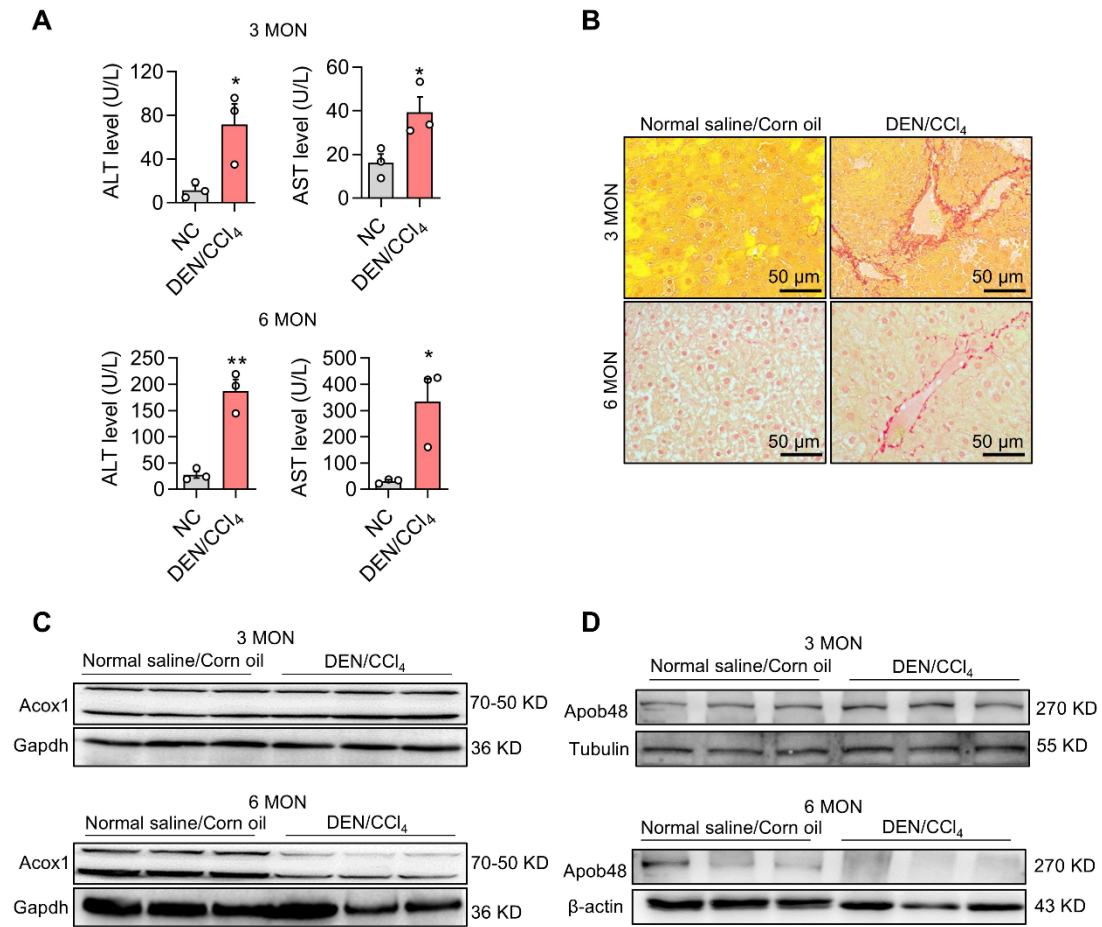
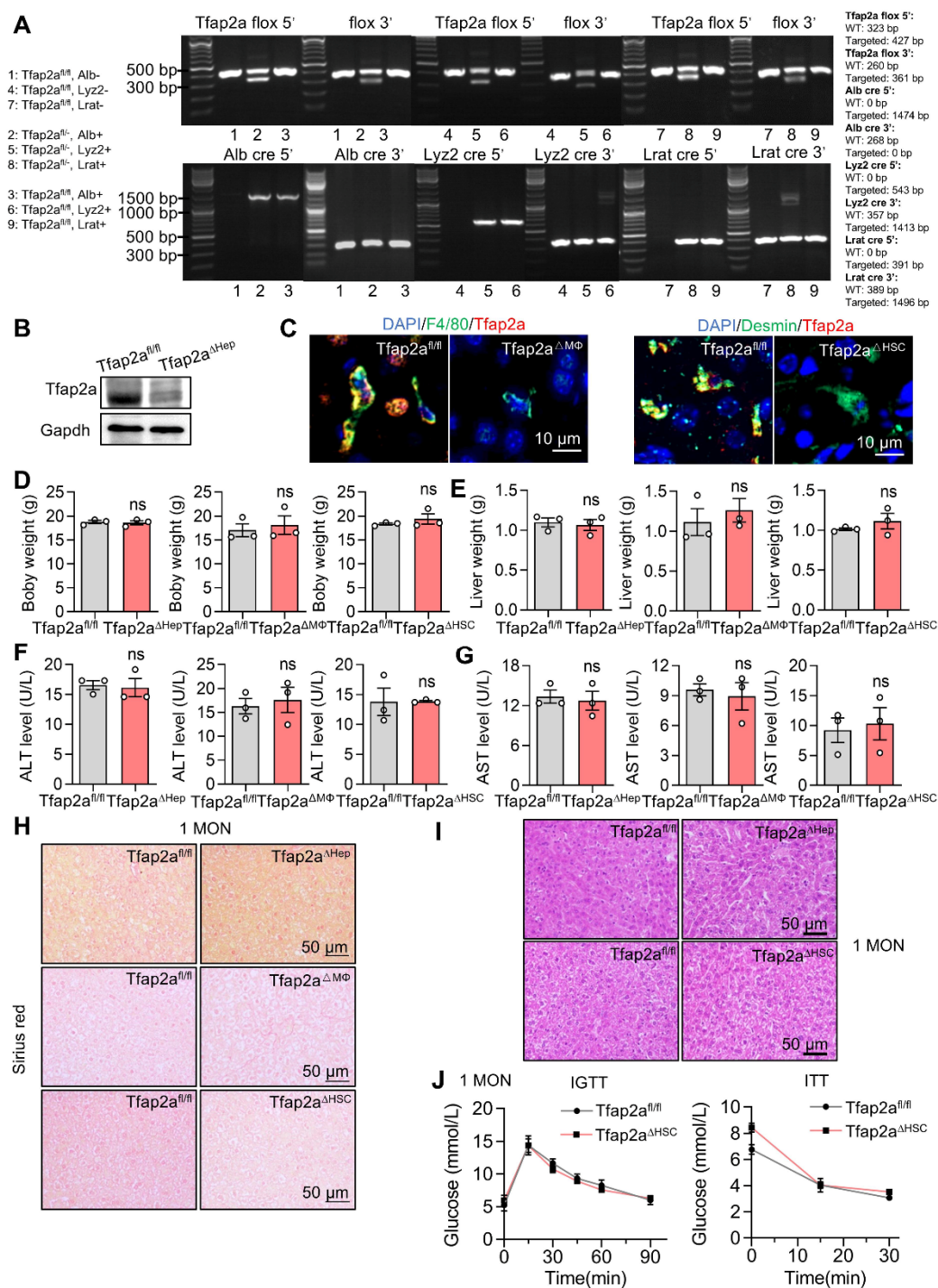


## SUPPLEMENTAL FIGURES AND FIGURE LEGENDS

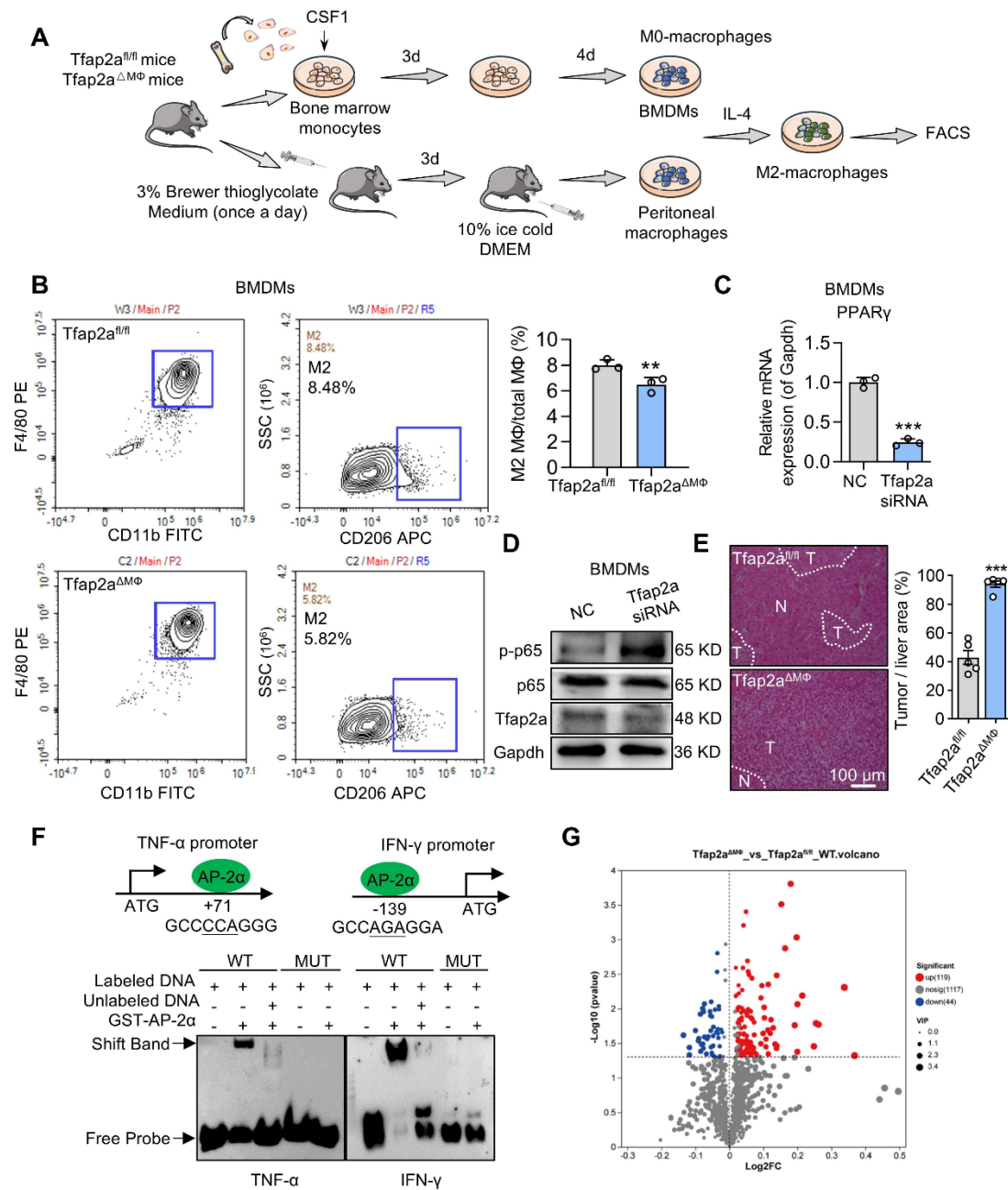


**Figure S1. The characterization of DEN/CCl<sub>4</sub>-induced HCC models.** A, ALT/AST detection for liver function in fibrosis and HCC models. B, Sirius red staining detecting the liver fibrosis at 3 months and 6 months. C, D, Western blot analysis of protein expression involved in fatty acid oxidation (Acox1) and transport (Apob48). \*, \*\* mean  $P < 0.05$  and  $P < 0.01$ .



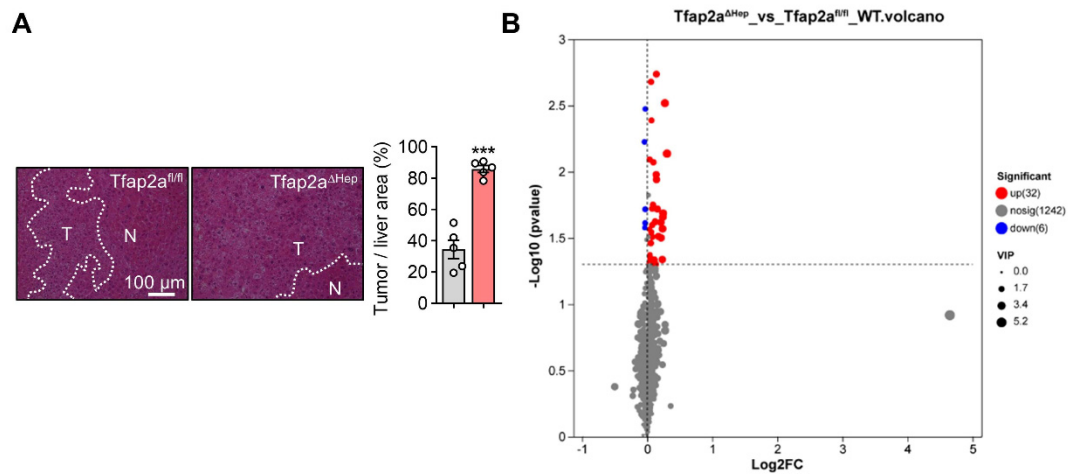
**Figure S2. Detection and phenotype analysis of Tfap2a knockout in livers.** A, Genotyping of three types of Tfap2a knockout mice. B, C, Western blots and ICC assays verified the knockout efficiency of Tfap2a in three conditional knockout mice. D-G, Effects of Tfap2a knockout in hepatocytes on body weight, liver weight and ALT/AST levels. H, Sirius red staining detecting liver fibrosis in Tfap2a<sup>ΔHep</sup>, Tfap2a<sup>ΔMΦ</sup>, Tfap2a<sup>ΔHSC</sup> mice and corresponding controls after 1 month. I, H&E staining showing

liver morphology and lipid droplet accumulation in the livers of  $Tfap2a^{\Delta Hep}$  mice and  $Tfap2a^{\Delta HSC}$  mice at 1 month. J, IGTT and ITT analysis of glucose change in  $Tfap2a^{\Delta HSC}$  mice and  $Tfap2a^{flox/flox}$  mice at 1 month. ns, no significance.

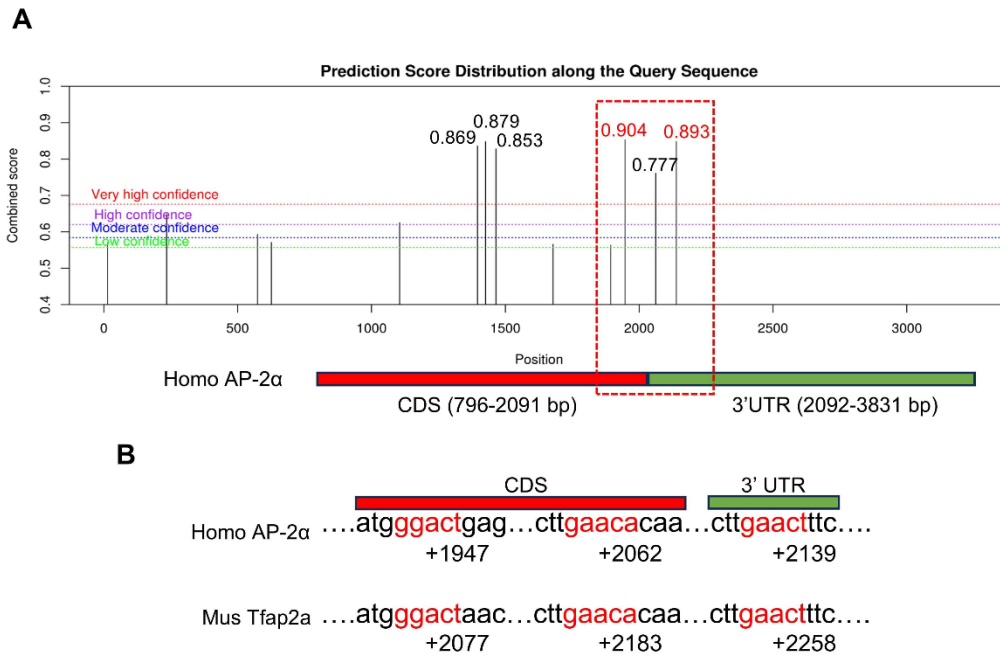


**Figure S3. The effects of  $Tfap2a$  knockout in macrophages on macrophage polarization.** A, The strategy depicting the isolation and treatment of macrophages from  $Tfap2a^{\Delta M\Phi}$  mice and  $Tfap2a^{fl/fl}$  mice. B, FACS analysis detecting the effects of  $Tfap2a$  knockout in BMDMs on the proportion of M2 macrophages. C, D, qRT-PCR

and Western blotting analysis showing the effects of Tfap2a knockout in macrophages on gene expression. E, Analysis of the tumor-to-liver area ratio using H&E staining with ImageJ software. N, Normal. T, Tumor. F, EMSA showing the binding of AP-2 $\alpha$  to TNF- $\alpha$  and IFN- $\gamma$  promoter *in vitro*. G, Non-targeted lipidomics analysis of differential lipids in Tfap2a $\Delta^{M\Phi}$  and Tfap2a $^{fl/fl}$  mouse liver. \*\*, \*\*\* mean  $P < 0.01$  and  $P < 0.001$ .



**Figure S4. The effects of Tfap2a knockout in hepatocytes on lipid metabolism and tumorigenesis.** A, Analysis of the tumor-to-liver area ratio using H&E staining of Tfap2a $\Delta^{Hep}$  and Tfap2a $^{fl/fl}$  mouse liver with ImageJ software. N, Normal. T, Tumor. B, Non-targeted lipidomics analysis of differential lipids in Tfap2a $\Delta^{Hep}$  and Tfap2a $^{fl/fl}$  mouse liver.



**Figure S5. The predicted m6A sites in the AP-2α 3' UTR.** A, The potential m6A sites in the AP-2α 3' UTR were predicted from the SRAMP website (<http://www.cuilab.cn/sramp>). B, The conserved m6A sites in the 3'UTR of human AP-2α and mouse Tfap2a.

## SUPPLEMENTAL TABLE

**Table S1. Primer pairs used in this study.**

| <b>Name</b>     | <b>Sequence(5'-to -3')</b> | <b>Purpose</b> |
|-----------------|----------------------------|----------------|
| Acc F           | CTCCCGATTCATAATTGGGTCTG    | qRT-PCR        |
| Acc R           | TCGACCTTGTTTTACTAGGTGC     |                |
| Fasn F          | CTCTGTTCACTATTGGACGC       | qRT-PCR        |
| Fasn R          | CGGAATTTCTGGGATTCAGCTTC    |                |
| Acly F          | CAGCCAAGGCAATTCAGAGC       | qRT-PCR        |
| Acly R          | CTCGACGTTTGATTAAGTGGTCT    |                |
| Scd1 F          | TCCATCATGAAGTGTGACGT       | qRT-PCR        |
| Scd1 R          | TACTCCTGCTTGCTGATCCAC      |                |
| Acox1 F         | GGATGGTAGTCCGGAGAACA       | qRT-PCR        |
| Acox1 R         | AGTCTGGATCGTTCAGAATCAAG    |                |
| Cpt1a F         | TGGCATCATCACTGGTGTGTT      | qRT-PCR        |
| Cpt1a R         | GTCTAGGGTCCGATTGATCTTTG    |                |
| Apbo48 F        | TTGGCAAACATGCATAGCATCC     | qRT-PCR        |
| Apbo48 R        | TCAAATTGGGACTCTCCTTTAGC    |                |
| Ppar $\gamma$ F | TATGGAGTGACATAGAGTGTGCT    | qRT-PCR        |
| Ppar $\gamma$ R | CCACTTCAATCCACCCAGAAAG     |                |
| Afp F           | CTTCCCTCATCCTCCTGCTAC      | qRT-PCR        |
| Afp R           | ACAAACTGGGTAAAGGTGATGG     |                |
| Gpc3 F          | CAGCCCGGACTCAAATGGG        | qRT-PCR        |
| Gpc3 R          | CAGCCGTGCTGTTAGTTGGTA      |                |
| $\alpha$ -Sma F | GTCCCAGACATCAGGGAGTAA      | qRT-PCR        |
| $\alpha$ -Sma R | TCGGATACTTCAGCGTCAGGA      |                |
| Col1a1 F        | GCTCCTCTTAGGGGCCACT        | qRT-PCR        |
| Col1a1 R        | CCACGTCTCACCATTGGGG        |                |
| Col3a1 F        | CTGTAACATGGAACTGGGGAAA     | qRT-PCR        |
| Col3a1 R        | CCATAGCTGAACTGAAAACCACC    |                |
| Col6a1 F        | CTGCTGCTACAAGCCTGCT        | qRT-PCR        |
| Col6a1 R        | CCCCATAAGGTTTCAGCCTCA      |                |
| Mmp-2 F         | CAAGTTCCCCGGCGATGTC        | qRT-PCR        |

|                  |                           |            |
|------------------|---------------------------|------------|
| Mmp-2 R          | TTCTGGTCAAGGTCACCTGTC     |            |
| Tgf- $\beta$ 1 F | TGATACGCCTGAGTGGCTGTCT    | qRT-PCR    |
| Tgf- $\beta$ 1 R | CACAAGAGCAGTGAGCGCTGAA    |            |
| Il-1 $\beta$ F   | TGGACCTTCCAGGATGAGGACA    | qRT-PCR    |
| Il-1 $\beta$ R   | GTTTCATCTCGGAGCCTGTAGTG   |            |
| Tnf- $\alpha$ F  | GGTGCCTATGTCTCAGCCTCTT    | qRT-PCR    |
| Tnf- $\alpha$ R  | GCCATAGAACTGATGAGAGGGAG   |            |
| Il-10 F          | CCCATTCCCTCGTCACGATCTC    | qRT-PCR    |
| Il-10 R          | TCAGACTGGTTTGGGATAGGTTT   |            |
| Ifn- $\gamma$ F  | CAGCAACAGCAAGGCGAAAAAGG   | qRT-PCR    |
| Ifn- $\gamma$ R  | TTTCCGCTTCCTGAGGCTGGAT    |            |
| Tfap2a F         | TTTTTCAGCTATGGACCGTCAC    | qRT-PCR    |
| Tfap2a R         | GAAGTCGGCATTAGGGGTGTG     |            |
| Gapdh F          | AGGTCGGTGTGAACGGATTTG     | qRT-PCR    |
| Gapdh R          | TGTAGACCATGTAGTTGAGGTCA   |            |
| AP-2 $\alpha$ F  | AGGTCAATCTCCCTACACGAG     | qRT-PCR    |
| AP-2 $\alpha$ R  | GGAGTAAGGATCTTGCGACTGG    |            |
| $\beta$ -ACTIN F | CACCATTGGCAATGAGCGGTTC    | RT-QPCR    |
| $\beta$ -ACTIN R | AGGTCTTTGCGGATGTCCACGT    |            |
| Tfap2a 5'arm F   | GGGTGCAAGCATAAAGGGATCAT   | Genotyping |
| Tfap2a 5'arm R   | GTTACCAAGCACAGGCATTGCC    |            |
| Tfap2a 3'arm F   | GCCAGAAATTCAAACCCAGCAA    | Genotyping |
| Tfap2a 3'arm R   | TGCGCCAATTAGAGCATCAAAG    |            |
| Alb 5'arm F      | ATGCCCACCAAAGTCATCAGTGTAG | Genotyping |
| Alb 5'arm R      | TGCTTGTGGAGCAATGTTGGTAG   |            |
| Alb 3'arm F      | GGGCAGTCTGGTACTTCCAAGCT   | Genotyping |
| Alb 3'arm R      | ATATCCCCTTGTTCCCTTTCTGC   |            |
| Lyz2 5'arm F     | AGTGCTGAAGTCCATAGATCGG    | Genotyping |
| Lyz2 5'arm R     | CTGATTCTCCTCATCACCAGG     |            |
| Lyz2 3'arm F     | AGTGCTGAAGTCCATAGATCGG    | Genotyping |
| Lyz2 3'arm R     | GTCACTCACTGCTCCCCTGT      |            |
| Lrat 5'arm F     | TGAGCCAAGCACTTTGGCTTC     | Genotyping |
| Lrat 5'arm R     | TCACATCCTCAGGTTTCAGCAGG   |            |

|                      |                                          |               |
|----------------------|------------------------------------------|---------------|
| Lrat 3'arm F         | TGAGCCAAGCACTTTGGCTTC                    | Genotyping    |
| Lrat 3'arm R         | AACAGGATGTCAGGCATTAGATGG                 |               |
| ACC-Promoter F       | GGTACCCGGGGTACCACGTCCAGTAAAG<br>GATGCACA | PCR           |
| ACC-Promoter R       | AAGCTTCCCAAGCTTTTGGGACATACCTA<br>GCCCTCA |               |
| FASN-Promoter<br>F   | GGTACCGCATTCCCATCCCGCACACGT              | PCR           |
| FASN-Promoter<br>R   | AAGCTTGAAGCGAAGGCGGCTGTT                 |               |
| SREBP-Promoter<br>F  | GGTACCATCAGGCCTGCTCACAAACAC              | PCR           |
| SREBP-Promoter<br>R  | AAGCTTTGGCATTTCGGTGGATGTCAG              |               |
| IL-10-Promoter F     | CGGGGTACCCTAGGAACACGCGAATGAG<br>A        | PCR           |
| IL-10-Promoter<br>R  | CCCAAGCTTGGAGAATGTCTAGTTCAGG<br>C        |               |
| FASN (+293)<br>WT F  | CGGAGGCGCCCGGGGCCCCGCGG                  | EMSA<br>Probe |
| FASN (+293)<br>WT R  | CCGCGGGGCCCCGGGCGCCTCCG                  |               |
| FASN (+293)<br>MUT F | CGGAGGCAATCGGGTACCCGCGG                  | EMSA<br>Probe |
| FASN (+293)<br>MUT R | CCGCGGGTACCCGATTGCCTCCG                  |               |
| FASN (-283)<br>WT F  | CGTCGGGGCCCGCGGGGCGGGAG                  | EMSA<br>Probe |
| FASN (-283)<br>WT R  | CTCCCGCCCCGCGGGCCCCGACG                  |               |
| FASN (-283)<br>MUT F | CGTCGGGAATCGCGTAGCGGGAG                  | EMSA<br>Probe |
| FASN (-283)          | CTCCCGCTACGCGATTCCCGACG                  |               |



---

|               |                           |       |
|---------------|---------------------------|-------|
| MUT R         |                           |       |
| ACC(-953) WT  | GGCCCACGCCTCAGGCACGAGAATC | EMSA  |
| F             |                           | Probe |
| ACC(-953) WT  | GATTCTCGTGCCTGAGGCGTGGGCC |       |
| R             |                           |       |
| ACC (-953)    | GGCCCACGATTCAGTAACGAGAATC | EMSA  |
| MUT F         |                           | Probe |
| ACC(-953)     | GATTCTCGTTACTGAATCGTGGGCC |       |
| MUT R         |                           |       |
| ACC (-401) WT | CGGGGCGGGCCCCCGGGGTCAGGC  | EMSA  |
| F             |                           | Probe |
| ACC (-401) WT | GCCTGACCCCGGGGGCCCGCCCCG  |       |
| R             |                           |       |
| ACC (-401)    | CGGGGCGGGATCCCGTAGTCAGGC  | EMSA  |
| MUT F         |                           | Probe |
| ACC (-401)    | GCCTGACTACGGGATCCCGCCCCG  |       |
| MUT R         |                           |       |
| ACC (-101) WT | GCGTGCGCGCCCCCGGGCGGCGC   | EMSA  |
| F             |                           | Probe |
| ACC (-101) WT | GCGCCGCCCCGGGGGCGCGCACGC  |       |
| R             |                           |       |
| ACC (-101)    | GCGTGCGCGATCCCGTACGGCGC   | EMSA  |
| MUT F         |                           | Probe |
| ACC (-101)    | GCGCCGTACGGGATCGCGCACGC   |       |
| MUT R         |                           |       |
| ACC (+140)    | GGCCCGTTGCCTGAGGCTTCCTGGC | EMSA  |
| WT F          |                           | Probe |
| ACC (+140)    | GCCAGGAAGCCTCAGGCAACGGGCC |       |
| WT R          |                           |       |
| ACC (+140)    | GGCCCGTTGATTGAGTATTCCTGGC | EMSA  |
| MUT F         |                           | Probe |
| ACC (+140)    | GCCAGGAATACTCAATCAACGGGCC |       |
| MUT R         |                           |       |

---

|                              |                            |               |
|------------------------------|----------------------------|---------------|
| SREBP1(-485)<br>WT F         | TGGGCCCAGGCCTGGGGCTTCCACT  | EMSA<br>Probe |
| SREBP1(-485)<br>WT R         | AGTGGAAGCCCCAGGCCTGGGCCCCA |               |
| SREBP1(-485)<br>MUT F        | TGGGCCCAGTACTGGATCTTCCACT  | EMSA<br>Probe |
| SREBP1(-485)<br>MUT R        | AGTGGAAGATCCAGTACTGGGCCCCA |               |
| SREBP1(+496)<br>WT F         | CGGTCATTCCCTCCGGCCCCGAGA   | EMSA<br>Probe |
| SREBP1(+496)<br>WT R         | TCTCGGGCCGGAGGGAATGACCG    |               |
| SREBP1(+496)<br>MUT F        | CGGTCATTTACTCCGATCCGAGA    | EMSA<br>Probe |
| SREBP1(+496)<br>MUT R        | TCTCGGATCGGAGTAAATGACCG    |               |
| IL-10(-1338)<br>WT F         | CAGCCCAGGCCAGGGCACCCA      | EMSA<br>Probe |
| IL-10(-1338)<br>WT R         | TGGGTGCCCTGGCCTGGGCTG      |               |
| IL-10(-1338)<br>MUT F        | CAGCCCAGATCAGTACACCCA      | EMSA<br>Probe |
| IL-10(-1338)<br>MUT R        | TGGGTGTACTGATCTGGGCTG      |               |
| TNF- $\alpha$ (+71)<br>WT F  | CAGGGGGGCCCCAGGGCTCCAG     | EMSA<br>Probe |
| TNF- $\alpha$ (+71)<br>WT R  | CTGGAGCCCTGGGGCCCCCCTG     |               |
| TNF- $\alpha$ (+71)<br>MUT F | CAGGGGGTAACCATTTCTCCAG     | EMSA<br>Probe |
| TNF- $\alpha$ (+71)<br>MUT R | CTGGAGAAATGGTTACCCCCTG     |               |
| IFN- $\gamma$ (-139) WT      | ACCAGCAGCCAGAGGAGGTGC      | EMSA          |

|                         |                                                                |       |
|-------------------------|----------------------------------------------------------------|-------|
| F                       |                                                                | Probe |
| IFN- $\gamma$ (-139) WT | GCACCTCCTCTGGCTGCTGGT                                          |       |
| R                       |                                                                |       |
| IFN- $\gamma$ (-139)    | ACCAGCAGATAGATAAGGTGC                                          | EMSA  |
| MUT F                   |                                                                | Probe |
| IFN- $\gamma$ (-139)    | GCACCTTATCTATCTGCTGGT                                          |       |
| MUT R                   |                                                                |       |
| FASN 131 F              | TGGCCCAAGCATTCCCATC                                            | ChIP  |
| FASN 131 R              | GACTTCCGCCTCCCGC                                               |       |
| FASN 165 F              | TCCTCATCCTCCGCTCTCG                                            | ChIP  |
| FASN 165 R              | TGTTGGTGGCTTTCCCCG                                             |       |
| ACC 182 F               | CCCCTTTCACAAGAGACCACA                                          | ChIP  |
| ACC 182 R               | GAACGTTGGCTCCACAACCTC                                          |       |
| SREBP1+496 F            | CCGTGACGTAATTGCGAGGT                                           | ChIP  |
| SREBP1+496 R            | TGGCATTTCGGTGGATGTCAG                                          |       |
| SREBP1-485 F            | GGCCTGGGACCCCTATAACT                                           | ChIP  |
| SREBP1-485 R            | TGTTTCTCCAGCACCAAGCA                                           |       |
| METTL3                  | CUGCAAGUAUGUUCACUAUGA<br>UCAUAGUGAACAUACUUGCAG                 | siRNA |
| ALKBH5                  | ACAAGUACUUCUUCGGCGA(dT)(dT)<br>UCGCCGAAGAAGUACUUGU(dT)(dT)     | siRNA |
| WTAP                    | AAGCUUUGGAGGGCAAGUACA(dT)(dT)<br>UGUACUUGCCCUCCAAAGCUU(dT)(dT) | siRNA |
| METTL14                 | AAGGAUGAGUUAUAGCUAAA<br>UUUAGCUAUUAACUCAUCCUU                  | siRNA |
| FTO                     | AUAGCCGCUGCUUGUGAGATT<br>UCUCACAAGCAGCGGCUAUUU                 | siRNA |
| YTHDF1                  | CCGCGUCUAGUUGUUGAUGAA<br>UUCAUGAACAAACUAGACGCGG                | siRNA |
| YTHDF2                  | AAGGACGUUCCCAAUAGCCAA<br>UUGGCUAUUGGGAACGUCCUU                 | siRNA |
| YTHDF3                  | UAAGUCAAGAAGACGUAUUA<br>UAAUACGUCUUCUUUGACUUA                  | siRNA |

|                      |                                                            |           |
|----------------------|------------------------------------------------------------|-----------|
| YTHDC1               | CGACCAGAAGAUUAUGAUUU<br>AAUAUCAUAAUCUUCUGGUCG              | siRNA     |
| YTHDC2               | GCCCACAGAUUGGCUUAUUUA<br>UAAAUAAAGCCAAUCUGUGGGC            | siRNA     |
| Mus Tfap-2a          | GCUCCACCUCGAAGUACAA(dT)(dT)<br>UUGUACUUCGAGGUGGAGC(dT)(dT) | siRNA     |
| Homo TFAP-2 $\alpha$ | GCAAGAUCCUUACUCCCACTT<br>GUGGGAGUAAGGAUCUUGCTT             | siRNA     |
| TFAP2a 3'UTR<br>F    | GGACTGAGTCACCACCTTCC                                       | MeRIP/RIP |
| TFAP2a 3'UTR<br>R    | CTGCGAATCGTGTTGCCAG                                        | MeRIP/RIP |

**Table S2. AP-2a expression and clinical characteristics**

| Clinical features            | Number | Overexpr<br>ession | AP-2a<br>Low<br>expression | No<br>expression | P Value           |
|------------------------------|--------|--------------------|----------------------------|------------------|-------------------|
| Total number                 | 60     | 16                 | 14                         | 30               |                   |
| Gender                       |        |                    |                            |                  | 0.9671            |
| Female                       | 20     | 5                  | 5                          | 10               |                   |
| Male                         | 40     | 11                 | 9                          | 20               |                   |
| Age                          |        |                    |                            |                  | 0.157             |
| (median,51.5 years)          |        |                    |                            |                  |                   |
| <                            | 30     | 6                  | 10                         | 14               |                   |
| ≥                            | 30     | 9                  | 5                          | 16               |                   |
| Histological<br>diagnosis    |        |                    |                            |                  | <b>&lt;0.0001</b> |
| Hepatitis                    | 13     | 4                  | 6                          | 3                |                   |
| Non-alcoholic fatty<br>liver | 10     | 5                  | 2                          | 3                |                   |
| Cirrhosis                    | 12     | 2                  | 2                          | 8                |                   |
| Hepatocellular<br>carcinoma  | 20     | 0                  | 5                          | 15               |                   |
| HCC histological<br>Grade    |        |                    |                            |                  | <b>&lt;0.0001</b> |
| Grade I                      | 3      | 0                  | 1                          | 2                |                   |
| Grade II                     | 10     | 0                  | 4                          | 6                |                   |
| Grade III                    | 7      | 0                  | 0                          | 7                |                   |
| Normal liver tissue          | 5      | 5                  | 0                          | 0                |                   |

**Table S3. WTAP expression and clinical characteristics**

| Clinical features            | Number | Overexpr<br>ession | WTAP<br>Low<br>expression | No<br>expression | P Value      |
|------------------------------|--------|--------------------|---------------------------|------------------|--------------|
| Total number                 | 60     | 25                 | 27                        | 8                |              |
| Gender                       |        |                    |                           |                  | 0.517        |
| Female                       | 20     | 7                  | 9                         | 4                |              |
| Male                         | 40     | 18                 | 18                        | 4                |              |
| Age                          |        |                    |                           |                  | 0.400        |
| (median,51.5<br>years)       |        |                    |                           |                  |              |
| <                            | 30     | 10                 | 15                        | 5                |              |
| ≥                            | 30     | 15                 | 12                        | 3                |              |
| Histological<br>diagnosis    |        |                    |                           |                  | 0.102        |
| Hepatitis                    | 13     | 5                  | 6                         | 2                |              |
| Non-alcoholic fatty<br>liver | 10     | 6                  | 4                         | 0                |              |
| Cirrhosis                    | 12     | 6                  | 5                         | 1                |              |
| Hepatocellular<br>carcinoma  | 20     | 8                  | 10                        | 2                |              |
| HCC histological<br>Grade    |        |                    |                           |                  | <b>0.008</b> |
| Grade I                      | 3      | 3                  | 0                         |                  |              |
| Grade II                     | 10     | 1                  | 7                         | 2                |              |
| Grade III                    | 7      | 4                  | 3                         |                  |              |
| Normal liver tissue          | 5      | 0                  | 2                         | 3                |              |

**Table S4. YTHDC1 expression and clinical characteristics**

| Clinical features             | Number | Overexpr<br>ession | YTHDC1<br>Low<br>expression | No<br>expression | P Value      |
|-------------------------------|--------|--------------------|-----------------------------|------------------|--------------|
| Total number                  | 60     | 36                 | 21                          | 3                |              |
| Gender                        |        |                    |                             |                  | >0.999       |
| Female                        | 20     | 12                 | 7                           | 1                |              |
| Male                          | 40     | 24                 | 14                          | 2                |              |
| Age<br>(median,51.5<br>years) |        |                    |                             |                  | 0.283        |
| <                             | 30     | 21                 | 9                           | 0                |              |
| ≥                             | 30     | 15                 | 13                          | 2                |              |
| Histological<br>diagnosis     |        |                    |                             |                  | <b>0.037</b> |
| Hepatitis                     | 13     | 6                  | 7                           | 0                |              |
| Non-alcoholic fatty<br>liver  | 10     | 7                  | 3                           | 0                |              |
| Cirrhosis                     | 12     | 6                  | 6                           | 0                |              |
| Hepatocellular<br>carcinoma   | 20     | 17                 | 3                           | 0                |              |
| HCC histological<br>Grade     |        |                    |                             |                  | <b>0.004</b> |
| Grade I                       | 3      | 2                  | 1                           | 0                |              |
| Grade II                      | 10     | 8                  | 2                           | 0                |              |
| Grade III                     | 7      | 7                  | 0                           | 0                |              |
| Normal liver tissue           | 5      | 0                  | 2                           | 3                |              |

**Table S5. FASN expression and clinical characteristics**

| Clinical features             | Number | Overexpr<br>ession | FASN<br>Low<br>expression | No<br>expression | P Value      |
|-------------------------------|--------|--------------------|---------------------------|------------------|--------------|
| Total number                  | 60     | 40                 | 18                        | 2                |              |
| Gender                        |        |                    |                           |                  | 0.675        |
| Female                        | 20     | 14                 | 5                         | 1                |              |
| Male                          | 40     | 25                 | 14                        | 1                |              |
| Age<br>(median,51.5<br>years) |        |                    |                           |                  | 0.111        |
| <                             | 30     | 22                 | 6                         | 2                |              |
| ≥                             | 30     | 18                 | 12                        | 0                |              |
| Histological<br>diagnosis     |        |                    |                           |                  | 0.068        |
| Hepatitis                     | 13     | 8                  | 5                         | 0                |              |
| Non-alcoholic fatty<br>liver  | 10     | 8                  | 2                         | 0                |              |
| Cirrhosis                     | 12     | 8                  | 4                         | 0                |              |
| Hepatocellular<br>carcinoma   | 20     | 16                 | 4                         | 0                |              |
| HCC histological<br>Grade     |        |                    |                           |                  | <b>0.007</b> |
| Grade I                       | 3      | 3                  | 0                         | 0                |              |
| Grade II                      | 10     | 9                  | 1                         | 0                |              |
| Grade III                     | 7      | 6                  | 1                         | 0                |              |
| Normal liver tissue           | 5      | 0                  | 3                         | 2                |              |