

*Medical Oncology*

Polymorphisms of HIF1A gene are associated with prognosis of early stage non-small cell  
lung cancer patients after surgery

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## **Supplementary Figure Captions**

### **Supplementary Fig 1 Kaplan-Meier curves of recurrence-free survival by dominant model in patient subgroups with different disease stages**

A) The analysis of rs2057482 in patients with early stage disease; B) rs2057482 in patients with advanced stage disease; C) rs2301113 in patients with early stage disease; D) rs2301113 in patients with advanced stage disease

### **Supplementary Fig 2 Kaplan-Meier curves of recurrence-free survival by dominant model in patient subgroups with different T-stages**

A) The analysis of rs2057482 in patients with early T-stage disease; B) rs2057482 in patients with advanced T-stage disease; C) rs2301113 in patients with early T-stage disease; D) rs2301113 in patients with advanced T-stage disease

### **Supplementary Fig 3 Kaplan-Meier curves of recurrence-free survival by dominant model in patient subgroups with different N-stages**

A) The analysis of rs2057482 in patients without lymph node involvement; B) rs2057482 in patients with positive lymph nodes involvement; C) rs2301113 in patients without lymph node involvement; D) rs2301113 in patients with positive lymph nodes involvement

**Table S1. Association of *HIF1A* SNPs with clinical outcomes of NSCLC patients**

| SNP                 | Genotype | Overall survival |                         |         | Recurrence-free survival |                         |         |
|---------------------|----------|------------------|-------------------------|---------|--------------------------|-------------------------|---------|
|                     |          | Death/total      | HR (95%CI) <sup>a</sup> | P value | Recurrence/total         | HR (95%CI) <sup>a</sup> | P value |
| rs2057482<br>3'-UTR | CC       | 110/344          | Ref.                    |         | 154/344                  | Ref.                    |         |
|                     | CT       | 33/128           | 0.89(0.60-1.32)         | 0.551   | 45/128                   | 0.77(0.55-1.08)         | 0.132   |
|                     | TT       | 5/19             | 0.61(0.25-1.51)         | 0.288   | 8/19                     | 0.73(0.35-1.51)         | 0.389   |
|                     | Dominant | 38/147           | 0.84(0.57-1.22)         | 0.347   | 53/147                   | 0.77(0.56-1.06)         | 0.111   |
|                     | Additive |                  | 0.84(0.62-1.14)         | 0.262   |                          | 0.81(0.63-1.06)         | 0.114   |
| rs2301113<br>Intron | AA       | 72/219           | Ref.                    |         | 101/219                  | Ref.                    |         |
|                     | AC       | 58/209           | 0.87(0.65-1.18)         | 0.442   | 82/209                   | 0.87(0.65-1.17)         | 0.371   |
|                     | CC       | 18/64            | 0.82(0.47-1.39)         | 0.457   | 24/64                    | 0.72(0.46-1.14)         | 0.174   |
|                     | Dominant | 76/273           | 0.84(0.64-1.11)         | 0.336   | 106/273                  | 0.83(0.63-1.10)         | 0.202   |
|                     | Additive |                  | 0.89(0.71-1.13)         | 0.352   |                          | 0.86(0.71-1.06)         | 0.135   |

Abbreviations: CI, confidence interval; HR, hazard ratio; Ref., reference.

<sup>a</sup>Adjusted for age, gender, smoking status, histology, TNM stage, differentiation, chemotherapy or radiotherapy.

**Table S2. Stratified analysis on association of *HIF1A* SNPs with prognosis in NSCLC patients**

| Variable                | rs2057482   |          |                         |                  |        |                         | rs2301113   |        |                         |                  |        |                         |
|-------------------------|-------------|----------|-------------------------|------------------|--------|-------------------------|-------------|--------|-------------------------|------------------|--------|-------------------------|
|                         | Death/total |          | HR <sup>a</sup> (95%CI) | Recurrence/total |        | HR <sup>a</sup> (95%CI) | Death/total |        | HR <sup>a</sup> (95%CI) | Recurrence/total |        | HR <sup>a</sup> (95%CI) |
|                         | CC          | CT/TT    |                         | CC               | CT/TT  |                         | AA          | AC/CC  |                         | AA               | AC/CC  |                         |
| <b>Age</b>              |             |          |                         |                  |        |                         |             |        |                         |                  |        |                         |
| ≤59                     | 50/173      | 20/70    | 0.79(0.46-1.37)         | 81/173           | 28/70  | 0.66(0.42-1.04)         | 27/109      | 43/134 | 1.17(0.71-1.92)         | 51/109           | 58/134 | 0.91(0.62-1.34)         |
| >59                     | 60/171      | 18/77    | 0.91(0.52-1.58)         | 73/171           | 25/77  | 1.00(0.62-1.60)         | 45/110      | 33/139 | 0.66(0.42-1.04)         | 50/110           | 48/139 | 0.79(0.52-1.18)         |
| <b>Gender</b>           |             |          |                         |                  |        |                         |             |        |                         |                  |        |                         |
| Female                  | 22/73       | 9/34     | 1.09(0.47-2.51)         | 36/73            | 12/34  | 0.84(0.42-1.69)         | 13/50       | 18/57  | 1.08(0.5-2.31)          | 24/50            | 24/57  | 0.93(0.52-1.68)         |
| Male                    | 88/271      | 129/1130 | 0.79(0.52-1.21)         | 118/271          | 41/113 | 0.75(0.52-1.08)         | 59/169      | 58/216 | 0.79(0.55-1.14)         | 77/169           | 82/216 | 0.81(0.59-1.11)         |
| <b>Smoking status</b>   |             |          |                         |                  |        |                         |             |        |                         |                  |        |                         |
| Never                   | 30/99       | 14/54    | 0.75(0.37-1.50)         | 48/99            | 21/54  | 0.60(0.35-1.05)         | 19/65       | 25/88  | 0.80(0.42-1.51)         | 32/65            | 37/88  | 0.72(0.44-1.19)         |
| Ever                    | 80/245      | 24/93    | 0.82(0.52-1.30)         | 106/245          | 32/93  | 0.80(0.54-1.20)         | 53/154      | 51/185 | 0.83(0.56-1.23)         | 69/154           | 69/185 | 0.86(0.61-1.20)         |
| <b>Histology</b>        |             |          |                         |                  |        |                         |             |        |                         |                  |        |                         |
| Squamous cell carcinoma | 60/201      | 19/68    | 0.96(0.57-1.63)         | 86/201           | 22/68  | 0.78(0.48-1.26)         | 43/131      | 36/136 | 0.82(0.52-1.29)         | 59/131           | 49/138 | 0.83(0.57-1.22)         |
| Adenocarcinoma          | 23/92       | 9/55     | 0.72(0.32-1.62)         | 40/92            | 15/55  | 0.58(0.31-1.08)         | 15/61       | 17/87  | 0.82(0.40-1.67)         | 29/61            | 26/87  | 0.61(0.35-1.06)         |
| Others*                 | 27/51       | 10/24    | 0.77(0.36-1.69)         | 28/51            | 16/24  | 1.29(0.64-2.59)         | 14/27       | 23/48  | 0.97(0.47-1.98)         | 13/27            | 31/48  | 1.62(0.82-3.23)         |
| <b>TNM stage</b>        |             |          |                         |                  |        |                         |             |        |                         |                  |        |                         |
| I/II                    | 60/200      | 12/86    | <b>0.42(0.22-0.80)</b>  | 75/200           | 22/86  | <b>0.60(0.36-0.97)</b>  | 38/130      | 34/134 | 0.71(0.44-1.15)         | 49/130           | 48/156 | 0.77(0.51-1.15)         |
| III                     | 50/144      | 26/61    | 1.54(0.94-2.53)         | 79/144           | 31/61  | 0.93(0.60-1.44)         | 34/89       | 42/117 | 1.07(0.68-1.70)         | 52/89            | 58/117 | 0.92(0.63-1.35)         |
| <b>Differentiation</b>  |             |          |                         |                  |        |                         |             |        |                         |                  |        |                         |
| Well/moderate           | 66/241      | 119/1020 | 0.66(0.39-1.12)         | 99/241           | 25/102 | <b>0.55(0.35-0.86)</b>  | 47/161      | 38/138 | 0.69(0.44-1.08)         | 70/161           | 54/183 | <b>0.65(0.45-0.94)</b>  |
| Poorly/undifferentiated | 44/103      | 19/45    | 0.86(0.48-1.56)         | 55/103           | 28/45  | 1.00(0.61-1.65)         | 25/58       | 38/90  | 0.97(0.58-1.62)         | 31/58            | 52/90  | 1.13(0.72-1.78)         |
| <b>Adjuvant therapy</b> |             |          |                         |                  |        |                         |             |        |                         |                  |        |                         |
| No                      | 33/84       | 11/43    | 0.85(0.45-1.60)         | 39/84            | 11/43  | 0.60(0.32-1.15)         | 22/56       | 22/71  | 0.84(0.49-1.45)         | 26/56            | 24/71  | 0.75(0.44-1.28)         |
| Yes                     | 77/260      | 27/1040  | 0.79(0.49-1.28)         | 115/260          | 42/104 | 0.81(0.56-1.18)         | 50/163      | 54/202 | 0.87(0.57-1.31)         | 75/163           | 82/202 | 0.89(0.64-1.23)         |

Abbreviations: CI, confidence interval; HR, hazard ratio; Ref., reference.

<sup>a</sup>Adjusted for age, gender, smoking status, histology, TNM stage, differentiation, chemotherapy radiotherapy.

Fig S1

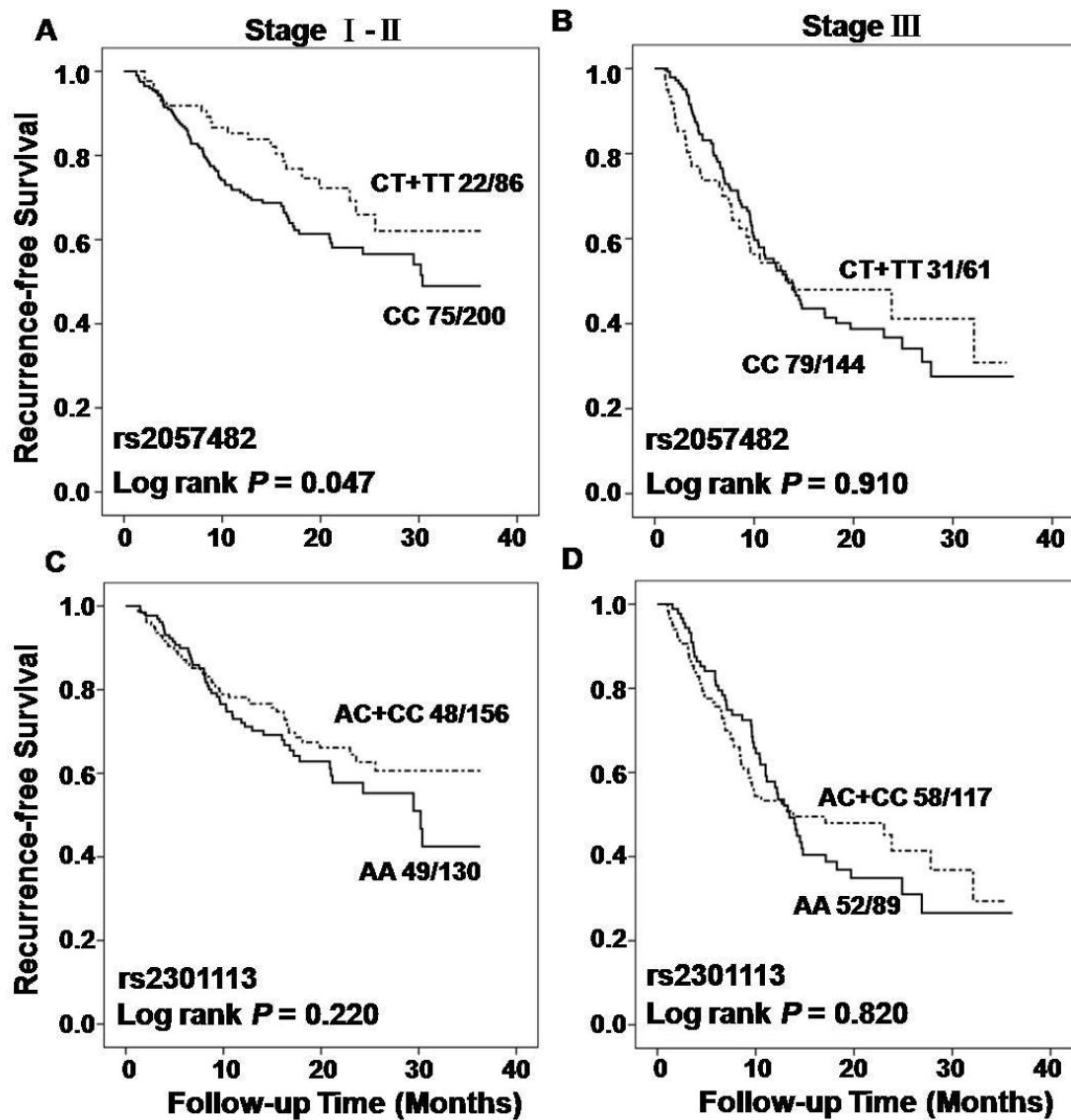


Fig S2

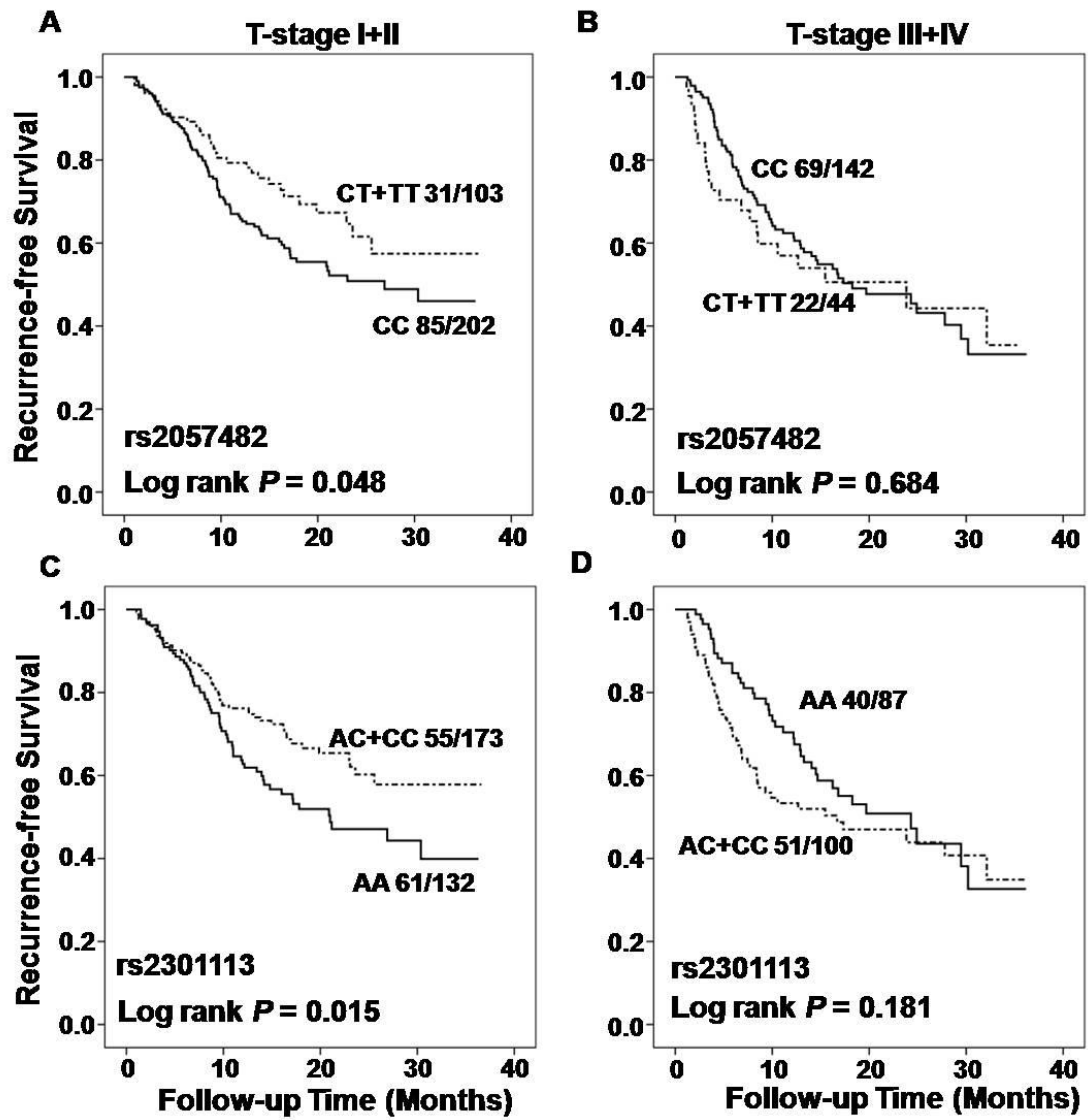


Fig S3

