Electronic Supplementary Material (ESI) for Materials Chemistry Frontiers.


**Supporting Information**

# A Cubic $Cu_2O$@Ag Substrate for Label-free SERS Classification of Hepatic Fibrosis and Hepatocellular Carcinoma

## 1. Physical characterization of $Cu_2O$, $Cu_2O$@Ag

The absorption characteristics were measured using a T10 CS UV−vis spectrophotometer from Beijing Purkinje General Instrument CO., Ltd. The $Cu_2O$ powder's X-ray diffraction (XRD) was analyzed utilizing the BRUKER D8 ADVANCE DAVINCI diffractometer with Cu Kα radiation (λ = 1.54056 Å). The morphology and lattice information of $Cu_2O$ and $Cu_2O$@Ag were analyzed using high-resolution transmission electron microscope (HR-TEM, Talos, HITACHI) and scanning electron microscope (SEM, HITACHI).

## 2. Diagram of preparation of $Cu_2O$@Ag

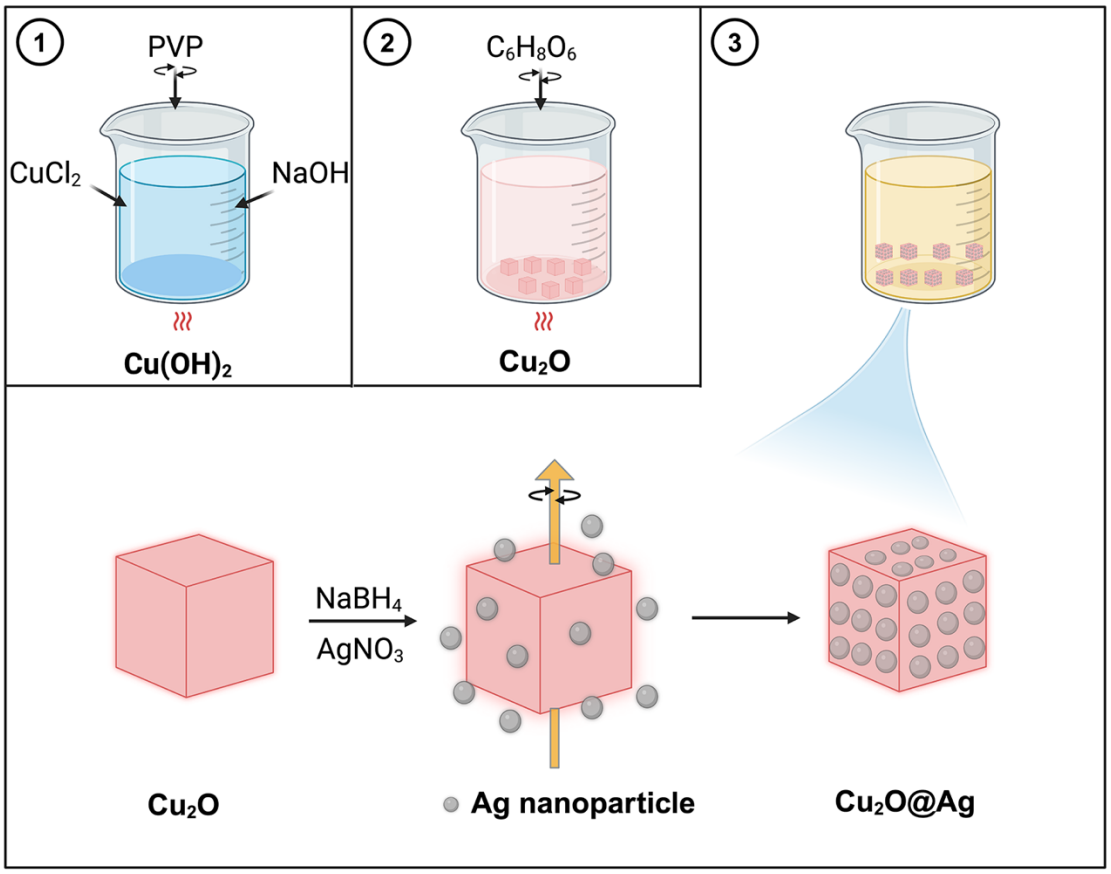


**Figure S1**. Synthesis route of $Cu_2O$@Ag.

### 3. Lattice fringe pattern of cubic $Cu_2O$

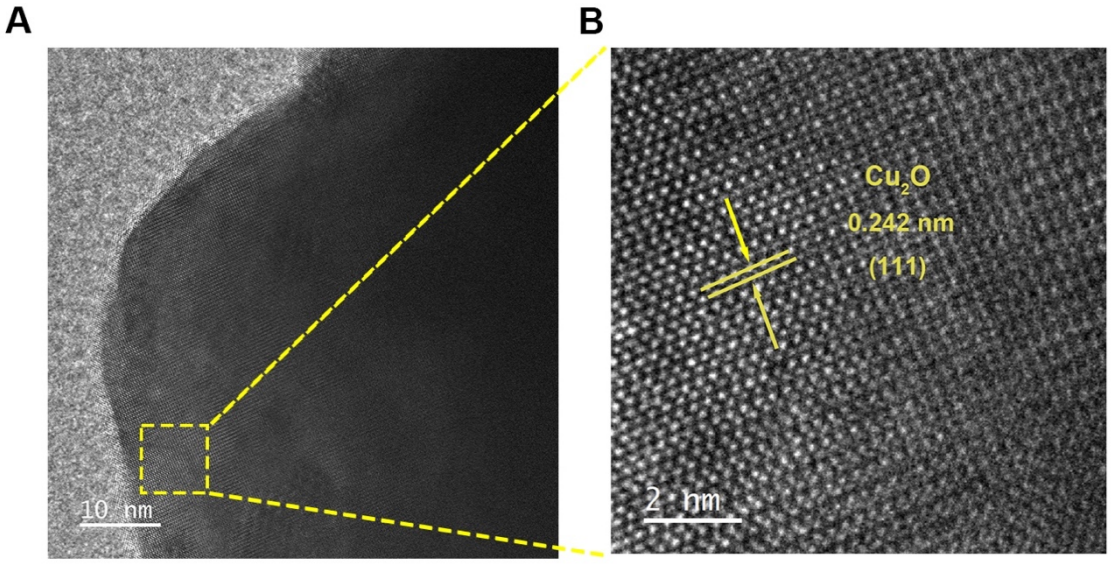


**Figure S2.** Lattice fringe pattern of cubic $Cu_2O$ under HRTEM.

## 4. Element map of cubic $Cu_2O$

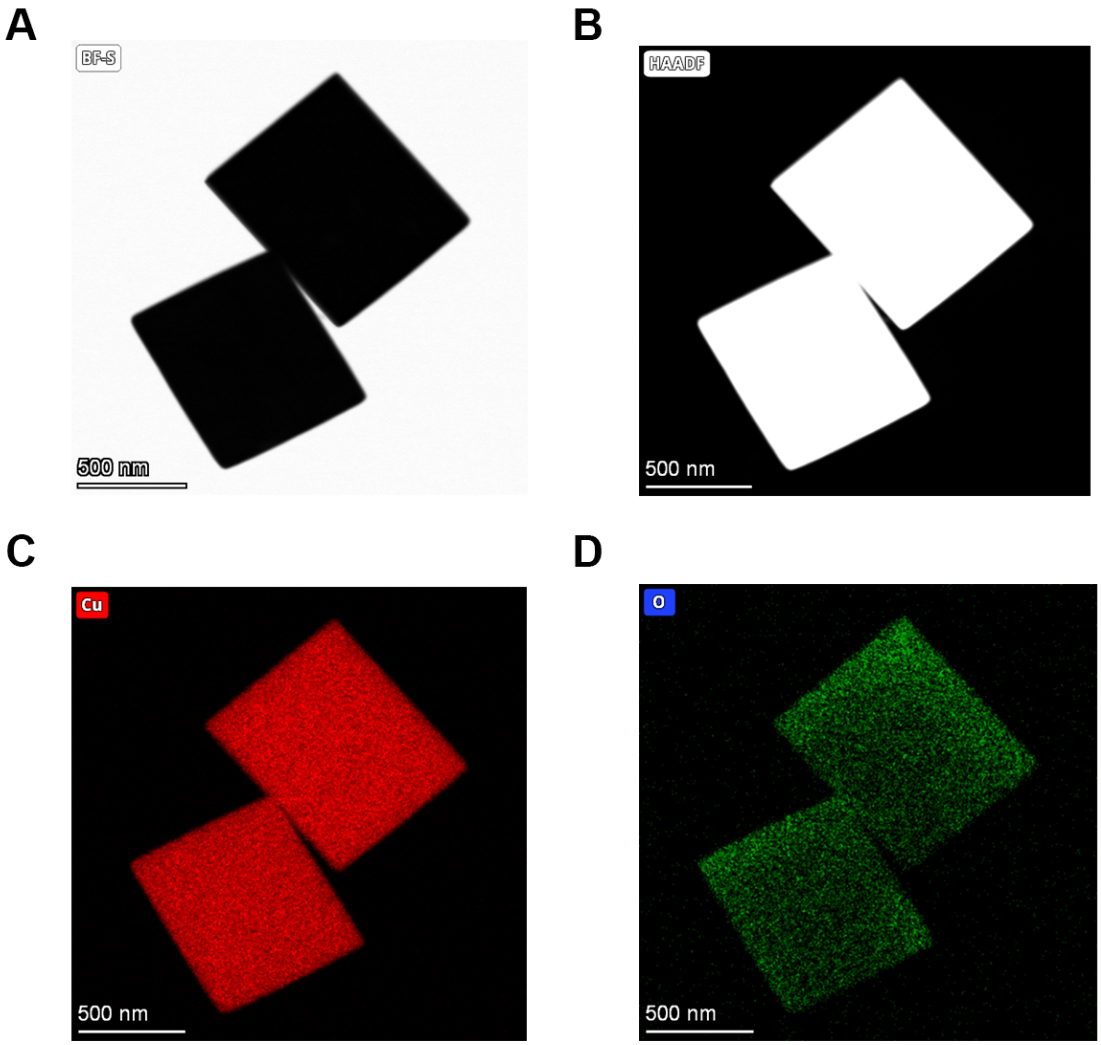


**Figure S3.** Element scanning images of cubic $Cu_2O$.

## 5. Morphology characterization of Ag nanoparticles

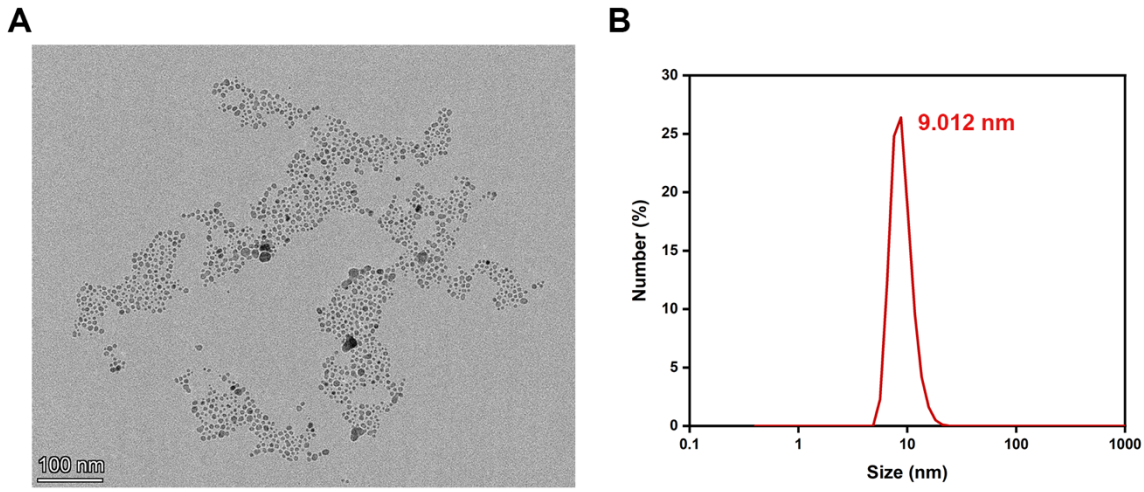


**Figure S4.** TEM and DLS images of Ag nanoparticles.

## 6. Characterization crystalline phase of Ag nanoparticles

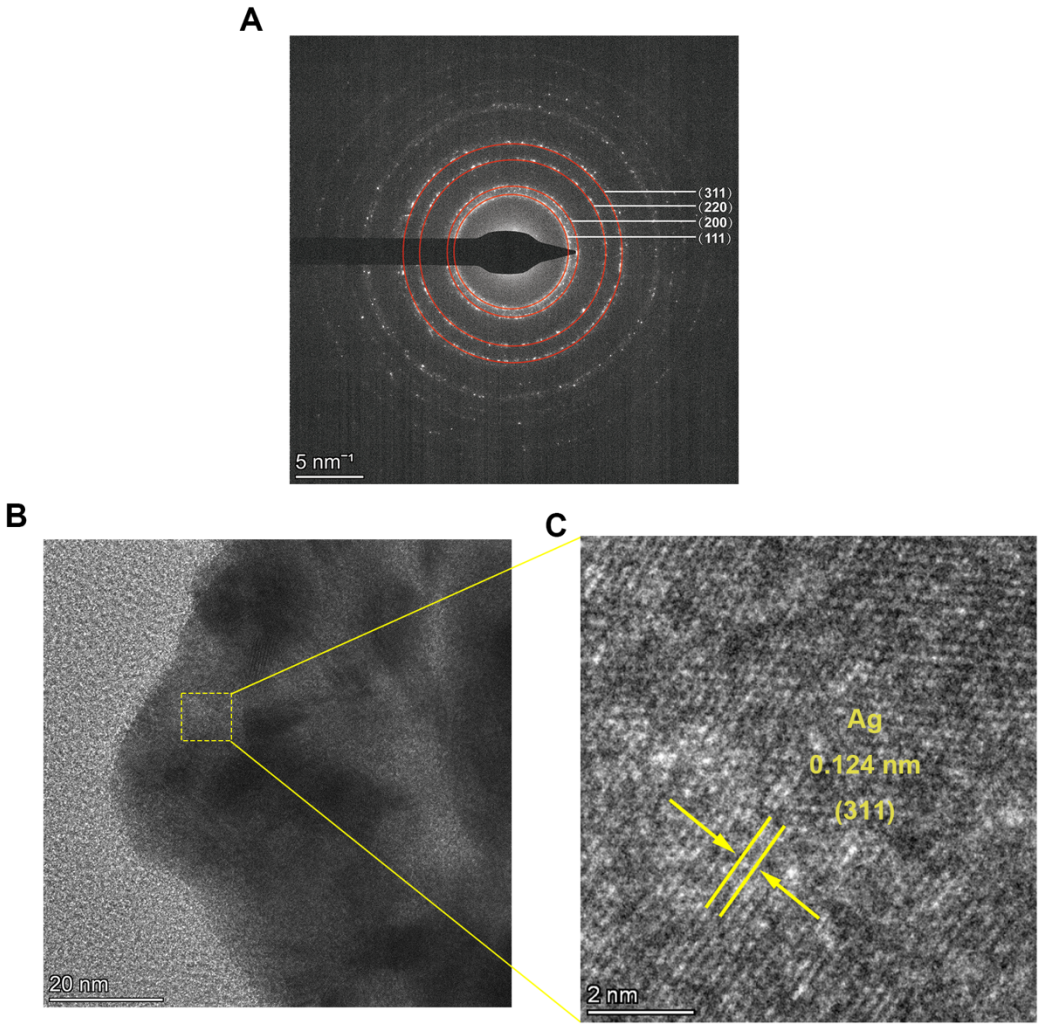


**Figure S5.** Selected area electron diffraction (SAED) and lattice fringe images of Ag nanoparticles.

## 7. Absorbance characterization of cubic $Cu_2O$, Ag nanoparticles and $Cu_2O$@Ag

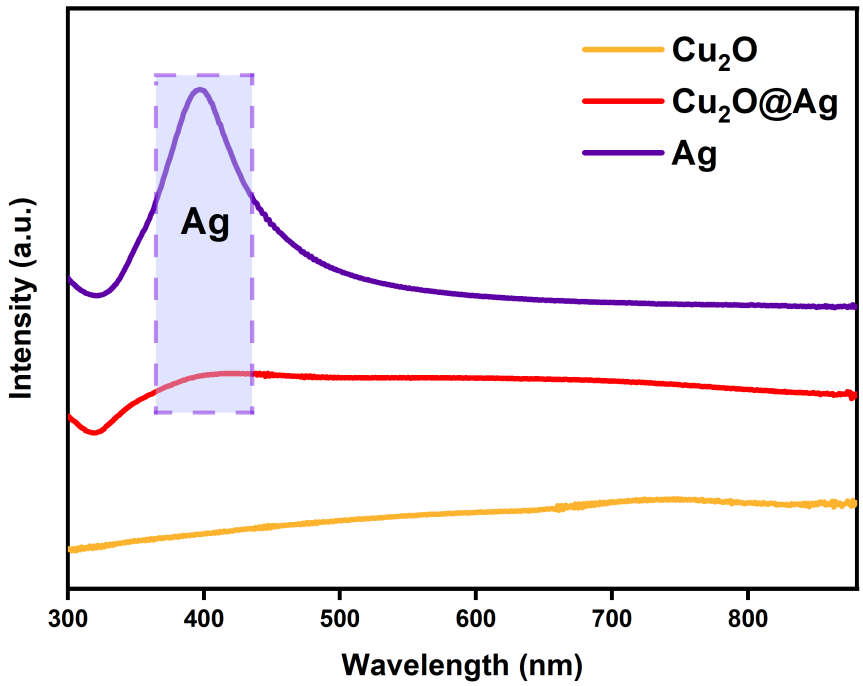


**Figure S6.** UV-vis spectra of cubic $Cu_2O$, Ag nanoparticles and $Cu_2O$@Ag.

**8. XRD characterization of cubic $Cu_2O$, Ag nanoparticles and $Cu_2O$@Ag**

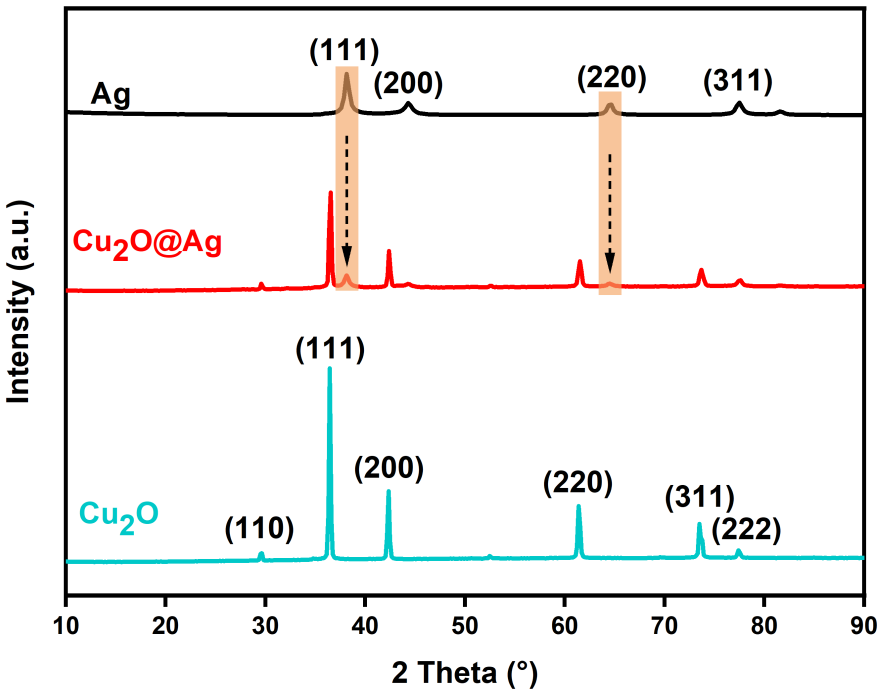


**Figure S7.** XRD spectra of cubic $Cu_2O$, Ag nanoparticles and $Cu_2O$@Ag.

## 9. Predicted results of test set for three Raman reporter molecules

Table S1. Predicted results with probability distribution of test set for AR, MB and R6G.

| True labels | Predicted labels | True/False 1/0 | Prediction probability for AR | Prediction probability for MB | Prediction probability for R6G |
|---|---|---|---|---|---|
| MB | MB | 1 | 0 | 1 | 1.2497E-129 |
| R6G | R6G | 1 | 1.2767E-204 | 1.86383E-87 | 1 |
| R6G | R6G | 1 | 3.6805E-209 | 9.0311E-107 | 1 |
| R6G | R6G | 1 | 5.0978E-224 | 1.2486E-107 | 1 |
| MB | MB | 1 | 3.4571E-199 | 1 | 4.94652E-97 |
| R6G | R6G | 1 | 3.7054E-211 | 2.15791E-93 | 1 |
| MB | MB | 1 | 3.5455E-191 | 1 | 2.14101E-87 |
| MB | MB | 1 | 1.9344E-173 | 1 | 2.11834E-74 |
| R6G | R6G | 1 | 1.6979E-216 | 9.6576E-101 | 1 |
| MB | MB | 1 | 2.5749E-188 | 1 | 2.60702E-76 |
| MB | MB | 1 | 1.6596E-253 | 1 | 2.0527E-117 |
| AR | AR | 1 | 1 | 6.4869E-300 | 1.4688E-298 |
| R6G | R6G | 1 | 7.9919E-203 | 2.00647E-95 | 1 |
| AR | AR | 1 | 1 | 1.0154E-232 | 1.5478E-229 |
| AR | AR | 1 | 1 | 1.954E-293 | 1.0042E-275 |

## 10. Averaged Raman spectra of label-free SERS detection of four types of hepatic cells

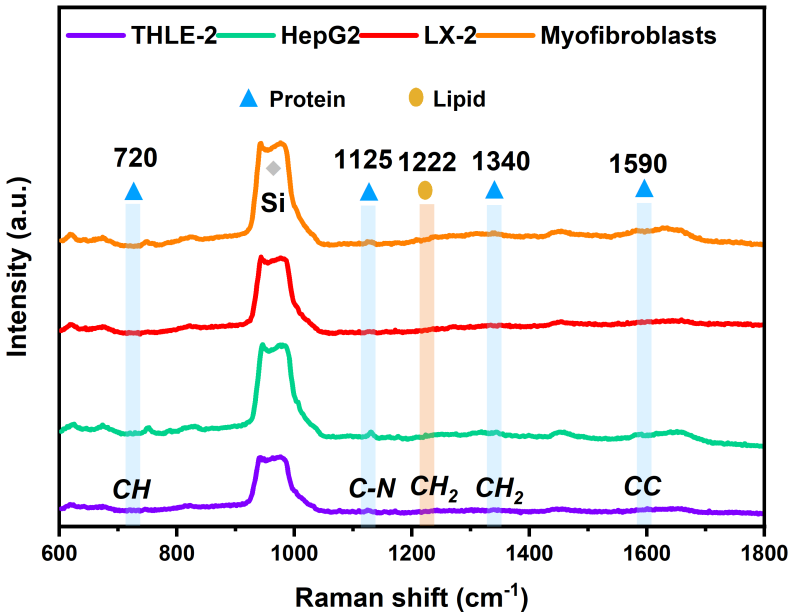


**Figure S8.** Averaged Raman spectra of label-free SERS detection of four types of hepatic cells.

**11. ROC curves for LDA classification of four types of hepatic cells**

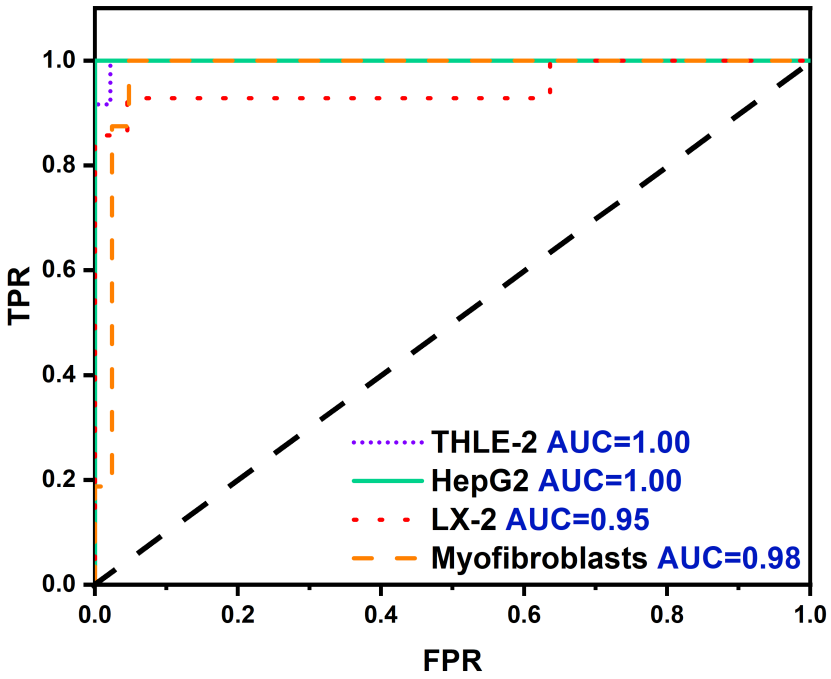


**Figure S9.** ROC curves for LDA classification of four types of hepatic cells.

## 12. Prediction results of four types of hepatic cells

**Table S2.** Table of classification and model prediction results of four types of hepatic cells.

| | Ture Type | Predicted Type | Prediction Result True 1/False 0 | Prediction Probability for THLE-2 | Prediction Probability for HepG2 | Prediction Probability for LX-2 | Prediction Probability for Myofibroblasts |
|---|---|---|---|---|---|---|---|
| 0 | HepG2 | HepG2 | 1 | 3.038E-10 | 0.999912608 | 8.7302E-05 | 9.01946E-08 |
| 1 | LX-2 | LX-2 | 1 | 0.013484438 | 2.01328E-06 | 0.985048856 | 0.001464692 |
| 2 | HepG2 | HepG2 | 1 | 1.38183E-10 | 0.999974533 | 2.54667E-05 | 6.00954E-10 |
| 3 | Myofibroblasts | Myofibroblasts | 1 | 1.17259E-10 | 3.20206E-13 | 6.40712E-09 | 0.999999993 |
| 4 | LX-2 | LX-2 | 1 | 0.012147091 | 3.24463E-07 | 0.98626332 | 0.001589265 |
| 5 | Myofibroblasts | Myofibroblasts | 1 | 0.187071304 | 1.09885E-06 | 0.059766298 | 0.753161299 |
| 6 | THLE-2 | THLE-2 | 1 | 0.999315596 | 2.35698E-14 | 0.000571607 | 0.000112797 |
| 7 | THLE-2 | THLE-2 | 1 | 0.996663381 | 3.80455E-10 | 0.003330891 | 5.72712E-06 |
| 8 | THLE-2 | THLE-2 | 1 | 0.937004311 | 2.83328E-10 | 0.061583502 | 0.001412186 |
| 9 | THLE-2 | THLE-2 | 1 | 0.860760211 | 3.73219E-10 | 0.13923836 | 1.42838E-06 |
| 10 | HepG2 | HepG2 | 1 | 4.44551E-19 | 1 | 8.17077E-11 | 9.51411E-13 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 11 | LX-2 | LX-2 | 1 | 0.005663981 | 3.04981E-05 | 0.984219755 | 0.010085766 |
| 12 | HepG2 | HepG2 | 1 | 1.15298E-17 | 0.999999994 | 6.05363E-09 | 8.64293E-12 |
| 13 | HepG2 | HepG2 | 1 | 1.54937E-14 | 0.999999998 | 1.26481E-09 | 8.75125E-10 |
| 14 | Myofibroblasts | Myofibroblasts | 1 | 2.90168E-07 | 3.27291E-11 | 0.000328545 | 0.999671165 |
| 15 | THLE-2 | THLE-2 | 1 | 0.996689312 | 4.03163E-13 | 0.001362829 | 0.001947859 |
| 16 | Myofibroblasts | Myofibroblasts | 1 | 1.15372E-08 | 5.70933E-13 | 7.76347E-08 | 0.999999911 |
| 17 | HepG2 | HepG2 | 1 | 3.47297E-12 | 0.999999006 | 8.98598E-07 | 9.50431E-08 |
| 18 | LX-2 | LX-2 | 1 | 1.21519E-05 | 5.68624E-07 | 0.999931227 | 5.60526E-05 |
| 19 | HepG2 | HepG2 | 1 | 9.90011E-09 | 0.997757896 | 0.002240885 | 1.20946E-06 |
| 20 | Myofibroblasts | Myofibroblasts | 1 | 9.3632E-07 | 1.63146E-05 | 0.000984279 | 0.99899847 |
| 21 | Myofibroblasts | Myofibroblasts | 1 | 2.10563E-05 | 5.65166E-09 | 0.002036868 | 0.99794207 |
| 22 | LX-2 | Myofibroblasts | 0 | 1.58622E-08 | 4.70729E-08 | 0.000126162 | 0.999873775 |
| 23 | LX-2 | THLE-2 | 0 | 0.794499978 | 3.26781E-07 | 0.185355006 | 0.02014469 |
| 24 | HepG2 | HepG2 | 1 | 1.03134E-06 | 0.962529224 | 0.037444167 | 2.55772E-05 |
| 25 | LX-2 | LX-2 | 1 | 0.001905643 | 1.39704E-05 | 0.997657186 | 0.000423201 |
| 26 | THLE-2 | THLE-2 | 1 | 0.999736118 | 4.41964E-15 | 0.000225596 | 3.8286E-05 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 27 | Myofibroblasts | Myofibroblasts | 1 | 1.33978E-06 | 2.07627E-14 | 1.88088E-08 | 0.999998641 |
| 28 | HepG2 | HepG2 | 1 | 3.98036E-16 | 0.999999993 | 6.73346E-09 | 4.63761E-12 |
| 29 | LX-2 | LX-2 | 1 | 0.00727351 | 7.92025E-08 | 0.967379557 | 0.025346854 |
| 30 | LX-2 | LX-2 | 1 | 0.010024355 | 1.14479E-06 | 0.989359004 | 0.000615496 |
| 31 | Myofibroblasts | Myofibroblasts | 1 | 9.17926E-06 | 2.0656E-05 | 0.00025028 | 0.999719884 |
| 32 | THLE-2 | THLE-2 | 1 | 0.997279339 | 5.85445E-12 | 0.002470448 | 0.000250212 |
| 33 | HepG2 | HepG2 | 1 | 5.42838E-14 | 0.999999484 | 5.09511E-07 | 6.04636E-09 |
| 34 | Myofibroblasts | Myofibroblasts | 1 | 0.000267972 | 3.38773E-07 | 0.002066098 | 0.997665591 |
| 35 | THLE-2 | THLE-2 | 1 | 0.894291699 | 5.43421E-09 | 0.004206697 | 0.101501598 |
| 36 | LX-2 | LX-2 | 1 | 2.4225E-05 | 1.68855E-08 | 0.996702522 | 0.003273236 |
| 37 | Myofibroblasts | Myofibroblasts | 1 | 0.00048778 | 8.50961E-09 | 0.008219431 | 0.99129278 |
| 38 | Myofibroblasts | Myofibroblasts | 1 | 6.35795E-07 | 4.60913E-05 | 0.002752833 | 0.99720044 |
| 39 | HepG2 | HepG2 | 1 | 2.96459E-17 | 1 | 7.82532E-11 | 1.73319E-14 |
| 40 | LX-2 | LX-2 | 1 | 6.18148E-05 | 4.96911E-08 | 0.999774611 | 0.000163524 |
| 41 | Myofibroblasts | THLE-2 | 0 | 0.712162266 | 1.98418E-10 | 0.231676848 | 0.056160886 |
| 42 | THLE-2 | THLE-2 | 1 | 0.987456662 | 7.9309E-12 | 0.01203701 | 0.000506328 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 43 | LX-2 | LX-2 | 1 | 0.01901725 | 2.56008E-06 | 0.965179252 | 0.015800937 |
| 44 | HepG2 | HepG2 | 1 | 5.0023E-08 | 0.997711686 | 0.001770342 | 0.000517922 |
| 45 | Myofibroblasts | THLE-2 | 0 | 0.888094383 | 2.10988E-09 | 0.053914297 | 0.057991318 |
| 46 | LX-2 | LX-2 | 1 | 0.000142187 | 0.000166504 | 0.996175972 | 0.003515337 |
| 47 | HepG2 | HepG2 | 1 | 1.76417E-14 | 0.999999967 | 3.32646E-08 | 7.72204E-11 |
| 48 | HepG2 | HepG2 | 1 | 1.06859E-08 | 0.999341786 | 0.000657759 | 4.44226E-07 |
| 49 | LX-2 | LX-2 | 1 | 0.000769411 | 8.52052E-08 | 0.991543497 | 0.007687007 |
| 50 | THLE-2 | THLE-2 | 1 | 0.999952525 | 3.48593E-14 | 4.40471E-05 | 3.42819E-06 |
| 51 | Myofibroblasts | Myofibroblasts | 1 | 4.33399E-05 | 5.07886E-08 | 0.000414135 | 0.999542475 |
| 52 | HepG2 | HepG2 | 1 | 9.52623E-11 | 0.999852154 | 0.000147797 | 4.83968E-08 |
| 53 | HepG2 | HepG2 | 1 | 6.4907E-15 | 0.999999951 | 4.88976E-08 | 1.22402E-10 |
| 54 | Myofibroblasts | THLE-2 | 0 | 0.398773564 | 3.24752E-09 | 0.387586766 | 0.213639666 |
| 55 | THLE-2 | THLE-2 | 1 | 0.999663211 | 2.84109E-15 | 0.000255357 | 8.14318E-05 |
| 56 | THLE-2 | THLE-2 | 1 | 0.99989375 | 4.31811E-14 | 0.000103731 | 2.51894E-06 |
| 57 | Myofibroblasts | Myofibroblasts | 1 | 2.84338E-08 | 4.95011E-09 | 0.074373904 | 0.925626062 |