051T  | ENSG00000223611 | FAM48B2     | X          | g.24331429C>A                      | p.Asp2Tyr            | missense      |
| CHC1052T | ENSG00000197872 | FAM49A      | 2          | g.16740786A>C                      | p.Ile260Ser          | missense      |
| CHC429T  | ENSG00000128923 | FAM63B      | 15         | g.59114015G>T                      | p.Glu408X            | nonsense      |
| CHC434T  | ENSG00000042062 | FAM65C      | 20         | g.49211912C>A                      | p.Glu678X            | nonsense      |
| CHC1052T | ENSG00000187790 | FANCM       | 14         | g.45645104A>T                      | p.Leu1049Phe         | missense      |
| CHC306T  | ENSG00000064763 | FAR2        | 12         | g.29450121T>C                      | p.Ile178Thr          | missense      |
| CHC433T  | ENSG00000124279 | FASTKD3     | 5          | g.7867364T>C                       | p.Asn278Ser          | missense      |
| CHC301T  | ENSG00000086570 | FAT2        | 5          | g.150934191G>T                     | p.Ser1226Tyr         | missense      |
| CHC121T  | ENSG00000196159 | FAT4        | 4          | g.126373142_126373143insA          | p.Leu3658ThrfsX10    | insertion     |
| CHC1065T | ENSG00000138829 | FBN2        | 5          | g.127670451C>A                     | p.Gln1353His         | missense      |
| CHC320T  | ENSG00000145780 | FEM1C       | 5          | g.114860919C>A                     | p.Asp314Tyr          | missense      |
| CHC433T  | ENSG00000171564 | FBG         | 4          | g.155490729T>C                     | p.Leu341Ser          | missense      |
| CHC614T  | ENSG00000137440 | FGFBP1      | 4          | g.15937894C>G                      | p.Arg121Leu          | missense      |
| CHC429T  | ENSG00000137460 | FHDC1       | 4          | g.153897444A>G                     | p.Lys1001Glu         | missense      |
| CHC1055T | ENSG00000134775 | FHOD3       | 18         | g.34192058G>T                      | p.Glu319Asp          | missense      |
| CHC301T  | ENSG00000118407 | FIUP1       | 6          | g.76023200C>T                      | p.Ser783Asn          | missense      |
| CHC614T  | ENSG00000136068 | FLNB        | 3          | g.58120403del                      | p.Gly1557AlafsX31    | deletion      |
| CHC433T  | ENSG00000037280 | FLT4        | 5          | g.180047310T>A                     | splicing             | intron        |
| CHC301T  | ENSG00000157827 | FMNL2       | 2          | g.153435429C>T                     | p.Pro245Ser          | missense      |
| CHC197T  | ENSG00000164694 | FNDC1       | 6          | g.159653367C>T                     | p.Pro608Leu          | missense      |
| CHC302T  | ENSG00000138759 | FRAS1       | 4          | g.79328946G>A                      | p.Trp1420X           | nonsense      |
| CHC1055T | ENSG00000172159 | FRMD3       | 9          | g.85928629C>A                      | p.Leu210Phe          | missense      |
| CHC302T  | ENSG00000156869 | FRS1        | 1          | g.100174614G>C                     | p.Ser574X            | nonsense      |
| CHC121T  | ENSG00000106328 | FSCN3       | 7          | g.127235893C>A                     | p.Ala226Glu          | missense      |
| CHC433T  | ENSG00000140564 | FURIN       | 15         | g.91425068del                      | p.Gly782AlafsX31     | deletion      |
| CHC429T  | ENSG00000082074 | FYB         | 5          | g.39202156C>T                      | p.Glu303Lys          | missense      |
| CHC320T  | ENSG00000105325 | FZR1        | 19         | g.3533382C>G                       | p.Arg445Gly          | missense      |
| CHC302T  | ENSG00000143458 | GABPB2      | 1          | g.151090437del                     | p.Gly351AlafsX26     | deletion      |
| CHC433T  | ENSG00000145863 | GABRA6      | 5          | g.161113327G>A                     | p.Asp44Asn           | missense      |
| CHC320T  | ENSG00000145864 | GABRB2      | 5          | g.160886741C>A                     | p.Trp116Leu          | missense      |
| CHC302T  | ENSG00000163285 | GABRG1      | 4          | g.46066503T>A                      | p.Asn194Tyr          | missense      |
| CHC306T  | ENSG00000117308 | GALE        | 1          | g.24122689C>T                      | p.Ala314Thr          | missense      |
| CHC429T  | ENSG00000156958 | GALK2       | 15         | g.49528110A>G                      | p.Tyr110Cys          | missense      |
| CHC301T  | ENSG00000174473 | GALNTL6     | 4          | g.173803975G>T                     | p.Asp320Tyr          | missense      |
| CHC1041T | ENSG00000128310 | GALR3       | 22         | g.38219640T>C                      | p.Val76Ala           | missense      |
| CHC1061T | ENSG00000213930 | GALT        | 9          | g.34646773C>A                      | p.Phe24Leu           | missense      |
| CHC051T  | ENSG00000183807 | GAS6        | 13         | g.114535391C>A                     | p.Asp342Tyr          | missense      |
| CHC306T  | ENSG00000084734 | GCKR        | 2          | g.27724006C>T                      | p.Pro185Leu          | missense      |
| CHC433T  | ENSG00000089154 | GCN1L1      | 12         | g.120589084C>T                     | p.Ala1392Thr         | missense      |
| CHC1035T | ENSG00000178295 | GEN1        | 2          | g.17961923G>A                      | p.Asp482Asn          | missense      |
| CHC433T  | ENSG00000125447 | GGA3        | 17         | g.73238979A>G                      | p.Leu181Pro          | missense      |
| CHC433T  | ENSG00000137563 | GGH         | 8          | g.63942752_63942753del             | p.Tyr83X             | deletion      |
| CHC1061T | ENSG00000152661 | GJA1        | 6          | g.121768961C>T                     | p.Ala323Val          | missense      |
| CHC301T  | ENSG00000197045 | GMFB        | 14         | g.54950479A>G                      | p.Ser4Pro            | missense      |
| CHC1035T | ENSG00000130755 | GMFG        | 19         | g.39820183C>G                      | splicing             | intron        |
| CHC155T  | ENSG00000114353 | GNAI2       | 3          | g.50290615T>C                      | p.Tyr155His          | missense      |
| CHC1041T | ENSG00000100522 | GNPNAT1     | 14         | g.53248574_53248608del             | p.Lys80SerfsX17      | deletion      |
| CHC197T  | ENSG00000135677 | GNS         | 12         | g.65130840_65130847del             | p.Glu345AspfsX26     | deletion      |
| CHC197T  | ENSG00000144674 | GOLGA4      | 3          | g.37367172del                      | p.Trp1467X           | deletion      |
| CHC205T  | ENSG00000066455 | GOLGA5      | 14         | g.93263954del                      | p.Pro58LeufsX21      | deletion      |
| CHC197T  | ENSG00000173230 | GOLGB1      | 3          | g.121413124T>G                     | p.Leu2077Phe         | missense      |
| CHC1035T | ENSG00000135052 | GOLM1       | 9          | g.88642739G>C                      | p.Thr400Lys          | missense      |
| CHC322T  | ENSG00000120370 | GORAB       | 1          | g.170521158del                     | p.Lys247SerfsX15     | deletion      |
| CHC434T  | ENSG00000186566 | GPATCH8     | 17         | g.42475011_42475025del             | p.Ala1474_Ala1478del | deletion      |
| CHC197T  | ENSG00000136235 | GNPMB       | 7          | g.23309730C>A                      | p.Asn467Lys          | missense      |
| CHC434T  | ENSG00000153292 | GPR110      | 6          | g.46995471_46995472insA            | p.Lys32AsnfsX7       | insertion     |
| CHC1035T | ENSG00000164393 | GPR111      | 6          | g.47649967G>T                      | p.Val490Phe          | missense      |
| CHC429T  | ENSG00000144820 | GPR128      | 3          | g.100328802C>G                     | p.Ile34Met           | missense      |
| CHC1035T | ENSG00000181619 | GPR135      | 14         | g.59930761G>A                      | p.Ser395Leu          | missense      |
| CHC433T  | ENSG00000187037 | GPR141      | 7          | g.37780260A>G                      | p.Lys89Glu           | missense      |
| CHC1035T | ENSG00000164199 | GPR98       | 5          | g.90015949G>T                      | p.Ala3178Ser         | missense      |

**Supplementary Table 3. List of all somatic mutations identified in the exome sequencing of 24 HCC**

| HCC-ID   | Ensembl Gene ID | Gene symbol | Chromosome | Nucleotide (genomic position hg19) | Amino Acid         | Mutation Type |
|----------|-----------------|-------------|------------|------------------------------------|--------------------|---------------|
| CHC1065T | ENSG00000173612 | GPRC6A      | 6          | g.117113552G>T                     | p.Thr845Lys        | missense      |
| CHC429T  | ENSG00000169258 | GPRIN1      | 5          | g.176025011G>T                     | p.Leu609Met        | missense      |
| CHC155T  | ENSG00000121957 | GPSM2       | 1          | g.109466721G>C                     | p.Ser567Thr        | missense      |
| CHC322T  | ENSG00000083307 | GRHL2       | 8          | g.102631864A>C                     | p.Asn399Thr        | missense      |
| CHC433T  | ENSG00000155511 | GRIA1       | 5          | g.153085558T>A                     | p.Phe585Tyr        | missense      |
| CHC1035T | ENSG00000120251 | GRIA2       | 4          | g.158242707C>A                     | p.Leu280Met        | missense      |
| CHC205T  | ENSG00000105737 | GRIK5       | 19         | g.42546751C>G                      | p.Glu476Gln        | missense      |
| CHC155T  | ENSG00000150086 | GRIN2B      | 12         | g.13716331A>G                      | p.Tyr1281His       | missense      |
| CHC434T  | ENSG00000077235 | GTF3C1      | 16         | g.27497443G>A                      | p.Arg1245Cys       | missense      |
| CHC258T  | ENSG00000152402 | GUCY1A2     | 11         | g.106810383T>C                     | p.Met337Val        | missense      |
| CHC429T  | ENSG00000164116 | GUCY1A3     | 4          | g.156638372_156638373insA          | p.His545GlnfsX17   | insertion     |
| CHC155T  | ENSG00000145681 | HAPLN1      | 5          | g.82940219G>T                      | p.Ser246Arg        | missense      |
| CHC051T  | ENSG00000128708 | HAT1        | 2          | g.172823364T>G                     | p.Ser239Arg        | missense      |
| CHC205T  | ENSG00000048052 | HDAC9       | 7          | g.19015534T>A                      | p.Leu1043Gln       | missense      |
| CHC433T  | ENSG00000165259 | HDX         | X          | g.83599258C>A                      | p.Glu554X          | nonsense      |
| CHC320T  | ENSG00000171495 | HEATR7B2    | 5          | g.41018834A>G                      | p.Trp878Arg        | missense      |
| CHC433T  | ENSG00000198265 | HELZ        | 17         | g.65141916_65141918del             | p.Thr904del        | deletion      |
| CHC433T  | ENSG00000103657 | HERC1       | 15         | g.63916477T>G                      | p.Gln4442Pro       | missense      |
| CHC1061T | ENSG00000138646 | HERC5       | 4          | g.89384746G>A                      | p.Gly251Asp        | missense      |
| CHC1035T | ENSG0000010704  | HFE         | 6          | g.26091742G>T                      | p.Ala181Ser        | missense      |
| CHC614T  | ENSG00000019991 | HGF         | 7          | g.81332001G>A                      | p.Arg695Cys        | missense      |
| CHC320T  | ENSG00000164161 | HHP1        | 4          | g.145568017G>A                     | p.Gly64Arg         | missense      |
| CHC614T  | ENSG00000197846 | HIST1H2BF   | 6          | g.26199992A>G                      | p.Asp69Gly         | missense      |
| CHC155T  | ENSG00000143341 | HMCN1       | 1          | g.186034381C>A                     | p.Pro2509Thr       | missense      |
| CHC433T  | ENSG00000108753 | HNF1B       | 17         | g.36070533_36070555del             | p.Ser388ProfsX4    | deletion      |
| CHC1061T | ENSG00000092199 | HNRNPC      | 14         | g.21702304del                      | p.Arg17ValfsX51    | deletion      |
| CHC322T  | ENSG00000170689 | HOXB9       | 17         | g.46700371C>T                      | p.Arg215Lys        | missense      |
| CHC197T  | ENSG00000107521 | HPS1        | 10         | g.100183582A>G                     | p.Leu487Pro        | missense      |
| CHC1052T | ENSG00000002587 | HS3ST1      | 4          | g.11401185_11401193del             | p.Leu146_Asp148del | deletion      |
| CHC1061T | ENSG00000122254 | HS3ST2      | 16         | g.22926390T>C                      | p.Val204Ala        | missense      |
| CHC614T  | ENSG00000176387 | HSD11B2     | 16         | g.67470705C>G                      | p.Tyr339X          | nonsense      |
| CHC1061T | ENSG00000142798 | HSPG2       | 1          | g.22179298G>A                      | p.Gln2207X         | nonsense      |
| CHC614T  | ENSG00000136273 | HUS1        | 7          | g.48016433A>C                      | p.Leu120X          | nonsense      |
| CHC614T  | ENSG00000214042 | IFNA7       | 9          | g.21201716A>T                      | p.Ile150Asn        | missense      |
| CHC1052T | ENSG00000161405 | IKZF3       | 17         | g.37922201G>A                      | p.Arg458Cys        | missense      |
| CHC429T  | ENSG00000115598 | ILRL2       | 2          | g.102828617C>T                     | p.Ser236Leu        | missense      |
| CHC429T  | ENSG00000162594 | IL23R       | 1          | g.67724232A>G                      | p.Ile437Met        | missense      |
| CHC306T  | ENSG00000175189 | INHBC       | 12         | g.57843732A>G                      | p.Tyr329Cys        | missense      |
| CHC302T  | ENSG00000204084 | INPP5B      | 1          | g.38397690A>T                      | p.Trp143Arg        | missense      |
| CHC051T  | ENSG00000164066 | INTU        | 4          | g.128637514_128637515del           | p.Tyr918CysfsX5    | deletion      |
| CHC1065T | ENSG00000176095 | IP6K1       | 3          | g.49770340A>G                      | p.Leu167Pro        | missense      |
| CHC1041T | ENSG00000159387 | IRX6        | 16         | g.55360333C>A                      | p.Ala44Glu         | missense      |
| CHC121T  | ENSG00000213949 | ITGA1       | 5          | g.52177831G>A                      | p.Ala251Thr        | missense      |
| CHC429T  | ENSG00000156886 | ITGAD       | 16         | g.31429802T>G                      | p.Ser899Arg        | missense      |
| CHC1035T | ENSG00000123104 | ITPR2       | 12         | g.26748469C>T                      | p.Glu1437Lys       | missense      |
| CHC614T  | ENSG00000148841 | ITPRIP      | 10         | g.106075076A>G                     | p.Val245Ala        | missense      |
| CHC433T  | ENSG00000161999 | JMJD8       | 16         | g.733021dup                        | p.Leu237ProfsX23   | duplication   |
| CHC1065T | ENSG00000112101 | KAL1        | X          | g.8522077G>A                       | p.Arg424X          | nonsense      |
| CHC1061T | ENSG00000120696 | KBTBD7      | 13         | g.41766431C>A                      | p.Glu655X          | nonsense      |
| CHC433T  | ENSG00000158445 | KCNB1       | 20         | g.47989865T>C                      | p.Ile744Met        | missense      |
| CHC433T  | ENSG00000182674 | KCNB2       | 8          | g.73848291C>A                      | p.Ala234Glu        | missense      |
| CHC301T  | ENSG00000116396 | KCNC4       | 1          | g.110765914C>G                     | p.Ser336Cys        | missense      |
| CHC1052T | ENSG00000206559 | KCNG1       | 20         | g.49626445G>A                      | p.Ala144Val        | missense      |
| CHC155T  | ENSG00000183960 | KCNH8       | 3          | g.19479854G>A                      | splicing           | intron        |
| CHC1061T | ENSG00000120457 | KCNJ5       | 11         | g.128786453T>C                     | p.Cys363Arg        | missense      |
| CHC1061T | ENSG00000173338 | KCNK7       | 11         | g.65361108_65361134del             | p.Val178_Pro186del | deletion      |
| CHC433T  | ENSG00000075043 | KCNQ2       | 20         | g.62044812A>C                      | p.Leu585Arg        | missense      |
| CHC433T  | ENSG00000120733 | KDM3B       | 5          | g.137766069G>T                     | p.Gln1675His       | missense      |
| CHC433T  | ENSG00000186280 | KDM4D       | 11         | g.94731546A>G                      | p.Lys337Arg        | missense      |
| CHC301T  | ENSG00000079999 | KEAP1       | 19         | g.10597426C>A                      | p.Glu593X          | nonsense      |
| CHC121T  | ENSG00000088247 | KHSRP       | 19         | g.6420453G>T                       | p.Pro152Gln        | missense      |
| CHC121T  | ENSG00000135709 | KIAA0513    | 16         | g.85111142G>T                      | p.Arg229Leu        | missense      |
| CHC051T  | ENSG00000164542 | KIAA0895    | 7          | g.36396656G>G                      | p.Ala241Val        | missense      |
| CHC614T  | ENSG00000005238 | KIAA1539    | 9          | g.35107957_35107958del             | p.Glu105GlyfsX26   | deletion      |
| CHC1061T | ENSG00000163808 | KIF15       | 3          | g.44872511G>A                      | splicing           | intron        |
| CHC1053T | ENSG00000112984 | KIF20A      | 5          | g.137521219_137521220del           | p.Glu49ArgfsX22    | deletion      |
| CHC433T  | ENSG00000116852 | KIF21B      | 1          | g.200945986C>A                     | p.Gly1441Val       | missense      |
| CHC1055T | ENSG00000186638 | KIF24       | 9          | g.34256399T>C                      | p.Glu1069Gly       | missense      |
| CHC155T  | ENSG00000189013 | KIR2DL4     | 19         | g.55317541T>G                      | p.Leu166Arg        | missense      |
| CHC155T  | ENSG00000126259 | KIRREL2     | 19         | g.36352049G>C                      | p.Arg361Pro        | missense      |
| CHC051T  | ENSG00000118263 | KLF7        | 2          | g.207988806G>C                     | p.Pro142Arg        | missense      |
| CHC429T  | ENSG00000197776 | KLHDC1      | 14         | g.50176515G>A                      | p.Gly86Arg         | missense      |
| CHC320T  | ENSG00000128607 | KLHDC10     | 7          | g.129736848G>A                     | splicing           | intron        |
| CHC302T  | ENSG00000172578 | KLHL6       | 3          | g.183217510A>T                     | p.Cys339Ser        | missense      |
| CHC1041T | ENSG00000167749 | KLK4        | 19         | g.51410260C>G                      | p.Gly232Ala        | missense      |
| CHC614T  | ENSG00000162869 | KLRAQ1      | 2          | g.48713866C>T                      | p.Ser472Leu        | missense      |
| CHC320T  | ENSG00000025800 | KPNA6       | 1          | g.32620321_32620329del             | p.Gln46ProfsX3     | deletion      |
| CHC306T  | ENSG00000111615 | KRR1        | 12         | g.75905317G>A                      | p.Gln21X           | nonsense      |
| CHC197T  | ENSG00000187242 | KRT12       | 17         | g.39021093C>A                      | p.Glu258X          | nonsense      |
| CHC429T  | ENSG00000198910 | L1CAM       | X          | g.153134061T>C                     | p.Asn501Asp        | missense      |
| CHC155T  | ENSG00000101680 | LAMA1       | 18         | g.6948416C>A                       | p.Gly2899Val       | missense      |
| CHC1065T | ENSG00000115365 | LANCL1      | 2          | g.211305335T>C                     | p.Tyr226Cys        | missense      |
| CHC1053T | ENSG00000132434 | LANCL2      | 7          | g.55493113G>A                      | p.Arg392Gln        | missense      |
| CHC1053T | ENSG00000131023 | LATS1       | 6          | g.149997395C>A                     | splicing           | intron        |
| CHC433T  | ENSG00000187173 | LCE2A       | 1          | g.152671515_152671556del           | p.Cys51_Gly64del   | deletion      |
| CHC1035T | ENSG00000168806 | LCMT2       | 15         | g.43620927G>C                      | p.Tyr587X          | nonsense      |
| CHC1065T | ENSG00000183722 | LHFP        | 13         | g.39952632G>C                      | p.Tyr139X          | nonsense      |
| CHC1065T | ENSG00000113594 | LIFR        | 5          | g.38486026T>G                      | p.Ile798Leu        | missense      |
| CHC433T  | ENSG00000174482 | LINGO2      | 9          | g.27949012A>T                      | p.Leu553Gln        | missense      |
| CHC301T  | ENSG00000188992 | LIP1        | 21         | g.15535738A>G                      | splicing           | intron        |
| CHC197T  | ENSG00000163431 | LMOD1       | 1          | g.201868607A>G                     | p.Ser512Pro        | missense      |
| CHC1065T | ENSG00000188076 | SCGB1C1     | 11         | g.193797G>C                        | p.Glu47Asp         | missense      |
| CHC429T  | ENSG00000072071 | LPHN1       | 19         | g.14266925A>T                      | p.Ile1046Asn       | missense      |
| CHC320T  | ENSG00000132793 | LPIN3       | 20         | g.39987430T>A                      | p.Leu827Gln        | missense      |
| CHC1061T | ENSG00000197324 | LRP10       | 14         | g.23345277T>C                      | p.Cys374Arg        | missense      |
| CHC1041T | ENSG00000172061 | LRRC15      | 3          | g.194080760T>C                     | p.Asn344Ser        | missense      |



**Supplementary Table 3. List of all somatic mutations identified in the exome sequencing of 24 HCC**

| HCC-ID   | Ensembl Gene ID | Gene symbol | Chromosome | Nucleotide (genomic position hg19) | Amino Acid        | Mutation Type |
|----------|-----------------|-------------|------------|------------------------------------|-------------------|---------------|
| CHC1061T | ENSG00000128606 | LRRIC17     | 7          | g.102574460C>T                     | p.Arg34Trp        | missense      |
| CHC1061T | ENSG00000131409 | LRRIC48     | 19         | g.51022137G>A                      | p.Ser278Leu       | missense      |
| CHC197T  | ENSG00000033122 | LRRIC7      | 1          | g.70504700G>T                      | p.Val1027Phe      | missense      |
| CHC197T  | ENSG00000133640 | LRRIQ1      | 12         | g.85623375C>T                      | p.Leu1635Phe      | missense      |
| CHC1065T | ENSG00000170382 | LRRN2       | 1          | g.204588258T>G                     | p.Lys288Thr       | missense      |
| CHC1035T | ENSG00000162951 | LRRTM1      | 2          | g.80530291G>T                      | p.His218Gln       | missense      |
| CHC429T  | ENSG00000160285 | LSS         | 21         | g.47647529C>A                      | p.Gly86Trp        | missense      |
| CHC121T  | ENSG00000145220 | LYAR        | 4          | g.4270343C>T                       | splicing          | intron        |
| CHC433T  | ENSG00000177239 | MAN1B1      | 9          | g.140003024C>G                     | p.Pro694Arg       | missense      |
| CHC1052T | ENSG00000172469 | MANEA       | 6          | g.96052781T>C                      | splicing          | intron        |
| CHC1061T | ENSG00000069535 | MAOB        | X          | g.43634507C>A                      | p.Glu384X         | nonsense      |
| CHC205T  | ENSG00000166963 | MAP1A       | 15         | g.43814680C>T                      | p.Arg337Trp       | missense      |
| CHC306T  | ENSG00000078018 | MAP2        | 2          | g.210574925A>T                     | p.Lys1674X        | nonsense      |
| CHC1065T | ENSG00000139625 | MAP3K12     | 12         | g.53875769del                      | p.Ser814AlafsX95  | deletion      |
| CHC614T  | ENSG00000107643 | MAPK8       | 10         | g.49609777G>G                      | p.Arg25Gln        | missense      |
| CHC301T  | ENSG00000127241 | MASP1       | 3          | g.186980342T>C                     | p.Tyr135Cys       | missense      |
| CHC433T  | ENSG00000171444 | MCC         | 5          | g.112440053C>A                     | splicing          | intron        |
| CHC1052T | ENSG00000076003 | MCM6        | 2          | g.136610401C>A                     | p.Asp571Tyr       | missense      |
| CHC155T  | ENSG00000112559 | MDFI        | 6          | g.41617362C>G                      | p.Pro89Ala        | missense      |
| CHC1035T | ENSG00000014641 | MDH1        | 2          | g.63832498G>T                      | p.Val272Phe       | missense      |
| CHC155T  | ENSG00000135679 | MDM2        | 12         | g.69222641T>A                      | p.Leu205Gln       | missense      |
| CHC433T  | ENSG00000146834 | MEPCE       | 7          | g.100030692C>T                     | p.Arg608Cys       | missense      |
| CHC051T  | ENSG00000116688 | MFN2        | 1          | g.12052699T>G                      | p.Ile88Ser        | missense      |
| CHC434T  | ENSG00000135596 | MICAL1      | 6          | g.109771564C>T                     | p.Arg377His       | missense      |
| CHC1053T | ENSG00000155545 | MIER3       | 5          | g.56233410A>C                      | p.Leu144X         | nonsense      |
| CHC429T  | ENSG00000186260 | MKL2        | 16         | g.14311048G>A                      | p.Asp140Asn       | missense      |
| CHC205T  | ENSG00000119684 | MLH3        | 14         | g.75514768del                      | p.Ser531ValfsX12  | deletion      |
| CHC429T  | ENSG00000099953 | MMP11       | 22         | g.24124458C>T                      | p.Pro374Leu       | missense      |
| CHC205T  | ENSG00000087245 | MMP2        | 16         | g.55522491C>T                      | p.Pro290Leu       | missense      |
| CHC433T  | ENSG00000137675 | MMP27       | 11         | g.102573614T>A                     | splicing          | intron        |
| CHC1061T | ENSG00000149968 | MMP3        | 11         | g.102709315T>C                     | p.Lys399Arg       | missense      |
| CHC121T  | ENSG00000100985 | MMP9        | 20         | g.44639662G>T                      | p.Glu208X         | nonsense      |
| CHC302T  | ENSG00000138722 | MMRN1       | 4          | g.90874208A>T                      | p.Tyr1109Phe      | missense      |
| CHC1065T | ENSG00000124217 | MOC53       | 20         | g.49576473G>T                      | p.Cys365Phe       | missense      |
| CHC121T  | ENSG00000116151 | MORN1       | 1          | g.2321390C>T                       | p.Gly41Glu        | missense      |
| CHC320T  | ENSG00000130830 | MPP1        | X          | g.154014569T>C                     | p.Asn196Ser       | missense      |
| CHC197T  | ENSG00000082126 | MPP4        | 2          | g.202545754_202545755del           | p.Tyr246ArgfsX6   | deletion      |
| CHC1035T | ENSG00000066382 | MPPED2      | 11         | g.30433059T>A                      | p.Asn281Tyr       | missense      |
| CHC320T  | ENSG00000166902 | MRPL16      | 11         | g.59573821T>C                      | p.X252TrpextX2    | missense      |
| CHC433T  | ENSG00000116221 | MRPL37      | 1          | g.54666230A>G                      | p.Tyr105Cys       | missense      |
| CHC197T  | ENSG00000053372 | MRT0A       | 1          | g.19584362G>G                      | p.Arg126Gln       | missense      |
| CHC433T  | ENSG00000166927 | MS4A7       | 11         | g.60156927T>G                      | p.Leu135Arg       | missense      |
| CHC433T  | ENSG00000127989 | MTERF       | 7          | g.91503452T>G                      | p.Gln219Pro       | missense      |
| CHC1053T | ENSG00000136371 | MTHFS       | 15         | g.80181570G>A                      | p.Arg82Trp        | missense      |
| CHC614T  | ENSG00000132613 | MTSSL       | 16         | g.70698552T>C                      | p.Ser474Gly       | missense      |
| CHC433T  | ENSG00000101057 | MYBL2       | 20         | g.42344613G>A                      | p.Trp663X         | nonsense      |
| CHC301T  | ENSG00000133454 | MYO18B      | 22         | g.26168334C>G                      | p.Leu576Val       | missense      |
| CHC322T  | ENSG00000197879 | MYO1C       | 17         | g.1383903_1383915del               | p.Gln271ProfxsX17 | deletion      |
| CHC302T  | ENSG00000141052 | MYOCD       | 17         | g.12666879C>G                      | p.Pro960Arg       | missense      |
| CHC301T  | ENSG00000170011 | MYRIP       | 3          | g.40231337_40231352del             | p.Ser350GlyfsX4   | deletion      |
| CHC205T  | ENSG00000078177 | N4BP2       | 4          | g.40122951A>G                      | p.Lys1074Glu      | missense      |
| CHC155T  | ENSG00000164134 | NAA15       | 4          | g.140281044A>G                     | p.Thr469Ala       | missense      |
| CHC1061T | ENSG00000102452 | NALCN       | 13         | g.102051476A>G                     | p.Met1?           | missense      |
| CHC429T  | ENSG00000067798 | NAV3        | 12         | g.78574716G>C                      | p.Lys1839Asn      | missense      |
| CHC1052T | ENSG00000151503 | NCAPD3      | 11         | g.134062741C>A                     | p.Asp630Tyr       | missense      |
| CHC1053T | ENSG00000146918 | NCAPG2      | 7          | g.158437057T>A                     | p.Arg1102Trp      | missense      |
| CHC320T  | ENSG00000124160 | NCOA5       | 20         | g.44695713C>T                      | p.Val204Met       | missense      |
| CHC433T  | ENSG00000196498 | NCOR2       | 12         | g.123470536_123470567del           | indels            | deletion      |
| CHC302T  | ENSG00000183091 | NEB         | 2          | g.152536496T>C                     | p.Tyr1028Cys      | missense      |
| CHC1035T | ENSG00000100906 | NFKBIA      | 14         | g.35871259T>C                      | p.Tyr305Ser       | missense      |
| CHC429T  | ENSG00000169760 | NLGN1       | 3          | g.173322644G>A                     | p.Ala86Thr        | missense      |
| CHC1061T | ENSG00000087095 | NLK         | 17         | g.26488207G>A                      | p.Met222Ile       | missense      |
| CHC433T  | ENSG00000167984 | NLR3        | 16         | g.3614016G>A                       | p.Leu308Phe       | missense      |
| CHC121T  | ENSG00000182261 | NLRP10      | 11         | g.7981542del                       | p.Cys540ValfsX2   | deletion      |
| CHC433T  | ENSG00000142405 | NLRP12      | 19         | g.54312893C>A                      | p.Gly674Trp       | missense      |
| CHC320T  | ENSG00000167634 | NLRP7       | 19         | g.55447696C>T                      | p.Glu745Lys       | missense      |
| CHC1052T | ENSG00000132911 | NMUR2       | 5          | g.151784262G>T                     | p.Thr138Asn       | missense      |
| CHC433T  | ENSG00000112992 | NNT         | 5          | g.43609382A>C                      | p.Lys29Gln        | missense      |
| CHC433T  | ENSG00000164867 | NOS3        | 7          | g.150695503A>T                     | p.His214Leu       | missense      |
| CHC1053T | ENSG00000134250 | NOTCH2      | 1          | g.120539757T>C                     | p.Tyr205Cys       | missense      |
| CHC1052T | ENSG00000074181 | NOTCH3      | 19         | g.15302568G>T                      | p.Pro264Thr       | missense      |
| CHC205T  | ENSG00000255346 | NOX5        | 15         | g.69318912C>A                      | p.Thr32Asn        | missense      |
| CHC1055T | ENSG00000151322 | NPAS3       | 14         | g.33684497A>T                      | p.Ile84Phe        | missense      |
| CHC1035T | ENSG00000174576 | NPAS4       | 11         | g.66192601C>T                      | p.Ser747Phe       | missense      |
| CHC1053T | ENSG00000185551 | NR2F2       | 15         | g.96880694T>G                      | p.Leu363Arg       | missense      |
| CHC306T  | ENSG00000151623 | NR3C2       | 4          | g.149075935A>C                     | p.Ile711Ser       | missense      |
| CHC205T  | ENSG00000073969 | NSF         | 17         | g.44788380_44788384del             | p.Ile508MetfsX3   | deletion      |
| CHC1053T | ENSG00000108256 | NUFIP2      | 17         | g.27613156T>C                      | p.Tyr619Cys       | missense      |
| CHC307T  | ENSG00000126883 | NUP214      | 9          | g.134003761T>A                     | p.Ile95Asn        | missense      |
| CHC307T  | ENSG00000110713 | NUP98       | 11         | g.3756520C>A                       | p.Gln481His       | missense      |
| CHC1035T | ENSG00000089127 | OAS1        | 12         | g.113348912G>T                     | p.Glu176Lys       | missense      |
| CHC433T  | ENSG00000147162 | OGT         | X          | g.70756182A>G                      | p.Ile64Met        | missense      |
| CHC205T  | ENSG00000138315 | OIT3        | 10         | g.74690322A>C                      | p.Gln465Pro       | missense      |
| CHC1035T | ENSG00000162600 | OMA1        | 1          | g.59002184C>G                      | splicing          | intron        |
| CHC320T  | ENSG00000122375 | OPN4        | 10         | g.88419072G>T                      | p.Gly227Val       | missense      |
| CHC121T  | ENSG00000170782 | OR10A4      | 11         | g.6897977G>T                       | p.Leu33Phe        | missense      |
| CHC434T  | ENSG00000206474 | OR10C1      | 6          | g.29408024C>T                      | p.Pro78Ser        | missense      |
| CHC1052T | ENSG00000177174 | OR14C36     | 1          | g.248512710A>G                     | p.Ile212Val       | missense      |
| CHC429T  | ENSG00000204700 | OR2J2       | 6          | g.29142247T>C                      | p.Tyr279His       | missense      |
| CHC1061T | ENSG00000176200 | OR4D11      | 11         | g.59271338G>A                      | p.Cys97Tyr        | missense      |
| CHC1052T | ENSG00000197428 | OR51D1      | 11         | g.4661451G>G                       | p.Arg144His       | missense      |
| CHC1041T | ENSG00000167360 | OR51Q1      | 11         | g.5444052A>G                       | p.Ile208Val       | missense      |
| CHC121T  | ENSG00000180974 | OR52E4      | 11         | g.5905850A>A                       | p.Thr110Ser       | missense      |
| CHC614T  | ENSG00000174942 | OR5R1       | 11         | g.56185444G>A                      | p.Arg89Cys        | missense      |
| CHC1035T | ENSG00000205330 | OR6C1       | 12         | g.55714811T>C                      | p.Val143Ala       | missense      |
| CHC121T  | ENSG00000150261 | OR8K1       | 11         | g.56113963T>A                      | p.Leu150Gln       | missense      |

Supplementary Table 3. List of all somatic mutations identified in the exome sequencing of 24 HCC

| HCC-ID   | Ensembl Gene ID | Gene symbol | Chromosome | Nucleotide (genomic position hg19) | Amino Acid         | Mutation Type |
|----------|-----------------|-------------|------------|------------------------------------|--------------------|---------------|
| CHC1065T | ENSG00000181689 | OR8K3       | 11         | g.56086321A>G                      | p.Asp180Gly        | missense      |
| CHC302T  | ENSG00000172377 | OR9I1       | 11         | g.57886072del                      | p.Ile282ThrfsX4    | deletion      |
| CHC429T  | ENSG00000006025 | OSBPL7      | 17         | g.45890631C>T                      | splicing           | intron        |
| CHC197T  | ENSG00000155719 | OTOA        | 16         | g.21726317C>A                      | p.Phe444Leu        | missense      |
| CHC205T  | ENSG00000187848 | P2RX2       | 12         | g.133198125T>C                     | p.Val354Ala        | missense      |
| CHC306T  | ENSG00000090621 | PABPC4      | 1          | g.40031047T>C                      | p.Met326Val        | missense      |
| CHC1052T | ENSG00000142619 | PADI3       | 1          | g.17596805G>A                      | p.Gly244Arg        | missense      |
| CHC429T  | ENSG00000007168 | PAFAH1B1    | 17         | g.2570374G>A                       | p.Trp94X           | nonsense      |
| CHC429T  | ENSG00000129116 | PALLD       | 4          | g.169432738C>T                     | p.Pro28Leu         | missense      |
| CHC1053T | ENSG00000135473 | PAN2        | 12         | g.56720433A>C                      | p.Asp410Glu        | missense      |
| CHC434T  | ENSG00000183760 | PAPL        | 19         | g.39590987G>T                      | p.Arg209Val        | missense      |
| CHC429T  | ENSG00000175193 | PARL        | 3          | g.183580547C>A                     | p.Val169Leu        | missense      |
| CHC429T  | ENSG00000138496 | PARP9       | 3          | g.122259427C>T                     | p.Gly588Arg        | missense      |
| CHC1061T | ENSG00000125618 | PAX8        | 2          | g.113999185A>C                     | p.Phe240Leu        | missense      |
| CHC433T  | ENSG00000108187 | PBLD        | 10         | g.70048359C>A                      | p.Gly191Val        | missense      |
| CHC121T  | ENSG00000163939 | PBRM1       | 3          | g.52702661_52702662del             | indels             | deletion      |
| CHC1035T | ENSG00000118946 | PCDH17      | 13         | g.58208192C>A                      | p.Asn504Lys        | missense      |
| CHC1035T | ENSG00000165194 | PCDH19      | X          | g.99662659C>A                      | p.Glu313X          | nonsense      |
| CHC433T  | ENSG00000204970 | PCDH11      | 5          | g.140389516C>A                     | p.Asp949Glu        | missense      |
| CHC205T  | ENSG00000124253 | PCK1        | 20         | g.56137204_56137205del             | p.Thr102SerfsX21   | deletion      |
| CHC1052T | ENSG00000160299 | PCNT        | 21         | g.47783782G>T                      | p.Asp848Tyr        | missense      |
| CHC320T  | ENSG00000100731 | PCNX        | 14         | g.71445081G>C                      | p.Arg676Gln        | missense      |
| CHC1055T | ENSG00000169174 | PCSK9       | 1          | g.55524200G>C                      | p.Trp461Cys        | missense      |
| CHC1065T | ENSG00000004799 | PDK4        | 7          | g.95216389T>C                      | p.Tyr343Cys        | missense      |
| CHC429T  | ENSG00000162493 | PDPN        | 1          | g.13933683C>T                      | p.Pro104Leu        | missense      |
| CHC197T  | ENSG00000181195 | PENK        | 8          | g.57353988C>A                      | p.Arg216Ile        | missense      |
| CHC307T  | ENSG00000109272 | PF4V1       | 4          | g.74719596C>G                      | p.Ala66Gly         | missense      |
| CHC433T  | ENSG00000170525 | PKFB3       | 10         | g.6255709A>C                       | p.Lys67Thr         | missense      |
| CHC1052T | ENSG00000154330 | PGM5        | 9          | g.71002385T>C                      | p.Ile193Thr        | missense      |
| CHC121T  | ENSG00000087495 | PHACTR3     | 20         | g.58349374C>T                      | p.Arg335Trp        | missense      |
| CHC1065T | ENSG00000111752 | PHC1        | 12         | g.9086508_9086520del               | p.Glu648SerfsX15   | deletion      |
| CHC433T  | ENSG00000134686 | PHC2        | 1          | g.33794500T>C                      | p.Asp798Gly        | missense      |
| CHC614T  | ENSG00000067177 | PHKA1       | X          | g.71825155C>A                      | p.Met927Ile        | missense      |
| CHC1035T | ENSG00000191444 | PHLDB1      | 11         | g.118498522G>C                     | p.Arg328Pro        | missense      |
| CHC433T  | ENSG00000116793 | PHTF1       | 1          | g.114240991T>C                     | p.Arg721Gly        | missense      |
| CHC1052T | ENSG00000165443 | PHYHIP1     | 10         | g.61005035A>G                      | p.Tyr272Cys        | missense      |
| CHC433T  | ENSG00000141720 | PIP4K2B     | 17         | g.36925987T>A                      | p.Tyr403Phe        | missense      |
| CHC429T  | ENSG00000154217 | PITPNC1     | 17         | g.6568843C>T                       | p.Leu280Phe        | missense      |
| CHC258T  | ENSG00000110697 | PITPNM1     | 11         | g.67265000_67265011del             | p.Pro641_Ser644del | deletion      |
| CHC433T  | ENSG00000107959 | PITRM1      | 10         | g.3202086C>A                       | p.Asp321Tyr        | missense      |
| CHC051T  | ENSG00000118762 | PKD2        | 4          | g.88983119A>G                      | p.Gln649Leu        | missense      |
| CHC155T  | ENSG00000105223 | PLD3        | 19         | g.40877707A>G                      | p.Tyr269Cys        | missense      |
| CHC155T  | ENSG00000076356 | PLXNA2      | 1          | g.208213051C>T                     | p.Gly1472Asp       | missense      |
| CHC258T  | ENSG00000221866 | PLXNA4      | 7          | g.131859679G>C                     | p.Ala1292Gly       | missense      |
| CHC429T  | ENSG00000196576 | PLXNB2      | 22         | g.50719053 T>A                     | p.Lys1347Met       | missense      |
| CHC121T  | ENSG00000175535 | PNLIP       | 10         | g.118307955A>G                     | p.Ile95Met         | missense      |
| CHC306T  | ENSG00000164087 | POC1A       | 3          | g.52179882C>A                      | p.Arg220Leu        | missense      |
| CHC429T  | ENSG00000124429 | POF1B       | X          | g.84622772C>T                      | splicing           | intron        |
| CHC429T  | ENSG00000188866 | POFUT2      | 21         | g.46705622G>T                      | p.Pro118His        | missense      |
| CHC051T  | ENSG00000143442 | POGZ        | 1          | g.151396685_151396687del           | p.Ala421del        | deletion      |
| CHC433T  | ENSG00000122678 | POLM        | 7          | g.44116189C>A                      | p.Asp252Tyr        | missense      |
| CHC433T  | ENSG00000130997 | POLN        | 4          | g.2214787G>T                       | p.Ser67X           | nonsense      |
| CHC429T  | ENSG00000186141 | POLR3C      | 1          | g.145609267del                     | p.Ile24LeufsX5     | deletion      |
| CHC322T  | ENSG00000166351 | POTED       | 21         | g.14987742T>C                      | p.Cys221Arg        | missense      |
| CHC320T  | ENSG00000143190 | POU2F1      | 1          | g.167358829_167358834del           | p.Pro275_Thr276del | deletion      |
| CHC306T  | ENSG00000130810 | PPAN        | 19         | g.10221193C>G                      | p.Leu312Val        | missense      |
| CHC306T  | ENSG00000243207 | PPAN-P2RY11 | 19         | g.10221193C>G                      | p.Leu312Val        | missense      |
| CHC302T  | ENSG00000112033 | PPARD       | 6          | g.35392508G>C                      | p.Asp344His        | missense      |
| CHC433T  | ENSG00000155846 | PPARGC1B    | 5          | g.149216051A>T                     | p.Gln678Leu        | missense      |
| CHC322T  | ENSG00000177380 | PPFIA3      | 19         | g.49652918_49652961del             | p.Gly1160ArgfsX27  | deletion      |
| CHC302T  | ENSG00000058272 | PPP1R12A    | 12         | g.80266606C>A                      | p.Gly117Val        | missense      |
| CHC1052T | ENSG00000154415 | PPP1R3A     | 7          | g.113520138C>G                     | p.Asp337His        | missense      |
| CHC1035T | ENSG00000158528 | PPP1R9A     | 7          | g.94539678G>T                      | p.Ala85Ser         | missense      |
| CHC155T  | ENSG00000249553 | PPP2R2B     | 5          | g.146077602_146077603insA          | p.Ile95TyrfsX3     | insertion     |
| CHC1061T | ENSG00000149923 | PPP4C       | 16         | g.30094740T>A                      | p.Leu110Gln        | missense      |
| CHC1041T | ENSG00000114885 | PPP5C       | 19         | g.46890450del                      | p.Phe335LeufsX15   | deletion      |
| CHC433T  | ENSG00000110075 | PPP6R3      | 11         | g.68337232A>G                      | p.Tyr382Cys        | missense      |
| CHC301T  | ENSG00000108946 | PRKAR1A     | 17         | g.66526077_66526095del             | p.Gln304LysfsX21   | deletion      |
| CHC155T  | ENSG00000114302 | PRKAR2A     | 3          | g.48789654G>A                      | p.Pro346Ser        | missense      |
| CHC614T  | ENSG00000166501 | PRKCB       | 16         | g.24135258G>A                      | p.Asp341Asn        | missense      |
| CHC1053T | ENSG00000007062 | PROM1       | 4          | g.16025950G>T                      | p.Thr221Asn        | missense      |
| CHC1035T | ENSG00000166450 | PRTG        | 15         | g.55967863T>C                      | p.Tyr467Cys        | missense      |
| CHC1035T | ENSG00000059915 | PSD         | 10         | g.104174840C>A                     | p.Asp302Tyr        | missense      |
| CHC433T  | ENSG00000146005 | PSD2        | 5          | g.139217341C>A                     | p.Asp599Glu        | missense      |
| CHC433T  | ENSG00000156011 | PSD3        | 8          | g.18729634G>C                      | p.Ser247Cys        | missense      |
| CHC306T  | ENSG00000152104 | PTPN14      | 1          | g.214557049_214557051del           | p.Glu716del        | deletion      |
| CHC205T  | ENSG00000070159 | PTPN3       | 9          | g.112143978A>T                     | p.Ile873Asn        | missense      |
| CHC433T  | ENSG00000144724 | PTPRG       | 3          | g.62118279A>T                      | p.Ser207Cys        | missense      |
| CHC433T  | ENSG00000155093 | PTPRN2      | 7          | g.157475495A>T                     | p.His641Gln        | missense      |
| CHC1035T | ENSG00000196090 | PTPRT       | 20         | g.41306605G>C                      | p.Pro352Ala        | missense      |
| CHC614T  | ENSG00000176894 | PXMP2       | 12         | g.133272505A>G                     | p.Tyr91Cys         | missense      |
| CHC429T  | ENSG00000109113 | RAB34       | 17         | g.27042288C>T                      | p.Trp203X          | nonsense      |
| CHC197T  | ENSG00000111540 | RAB5B       | 12         | g.56384584A>G                      | p.Tyr145Cys        | missense      |
| CHC1061T | ENSG00000214842 | RAD51AP2    | 2          | g.17698119C>A                      | p.Gly522X          | nonsense      |
| CHC433T  | ENSG00000002016 | RAD52       | 12         | g.1023168G>T                       | p.Gln363Lys        | missense      |
| CHC1035T | ENSG00000164080 | RAD54L2     | 3          | g.51691608del                      | p.Pro1080LeufsX147 | deletion      |
| CHC253T  | ENSG00000188559 | RALGAP2     | 20         | g.20507002_20507014del             | indels             | deletion      |
| CHC434T  | ENSG00000075391 | RASAL2      | 1          | g.178412048dup                     | p.Asp390GlyfsX4    | duplication   |
| CHC433T  | ENSG00000165105 | RASEF       | 9          | g.85613331A>T                      | p.Val585Glu        | missense      |
| CHC155T  | ENSG00000198774 | RASSF9      | 12         | g.86199412A>T                      | p.Trp126Arg        | missense      |
| CHC1053T | ENSG00000162275 | RBM15       | 1          | g.110882914G>A                     | p.Gly296Asp        | missense      |
| CHC121T  | ENSG00000091009 | RBM27       | 5          | g.145609449G>A                     | p.Asp189Asn        | missense      |
| CHC306T  | ENSG00000188739 | RBM34       | 1          | g.235301490C>A                     | splicing           | intron        |
| CHC301T  | ENSG00000056586 | RC3H2       | 9          | g.125621361T>C                     | p.Thr624Ala        | missense      |
| CHC433T  | ENSG00000167771 | RCOR2       | 11         | g.63679989_63679999del             | p.Tyr347LeufsX39   | deletion      |
| CHC302T  | ENSG00000084093 | REST        | 4          | g.57798059A>T                      | p.His1012Leu       | missense      |

**Supplementary Table 3. List of all somatic mutations identified in the exome sequencing of 24 HCC**

| HCC-ID   | Ensembl Gene ID | Gene symbol   | Chromosome | Nucleotide (genomic position hg19) | Amino Acid         | Mutation Type |
|----------|-----------------|---------------|------------|------------------------------------|--------------------|---------------|
| CHC121T  | ENSG00000108370 | RGS9          | 17         | g.63221138C>T                      | p.Pro476Ser        | missense      |
| CHC433T  | ENSG00000153561 | RMNDSA        | 2          | g.86968076C>T                      | p.Leu57Phe         | missense      |
| CHC433T  | ENSG00000180537 | RNF182        | 6          | g.13977482T>A                      | p.Cys44X           | nonsense      |
| CHC1052T | ENSG00000152193 | RNF219        | 13         | g.79190319C>A                      | p.Ser526Ile        | missense      |
| CHC1061T | ENSG00000137075 | RNF38         | 9          | g.36356380G>A                      | p.Pro277Ser        | missense      |
| CHC1052T | ENSG00000069667 | RORA          | 15         | g.60797803del                      | p.Lys315AsnfsX10   | deletion      |
| CHC258T  | ENSG00000136643 | RPS6K1        | 1          | g.213303065del                     | p.Arg223LeufsX8    | deletion      |
| CHC1061T | ENSG00000198208 | RPS6K1L       | 14         | g.75373288G>C                      | p.His530Gln        | missense      |
| CHC1055T | ENSG00000189306 | RRP7A         | 22         | g.42910686_42910687insT            | indels             | insertion     |
| CHC306T  | ENSG00000114767 | RRP9          | 3          | g.51968546C>A                      | p.Arg401Leu        | missense      |
| CHC051T  | ENSG00000132026 | RTBDN         | 19         | g.12939741T>C                      | p.Thr98Ala         | missense      |
| CHC320T  | ENSG00000160753 | RUSC1         | 1          | g.155296579G>T                     | p.Gln690His        | missense      |
| CHC155T  | ENSG00000163785 | RYK           | 3          | g.133921646 A>C                    | p.Val235Gly        | missense      |
| CHC155T  | ENSG00000232040 | SCAND3        | 6          | g.28540650G>A                      | p.Leu1006Phe       | missense      |
| CHC433T  | ENSG00000136531 | SCN2A         | 2          | g.166223828A>T                     | p.Asn1208Tyr       | missense      |
| CHC121T  | ENSG00000153253 | SCN3A         | 2          | g.165947448C>T                     | p.Gly1739Arg       | missense      |
| CHC205T  | ENSG00000111319 | SCNN1A        | 12         | g.6465044T>C                       | p.Asn352Ser        | missense      |
| CHC1053T | ENSG00000168447 | SCNN1B        | 16         | g.23359963C>G                      | p.Gln15Glu         | missense      |
| CHC121T  | ENSG00000175356 | SCUBE2        | 11         | g.9043424T>C                       | p.Lys921Arg        | missense      |
| CHC205T  | ENSG00000165525 | SDCCAG1       | 14         | g.50295058 T>C                     | p.Lys480Arg        | missense      |
| CHC1053T | ENSG00000073578 | SDHA          | 5          | g.256525_256533del                 | p.Ser663X          | deletion      |
| CHC320T  | ENSG00000166562 | SEC11C        | 18         | g.56816776_56816783del             | p.Val41CysfsX15    | deletion      |
| CHC1052T | ENSG00000101310 | SEC23B        | 20         | g.18513307G>T                      | splicing           | intron        |
| CHC1041T | ENSG00000187742 | SECISBP2      | 9          | g.91972406A>G                      | p.Lys732Glu        | missense      |
| CHC121T  | ENSG00000170381 | SEMA3E        | 7          | g.83035340C>A                      | p.Lys283Asn        | missense      |
| CHC197T  | ENSG00000111897 | SERINC1       | 6          | g.122775025G>T                     | p.Ala160Asp        | missense      |
| CHC121T  | ENSG00000021355 | SERPIN1       | 6          | g.2840750G>T                       | p.Pro24Gln         | missense      |
| CHC429T  | ENSG00000183431 | SF3A3         | 1          | g.38449882G>T                      | p.His143Asn        | missense      |
| CHC1035T | ENSG00000087365 | SF3B2         | 11         | g.65835682G>A                      | p.Glu832Lys        | missense      |
| CHC322T  | ENSG00000189091 | SF3B3         | 16         | g.70582331G>T                      | p.Arg463Leu        | missense      |
| CHC205T  | ENSG00000164023 | SGMS2         | 4          | g.108824469T>A                     | p.His218Gln        | missense      |
| CHC434T  | ENSG00000148341 | SH3GLB2       | 9          | g.131783430C>T                     | p.Glu92Lys         | missense      |
| CHC1041T | ENSG00000172985 | SH3RF3        | 2          | g.110015263 C>T                    | p.Thr388Met        | missense      |
| CHC302T  | ENSG00000161681 | SHANK1        | 19         | g.51189537G>T                      | p.Ala845Glu        | missense      |
| CHC051T  | ENSG00000182199 | SHMT2         | 12         | g.57626053A>G                      | p.Glu191Gly        | missense      |
| CHC1053T | ENSG00000168779 | SHOX2         | 3          | g.15781778C>A                      | splicing           | intron        |
| CHC1055T | ENSG00000105366 | SIGLEC8       | 19         | g.51955889T>C                      | splicing           | intron        |
| CHC301T  | ENSG00000129450 | SIGLEC9       | 19         | g.51628458C>A                      | p.Thr76Lys         | missense      |
| CHC1035T | ENSG00000160584 | SIK3          | 11         | g.116744237T>C                     | p.Lys508Arg        | missense      |
| CHC051T  | ENSG00000197555 | SIPA1L1       | 14         | g.72139195G>T                      | p.Gly987Val        | missense      |
| CHC433T  | ENSG00000100625 | SIX4          | 14         | g.61180349C>A                      | p.Val708Phe        | missense      |
| CHC614T  | ENSG00000182628 | SKA2          | 17         | g.57196831T>C                      | p.Glu49Gly         | missense      |
| CHC301T  | ENSG00000174327 | SLC16A13      | 17         | g.6941603_6941614del               | p.Gln160_Leu163del | deletion      |
| CHC433T  | ENSG00000118596 | SLC16A7       | 12         | g.60168617T>A                      | p.Leu181Met        | missense      |
| CHC307T  | ENSG00000105143 | SLC1A6        | 19         | g.15065076G>A                      | p.Thr412Ile        | missense      |
| CHC1065T | ENSG00000144136 | SLC20A1       | 2          | g.113420482 G>T                    | p.Lys640Asn        | missense      |
| CHC320T  | ENSG00000170482 | SLC23A1       | 5          | g.138713965_138713966insC          | p.Leu423AlafsX7    | insertion     |
| CHC1053T | ENSG00000040864 | SLC25A13      | 7          | g.95761164_95761165insAT           | p.Pro496PhefsX14   | insertion     |
| CHC1035T | ENSG00000155287 | SLC25A28      | 10         | g.101371024C>T                     | p.Arg226His        | missense      |
| CHC433T  | ENSG00000197496 | SLC2A10       | 20         | g.45358052G>A                      | p.Gly491Asp        | missense      |
| CHC302T  | ENSG00000170385 | SLC30A1       | 1          | g.211749293_211749294del           | p.Val322CysfsX15   | deletion      |
| CHC205T  | ENSG00000164756 | SLC30A8       | 8          | g.118165285C>A                     | p.Ser125X          | nonsense      |
| CHC433T  | ENSG00000138459 | SLC35A5       | 3          | g.112299965dup                     | p.Leu334PhefsX19   | duplication   |
| CHC1035T | ENSG00000160190 | SLC37A1       | 21         | g.43994977G>C                      | p.Trp491Cys        | missense      |
| CHC1061T | ENSG00000139974 | SLC38A6       | 14         | g.61449305G>A                      | p.Gly62Asp         | missense      |
| CHC320T  | ENSG00000141424 | SLC39A6       | 18         | g.33703604T>C                      | p.Ile332Val        | missense      |
| CHC1053T | ENSG00000149150 | SLC43A1       | 11         | g.57268779G>A                      | p.Gln60X           | nonsense      |
| CHC1052T | ENSG00000167703 | SLC43A2       | 17         | g.1479025C>T                       | p.Gly528Asp        | missense      |
| CHC155T  | ENSG00000164889 | SLC4A2        | 7          | g.150772379G>A                     | p.Gly1029Ser       | missense      |
| CHC301T  | ENSG00000117834 | SLC5A9        | 1          | g.48698175G>A                      | splicing           | intron        |
| CHC301T  | ENSG00000151012 | SLC7A11       | 4          | g.139106331C>T                     | p.Ala287Thr        | missense      |
| CHC614T  | ENSG00000183023 | SLC8A1        | 2          | g.40366760A>G                      | p.Tyr776His        | missense      |
| CHC1041T | ENSG00000090020 | SLC9A1        | 1          | g.27434217T>G                      | p.Tyr402Pro        | missense      |
| CHC205T  | ENSG00000066230 | SLC9A3        | 5          | g.492032_492033insC                | p.Ile123HisfsX79   | insertion     |
| CHC121T  | ENSG00000166750 | SLFN5         | 17         | g.33586053C>A                      | p.Ser115Tyr        | missense      |
| CHC1052T | ENSG00000184347 | SLIT3         | 5          | g.168096806C>T                     | p.Gly1440Ser       | missense      |
| CHC433T  | ENSG00000178235 | SLITRK1       | 13         | g.84454111A>T                      | p.Val511Glu        | missense      |
| CHC302T  | ENSG00000102038 | SMARCA1       | X          | g.128649922C>T                     | p.Glu160Lys        | missense      |
| CHC1041T | ENSG00000080503 | SMARCA2       | 9          | g.2039655del                       | p.Arg183GlufsX5    | deletion      |
| CHC1053T | ENSG00000163104 | SMARCA2       | 4          | g.95191952A>G                      | p.Ile519Val        | missense      |
| CHC301T  | ENSG00000099956 | SMARCB1       | 22         | g.24145583G>T                      | p.Arg201Leu        | missense      |
| CHC1055T | ENSG00000100796 | SMEK1         | 14         | g.91937183A>G                      | p.Leu540Ser        | missense      |
| CHC614T  | ENSG00000138041 | SMEK2         | 2          | g.55816053T>G                      | p.Thr321Pro        | missense      |
| CHC320T  | ENSG00000143740 | SNAP47        | 1          | g.227946961G>C                     | p.Val300Met        | missense      |
| CHC121T  | ENSG00000163788 | SNRK          | 3          | g.43344873C>A                      | p.Leu60Val         | missense      |
| CHC433T  | ENSG00000249481 | SPATS1        | 6          | g.44344131G>T                      | p.Leu265Phe        | missense      |
| CHC197T  | ENSG00000065526 | SPEN          | 1          | g.16259206dup                      | p.Pro2158AlafsX26  | duplication   |
| CHC1035T | ENSG00000152377 | SPOCK1        | 5          | g.136314446del                     | p.Pro406GlnfsX8    | deletion      |
| CHC306T  | ENSG00000121067 | SPOP          | 17         | g.47696415G>C                      | p.Phe136Leu        | missense      |
| CHC1061T | ENSG00000169474 | SPRR1A        | 1          | g.152957738del                     | p.Pro12HisfsX10    | deletion      |
| CHC1055T | ENSG00000161011 | SQSTM1        | 5          | g.179260586G>A                     | splicing           | intron        |
| CHC301T  | ENSG00000080603 | SRCA1         | 16         | g.30744772T>A                      | splicing           | intron        |
| CHC205T  | ENSG00000174780 | SRP72         | 4          | g.57337912A>G                      | p.Tyr86Cys         | missense      |
| CHC1052T | ENSG00000116350 | SRSF4         | 1          | g.29481412C>A                      | p.Arg125Leu        | missense      |
| CHC320T  | ENSG00000144057 | ST6GAL2       | 2          | g.107459971del                     | p.Glu155SerfsX19   | deletion      |
| CHC1041T | ENSG00000048666 | ST7           | 7          | g.116830931G>C                     | p.Glu399Lys        | missense      |
| CHC1055T | ENSG00000148488 | ST8IA6        | 10         | g.17365104T>C                      | p.Thr230Ala        | missense      |
| CHC121T  | ENSG00000138134 | STAMBPL1      | 10         | g.90665347A>T                      | p.Arg60Trp         | missense      |
| CHC121T  | ENSG00000170581 | STAT2         | 12         | g.56745235C>A                      | splicing           | intron        |
| CHC121T  | ENSG00000124214 | STAU1         | 20         | g.47734596A>C                      | p.Ser409Arg        | missense      |
| CHC205T  | ENSG00000040341 | STAU2         | 8          | g.74495040C>A                      | p.Gly396Val        | missense      |
| CHC433T  | ENSG00000125834 | STK35         | 20         | g.2097579T>G                       | p.Val387Gly        | missense      |
| CHC429T  | ENSG00000101109 | STK4          | 20         | g.43623818G>A                      | p.Ala205Thr        | missense      |
| CHC1052T | ENSG00000068781 | STON1-GTF2A1L | 2          | g.48872191C>G                      | p.Ala812Gly        | missense      |
| CHC434T  | ENSG00000165730 | STOX1         | 10         | g.70644659G>T                      | p.Leu369Phe        | missense      |
| CHC121T  | ENSG00000125695 | STRADA        | 17         | g.61784056C>G                      | p.Gly266Ala        | missense      |

**Supplementary Table 3. List of all somatic mutations identified in the exome sequencing of 24 HCC**

| HCC-ID   | Ensembl Gene ID | Gene symbol | Chromosome | Nucleotide (genomic position hg19) | Amino Acid        | Mutation Type |
|----------|-----------------|-------------|------------|------------------------------------|-------------------|---------------|
| CHC051T  | ENSG00000079950 | STX7        | 6          | g.132785152A>G                     | p.Ser225Pro       | missense      |
| CHC614T  | ENSG00000060140 | STYK1       | 12         | g.10782124C>T                      | p.Asp201Asn       | missense      |
| CHC197T  | ENSG00000135316 | SYNCRIP     | 6          | g.86346836T>G                      | p.Asp172Ala       | missense      |
| CHC051T  | ENSG00000146383 | TAAR6       | 6          | g.132891657C>A                     | p.Pro66Gln        | missense      |
| CHC1035T | ENSG00000237110 | TAAR9       | 6          | g.132860372A>T                     | p.Tyr315Phe       | missense      |
| CHC1053T | ENSG00000122728 | TAFL1       | 9          | g.32631796T>A                      | p.Lys1261Met      | missense      |
| CHC433T  | ENSG00000106290 | TAFA6       | 7          | g.99709773C>G                      | p.Glu263Asp       | missense      |
| CHC614T  | ENSG00000177565 | TBL1XR1     | 3          | g.176765120C>T                     | p.Gly278Arg       | missense      |
| CHC121T  | ENSG00000121075 | TBX4        | 17         | g.59543205A>T                      | p.Lys103X         | nonsense      |
| CHC433T  | ENSG00000165929 | TC2N        | 14         | g.92264242T>A                      | p.Arg248X         | nonsense      |
| CHC155T  | ENSG00000148737 | TCF7L2      | 10         | g.114912162_114912163insT          | p.Met411IlefsX12  | insertion     |
| CHC301T  | ENSG00000176148 | TCP1L11     | 11         | g.33087377C>T                      | p.Thr325Ile       | missense      |
| CHC306T  | ENSG00000111077 | TENC1       | 12         | g.53453654_53453661del             | p.His754CysfsX5   | deletion      |
| CHC205T  | ENSG00000070759 | TESK2       | 1          | g.45811097_45811106del             | p.Lys375ValfsX3   | deletion      |
| CHC302T  | ENSG00000138336 | TEF1        | 10         | g.70333249A>G                      | p.His385Arg       | missense      |
| CHC1061T | ENSG00000091513 | TF          | 3          | g.133476673G>T                     | p.Asp311Tyr       | missense      |
| CHC1035T | ENSG00000042832 | TG          | 8          | g.133900392G>T                     | p.Gln780His       | missense      |
| CHC1061T | ENSG00000198959 | TGM2        | 20         | g.36775212C>A                      | p.Gly256Cys       | missense      |
| CHC434T  | ENSG00000115970 | THADA       | 2          | g.43779021G>A                      | p.Leu952Phe       | missense      |
| CHC433T  | ENSG00000172673 | THEMIS      | 6          | g.128134048C>A                     | p.Asp580Tyr       | missense      |
| CHC1055T | ENSG00000151923 | TIAL1       | 10         | g.121337183A>G                     | p.Tyr225His       | missense      |
| CHC433T  | ENSG00000104980 | TIMM44      | 19         | g.7999948A>G                       | splicing          | intron        |
| CHC434T  | ENSG00000104067 | TJP1        | 15         | g.29997948G>A                      | p.Pro1618Ser      | missense      |
| CHC301T  | ENSG00000146872 | TLK2        | 17         | g.60679446A>C                      | p.Lys588Asn       | missense      |
| CHC205T  | ENSG00000103534 | TMC5        | 16         | g.19501748C>T                      | p.Arg869X         | nonsense      |
| CHC197T  | ENSG00000118600 | TMEM5       | 12         | g.64196101G>T                      | p.Gly220Val       | missense      |
| CHC197T  | ENSG00000126106 | TMEM53      | 1          | g.45120629G>A                      | p.Pro146Ser       | missense      |
| CHC1065T | ENSG00000164953 | TMEM67      | 8          | g.94792905G>T                      | p.Ala267Ser       | missense      |
| CHC1041T | ENSG00000116857 | TMEM9       | 1          | g.201104822G>T                     | p.Thr174Lys       | missense      |
| CHC433T  | ENSG00000198092 | TMPRSS11F   | 4          | g.68934471A>T                      | p.Val207Asp       | missense      |
| CHC434T  | ENSG00000041982 | TNC         | 9          | g.117836008G>A                     | p.Gln1030X        | nonsense      |
| CHC1061T | ENSG00000120889 | TNFRSF10B   | 8          | g.22880326C>A                      | p.Gly394Val       | missense      |
| CHC121T  | ENSG00000240505 | TNFRSF13B   | 17         | g.16843685G>A                      | p.Gln196X         | nonsense      |
| CHC433T  | ENSG00000127863 | TNFRSF19    | 13         | g.24234562A>C                      | p.Arg223Ser       | missense      |
| CHC121T  | ENSG00000118194 | TNNT2       | 1          | g.201328756C>G                     | p.Gln279His       | missense      |
| CHC1053T | ENSG00000079308 | TNS1        | 2          | g.218677154G>C                     | p.Leu1553Val      | missense      |
| CHC197T  | ENSG00000136205 | TNS3        | 7          | g.47342994A>T                      | p.Leu1004Gln      | missense      |
| CHC301T  | ENSG00000168477 | TNXB        | 6          | g.32029976C>A                      | p.Gly2376Cys      | missense      |
| CHC197T  | ENSG00000141232 | TOB1        | 17         | g.48941255_48941316del             | p.Arg22AlafsX5    | deletion      |
| CHC1035T | ENSG00000115705 | TPO         | 2          | g.1440130G>T                       | p.Arg152Ser       | missense      |
| CHC253T  | ENSG00000116176 | TPSG1       | 16         | g.1272273G>A                       | p.Arg194Trp       | missense      |
| CHC121T  | ENSG00000170638 | TRABD       | 22         | g.50635960C>G                      | p.Ser205Cys       | missense      |
| CHC197T  | ENSG00000131323 | TRAF3       | 14         | g.103371846_103371858del           | p.Arg479MetfsX12  | deletion      |
| CHC433T  | ENSG00000183763 | TRAIIP      | 3          | g.49879373C>T                      | splicing          | intron        |
| CHC301T  | ENSG00000167632 | TRAPP9      | 8          | g.141460993C>A                     | p.Glu258Asp       | missense      |
| CHC121T  | ENSG00000186439 | TRDN        | 6          | g.123714817C>A                     | p.Gly353X         | nonsense      |
| CHC429T  | ENSG00000204613 | TRIM10      | 6          | g.30126187C>A                      | p.Glu249X         | nonsense      |
| CHC429T  | ENSG00000168930 | TRIM49      | 11         | g.89536959C>G                      | p.Glu138Asp       | missense      |
| CHC433T  | ENSG00000125733 | TRIP10      | 19         | g.6744824T>C                       | p.Leu268Pro       | missense      |
| CHC429T  | ENSG00000083067 | TRPM3       | 9          | g.73233817C>T                      | p.Gly763Asp       | missense      |
| CHC1055T | ENSG00000070985 | TRPM5       | 11         | g.2441602C>T                       | p.Gly167Ser       | missense      |
| CHC434T  | ENSG00000144481 | TRPM8       | 2          | g.234847747G>A                     | p.Ala152Thr       | missense      |
| CHC1065T | ENSG00000126467 | TSK5        | 19         | g.50251699C>A                      | p.Ala143Ser       | missense      |
| CHC433T  | ENSG00000113312 | TTC1        | 5          | g.159476614A>G                     | p.Tyr212Cys       | missense      |
| CHC1055T | ENSG00000171853 | TTC15       | 2          | g.3428301G>A                       | p.Trp428X         | nonsense      |
| CHC320T  | ENSG00000198677 | TTC37       | 5          | g.94852850C>G                      | p.Arg764Thr       | missense      |
| CHC307T  | ENSG00000101407 | TTI1        | 20         | g.36642037T>G                      | p.Lys61Thr        | missense      |
| CHC433T  | ENSG00000155657 | TTN         | 2          | g.179623870T>A                     | p.Lys3382X        | nonsense      |
| CHC433T  | ENSG00000251297 | TUBB4Q      | 4          | g.190903858C>A                     | p.Glu375X         | nonsense      |
| CHC1035T | ENSG00000086288 | TXNDC3      | 7          | g.37904023del                      | p.Ile177LeufsX8   | deletion      |
| CHC1053T | ENSG00000156521 | TYSD1       | 10         | g.71899684A>C                      | p.Leu566Arg       | missense      |
| CHC1055T | ENSG00000033178 | UBA6        | 4          | g.68562417_68562443del             | indels            | deletion      |
| CHC301T  | ENSG00000130560 | UBAC1       | 9          | g.138845556_138845557insC          | p.Lys102GlnfsX4   | insertion     |
| CHC155T  | ENSG00000177889 | UBE2N       | 12         | g.93804509C>A                      | splicing          | intron        |
| CHC121T  | ENSG00000110344 | UBE4A       | 11         | g.118267042C>A                     | p.Pro1037Thr      | missense      |
| CHC433T  | ENSG00000127481 | UBR4        | 1          | g.19468160T>G                      | p.His2764Pro      | missense      |
| CHC1052T | ENSG00000198722 | UNC13B      | 9          | g.35378318A>T                      | p.Lys615X         | nonsense      |
| CHC1041T | ENSG00000135093 | USP30       | 12         | g.109511319_109511344del           | p.Cys234X         | deletion      |
| CHC1052T | ENSG00000170832 | USP32       | 17         | g.58282831T>C                      | p.Ile1076Val      | missense      |
| CHC121T  | ENSG00000170242 | USP47       | 11         | g.11971500A>T                      | p.Glu1070Val      | missense      |
| CHC1053T | ENSG00000170236 | USP50       | 15         | g.50793033del                      | p.Asn313ThrfsX69  | deletion      |
| CHC429T  | ENSG00000156697 | UTP14A      | X          | g.129054452A>C                     | p.Lys258Gln       | missense      |
| CHC433T  | ENSG00000026025 | VIM         | 10         | g.17277300C>G                      | p.Arg381Gly       | missense      |
| CHC1055T | ENSG00000223501 | VPS52       | 6          | g.33219393G>A                      | p.Arg643Cys       | missense      |
| CHC1061T | ENSG00000120688 | WBP4        | 13         | g.41639199del                      | p.Arg43GlyfsX31   | deletion      |
| CHC1052T | ENSG00000138442 | WDR12       | 2          | g.203757417C>G                     | p.Asp222His       | missense      |
| CHC433T  | ENSG00000065183 | WDR3        | 1          | g.118492616A>T                     | splicing          | intron        |
| CHC1065T | ENSG00000158023 | WDR66       | 12         | g.122395042T>C                     | p.Val533Ala       | missense      |
| CHC253T  | ENSG00000133316 | WDR74       | 11         | g.62606991C>G                      | p.Gly18Arg        | missense      |
| CHC155T  | ENSG00000140527 | WDR93       | 15         | g.90260173T>C                      | p.Leu263Ser       | missense      |
| CHC121T  | ENSG00000075035 | WSCD2       | 12         | g.108618534del                     | p.Gly235AlafsX15  | deletion      |
| CHC429T  | ENSG00000206579 | XKR4        | 8          | g.56436337G>A                      | p.Gly502Ser       | missense      |
| CHC197T  | ENSG00000221947 | XKR9        | 8          | g.71593349T>C                      | p.Val19Ala        | missense      |
| CHC253T  | ENSG00000196419 | XRCC6       | 22         | g.42052974_42052993del             | p.Ala454GlnfsX7   | deletion      |
| CHC1061T | ENSG00000100811 | YY1         | 14         | g.100743917A>G                     | p.Lys409Glu       | missense      |
| CHC433T  | ENSG00000163374 | YY1AP1      | 1          | g.155646500G>A                     | p.His193Tyr       | missense      |
| CHC1052T | ENSG00000169064 | ZBBX        | 3          | g.166958663G>A                     | p.Ser774Phe       | missense      |
| CHC320T  | ENSG00000185670 | ZBTB3       | 11         | g.62519564A>T                      | p.X575LysfsX6     | missense      |
| CHC307T  | ENSG00000166860 | ZBTB39      | 12         | g.57397116_57397122del             | p.Met527SerfsX124 | deletion      |
| CHC433T  | ENSG00000204859 | ZBTB48      | 1          | g.6649028C>T                       | p.Pro608Leu       | missense      |
| CHC322T  | ENSG00000083223 | ZCCHC6      | 9          | g.88924865T>C                      | p.Tyr1149Cys      | missense      |
| CHC320T  | ENSG00000102383 | ZDHC15      | X          | g.74698796G>C                      | p.Ala63Asp        | missense      |
| CHC197T  | ENSG00000186908 | ZDHC17      | 12         | g.77220773G>T                      | p.Trp328Leu       | missense      |
| CHC1035T | ENSG00000091656 | ZFH4        | 8          | g.77620035A>T                      | p.Asn949Tyr       | missense      |
| CHC433T  | ENSG00000062370 | ZFP112      | 19         | g.44831839T>A                      | p.Glu830Val       | missense      |
| CHC155T  | ENSG00000204644 | ZFP57       | 6          | g.29640818G>T                      | p.Thr357Asn       | missense      |

**Supplementary Table 3. List of all somatic mutations identified in the exome sequencing of 24 HCC**

| HCC-ID   | Ensembl Gene ID | Gene symbol | Chromosome | Nucleotide (genomic position hg19) | Amino Acid        | Mutation Type |
|----------|-----------------|-------------|------------|------------------------------------|-------------------|---------------|
| CHC155T  | ENSG00000169946 | ZFPM2       | 8          | g.106814470G>T                     | p.Arg720Ser       | missense      |
| CHC051T  | ENSG00000005889 | ZFX         | X          | g.24229375T>C                      | p.Ile767Thr       | missense      |
| CHC205T  | ENSG00000165156 | ZHX1        | 8          | g.124265860A>T                     | p.Ile776Lys       | missense      |
| CHC302T  | ENSG00000043355 | ZIC2        | 13         | g.100635295T>G                     | p.Val326Gly       | missense      |
| CHC1052T | ENSG00000152926 | ZNF117      | 7          | g.64439872T>A                      | p.Asn26Ile        | missense      |
| CHC1055T | ENSG00000176293 | ZNF135      | 19         | g.58573055C>G                      | p.Phe59Leu        | missense      |
| CHC155T  | ENSG00000163848 | ZNF148      | 3          | g.124951325T>A                     | p.Ser749Cys       | missense      |
| CHC433T  | ENSG00000160321 | ZNF208      | 19         | g.22156815A>G                      | p.Tyr341His       | missense      |
| CHC301T  | ENSG00000167840 | ZNF232      | 17         | g.5013123C>A                       | p.Glu22X          | nonsense      |
| CHC302T  | ENSG00000213096 | ZNF254      | 19         | g.24288792del                      | p.Trp27CysfsX15   | deletion      |
| CHC306T  | ENSG00000090612 | ZNF268      | 12         | g.133768187A>G                     | p.Asn116Ser       | missense      |
| CHC205T  | ENSG00000182986 | ZNF320      | 19         | g.53383988G>T                      | p.Thr464Asn       | missense      |
| CHC1061T | ENSG00000189180 | ZNF33A      | 10         | g.38344510G>T                      | p.Gln486His       | missense      |
| CHC322T  | ENSG00000169981 | ZNF35       | 3          | g.44700400G>C                      | p.Cys182Ser       | missense      |
| CHC1035T | ENSG00000178338 | ZNF354B     | 5          | g.178310772G>C                     | p.Cys440Ser       | missense      |
| CHC1053T | ENSG00000198521 | ZNF43       | 19         | g.21992119 A>T                     | p.Asn240Lys       | missense      |
| CHC320T  | ENSG00000256807 | ZNF432      | 19         | g.52537268T>C                      | p.Tyr555Cys       | missense      |
| CHC301T  | ENSG00000140987 | ZNF434      | 16         | g.3433115C>A                       | p.Gly399X         | nonsense      |
| CHC306T  | ENSG00000196263 | ZNF471      | 19         | g.57029880T>A                      | p.Ser64Thr        | missense      |
| CHC306T  | ENSG00000142528 | ZNF473      | 19         | g.50550026C>T                      | p.His776Tyr       | missense      |
| CHC197T  | ENSG00000197037 | ZNF498      | 7          | g.99217399A>T                      | p.Gln57Leu        | missense      |
| CHC1052T | ENSG00000198633 | ZNF534      | 19         | g.52941267C>T                      | p.Pro198Leu       | missense      |
| CHC1053T | ENSG00000172006 | ZNF554      | 19         | g.2823070A>G                       | p.Glu29Gly        | missense      |
| CHC302T  | ENSG00000198028 | ZNF560      | 19         | g.9577515A>T                       | p.Leu703X         | nonsense      |
| CHC429T  | ENSG00000189144 | ZNF573      | 19         | g.38230055C>G                      | p.Glu446Gln       | missense      |
| CHC614T  | ENSG00000189190 | ZNF600      | 19         | g.53268984del                      | p.Phe675LeufsX7   | deletion      |
| CHC301T  | ENSG00000167554 | ZNF610      | 19         | g.52869830A>G                      | p.Tyr400Cys       | missense      |
| CHC614T  | ENSG00000160352 | ZNF714      | 19         | g.21281677 T>G                     | p.Trp35Gly        | missense      |
| CHC155T  | ENSG00000170396 | ZNF804A     | 2          | g.185801897_185801907del           | p.Ser593GluufsX29 | deletion      |
| CHC205T  | ENSG00000198783 | ZNF830      | 17         | g.33289670C>G                      | p.Ser362Cys       | missense      |
| CHC433T  | ENSG00000176371 | ZSCAN2      | 15         | g.85165076A>T                      | p.Arg550Ser       | missense      |
| CHC302T  | ENSG00000180532 | ZSCAN4      | 19         | g.58189906A>G                      | p.Tyr312Cys       | missense      |
| CHC197T  | ENSG00000131848 | ZSCAN5A     | 19         | g.56733297C>A                      | p.Gly380Cys       | missense      |
| CHC155T  | ENSG00000162415 | ZSWIM5      | 1          | g.45553765T>A                      | p.His247Leu       | missense      |

**Supplementary Table 4. Correlation between clinical, pathological and genomic features.**

| <b>Correlation with clinical and pathological features</b> |  |
|--|--|
| HBV infection  | IRF2 mutation (P=0.003); no CTNNB1 mutation (P=0.001); High FAA (P=0.01*); Homozygous deletion (P=0.03)  |
| Alcohol intake   | ARID1A mutation (P=0.002)  |
| No etiology  | HNF1A mutation (P=0.008)   |
| Age < 60 years   | IRF2 mutation (P =0.002), no CTNNB1 mutation (P=0.05)  |
| Poor tumor differentiation (Edmondson III-IV)              | High FAA (P=0.04*); High ploidy (P=0.03*) ; Homozygous deletion (P=0.04)   |
| Well tumor differentiation (Edmondson I-II)                | High level G>T transversion (P=0.01*); HNF1A mutation (P=0.03)   |
| Non-cirrhotic liver  | High FAA (P=0.04*); high level G>T transversion (P=0.01*); RPS6KA3 mutation (P=0.05)   |
| Large tumors (>50 mm)                                      | High FAA (P=0.004*)  |
| High serum Alpha Foeto Protein (≥24 ng/ml)                 | High ploidy (P=0.01*); High FAA (P=0.03*); no CTNNB1 mutation (P=0.03); Homozygous deletion (P=0.008)  |
| Microscopic vascular invasion                              | Homozygous deletion (P=0.009)  |
|  |  |
| <b>Correlation between gene alterations</b>                |  |
| High FAA   | High ploidy (P=1E-07*); G1-G3 transcriptomic (P=6E-05*); TP53 mutation (P=0.003*); AXIN1 mutation (P=0.02*); IRF2 mutation (P=0.01*); Homozygous deletion (P=0.00001*) |
| CTNNB1 mutation  | G5-G6 transcriptomic (P<1E-9); NFE2L2 mutation (P=0.01); ARID1A mutation (P=0.05); no TP53 mutation (P=0.0001); no AXIN1 mutation (P=0.006)                            |
| TP53 mutation  | G3 transcriptomic (P=0.0001)   |
| RPS6KA3 mutation   | AXIN1 mutation (P=0.02)  |
| IRF2 mutation  | G2 transcriptomic (P=0.0002)   |
| IL6ST mutation   | G6 transcriptomic (P=0.02)   |
| HNF1A mutation   | G4 transcriptomic (P=0.04)   |

\*Kruskal Wallis test

**Supplementary Table 5: Focal Amplifications**

| #HCC-ID  | Copy number | Start position (in bp) | End position (in bp) | Cytoband | Genes  |
|----------|-------------|------------------------|----------------------|----------|--|
| CHC014T  | 6           | 73776674               | 73959878             | 1p31.1   |  |
| CHC014T  | 6           | 80208060               | 80416986             | 1p31.1   |  |
| CHC304T  | 7           | 115862255              | 115922523            | 1p13.2   |  |
| CHC309T  | 5           | 154750817              | 155186728            | 1q21.3   | ADAM15, DPM3, RAG1AP1, TRIM46, THBS3, EFNA4, CKS1B, EFNA1, PMVK, SHC1, MTX1, MUC1, DCST2, PBXIP1, LENE, KRTPCAP2, MIR92B, ZBTB7B, FLAD1, DCST1, EFNA3, PYGO2                   |
| CHC794T  | 6           | 156300083              | 156560501            | 1q22     | TTC24, C1orf182, C1orf61, IQGAP3, RHBG, MEF2D, MIR9-1  |
| CHC314T  | 5           | 204440602              | 204632480            | 1q32.1   | MDM4   |
| CHC961T  | 6           | 217085750              | 217145697            | 1q41     |  |
| CHC205T  | 6           | 239587513              | 239659952            | 1q43     |  |
| CHC031T  | 5           | 54708409               | 55151439             | 2p16.2   | RPL23AP32, SPTBN1  |
| CHC028T  | 6           | 126395813              | 127894614            | 2q14.3   | BIN1, GYPC   |
| CHC028T  | 6           | 165047346              | 167056427            | 2q24.3   | SCN1A, SCN3A, GRB14, GALNT3, SCN2A, COBLL1, SLC38A11, TTC21B, SNORA70F, CSRNP3   |
| CHC1065T | 5           | 192335295              | 195160637            | 2q32.3   | PCGEM1, SDPR, TMEFF2, OBFCA  |
| CHC1052T | 6           | 189910073              | 190237100            | 3q28     | TMEM207, CLDN16, CLDN1   |
| CHC1055T | 6           | 11425013               | 12099334             | 4p15.33  |  |
| CHC1055T | 5           | 13265682               | 13484419             | 4p15.33  | HSP90A2P2  |
| CHC1055T | 4           | 13940962               | 14099570             | 4p15.33  |  |
| CHC254T  | 8           | 55108295               | 55257610             | 4q12     |  |
| CHC339T  | 6           | 57368167               | 58136697             | 4q12     | REST, HOPX, IGFBP7, SPINK2, ARL9, C4orf14, POLR2B  |
| CHC018T  | 6           | 66431910               | 67459960             | 4q13.1   |  |
| CHC1154T | 6           | 2866347                | 3104266              | 5p15.33  |  |
| CHC1154T | 6           | 3126446                | 4907777              | 5p15.33  | IRX1   |
| CHC1065T | 4           | 29342141               | 29625795             | 5p13.3   |  |
| CHC1154T | 6           | 42483694               | 43899601             | 5p13.1   | PAIP1, SEPP1, HMGC1, CCL28, C5orf34, CCDC152, ZNF131, MGC42105, C5orf28, NNT, LOC153684, C5orf39   |
| CHC211T  | 5           | 65186000               | 66518705             | 5q12.3   | ERBB2IP, CD180, LOC100303749, MAST4, SFRS12  |
| CHC211T  | 6           | 73710425               | 76147233             | 5q13.3   | C5orf37, GFM2, HMGC1, HEXB, ANKRD31, ENC1, NSA2, COL4A3BP, GCNT4, FAM169A, SV2C, IQGAP2, F2RL2, POLK, F2R, F2RL1, NCRUPAR  |
| CHC304T  | 6           | 1374278                | 2064263              | 6p25.3   | FOXO1, FOXF2   |
| CHC097T  | 6           | 27835931               | 27847516             | 6p22.1   | HIST1H3I, HIST1H4L   |
| CHC794T  | 5           | 43187767               | 43900442             | 6p21.1   | XPO5, SLC22A7, POLH, VEGFA, ABCG10, YIPF3, RSPH9, CRIP3, DLK2, MAD2L1BP, C6orf108, ZNF318, C6orf154, POLR1C, GTPBP2, MRPS18A, TTBK1, TJAP1                                     |
| CHC033T  | 8           | 63961693               | 64269846             | 6q12     | LGSN   |
| CHC301T  | 5           | 64269848               | 65171418             | 6q12     | PHF3, PTP4A1   |
| CHC237T  | 5           | 66746844               | 67995170             | 6q12     |  |
| CHC242T  | 5           | 18864041               | 18935766             | 7p21.1   |  |
| CHC303T  | 8           | 70145074               | 70209636             | 7q11.22  |  |
| CHC303T  | 8           | 70387954               | 70521775             | 7q11.22  |  |
| CHC314T  | 5           | 79730562               | 80354228             | 7q21.11  |  |
| CHC121T  | 6           | 81176805               | 81273755             | 7q21.11  | GNAI1, CD36, GNAT3   |
| CHC154T  | 5           | 128169980              | 128866388            | 7q32.1   | FLJ45340, IRF5, LOC407835, LOC286016, ATP6V1F, CALU, TNPO3, SMO, OPN1SW, FLNC, CDC136, FAM71F1, KCP, FAM71F2, TSPAN33  |
| CHC465T  | 5           | 150977228              | 151926614            | 7q36.1   | RHEB, GALNT11, WDR86, PRKAG2, NUB1, CRYGN, GALNTL5   |
| CHC051T  | 5           | 32716484               | 35319480             | 8p12     | DUSP26, FUT10, MAK16, C8orf41, RNF122  |
| CHC097T  | 8           | 34674920               | 34856370             | 8p12     |  |
| CHC301T  | 5           | 34889072               | 35316787             | 8p12     |  |
| CHC097T  | 6           | 35247298               | 35429072             | 8p12     |  |
| CHC1052T | 8           | 39495326               | 39587863             | 8p11.22  |  |
| CHC097T  | 7           | 40243955               | 40565815             | 8p11.21  |  |
| CHC1052T | 8           | 42858300               | 43195671             | 8p11.21  | SGK196, FNTA, HGSNAT   |
| CHC051T  | 6           | 53363938               | 53579553             | 8q11.23  | FAM150A  |
| CHC302T  | 6           | 55437525               | 55476998             | 8q11.23  |  |
| CHC302T  | 5           | 56448941               | 57707933             | 8q12.1   | TGS1, RPS20, SDR16C6, MOS, LYN, PENK, SNORD54, CHCHD7, PLAG1, TMEM68, SDR16C5  |
| CHC302T  | 5           | 61984700               | 63436368             | 8q12.2   | ASPH, CLVS1  |
| CHC327T  | 7           | 80264466               | 82017371             | 8q21.13  | ZBTB10, TPD52, HEY1, STMN2, MRPS28, ZNF704   |
| CHC226T  | 6           | 83293873               | 84974523             | 8q21.13  |  |
| CHC399T  | 5           | 88696840               | 88740928             | 8q21.3   |  |
| CHC154T  | 5           | 13588522               | 13854996             | 10p13    | PRPF18   |
| CHC033T  | 8           | 114966497              | 115807015            | 10q25.3  | CASP7, C10orf81, NHLRC2, HAPB2, ADRB1, NRAP, DCLRE1A   |
| CHC033T  | 8           | 116040002              | 116519520            | 10q25.3  | AFAP1L2, ABLIM1  |
| CHC1065T | 5           | 117996151              | 118116033            | 10q25.3  |  |
| CHC129T  | 6           | 30246777               | 30829829             | 11p14.1  | FSHB, MPPED2, C11orf46   |
| CHC245T  | 8           | 67479309               | 69604526             | 11q13.2  | CHKA, SUV420H1, C11orf24, NDUF8, FGF4, MTL5, CPT1A, ORAOV1, ALDH3B1, IGHMBP2, UNC93B1, MRGPRF, CCND1, TCIRG1, MRPL21, SAFS3, GAL, FGF19, MYEOV, LRP5, TPCN2, LOC645332, MRGPRD |
| CHC008T  | 5           | 68346484               | 69585786             | 11q13.2  | MTL5, CPT1A, ORAOV1, IGHMBP2, MRGPRF, CCND1, MRPL21, GAL, FGF19, MYEOV, TPCN2, MRGPRD  |
| CHC793T  | 5           | 72093615               | 72276605             | 11q13.4  |  |
| CHC918T  | 6           | 117128272              | 117428277            | 11q23.3  | BACE1, CEP164  |
| CHC226T  | 7           | 21531438               | 22358857             | 12p12.1  | ABCC9, GOLT1B, CMAS, RECQL, KCNJB8, C12orf39, LDHB, PYROXD1, GYS2  |
| CHC031T  | 8           | 22945809               | 23599348             | 12p12.1  |  |
| CHC226T  | 5           | 23677561               | 23700774             | 12p12.1  |  |
| CHC303T  | 7           | 53714869               | 54324068             | 12q13.13 | SP7, SP1, CALCOCO1, AMHR2, NPF, ATP5G2, PCBP2, ATF7, TARBP2, PRR13, MAP3K12  |
| CHC303T  | 8           | 59575431               | 61320898             | 12q14.1  | SLC16A7  |
| CHC033T  | 8           | 82113311               | 82378975             | 13q31.1  |  |
| CHC033T  | 8           | 86071403               | 88963675             | 13q31.1  | SLITRK5, SLITRK6   |
| CHC961T  | 5           | 99527028               | 99670270             | 13q32.3  |  |
| CHC430T  | 5           | 73490925               | 74130927             | 16q22.3  |  |
| CHC430T  | 5           | 76372980               | 76624462             | 16q23.1  |  |
| CHC430T  | 5           | 79460568               | 79651292             | 16q23.2  | MAF  |
| CHC126T  | 6           | 27502030               | 28479798             | 17q11.2  | GIT1, CRYBA1, ANKRD13B, SSH2, MIR423, NUFIP2, ABHD15, TP53I13, TAOK1, EFCAB5, CORO6  |
| CHC437T  | 5           | 28551666               | 28812119             | 17q11.2  | CPD, TMIGD1, BLMH  |
| CHC1052T | 7           | 37201756               | 37288064             | 17q12    |  |

**Supplementary Table 5: Focal Amplifications**

| #HCC-ID  | Copy number | Start position (in bp) | End position (in bp) | Cytoband | Genes   |
|----------|-------------|------------------------|----------------------|----------|---|
| CHC126T  | 8           | 37770006               | 40107808             | 17q12    | KRT40,TMEM99,ZPBP2,PPP1R1B,ACLY,CDC6,CASC3,KRT17,KRT10,KRT34,KRT37,KRTA<br>P1-1,KRTAP2-2,KRT13,KRT24,KRT222,KRTAP1-<br>3,RARA,KRT15,KRT23,ERBB2,MED24,KRT12,KRT27,KRTAP3-3,KRTAP3-2,KRTAP3-<br>1,KRTAP1-5,KRTAP4-12,KRTAP4-5,KRTAP4-4,KRTAP4-3,KRTAP4-2,KRTAP4-1,KRTAP9-<br>2,KRTAP9-3,KRTAP9-9,KRTAP9-8,KRTAP9-4,KRTAP17-<br>1,KRT33B,KRT35,KRT32,EIF1,SCG5,NT5C3L,ORMDL3,KRT38,KRT9,KRTAP4-7,KRTAP4-<br>11,STARD3,HAP1,NR1D1,TOP2A,PGAP3,C17orf37,KRT19,FKBP10,SMARCE1,IKZF3,GJD<br>3,KLHL10,CSF3,KRT20,PSMD3,GSDMA,JUP,RAPGEF1,TCAP,GAST,THRA,WIPF2,TNS4,I<br>GFBP4,LOC730755,KLHL11,SNORD124,KRT33A,GSDMB,CCR7,KRT16,PNMT,GRB7,KRT<br>36,KRTAP4-8,KRT28,KRT25,KRTAP4-9,KRTAP2-1,KRT31,KRTAP2-<br>4,KRT14,KRT26,KRT39,MSL1 |
| CHC399T  | 5           | 2641036                | 2817051              | 18p11.32 | SMCHD1  |
| CHC399T  | 5           | 13177131               | 13487484             | 18p11.21 |   |
| CHC399T  | 5           | 13590753               | 13680931             | 18p11.21 | C18orf1   |
| CHC155T  | 5           | 64801046               | 65220233             | 18q22.1  | DSEL  |
| CHC1055T | 8           | 21215213               | 21277422             | 19p12    |   |
| CHC1055T | 4           | 22779199               | 23447298             | 19p12    | ZNF99,ZNF492  |
| CHC794T  | 8           | 49783102               | 50301544             | 19q13.33 | CD37,SNORD32A,SNORD35B,PTH2,RRAS,CPT1C,SLC17A7,SNORD35A,RCN3,PIH1D1,F<br>CGRT,SLC6A16,TEAD2,RPL13A,RPS11,NOSIP,TSKS,SNORD33,SCAF1,IRF3,ALDH16A1,P<br>RRG2,SNORD34,BCL2L12,CCDC155,FLT3LG,C19orf76,PRR12,PRMT1,DKKL1,RPL13AP5<br>,MIR150   |
| CHC129T  | 5           | 34555834               | 34612159             | 21q22.11 |   |
| CHC033T  | 8           | 18913603               | 19365285             | 22q11.21 | TSSK2,DGCR2,CLTCL1,DGCR14,GSC2,DGCR5,SLC25A1,DGCR9,DGCR11,DGCR10  |
| CHC033T  | 8           | 20854162               | 21814927             | 22q11.21 | RIMBP3C,PI4KA,MED15,LZTR1,SLC7A4,AIFM3,SNAP29,HIC2,RIMBP3B,MGC16703,P2<br>RX6,CRKL,THAP7,POM121L8P,POM121L4P,TMEM191A,LOC400891,FUJ39582,SERPIN<br>D1,P2RX6P  |



**Supplementary Table 6: Homozygous deletion**

| #HCC-ID  | Start position (in bp) | End position (in bp) | Cytoband | Genes  |
|----------|------------------------|----------------------|----------|--|
| CHC320T  | 1619542                | 1680218              | 1p36.33  | SLC35E2,CDK11B,CDK11A,LOC728661,MMP23A   |
| CHC441T  | 3577322                | 3616600              | 1p36.32  | TP73   |
| CHC317T  | 7971079                | 8652153              | 1p36.23  | ERRFI1,RERE,PARK7,TNFRSF9,SLC45A1  |
| CHC317T  | 21682435               | 21766452             | 1p36.12  |  |
| CHC402T  | 41013016               | 41054113             | 1p34.2   | ZNF684   |
| CHC218T  | 50918389               | 51462438             | 1p32.3   | CDKN2C,FAF1  |
| CHC046T  | 178665594              | 178684822            | 1q25.2   |  |
| CHC441T  | 204231501              | 204389313            | 1q32.1   | PPP1R15B,PLEKHA6,LOC127841   |
| CHC218T  | 65524098               | 65680309             | 2p14     | SPRED2   |
| CHC441T  | 65561393               | 65741614             | 2p14     | SPRED2   |
| CHC304T  | 141466385              | 142035285            | 2q22.1   | LRP1B  |
| CHC218T  | 186865607              | 187084688            | 2q32.1   |  |
| CHC208T  | 232779224              | 234694176            | 2q37.1   | ALPP,NPPC,UGT1A5,UGT1A9,UGT1A4,UGT1A8,UGT1A10,KCNJ13,GIGYF2,UGT1A6,SAG,EIF4E2,DGKD,UGT1A3,CHRNA,CHRND,UGT1A7,NEU2,TIGD1,ALPPL2,DNAJB3,NGEF,UGT1A1,INPP5D,C2orf82,USP40,DIS3L2,SCARNA5,SCARNA6,ATG16L1,ALPI,ECEL1,EFHD1,ECEL1P2   |
| CHC254T  | 233097787              | 233155565            | 2q37.1   | DIS3L2   |
| CHC218T  | 65750653               | 65776339             | 3p14.1   | MAGI1  |
| CHC226T  | 68512005               | 68678210             | 3p14.1   | FAM19A1  |
| CHC218T  | 71074195               | 71254192             | 3p13     | FOXP1  |
| CHC218T  | 114034099              | 114598528            | 3q13.31  | ZBTB20,MIR568  |
| CHC1199T | 162123180              | 162155075            | 3q26.1   |  |
| CHC317T  | 38980065               | 39016074             | 4p14     | TMEM156  |
| CHC218T  | 39496273               | 39614822             | 4p14     | C4orf34,UGDH   |
| CHC130T  | 44078423               | 44093498             | 4p13     |  |
| CHC317T  | 62416500               | 62498950             | 4q13.1   | LPHN3  |
| CHC123T  | 98701199               | 98809573             | 4q22.3   | C4orf37  |
| CHC304T  | 108060030              | 108083470            | 4q25     |  |
| CHC1199T | 122281108              | 122289862            | 4q27     | QRFPR  |
| CHC239T  | 171252195              | 171312560            | 4q33     |  |
| CHC239T  | 184882783              | 185220261            | 4q35.1   | STOX2,ENPP6  |
| CHC034T  | 184892635              | 185370065            | 4q35.1   | STOX2,ENPP6,IRF2   |
| CHC018T  | 185034184              | 185382060            | 4q35.1   | ENPP6,IRF2   |
| CHC012T  | 185148190              | 185400747            | 4q35.1   | IRF2   |
| CHC239T  | 185282465              | 185490725            | 4q35.1   | IRF2   |
| CHC1035T | 13201513               | 13367396             | 5p15.2   |  |
| CHC891T  | 91575925               | 91893094             | 5q14.3   |  |
| CHC121T  | 100955049              | 101168136            | 6q16.3   | ASCC3  |
| CHC961T  | 108641306              | 109574094            | 6q21     | FOXO3,LACE1,SESN1,C6orf182,ARMC2   |
| CHC794T  | 109863159              | 109917531            | 6q21     | AKD1   |
| CHC218T  | 128313089              | 128691352            | 6q22.33  | PTPRK  |
| CHC218T  | 148270823              | 148328366            | 6q24.3   |  |
| CHC609T  | 166767384              | 166787242            | 6q27     | BRP44L   |
| CHC301T  | 169924120              | 170142385            | 6q27     | WDR27,PHF10,TCTE3,C6orf120   |
| CHC469T  | 78256343               | 78492641             | 7q21.11  | MAGI2  |
| CHC218T  | 110677657              | 110733716            | 7q31.1   | IMMP2L,LRRN3   |
| CHC218T  | 111596968              | 111723487            | 7q31.1   | DOCK4  |
| CHC1055T | 3668652                | 3826044              | 8p23.2   | CSMD1  |
| CHC1055T | 3829248                | 3854986              | 8p23.2   | CSMD1  |
| CHC123T  | 13185927               | 13209660             | 8p22     | DLC1   |
| CHC441T  | 17655407               | 17748919             | 8p22     | FGL1,MTUS1   |
| CHC031T  | 17739539               | 17759862             | 8p22     | FGL1   |
| CHC441T  | 22210235               | 22340498             | 8p21.3   | SLC39A14,PIWIL2,PPP3CC   |
| CHC441T  | 25269103               | 25318252             | 8p21.2   | DOCK5,GNRH1,KCTD9,CDCA2  |
| CHC441T  | 38754531               | 38793681             | 8p11.22  | PLEKHA2  |
| CHC1053T | 51029372               | 51042155             | 8q11.21  | SNTG1  |
| CHC441T  | 3989790                | 4310557              | 9p24.2   | GLIS3  |
| CHC304T  | 9253588                | 9516347              | 9p23     | PTPRD  |
| CHC254T  | 12464877               | 12586943             | 9p23     |  |
| CHC031T  | 21557407               | 22207036             | 9p21.3   | CDKN2BAS,CDKN2B,C9orf53,CDKN2A,MTAP,LOC554202  |
| CHC205T  | 21712194               | 22081396             | 9p21.3   | CDKN2BAS,CDKN2B,C9orf53,CDKN2A,MTAP  |
| CHC130T  | 21920347               | 21997871             | 9p21.3   | CDKN2BAS,C9orf53,CDKN2A  |
| CHC433T  | 21953138               | 22044121             | 9p21.3   | CDKN2BAS,CDKN2B,C9orf53,CDKN2A   |
| CHC235T  | 21954954               | 22056498             | 9p21.3   | CDKN2BAS,CDKN2B,C9orf53,CDKN2A   |
| CHC1069T | 21966222               | 22028800             | 9p21.3   | CDKN2BAS,CDKN2B,C9orf53,CDKN2A   |
| CHC218T  | 21980152               | 22130064             | 9p21.3   | CDKN2BAS,CDKN2B,CDKN2A   |
| CHC793T  | 21990458               | 22088259             | 9p21.3   | CDKN2BAS,CDKN2B,CDKN2A   |
| CHC218T  | 22861228               | 22963772             | 9p21.3   |  |
| CHC218T  | 112418912              | 112924175            | 9q31.3   | PALM2,AKAP2,PALM2-AKAP2  |
| CHC158T  | 52558493               | 52616921             | 10q11.23 | A1CF   |
| CHC158T  | 65000494               | 65194128             | 10q21.3  | JMJD1C,MIR1296   |
| CHC313T  | 89406642               | 89807851             | 10q23.2  | PTEN,PAPSS2,ATAD1,KILLIN,CFLP1   |
| CHC1055T | 89495365               | 89725731             | 10q23.2  | PTEN,PAPSS2,ATAD1,KILLIN,CFLP1   |
| CHC218T  | 96547464               | 96682513             | 10q23.33 | CYP2C19  |
| CHC218T  | 104241684              | 104531049            | 10q24.32 | SFXN2,SUFU,TRIM8,ARL3,ACTR1A,C10orf26  |
| CHC218T  | 109453933              | 109800375            | 10q25.1  |  |
| CHC239T  | 122762147              | 122787761            | 10q26.12 |  |
| CHC218T  | 131361225              | 131457178            | 10q26.3  | MGMT   |
| CHC014T  | 25455060               | 26018892             | 11p14.3  |  |
| CHC441T  | 46469901               | 46692869             | 11p11.2  | KIAA0652,AMBRA1,HARBI1   |
| CHC317T  | 129065881              | 129115637            | 11q24.3  |  |
| CHC441T  | 12829915               | 12912803             | 12p13.1  | APOLD1,GPR19,CDKN1B  |
| CHC014T  | 28605427               | 28719699             | 12p11.22 | CCDC91   |
| CHC1199T | 45613496               | 47562926             | 12q12    | SFRS2IP,AMIGO2,SLC38A4,ANO6,ARID2,SLC38A1,SLC38A2,LOC400027  |
| CHC043T  | 50841058               | 53094938             | 12q13.12 | ACVRL1,SMAGP,KRT80,KRT71,KRT75,TMPRSS12,LETMD1,DIP2B,CSRNP2,BIN2,SLC4A8,ACVR1B,ANKRD33,GRASP,KRT81,KRT83,KRT85,KRT6C,KRT72,LARP4,KRT6B,KRT6A,NR4A1,KRT2,DAZAP2,METTL7A,KRT7,KRT5,KRT1,POU6F1,KRT86,CELA1,TFCP2,GALN T6,SLC11A2,HIGD1C,ATF1,C12orf44,SCN8A,KRT73,KRT74,KRT77,LOC283404,FIGLN2,KRT84,KRT82 |
| CHC1146T | 104845733              | 104849026            | 12q23.3  |  |
| CHC129T  | 33678506               | 33754515             | 13q13.1  | STARD13  |

**Supplementary Table 6: Homozygous deletion**

| #HCC-ID  | Start position (in bp) | End position (in bp) | Cytoband | Genes  |
|----------|------------------------|----------------------|----------|--|
| CHC158T  | 48901433               | 49002353             | 13q14.2  | LPAR6, RB1   |
| CHC137T  | 56493080               | 56605491             | 13q21.1  |  |
| CHC242T  | 70733845               | 70778216             | 13q21.33 |  |
| CHC226T  | 75331094               | 75494108             | 13q22.1  |  |
| CHC441T  | 58701881               | 58794000             | 14q23.1  | PSMA3, ARID4A, ACTR10, FLJ31306  |
| CHC226T  | 44897746               | 45094018             | 15q21.1  | TRIM69, B2M, SPG11, PATL2  |
| CHC012T  | 203255                 | 362637               | 16p13.3  | ITFG3, HBA2, AXIN1, HBQ1, ARHGDIG, RGS11, PDIA2, HBA1, HBZ, LUC7L, HBM             |
| CHC031T  | 265160                 | 341078               | 16p13.3  | ITFG3, AXIN1, ARHGDIG, RGS11, PDIA2, LUC7L   |
| CHC1199T | 347185                 | 357139               | 16p13.3  | AXIN1  |
| CHC014T  | 349222                 | 377793               | 16p13.3  | AXIN1  |
| CHC1154T | 19941969               | 19971789             | 16p12.3  |  |
| CHC018T  | 20509697               | 20552074             | 16p12.3  | ACSM2B   |
| CHC081T  | 65986968               | 66130755             | 16q21    |  |
| CHC250T  | 72823076               | 73087493             | 16q22.2  | ZFH3   |
| CHC158T  | 78201954               | 78504997             | 16q23.1  | WWOX   |
| CHC014T  | 78817230               | 79079658             | 16q23.1  | WWOX   |
| CHC130T  | 89094244               | 89122738             | 16q24.3  |  |
| CHC469T  | 2641106                | 2860023              | 17p13.3  | RAP1GAP2, MIR1253  |
| CHC218T  | 9097934                | 9304542              | 17p13.1  | NTN1, STX8   |
| CHC137T  | 10765210               | 10830183             | 17p12    |  |
| CHC226T  | 16068423               | 16219791             | 17p11.2  | NCOR1, PIGL, MIR1288   |
| CHC441T  | 25630652               | 25759163             | 18q12.1  | CDH2   |
| CHC402T  | 65290715               | 65318535             | 18q22.1  |  |
| CHC033T  | 66758990               | 66758996             | 18q22.1  |  |
| CHC1035T | 1                      | 406369               | 19p13.3  | THEG, PPA2C, C2CD4C, MIER2, FAM138A, FAM138F, FAM138C, FLJ45445, OR4F17, LOC375690 |
| CHC441T  | 1124032                | 1189481              | 19p13.3  | SBN02  |
| CHC614T  | 1132638                | 1238898              | 19p13.3  | C19orf26, SBN02, STK11   |
| CHC441T  | 2050824                | 2221791              | 19p13.3  | MKNK2, MOBKL2A, C19orf36, DOT1L, AP3D1   |
| CHC301T  | 2141210                | 2211049              | 19p13.3  | DOT1L, AP3D1   |
| CHC441T  | 11023435               | 11146498             | 19p13.2  | CARM1, SMARCA4, YIPF2, C19orf52  |
| CHC235T  | 43368962               | 43556842             | 19q13.2  | PSG11, PSG6, PSG7, PSG1  |
| CHC208T  | 54717302               | 54759570             | 19q13.42 | LILRB5, LILRB3, LILRA6   |
| CHC304T  | 15058883               | 15113007             | 20p12.1  | MACROD2  |
| CHC441T  | 23348888               | 23392839             | 21q21.1  |  |
| CHC013T  | 27336169               | 27548329             | 21q21.3  | APP  |
| CHC013T  | 32736170               | 33090757             | 21q22.11 | SFRS15, SOD1, TIAM1  |
| CHC909T  | 18624959               | 18631364             | 22q11.21 |  |
| CHC441T  | 24707113               | 24865186             | 22q11.23 | C22orf45, CYTSA, ADORA2A   |
| CHC218T  | 28411919               | 29083204             | 22q12.1  | TTC28  |
| CHC239T  | 6451753                | 8141016              | Xp22.31  | HDHD1A, STS, VCX3A, PNPLA4, VCX2, VCX, MIR651                                      |
| CHC303T  | 9456802                | 9543469              | Xp22.31  | TBL1X  |
| CHC014T  | 10458876               | 10621475             | Xp22.2   | MID1   |
| CHC137T  | 28770686               | 29133142             | Xp21.3   | IL1RAPL1   |
| CHC130T  | 36786480               | 37191430             | Xp21.1   | FAM47C   |
| CHC1192T | 53087477               | 53115704             | Xp11.22  | GPR173, TSPYL2   |
| CHC307T  | 82330914               | 82460172             | Xq21.1   |  |
| CHC218T  | 96165910               | 97165453             | Xq21.33  | DIAPH2   |
| CHC441T  | 96441494               | 96623615             | Xq21.33  | DIAPH2   |
| CHC218T  | 104311117              | 104454049            | Xq22.3   | IL1RAPL2   |
| CHC218T  | 111421285              | 111609731            | Xq23     | ZCCHC16  |
| CHC034T  | 134809429              | 134865393            | Xq26.3   | CT45A1   |

**Supplementary table 7. Complete list of gene mutations found in a series of validation of 125 HCC.**

| #HCC-ID  | Ensembl Gene ID | Gene symbol | Chromosome | Nucleotide (genomic hg19)  | cDNA               | Amino Acid           |
|----------|-----------------|-------------|------------|----------------------------|--------------------|----------------------|
| CHC013T  | ENSG00000168036 | CTNNB1      | 3          | g.41266124A>G              | c.121A>G           | p.Thr41Ala           |
| CHC028T  | ENSG00000168036 | CTNNB1      | 3          | g.41266098A>G              | c.95A>G            | p.Asp32Gly           |
| CHC037T  | ENSG00000168036 | CTNNB1      | 3          | g.41266137C>T              | c.134C>T           | p.Ser45Phe           |
| CHC046T  | ENSG00000168036 | CTNNB1      | 3          | g.41266103G>A              | c.100G>A           | p.Gly34Arg           |
| CHC051T  | ENSG00000168036 | CTNNB1      | 3          | g.41266100T>C              | c.97T>C            | p.Ser33Pro           |
| CHC059T  | ENSG00000168036 | CTNNB1      | 3          | g.41266124A>G              | c.121A>G           | p.Thr41Ala           |
| CHC097T  | ENSG00000168036 | CTNNB1      | 3          | g.41266136T>C              | c.133T>C           | p.Ser45Pro           |
| CHC115T  | ENSG00000168036 | CTNNB1      | 3          | g.41266136T>C              | c.133T>C           | p.Ser45Pro           |
| CHC121T  | ENSG00000168036 | CTNNB1      | 3          | g.41266136T>G              | c.133T>G           | p.Ser45Ala           |
| CHC130T  | ENSG00000168036 | CTNNB1      | 3          | g.41266101C>T              | c.98C>T            | p.Ser33Phe           |
| CHC164T  | ENSG00000168036 | CTNNB1      | 3          | g.41266110A>C              | c.107A>C           | p.His36Pro           |
| CHC168T  | ENSG00000168036 | CTNNB1      | 3          | g.41266101C>G              | c.98C>G            | p.Ser33Cys           |
| CHC197T  | ENSG00000168036 | CTNNB1      | 3          | g.41266137C>T              | c.134C>T           | p.Ser45Phe           |
| CHC211T  | ENSG00000168036 | CTNNB1      | 3          | g.41265926_41266306del     | c.14-91_241+62del  | deletion exon 3      |
| CHC230T  | ENSG00000168036 | CTNNB1      | 3          | g.41268766A>T              | c.1004A>T          | p.Lys335Ile          |
| CHC242T  | ENSG00000168036 | CTNNB1      | 3          | g.41266136T>C              | c.133T>C           | p.Ser45Pro           |
| CHC252T  | ENSG00000168036 | CTNNB1      | 3          | g.41268766A>T              | c.1004A>T          | p.Lys335Ile          |
| CHC301T  | ENSG00000168036 | CTNNB1      | 3          | g.41266107T>G              | c.104T>G           | p.Ile35Ser           |
| CHC302T  | ENSG00000168036 | CTNNB1      | 3          | g.41266137C>A              | c.134C>A           | p.Ser45Tyr           |
| CHC303T  | ENSG00000168036 | CTNNB1      | 3          | g.41266110A>C              | c.107A>C           | p.His36Pro           |
| CHC317T  | ENSG00000168036 | CTNNB1      | 3          | g.41266124A>G              | c.121A>G           | p.Thr41Ala           |
| CHC320T  | ENSG00000168036 | CTNNB1      | 3          | g.41266113C>G              | c.110C>G           | p.Ser37Cys           |
| CHC333T  | ENSG00000168036 | CTNNB1      | 3          | g.41266107T>G              | c.104T>G           | p.Ile35Ser           |
| CHC335T  | ENSG00000168036 | CTNNB1      | 3          | g.41266100T>C              | c.97T>C            | p.Ser33Pro           |
| CHC361TB | ENSG00000168036 | CTNNB1      | 3          | g.41265566_41266581del     | c.7_378del         | p.Thr3_Ala126del     |
| CHC399T  | ENSG00000168036 | CTNNB1      | 3          | g.41266101C>G              | c.98C>G            | p.Ser33Cys           |
| CHC429T  | ENSG00000168036 | CTNNB1      | 3          | g.41266101C>G              | c.98C>G            | p.Ser33Cys           |
| CHC430T  | ENSG00000168036 | CTNNB1      | 3          | g.41266136T>C              | c.133T>C           | p.Ser45Pro           |
| CHC433T  | ENSG00000168036 | CTNNB1      | 3          | g.41266098A>G              | c.95A>G            | p.Asp32Gly           |
| CHC437T  | ENSG00000168036 | CTNNB1      | 3          | g.41266124A>G              | c.121A>G           | p.Thr41Ala           |
| CHC469T  | ENSG00000168036 | CTNNB1      | 3          | g.41266103G>A              | c.100G>A           | p.Gly34Arg           |
| CHC609T  | ENSG00000168036 | CTNNB1      | 3          | g.41266113C>G              | c.110C>G           | p.Ser37Cys           |
| CHC614T  | ENSG00000168036 | CTNNB1      | 3          | g.41266125C>A              | c.122C>A           | p.Thr41Asn           |
| CHC798T  | ENSG00000168036 | CTNNB1      | 3          | g.41266101C>G              | c.98C>G            | p.Ser33Cys           |
| CHC918T  | ENSG00000168036 | CTNNB1      | 3          | g.41266137C>T              | c.134C>T           | p.Ser45Phe           |
| CHC983T  | ENSG00000168036 | CTNNB1      | 3          | g.41274899G>T              | c.1149G>T          | p.Trp383Cys          |
| CHC983T  | ENSG00000168036 | CTNNB1      | 3          | g.41242294A>G              | c.874A>G           | p.Lys292Glu          |
| CHC1040T | ENSG00000168036 | CTNNB1      | 3          | g.41266136T>C              | c.133T>C           | p.Ser45Pro           |
| CHC1041T | ENSG00000168036 | CTNNB1      | 3          | g.41266098A>T              | c.95A>T            | p.Asp32Val           |
| CHC1052T | ENSG00000168036 | CTNNB1      | 3          | g.41266129_41266134dup     | c.126_131dup       | p.Ala43_Pro44dup     |
| CHC1069T | ENSG00000168036 | CTNNB1      | 3          | g.41266098A>C              | c.95A>C            | p.Asp32Ala           |
| CHC1146T | ENSG00000168036 | CTNNB1      | 3          | g.41266100T>C              | c.97T>C            | p.Ser33Pro           |
| CHC008T  | ENSG00000141510 | TP53        | 17         | g.7578272G>C               | c.577C>G           | p.His193Asp          |
| CHC013T  | ENSG00000141510 | TP53        | 17         | g.7577556C>A               | c.725G>T           | p.Cys242Phe          |
| CHC014T  | ENSG00000141510 | TP53        | 17         | g.7577534C>A               | c.747G>T           | p.Arg249Ser          |
| CHC033T  | ENSG00000141510 | TP53        | 17         | g.7577556C>T               | c.725G>A           | p.Cys242Tyr          |
| CHC037T  | ENSG00000141510 | TP53        | 17         | g.7579420dup               | c.267dup           | p.Ser90LeufsX59      |
| CHC043T  | ENSG00000141510 | TP53        | 17         | g.7577534C>A               | c.747G>T           | p.Arg249Ser          |
| CHC046T  | ENSG00000141510 | TP53        | 17         | g.7577610T>C               | c.673-2A>G         | splicing             |
| CHC100T  | ENSG00000141510 | TP53        | 17         | g.7577081T>A               | c.857A>T           | p.Glu286Val          |
| CHC126T  | ENSG00000141510 | TP53        | 17         | g.7577085C>T               | c.853G>A           | p.Glu285Lys          |
| CHC129T  | ENSG00000141510 | TP53        | 17         | g.7578445A>C               | c.485T>G           | p.Ile162Ser          |
| CHC137T  | ENSG00000141510 | TP53        | 17         | g.7574012C>A               | c.1015G>T          | p.Glu339X            |
| CHC154T  | ENSG00000141510 | TP53        | 17         | g.7577602del               | c.679del           | p.Ser227LeufsX20     |
| CHC208T  | ENSG00000141510 | TP53        | 17         | g.7578190T>G               | c.659A>C           | p.Tyr220Ser          |
| CHC226T  | ENSG00000141510 | TP53        | 17         | g.7577534C>A               | c.747G>T           | p.Arg249Ser          |
| CHC229T  | ENSG00000141510 | TP53        | 17         | g.7578212G>A               | c.637C>T           | p.Arg213X            |
| CHC245T  | ENSG00000141510 | TP53        | 17         | g.7577550C>T               | c.731G>A           | p.Gly244Asp          |
| CHC254T  | ENSG00000141510 | TP53        | 17         | g.7577568C>A               | c.713G>T           | p.Cys238Phe          |
| CHC304T  | ENSG00000141510 | TP53        | 17         | g.7579398_7579439dup       | c.248_289dup       | p.Ala83_Ser96dup     |
| CHC314T  | ENSG00000141510 | TP53        | 17         | g.7578395G>A               | c.535C>T           | p.His179Tyr          |
| CHC327T  | ENSG00000141510 | TP53        | 17         | g.7577545T>C               | c.736A>G           | p.Met246Val          |
| CHC402T  | ENSG00000141510 | TP53        | 17         | g.7577535C>T               | c.746G>A           | p.Arg249Lys          |
| CHC793T  | ENSG00000141510 | TP53        | 17         | g.7573982C>A               | c.1045G>T          | p.Glu349X            |
| CHC882T  | ENSG00000141510 | TP53        | 17         | g.7577058C>A               | c.880G>T           | p.Glu294X            |
| CHC1035T | ENSG00000141510 | TP53        | 17         | g.7577534C>A               | c.747G>T           | p.Arg249Ser          |
| CHC1055T | ENSG00000141510 | TP53        | 17         | g.7579502_7579518dup       | c.169_185dup       | p.Ala63ThrfsX66      |
| CHC1061T | ENSG00000141510 | TP53        | 17         | g.7574017C>A               | c.1010G>T          | p.Arg337Leu          |
| CHC013T  | ENSG00000117713 | ARID1A      | 1          | g.27106961_27106969del     | c.6572_6580del     | p.Ser2191_Gly2193del |
| CHC014T  | ENSG00000117713 | ARID1A      | 1          | g.27089676C>T              | c.2632C>T          | p.Gln878X            |
| CHC100T  | ENSG00000117713 | ARID1A      | 1          | g.27107082_27107094del     | c.6693_6705del     | p.Met2231IlefsX32    |
| CHC121T  | ENSG00000117713 | ARID1A      | 1          | g.27023209_27023228del     | c.315_334del       | p.Asn106ProfsX4      |
| CHC155T  | ENSG00000117713 | ARID1A      | 1          | g.27056173dup              | c.1169dup          | p.Met390IlefsX10     |
| CHC205T  | ENSG00000117713 | ARID1A      | 1          | g.27099939_27099964delinsG | c.3818_3843delinsG | p.Met1273AArgfsX8    |
| CHC211T  | ENSG00000117713 | ARID1A      | 1          | g.27106934_27106953del     | c.6545_6564del     | p.Ala2182GlufsX36    |
| CHC230T  | ENSG00000117713 | ARID1A      | 1          | g.27023381G>A              | c.487G>A           | p.Ala163Thr          |
| CHC241T  | ENSG00000117713 | ARID1A      | 1          | g.27089501dup              | c.2457dup          | p.Asn820GlnfsX52     |
| CHC303T  | ENSG00000117713 | ARID1A      | 1          | g.27107163_27107181del     | c.6774_6792del     | p.Leu2259ArgfsX2     |
| CHC320T  | ENSG00000117713 | ARID1A      | 1          | g.27106640T>A              | c.6251T>A          | p.Val2084Asp         |
| CHC335T  | ENSG00000117713 | ARID1A      | 1          | g.27106649G>A              | c.6260G>A          | p.Gly2087Glu         |
| CHC339T  | ENSG00000117713 | ARID1A      | 1          | g.27106159delinsAA         | c.5770delinsAA     | p.Glu1924LysfsX5     |
| CHC433T  | ENSG00000117713 | ARID1A      | 1          | g.27023909del              | c.1015del          | p.Ala339LeufsX24     |
| CHC434T  | ENSG00000117713 | ARID1A      | 1          | g.27023909_27023923del     | c.1015_1029del     | p.Ala345_Ala349del   |

**Supplementary table 7. Complete list of gene mutations found in a series of validation of 125 HCC.**

| #HCC-ID  | Ensembl Gene ID | Gene symbol | Chromosome | Nucleotide (genomic hg19)              | cDNA                           | Amino Acid         |
|----------|-----------------|-------------|------------|--|--------------------------------|--------------------|
| CHC437T  | ENSG00000117713 | ARID1A      | 1          | g.27097692dup                          | c.3281dup                      | p.Gln1095AlafsX10  |
| CHC445T  | ENSG00000117713 | ARID1A      | 1          | g.27087897_27087911delinsT             | c.2184_2198delinsT             | p.Pro729GlyfsX83   |
| CHC983T  | ENSG00000117713 | ARID1A      | 1          | g.27099008C>T                          | c.3424C>T                      | p.Gln1142X         |
| CHC1040T | ENSG00000117713 | ARID1A      | 1          | g.27056214C>T                          | c.1210C>T                      | p.Gln404X          |
| CHC1053T | ENSG00000117713 | ARID1A      | 1          | g.27023213_27023222del                 | c.319_328del                   | p.Ala107GlyfsX4    |
| CHC018T  | ENSG00000103126 | AXIN1       | 16         | g.396458G>A                            | c.568C>T                       | p.Gln190X          |
| CHC226T  | ENSG00000103126 | AXIN1       | 16         | g.347764_347765del                     | c.1741_1742del                 | p.Ser581CysfsX9    |
| CHC237T  | ENSG00000103126 | AXIN1       | 16         | g.364557_364563dup                     | c.999_1005dup                  | p.Thr336ValfsX17   |
| CHC250T  | ENSG00000103126 | AXIN1       | 16         | g.347143G>T                            | c.1868C>A                      | p.Ser623X          |
| CHC306T  | ENSG00000103126 | AXIN1       | 16         | g.396233C>A                            | c.793G>T                       | p.Gly265X          |
| CHC314T  | ENSG00000103126 | AXIN1       | 16         | g.360068del                            | c.1021del                      | p.Asp341MetfsX73   |
| CHC327T  | ENSG00000103126 | AXIN1       | 16         | g.348113C>A                            | c.1393G>T                      | p.Glu465X          |
| CHC434T  | ENSG00000103126 | AXIN1       | 16         | g.347772G>T                            | c.1734C>A                      | p.Tyr578X          |
| CHC438T  | ENSG00000103126 | AXIN1       | 16         | g.396962G>A                            | c.64C>T                        | p.Arg22X           |
| CHC1052T | ENSG00000103126 | AXIN1       | 16         | g.397014T>G                            | c.12A>C                        | p.Gln4His          |
| CHC1053T | ENSG00000103126 | AXIN1       | 16         | g.347930C>T                            | c.1576G>A                      | p.Ala526Thr        |
| CHC1065T | ENSG00000103126 | AXIN1       | 16         | g.354326dup                            | c.1232dup                      | p.Arg412AlafsX12   |
| CHC1154T | ENSG00000103126 | AXIN1       | 16         | g.347929G>A                            | c.1577C>T                      | p.Ala526Val        |
| CHC1190T | ENSG00000103126 | AXIN1       | 16         | g.347909G>A                            | c.1597C>T                      | p.Arg533X          |
| CHC1201T | ENSG00000103126 | AXIN1       | 16         | g.347903C>T                            | c.1603G>A                      | p.Val535Ile        |
| CHC237T  | ENSG00000103126 | AXIN1       | 16         | g.348122C>T                            | c.1384G>A                      | p.Ala462Thr        |
| CHC018T  | ENSG00000177189 | RPS6KA3     | X          | g.20183143_20183145delinsC             | c.1636_1638delinsG             | p.Leu546ValfsX4    |
| CHC034T  | ENSG00000177189 | RPS6KA3     | X          | g.20185706C>T                          | c.1602+1G>A                    | splicing           |
| CHC037T  | ENSG00000177189 | RPS6KA3     | X          | g.20183078A>T                          | c.1703T>A                      | p.Leu568Gln        |
| CHC115T  | ENSG00000177189 | RPS6KA3     | X          | g.20206653C>G                          | c.594-1G>C                     | splicing           |
| CHC226T  | ENSG00000177189 | RPS6KA3     | X          | g.20206644A>G                          | c.602T>C                       | p.Leu201Pro        |
| CHC258T  | ENSG00000177189 | RPS6KA3     | X          | g.20194611C>A                          | c.940G>T                       | p.Gly314X          |
| CHC309T  | ENSG00000177189 | RPS6KA3     | X          | g.20181087_20181095delinsC             | c.1828_1836delinsG             | p.Thr610AspfsX11   |
| CHC429T  | ENSG00000177189 | RPS6KA3     | X          | g.20222175T>C                          | c.290A>G                       | p.Tyr97Cys         |
| CHC434T  | ENSG00000177189 | RPS6KA3     | X          | g.20206044A>T                          | c.676T>A                       | p.Tyr226Asn        |
| CHC1044T | ENSG00000177189 | RPS6KA3     | X          | g.20284689C>A                          | c.62G>T                        | p.Ser21Ile         |
| CHC1053T | ENSG00000177189 | RPS6KA3     | X          | g.20181154A>C                          | c.1769T>G                      | p.Leu590X          |
| CHC1154T | ENSG00000177189 | RPS6KA3     | X          | g.20185727C>A                          | c.1582G>T                      | p.Glu528X          |
| CHC1044T | ENSG00000177189 | RPS6KA3     | X          | g.20205954C>T                          | c.766G>A                       | p.Val256Met        |
| CHC1053T | ENSG00000177189 | RPS6KA3     | X          | g.20205972C>T                          | c.748G>A                       | p.Asp250Asn        |
| CHC154T  | ENSG00000135100 | HNF1        | 12         | g.121432125dup                         | c.872dup                       | p.Gly292ArgfsX25   |
| CHC154T  | ENSG00000135100 | HNF1        | 12         | g.121432002A>C                         | c.749A>C                       | p.Gln250Pro        |
| CHC155T  | ENSG00000135100 | HNF1        | 12         | g.121437143C>T                         | c.1574C>T                      | p.Thr525Ile        |
| CHC196T  | ENSG00000135100 | HNF1        | 12         | g.121426688A>T                         | c.379A>T                       | p.Asn127Tyr        |
| CHC196T  | ENSG00000135100 | HNF1        | 12         | g.121426804G>T                         | c.495G>T                       | p.Trp165Cys        |
| CHC465T  | ENSG00000135100 | HNF1        | 12         | g.121416642_121416653del               | c.71_82del                     | p.Ile27_Leu30del   |
| CHC465T  | ENSG00000135100 | HNF1        | 12         | g.121432000_121432017del               | c.747_764del                   | p.Gln250_Gly255del |
| CHC1061T | ENSG00000135100 | HNF1        | 12         | g.121426649_121426652de                | c.340_343del                   | p.Arg114TrpfsX40   |
| CHC1061T | ENSG00000135100 | HNF1        | 12         | g.121431485_121431515del               | c.689_713+6del                 | p.Glu230GlyfsX104  |
| CHC059T  | ENSG00000116044 | NFE2L2      | 2          | g.178098797_178098805del               | c.240_248del                   | p.Gly81_Phe83del   |
| CHC205T  | ENSG00000116044 | NFE2L2      | 2          | g.178098959T>C                         | c.86A>G                        | p.Asp29Gly         |
| CHC317T  | ENSG00000116044 | NFE2L2      | 2          | g.178098807T>G                         | c.238A>C                       | p.Thr80Pro         |
| CHC614T  | ENSG00000116044 | NFE2L2      | 2          | g.178098789T>A                         | c.256A>T                       | p.Ile86Phe         |
| CHC1040T | ENSG00000116044 | NFE2L2      | 2          | g.178098799T>G                         | c.246A>C                       | p.Glu82Asp         |
| CHC1041T | ENSG00000116044 | NFE2L2      | 2          | g.178098807T>G                         | c.238A>C                       | p.Thr80Pro         |
| CHC1069T | ENSG00000116044 | NFE2L2      | 2          | g.178098803C>A                         | c.242G>T                       | p.Gly81Val         |
| CHC1190T | ENSG00000116044 | NFE2L2      | 2          | g.178098960C>G                         | c.85G>C                        | p.Asp29His         |
| CHC614T  | ENSG00000116044 | NFE2L2      | 2          | g.178098800T>C                         | c.245A>G                       | p.Glu82Gly         |
| CHC123T  | ENSG00000189079 | ARID2       | 12         | g.46243449G>A                          | c.1802G>A                      | p.Arg601Gln        |
| CHC126T  | ENSG00000189079 | ARID2       | 12         | g.46240646_46240647dup                 | c.1506_1507dup                 | p.Ala503GlyfsX4    |
| CHC429T  | ENSG00000189079 | ARID2       | 12         | g.46244040G>T                          | c.2134G>T                      | p.Glu712X          |
| CHC614T  | ENSG00000189079 | ARID2       | 12         | g.46287229C>G                          | c.5174C>G                      | p.Ser1725X         |
| CHC725T  | ENSG00000189079 | ARID2       | 12         | g.46245893_46245894insGTTAGGTGAGATTGGA | c.3987_3988insGTTAGGTGAGATTGGA | p.Leu1330ValfsX3   |
| CHC1044T | ENSG00000189079 | ARID2       | 12         | g.46231153C>G                          | c.1073C>G                      | p.Thr358Ser        |
| CHC429T  | ENSG00000189079 | ARID2       | 12         | g.46243361A>G                          | c.1716-2A>G                    | splicing           |
| CHC205T  | ENSG00000150394 | CDH8        | 16         | g.60412498G>C                          | c.856C>G                       | p.Pro286Ala        |
| CHC429T  | ENSG00000150394 | CDH8        | 16         | g.60412513A>G                          | c.841T>C                       | p.Tyr281His        |
| CHC1199T | ENSG00000150394 | CDH8        | 16         | g.60318497A>C                          | c.1536+2T>G                    | splicing           |
| CHC339T  | ENSG00000168310 | IRF2        | 4          | g.185329422_185329435del               | c.412-6_419del                 | deletion           |
| CHC398T  | ENSG00000168310 | IRF2        | 4          | g.185339323T>G                         | c.409A>C                       | p.Lys137Gln        |
| CHC059T  | ENSG00000134352 | IL6ST       | 5          | g.55260053_55260055del                 | c.577_579del                   | p.Asn193del        |
| CHC469T  | ENSG00000134352 | IL6ST       | 5          | g.55260061_55260075del                 | c.557_571del                   | p.Tyr186_Tyr190del |
| CHC205T  | ENSG00000101292 | PROKR2      | 20         | g.5294732A>G                           | c.284T>C                       | p.Leu95Pro         |
| CHC429T  | ENSG00000101292 | PROKR2      | 20         | g.5283292del                           | c.549del                       | p.Ile184LeufsX56   |
| CHC037T  | ENSG00000133703 | KRAS        | 12         | g.25380275T>A                          | c.183A>T                       | p.Gln61His         |
| CHC339T  | ENSG00000133703 | KRAS        | 12         | g.25398285C>T                          | c.34G>A                        | p.Gly12Ser         |
| CHC137T  | ENSG00000134982 | APC         | 5          | g.112175957dup                         | c.4666dup                      | p.Thr1556AsnfsX3   |
| CHC205T  | ENSG00000134982 | APC         | 5          | g.112176007dup                         | c.4716dup                      | p.Glu1573X         |
| CHC235T  | ENSG00000121879 | PIK3CA      | 3          | g.178952085A>G                         | c.3140A>G                      | p.His1047Arg       |
| CHC438T  | ENSG00000121879 | PIK3CA      | 3          | g.178952085A>T                         | c.3140A>T                      | p.His1047Leu       |
| CHC469T  | ENSG00000147889 | CDKN2A      | 9          | g.21971096C>A                          | c.262G>T                       | p.Glu88X           |

**Supplementary Table 8: Pathway significantly enriched in the 1150 genes altered by either mutation or homozygous deletion**

| Pathway Names                         | p-values | FDR p-values |
|---------------------------------------|----------|--------------|
| Phosphatidylinositol signaling system | 0.001    | 0.01         |
| Wnt signaling pathway                 | 0.001    | 0.01         |
| Long-term potentiation                | 0.001    | 0.01         |
| Axon guidance                         | 0.003    | 0.02         |
| Focal adhesion                        | 0.004    | 0.02         |
| Cell cycle                            | 0.005    | 0.02         |
| Complement and coagulation cascades   | 0.005    | 0.03         |
| p53 signaling pathway                 | 0.02     | 0.06         |
| Gap junction                          | 0.02     | 0.06         |
| ECM-receptor interaction              | 0.02     | 0.07         |
| MAPK signaling pathway                | 0.02     | 0.07         |
| Apoptosis                             | 0.03     | 0.09         |
| Adherens junction                     | 0.03     | 0.1          |
| B cell receptor signaling pathway     | 0.03     | 0.1          |
| Insulin signaling pathway             | 0.03     | 0.1          |
| Ubiquitin mediated proteolysis        | 0.03     | 0.1          |