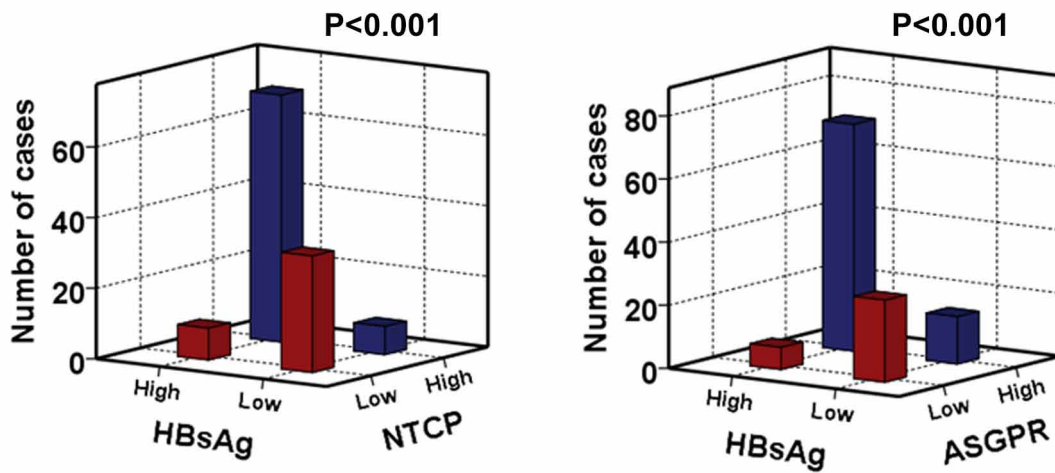
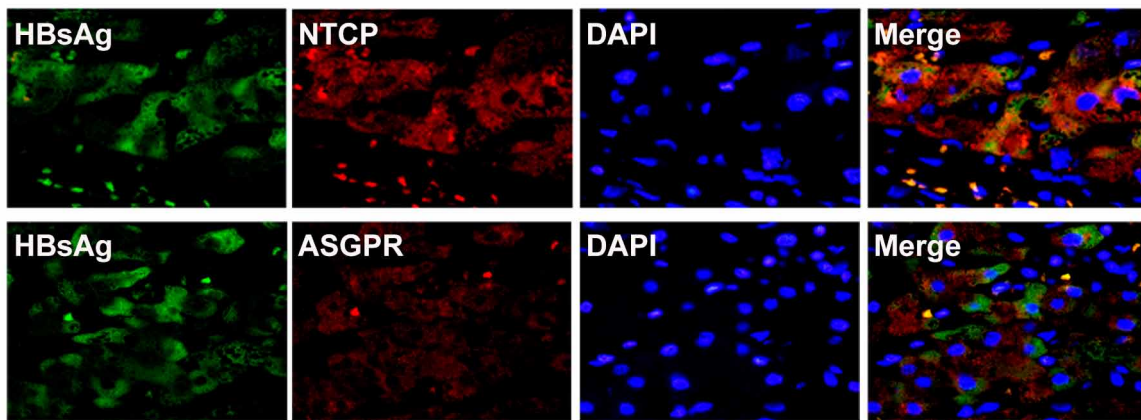


SUPPLEMENTARY FIGURES AND TABLES

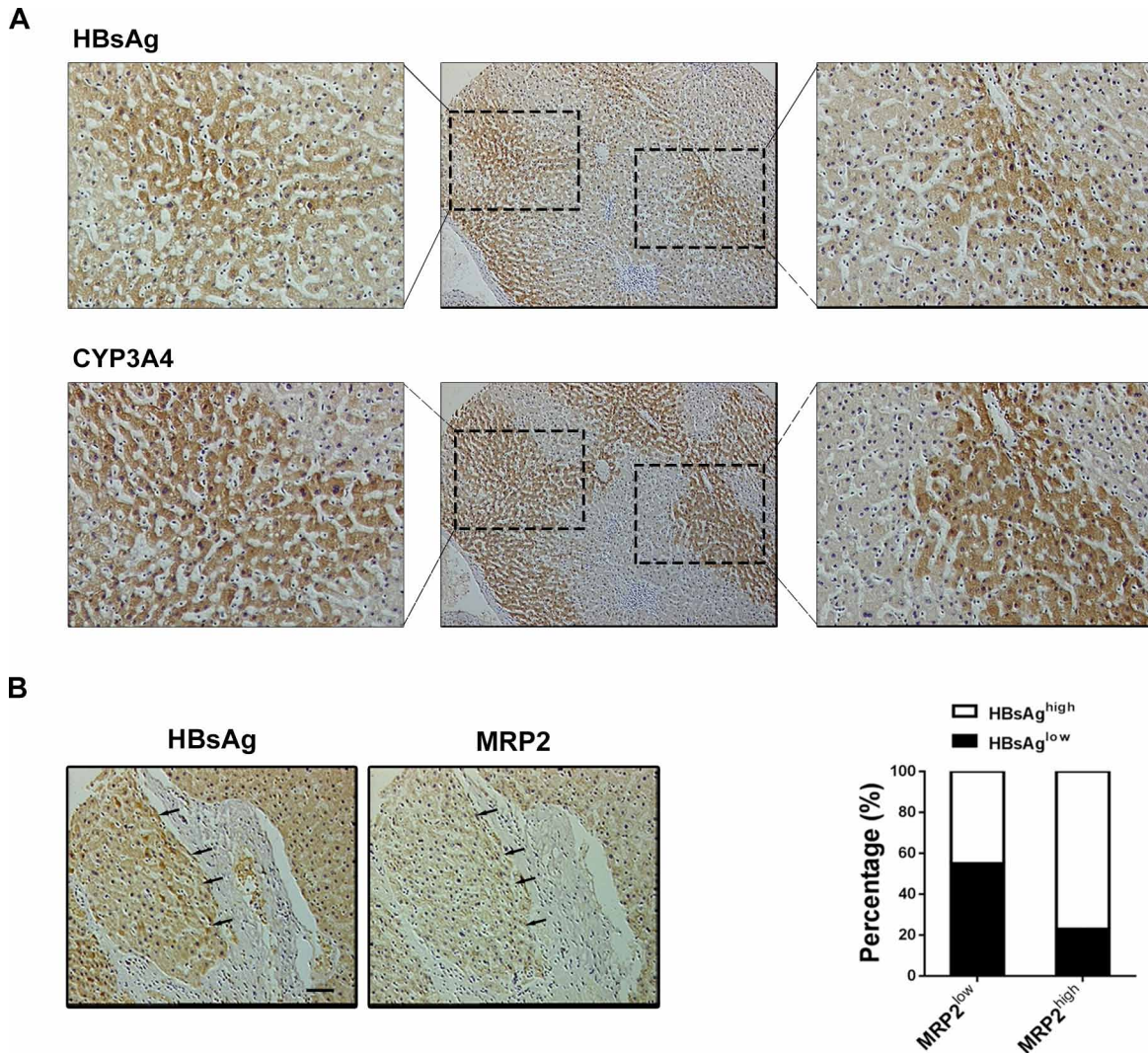
A



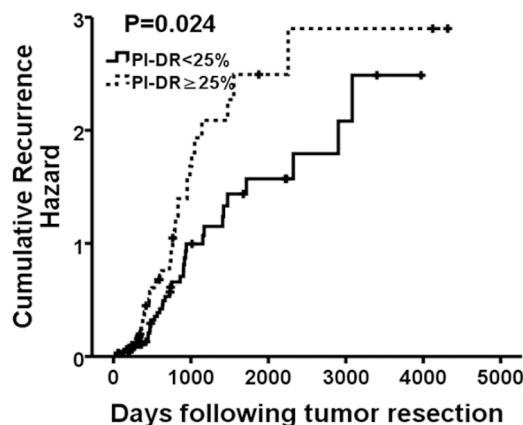
B



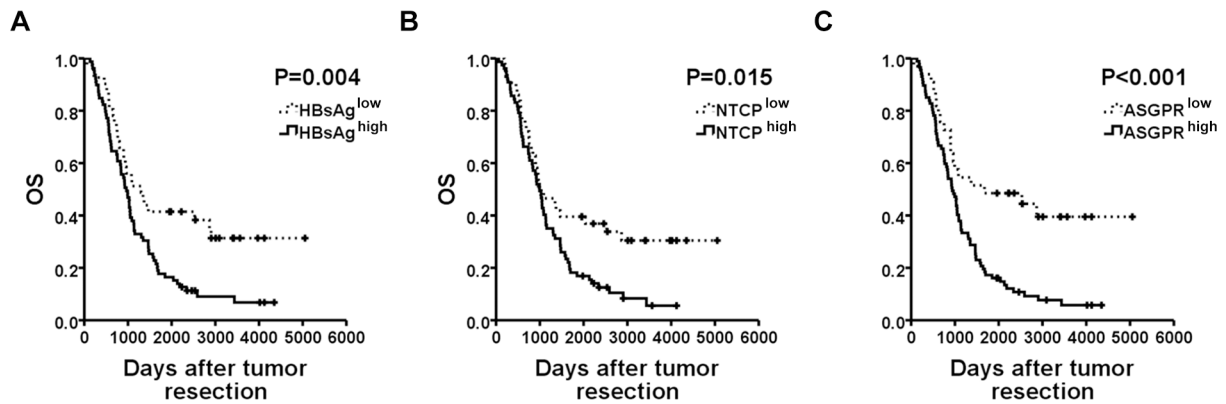
**Supplementary Figure S1: The correlation between peritumoral expression of HBsAg and NTCP or ASGPR.** A. The surrounding tumor tissues with different HBsAg expression have different levels of NTCP ( $P < 0.001$ ) and ASGPR ( $P < 0.001$ ). B. Some cases of peri-tumor with intensive HBsAg staining showing high expression of NTCP or ASGPR staining.



**Supplementary Figure S2: Expression of HBsAg on mature hepatocytes.** A. The immunostaining of CYP3A4, as a cytochrome enzyme exhibited by mature hepatocytes, showed a co-expression with HBsAg, which confirmed that HBV infection was mainly distributed in the central vein zone. B. The immunostaining showed that MRP2 expression, as a polarization marker of hepatocytes, was consistent with HBsAg expression.



**Supplementary Figure S3: Cumulative recurrence hazard analysis about PI-DR.** Higher PI-DR could contribute to the risk of HCC recurrence ( $P < 0.05$ )



**Supplementary Figure S4: Overexpression of peritumoral HBsAg, NTCP and ASGPR is associated with poorer OS.** Survival analyses showed that patients with high peritumoral HBsAg were more likely to have shorter OS **A**, and with overexpression of NTCP or ASGPR were also associated with poorer prognosis **B**.

**Supplementary Table S1: Patient demographic and baseline characteristics**

| Variables              | Values                     | Percent     |
|------------------------|----------------------------|-------------|
| Age (years)            | 53.02 ± 11.62              |             |
| Gender (Male/Female)   | 97/22                      | 80.8%/19.2% |
| Tumor size (cm)        | 5.9 ± 3.2                  |             |
| Lymph node metastasis  | 10                         | 8.3%        |
| Microvascular invasion | 69                         | 57.5%       |
| Tumor encapsulation    | 63                         | 52.5%       |
| Edmondson grade        |                            |             |
| I, II                  | 84                         | 70%         |
| III, IV                | 36                         | 30%         |
| TNM                    |                            |             |
| I, II                  | 110                        | 91.7%       |
| III                    | 10                         | 8.3%        |
| α-Fetoprotein (ng/mL)  | 335.2 ± 411.3 (1.7–1000.0) |             |
| Preoperative ALT (U/L) | 58.6 ± 38.5 (7.8–232.2)    |             |
| Preoperative AST (U/L) | 41.2 ± 19.4 (2.3–118.3)    |             |

**Supplementary Table S2: Demographic and clinicopathologic features of HBsAg-positive hepatocellular carcinoma patients stratified by peritumoral expression of HBsAg, NTCP or ASGPR**

| Variables                     | Peritumoral HBsAg density |      | <i>P</i> | Peritumoral NTCP density |      | <i>P</i> | Peritumoral ASGPR density |      | <i>P</i> |
|-------------------------------|---------------------------|------|----------|--------------------------|------|----------|---------------------------|------|----------|
|                               | Low                       | High |          | Low                      | High |          | Low                       | High |          |
| <b>Age (years)</b>            |                           |      |          |                          |      |          |                           |      |          |
| < 60                          | 31                        | 63   | 0.602    | 32                       | 62   | 0.437    | 25                        | 69   | 0.673    |
| <b>Male Gender</b>            | 33                        | 64   | 0.945    | 36                       | 61   | 0.548    | 27                        | 70   | 0.866    |
| <b>Tumor size (cm)</b>        |                           |      |          |                          |      |          |                           |      |          |
| ≥ 5                           | 19                        | 56   | 0.008    | 20                       | 55   | 0.007    | 14                        | 61   | 0.005    |
| <b>Tumor encapsulation</b>    |                           |      |          |                          |      |          |                           |      |          |
| Yes                           | 20                        | 43   | 0.557    | 21                       | 42   | 0.548    | 15                        | 48   | 0.341    |
| <b>Microvascular invasion</b> |                           |      |          |                          |      |          |                           |      |          |
| Yes                           | 7                         | 62   | < 0.001  | 13                       | 56   | < 0.001  | 9                         | 60   | < 0.001  |
| <b>Edmondson grade</b>        |                           |      |          |                          |      |          |                           |      |          |
| I, II                         | 34                        | 50   | 0.026    | 32                       | 52   | 0.430    | 27                        | 57   | 0.082    |
| III, IV                       | 7                         | 29   |          | 11                       | 25   |          | 6                         | 30   |          |
| <b>TNM</b>                    |                           |      |          |                          |      |          |                           |      |          |
| I, II                         | 37                        | 73   | 0.734    | 39                       | 71   | 0.744    | 31                        | 79   | 0.725    |
| III                           | 4                         | 6    |          | 4                        | 6    |          | 2                         | 8    |          |
| <b>AFP (ng/mL)</b>            |                           |      |          |                          |      |          |                           |      |          |
| < 400                         | 21                        | 58   | 0.015    | 24                       | 55   | 0.084    | 16                        | 63   | 0.014    |
| ≥ 400                         | 20                        | 21   |          | 19                       | 22   |          | 17                        | 24   |          |

**Supplementary Table S3: Univariate analyses of factors associated with overall survival (OS) and disease free survival (RFS)**

| Factors                                   | OS    | RFS   |
|---|-------|-------|
| <b>Age:</b> < 60 vs. ≥ 60 years           | 0.922 | 0.393 |
| <b>Gender:</b> Male vs. Female            | 0.359 | 0.714 |
| <b>Tumor size:</b> < 5 vs. ≥ 5 cm         | 0.002 | 0.005 |
| <b>Tumor encapsulation:</b> no vs. yes    | 0.304 | 0.279 |
| <b>Microvascular invasion:</b> no vs. yes | 0.026 | 0.055 |
| <b>Edmondson grade:</b> I, II vs. III, IV | 0.203 | 0.424 |
| <b>TNM:</b> I, II vs. III                 | 0.171 | 0.342 |
| <b>AFP:</b> < 400 vs. ≥ 400               | 0.869 | 0.777 |
| <b>HBsAg expression:</b> Low vs. High     | 0.005 | 0.017 |
| <b>NTCP expression:</b> Low vs. High      | 0.017 | 0.003 |
| <b>ASGPR expression:</b> Low vs. High     | 0.001 | 0.002 |

Factors with  $P < 0.100$  were selected for subsequent multivariate analysis.