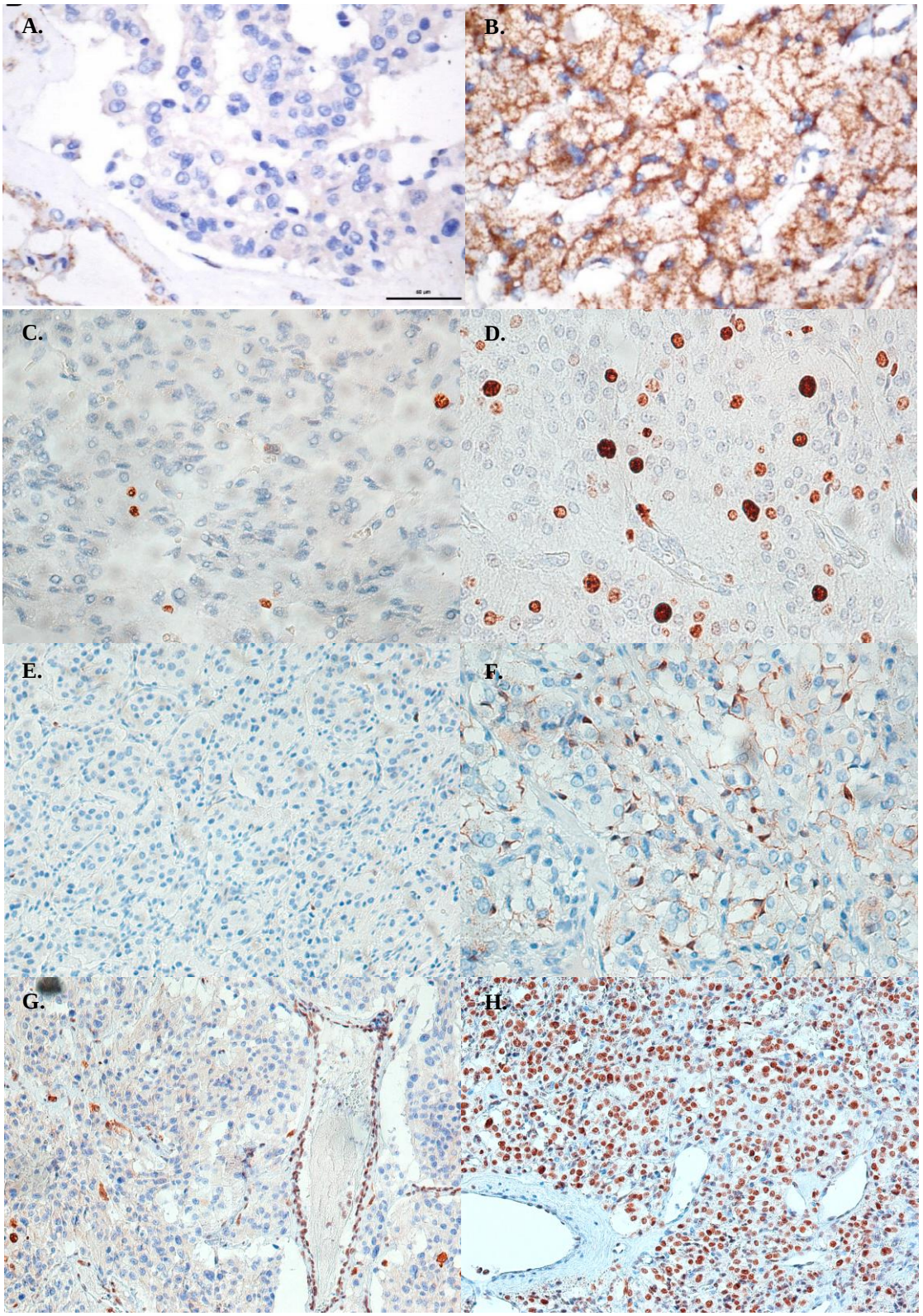
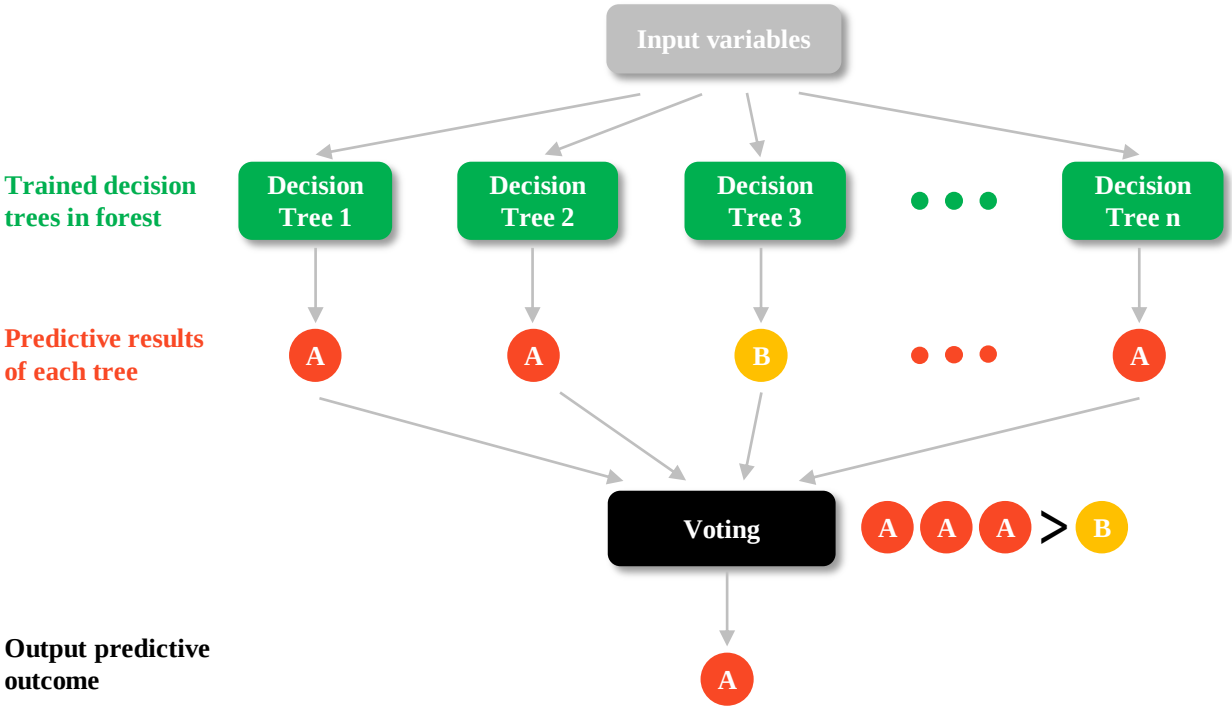
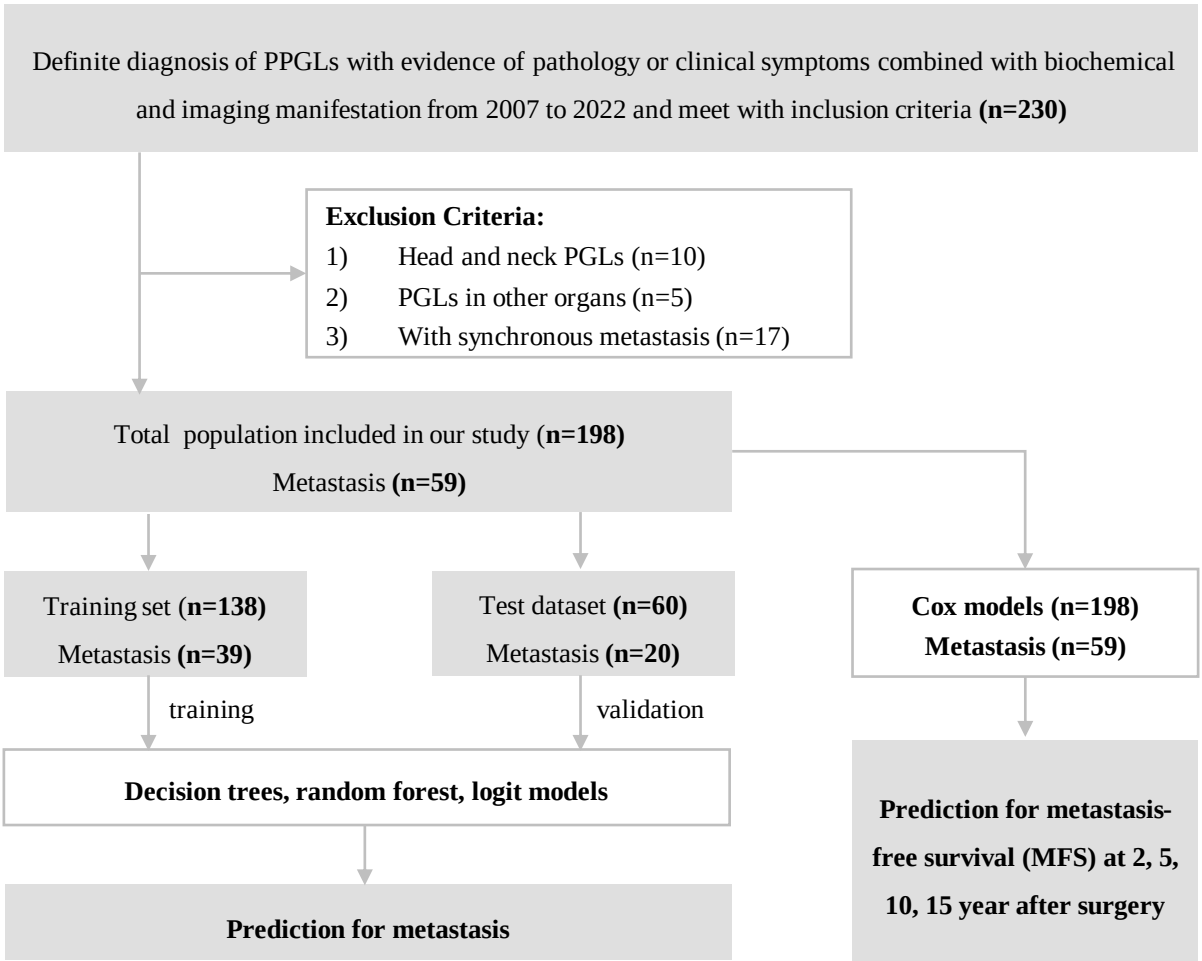
The Supplemental Figures



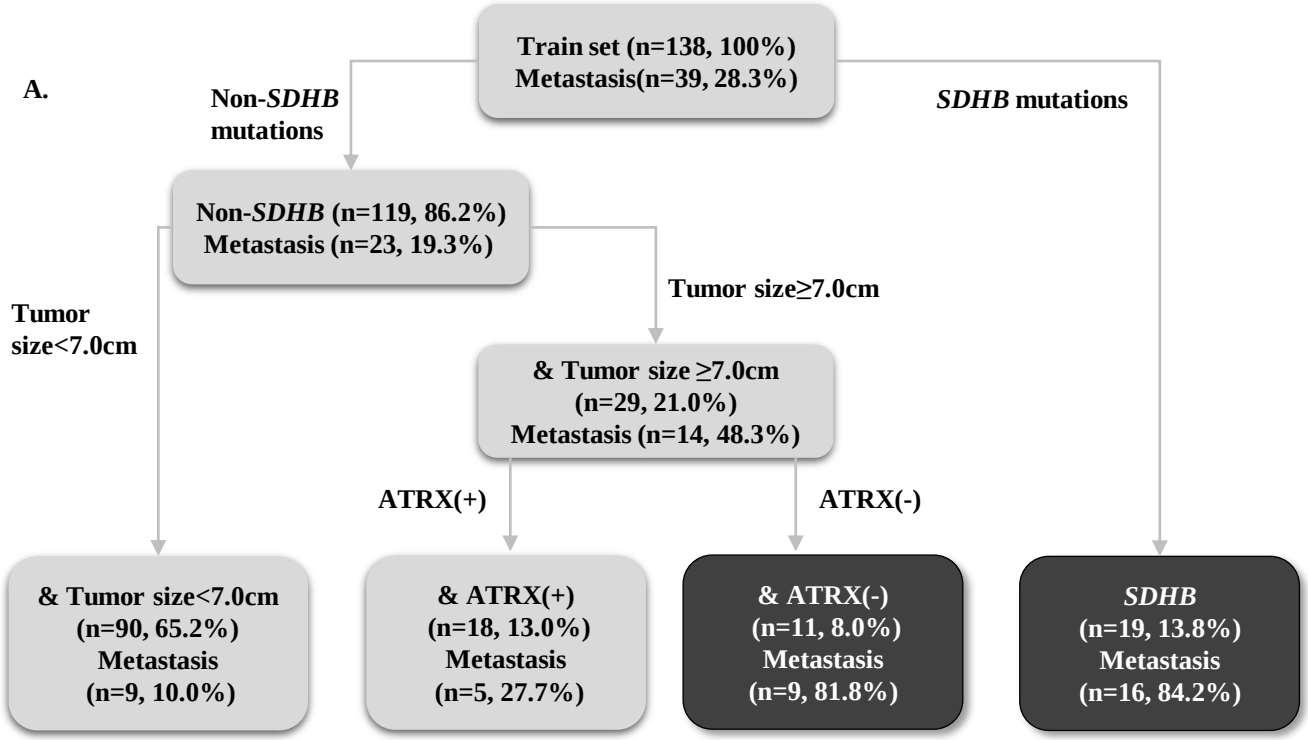
The Supplemental Figure 1. The immunohistochemistry (IHC) results of SDHB, KI-67, S-100 and ATRX. **A.** Negative staining of SDHB in the cytoplasm of tumor cells but preserved staining in the adjacent vascular endothelial cells (×400). **B.** Positive expression of SDHB with bore granular staining in the cytoplasm of the tumor cells (×400). A KI-67 proliferation index was evaluated manually in the hottest spot selected by counting positively stained cells per 100 tumor cells only on a photographic field at ×200 magnification (0.15 mm^2). At least 500 cells were independently evaluated. KI-67 index of 2% and 15% shown in **C.** and **D.** (×400), respectively. **E.** Negative IHC of S-100 defined as non-staining or staining in less than 1% of sustentacular cells (×200) and **F.** positive IHC of S-100 in more than 1% (×400). **G.** Negative IHC of ATRX with non-staining in tumor cells nuclear but preserved staining within adjacent stromal cells (×200) and **H.** positive IHC with staining in tumor cells nuclear (×200).

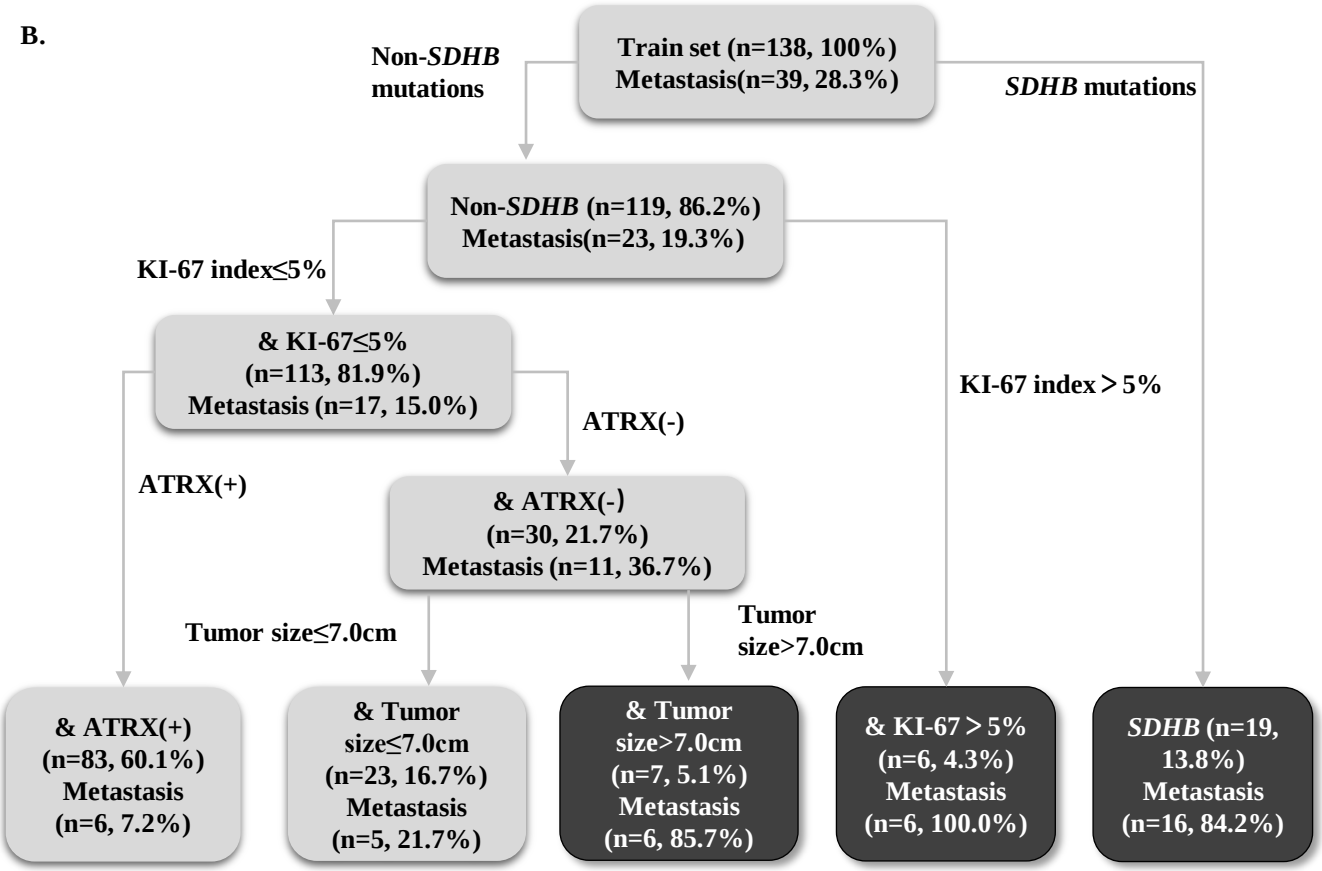


The Supplemental Figure 2. The pattern diagram of Randomized Forest (RF). Multiple decision trees will be trained simutaneously with different variables selected by the lowest out-of-bag (OOB) error. After the sample entering RF, each tree in RF will provide a predictive result and the final predictive outcome will be output through voting.

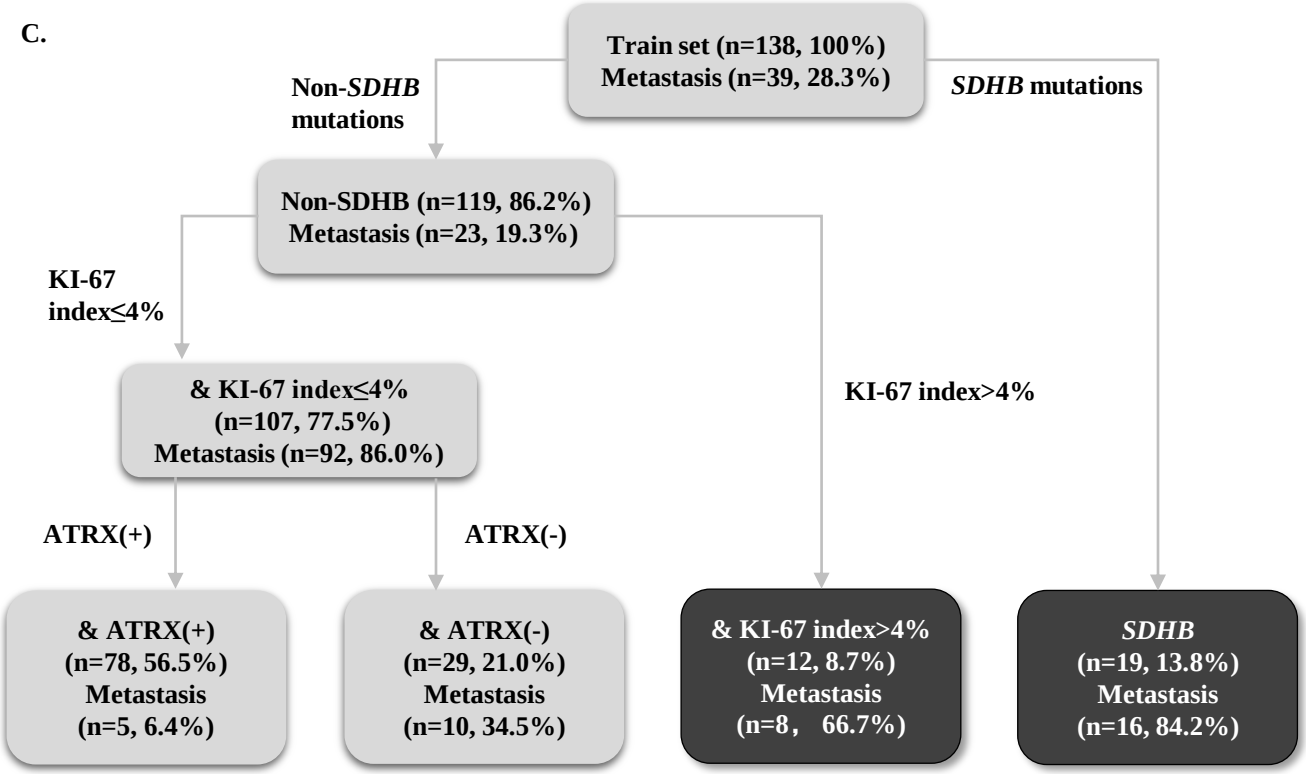


The Supplemental Figure 3. The flow diagram of the study design.

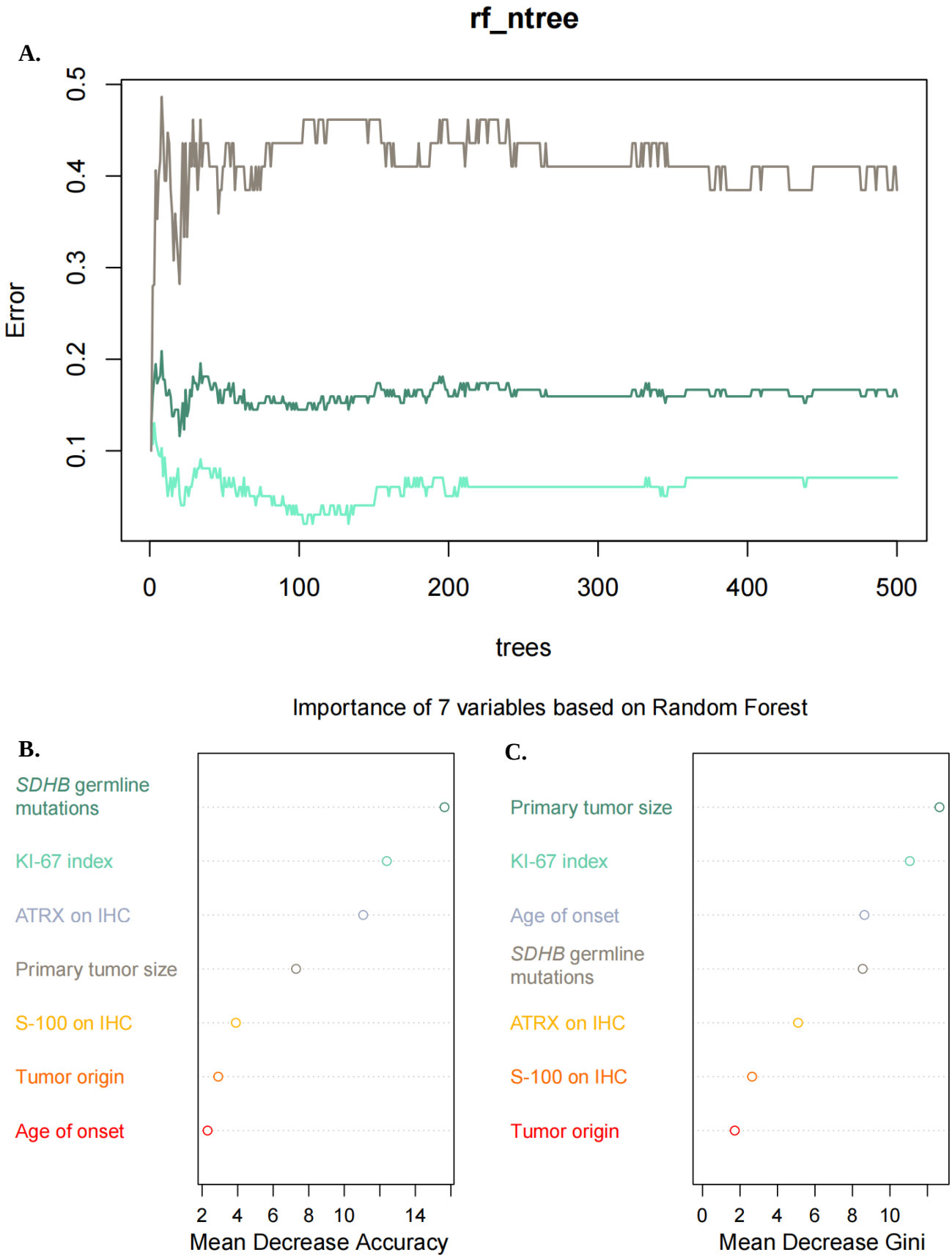




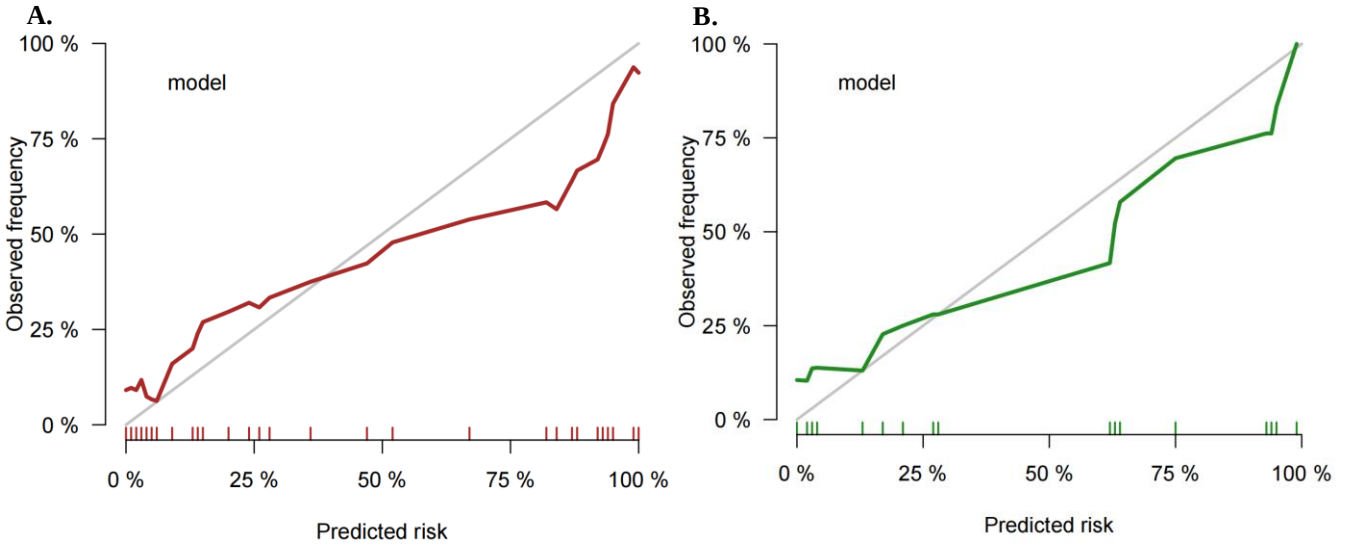
The Supplemental Figure 4. The pattern diagram of **A.** ID3, **B.** C4.5 and **C.** conditional inference tree models.



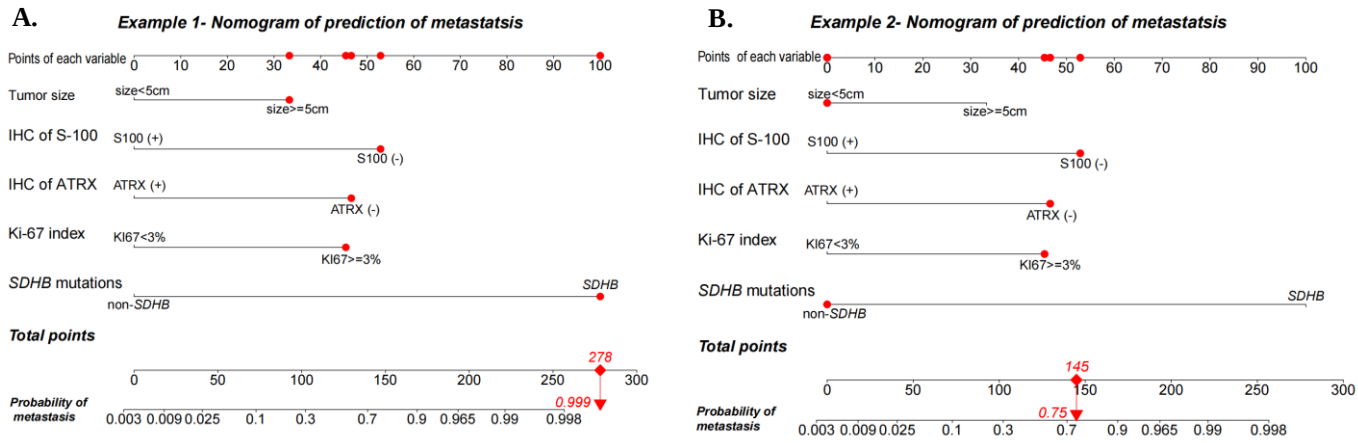
The Supplemental Figure 4. The pattern diagram of **A.** ID3, **B.** C4.5 and **C.** conditional inference tree models.



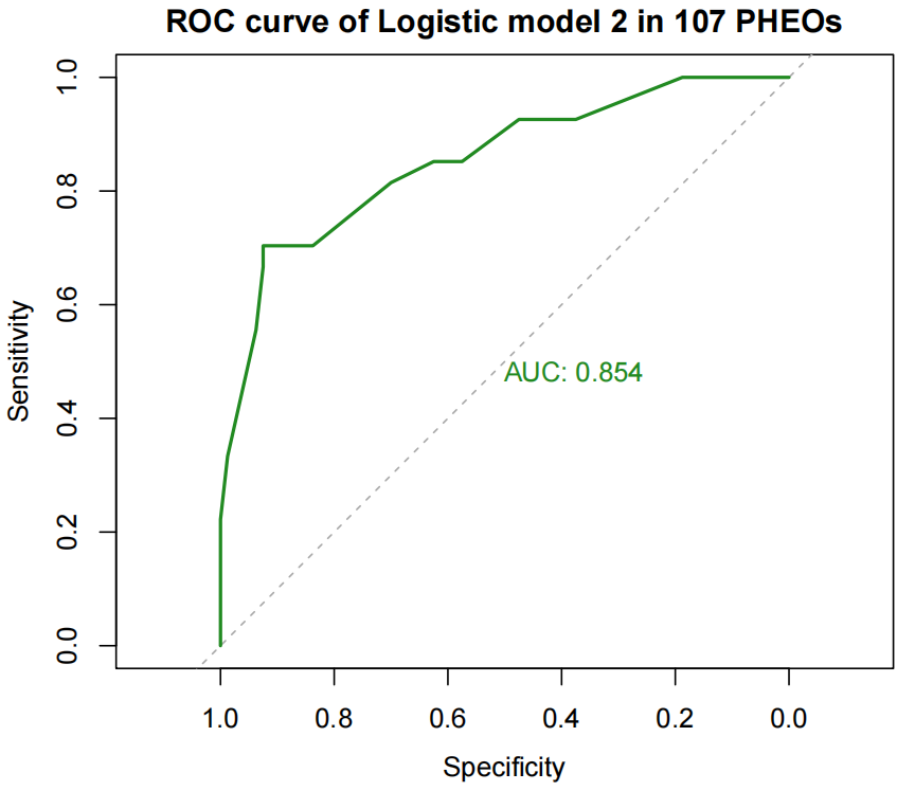
The Supplemental Figure 5. A. Error rate curve of random forest (RF) demonstrated the error in out-of-bag (OBB) sample classification with increasing tree growth. Error rates stabilize after approximately 220 trees growing. The uppermost grey-brown line represents error rate of classification of metastasis, the middle dark-green line for error rate of classification of non-metastasis and the nethermost green line for the false classification of non-metastasis. The importance of seven predictors were evaluated based on **B.** the mean decrease of accuracy and **C.** mean Gini coefficient after omitting each factor in RF model.



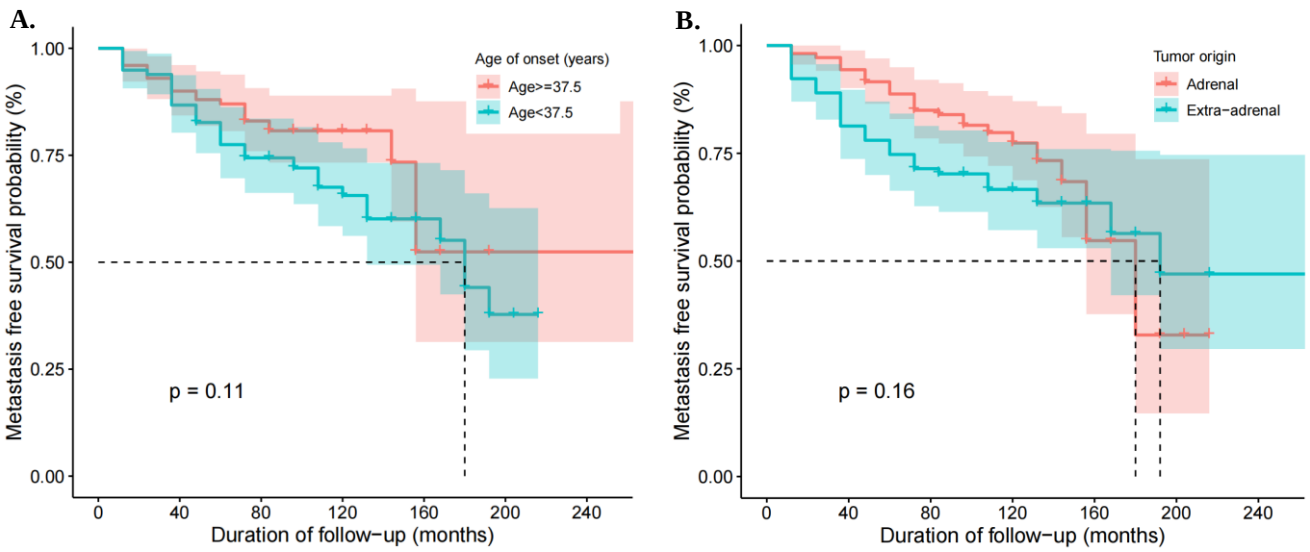
The Supplemental Figure 6. The calibration plot of **A.** logit model 1 (KI-67 index and tumor size as continuous variables) and **B.** logit model 2 (KI-67 index and tumor size as categorical variables with the cutoff of 3% and 5cm). The horizontal axis represents predicted risk of metastases by models and the vertical axis represents the actually observed results.



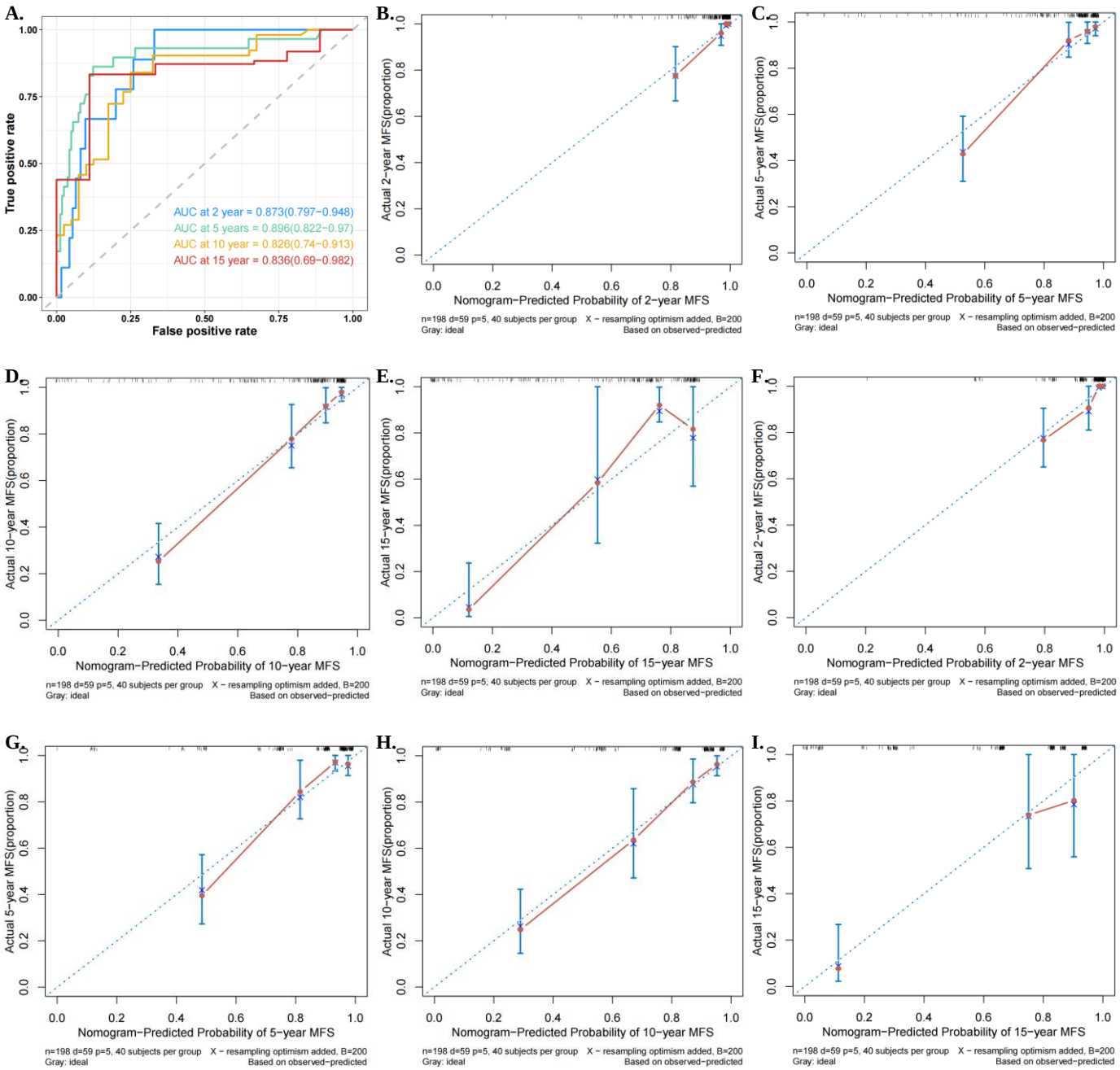
The Supplemental Figure 7. Two examples on how to use the nomogram to predict metastasis of PPGLs. **A.** In the example 1, the patient carry *SDHB* pathogenic germline mutation and her tumor is 10.0 cm assessed by contrast-enhanced CT, whose FFPE tissue showed negative IHC staining of both S-100 and ATRX and Ki-67 index of 10%. According to the nomogram, after summing up points of each variable (marked by red points), the total point reaches 278 and its predictive probability of metastasis is 99.9%. Actually, this patient develop metastases at 2rd year after surgery. **B.** In the example 2, the patient don't carry *SDHB* mutations. Her tumor is 4.6cm but showed Ki-67 of 5% and negative IHC staining of both ATRX and S-100 on FFPE tissue. According to the nomogram, after summing up points of each variable (marked by red points), the total point reaches 145 and its predictive probability of metastasis is 75.0%. Actually, this patient develop metastases at 4th year after surgery.



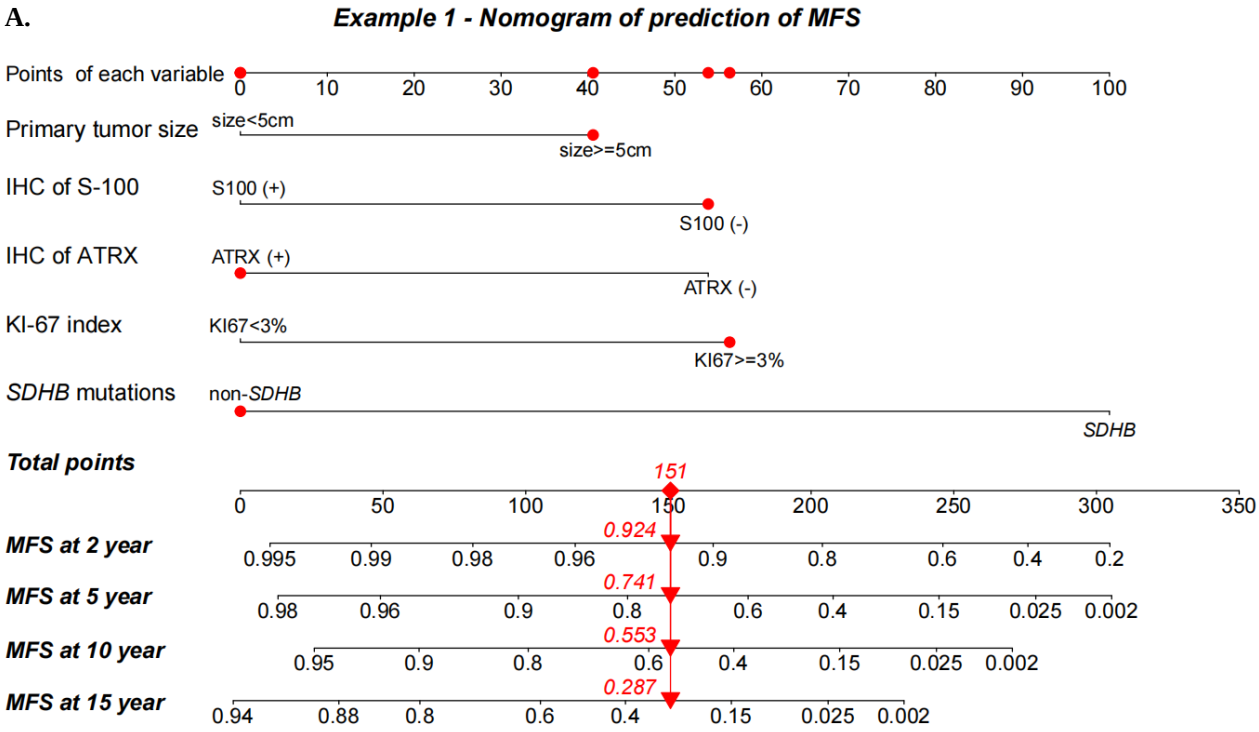
The Supplemental Figure 8. The ROC curve of logit model 2 (KI-67 index and tumor size as categorical variables with the cutoff of 3% and 5cm) in predicting metastasis of 107 patients with PHEOs showed an AUC of 0.854 (95% CI: 0.766-0.942).

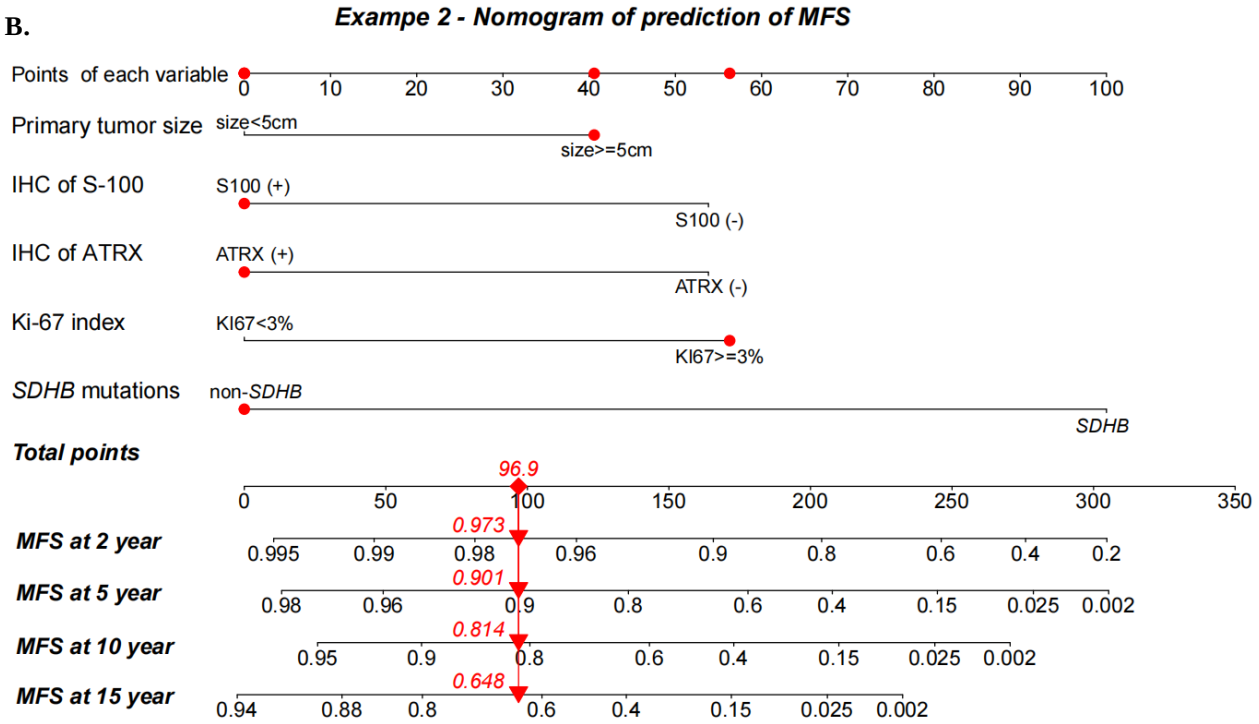


The Supplemental Figure 9. Survival curve of metastasis-free survival (MFS) **A.** between patients with age of onset younger than 37.5 years and older than 37.5 years (P=0.110) and **B.** between adrenal tumors and extra-adrenal tumors (P=0.160).

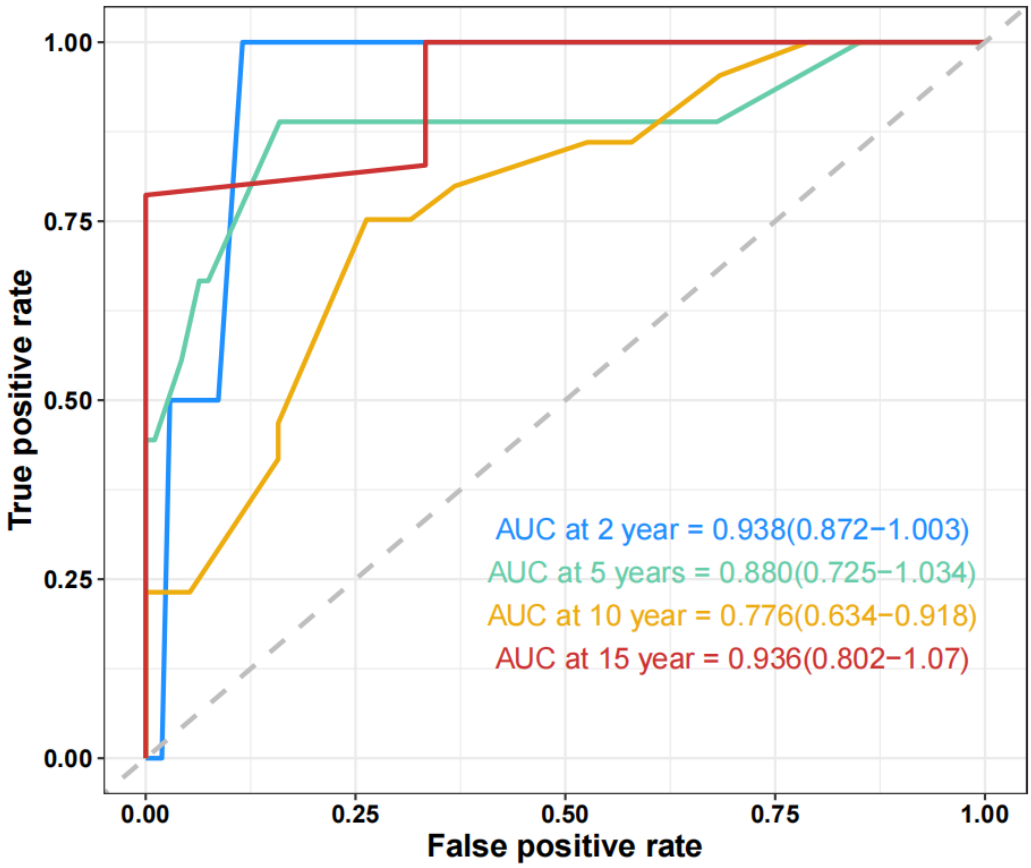


The Supplemental Figure 10. **A.** The ROC curve and AUC of Cox model 1 (with both tumor size and KI-67 index continuous variables). The calibration curve of Cox model 1 in predicting the probability of metastasis-free survival (MFS) at **B.** 2, **C.** 5, **D.** 10 and **E.** 15 year after surgery and the calibration curve of Cox model 2 (in which both tumor size and KI-67 index were categorical variables with the threshold of 5cm and 3%, respectively) in predicting MFS at **F.** 2, **G.** 5, **H.** 10 and **I.** 15 year after surgery.





The Supplemental Figure 11. Two examples on how to use the nomogram to predict MFS of PPGLs. **A.** In the example 1, the patient don't carry *SDHB* pathogenic germline mutation and his tumor is 8.4 cm assessed by contrast-enhanced CT, whose FFPE tissue showed negative IHC staining of S-100 but positive staining of ATRX and Ki-67 index of 10%. According to the nomogram, after summing up points of each variable (marked by red points), the total point reaches 151 and its predictive metastasis-free survival (MFS) at 2 year, 5 year, 10 year and 15 year after surgery were 92.4%, 74.1%, 55.3% and 28.7%, respectively. Actually, this patients develop metastases at 12th year after surgery. **B.** In the example 2, the patient don't carry *SDHB* mutations. Her tumor is 5.2 cm but showed Ki-67 of 4% and positive IHC of both ATRX and S-100 on FFPE tissue. According to the nomogram, after summing up points of each variable (marked by red points), the total point reaches 96.9 and its predictive metastasis-free survival (MFS) at 2 year, 5 year, 10 year and 15 year after surgery were 97.3%, 90.1%, 81.4% and 64.8% respectively. Actually, this patients don't develop metastases during the nine years after surgery.



The Supplemental Figure 12. The ROC curve and AUC of Cox model 2 (with both tumor size and KI-67 index categorical variables) in predicting 2-year-, 5-year-, 10-year- and 15-year-MFS after surgery in 107 patients with pheochromocytomas (PHEOs).