Supplemental Figure 1.
(**A**) Principal component analysis (PCA) of all GIST specimens (top) and only *KIT*, *PDGFRA*, and *SDH*-deficient specimens (bottom) as calculated by DESeq2 for R (n=75, clinicopathologic characteristics are available in Supplemental Table 1).

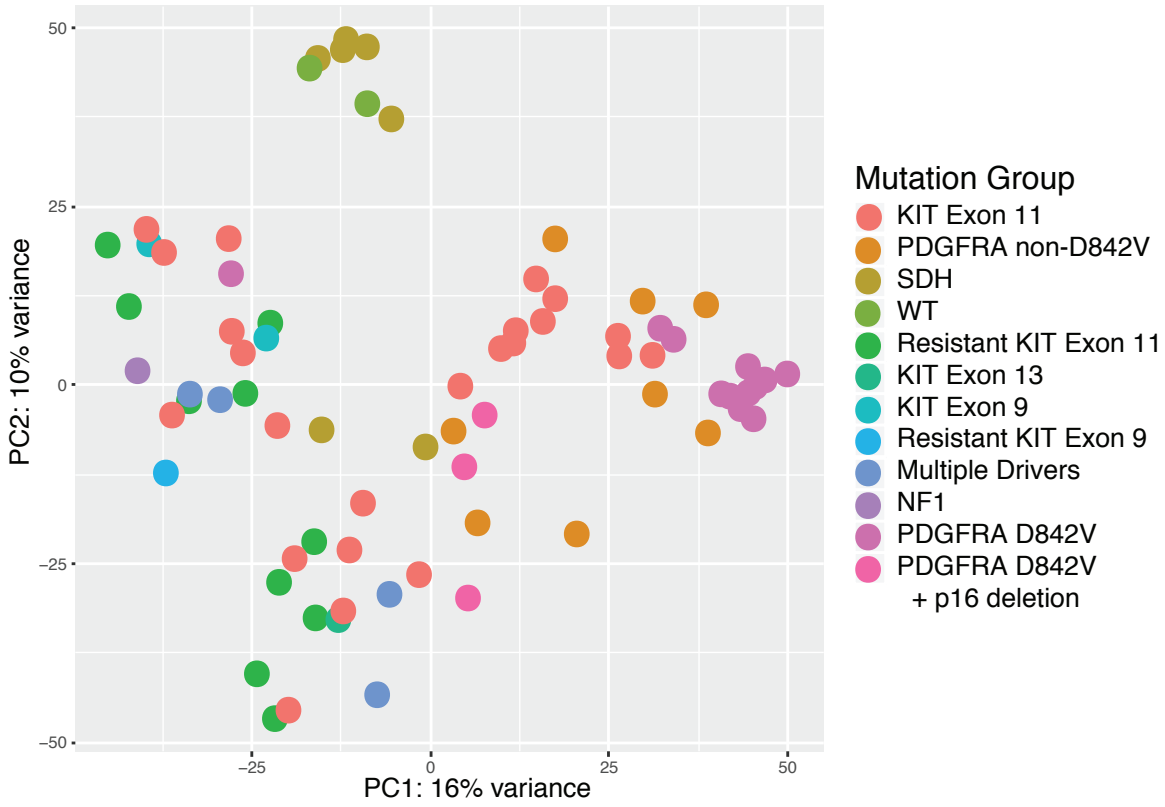
Supplemental Figure 2.
(**A**) (top) ESTIMATE and (bottom) Cyt scores by mitotic rate (left) and tumor sizes (middle and right) in all *KIT* and *PDGFRA*-mutant GISTs (n=61). (**B**) (top) ESTIMATE and (bottom) Cyt scores by mitotic rate (left) and tumor sizes (middle and right) in UPG *KIT* and *PDGFRA*-mutant GISTs (n=22). (**C**) ESTIMATE scores by mitotic rate in (left) UPG *KIT* and (right) UPG *PDGFRA*-mutant GISTs. High mitotic rate = $\geq$5 mitoses/hpf. Low mitotic rate = <5 mitoses/hpf. UPG = untreated, primary, gastric. *p<0.05, t-test. Bars, median.

Supplemental Figure 3.
(**A**) Demonstration of overfitting. On the left, using all 117 immune features to develop the random forest model on the All *KIT* vs. All *PDGFRA* training set (n=50) results in a 72.7% accuracy (red font) on the testing set (n=11). Decreasing the number of features included to 10, 8, and 6 results in an improvement in model accuracy on the testing set to 72.7%, 81.8%, and 90.9% respectively. (**B**) Retrained All *KIT* vs. All *PDGFRA* model with the top 6 features identified in Figure 6A excluded. (Left) Random forest modeling with 5-fold cross-validation of *KIT* and *PDGFRA*-mutant GIST specimens was performed. Training set created by partitioning 80% (n=50) of *KIT* and *PDGFRA* samples from Supplemental Table 3. Confusion matrix (middle) indicates assessment of model fit to training set. (Left) Predictive capacity of model on remaining *KIT* and *PDGFRA*-mutant GIST testing set (n=11), showing decreased classifier performance to 72.7% (red). Accuracy, sensitivity, specificity, and p-value [Acc >No Information Rate] of models are shown, as calculated by caret package for R.

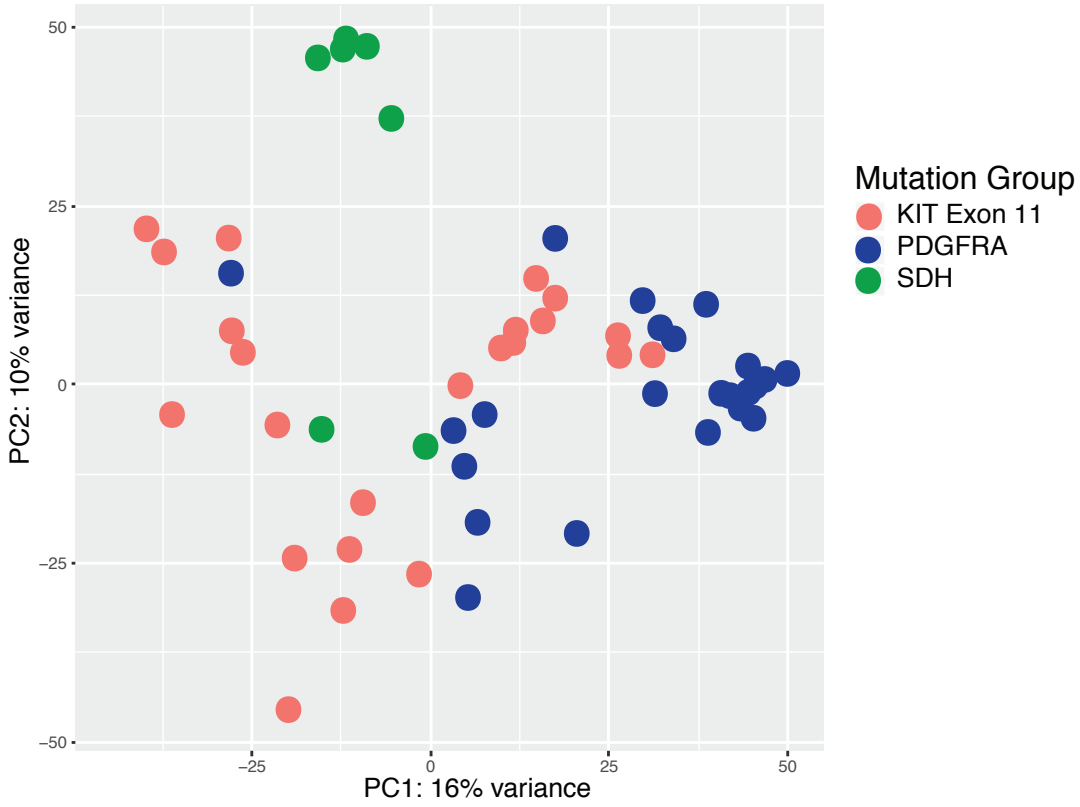
Supplemental Figure 4.
(**A**) ESTIMATE and Cyt scores in *PDGFRA*-mutant GIST samples that were correctly classified as *PDGFRA*-mutant (n=14) and incorrectly classified as *KIT*-mutant (n=6) by our All *KIT* vs. All *PDGFRA*-mutant random forest model (Figure 6A-C). (**B**) Distribution of top 6 features identified by random forest modeling in *KIT*-mutant tumors correctly classified as *KIT* and incorrectly classified as *PDGFRA* by our All *KIT* and All *PDGFRA*-mutant random forest model.

Supplemental Figure 5.
Western blot showing PD-L1 protein expression correlates with PD-L1 mRNA expression calculated by DESeq2. Human GIST numbers and mutation status are shown. KIT = *KIT*-mutant, SDHD = *SDH*-deficient.

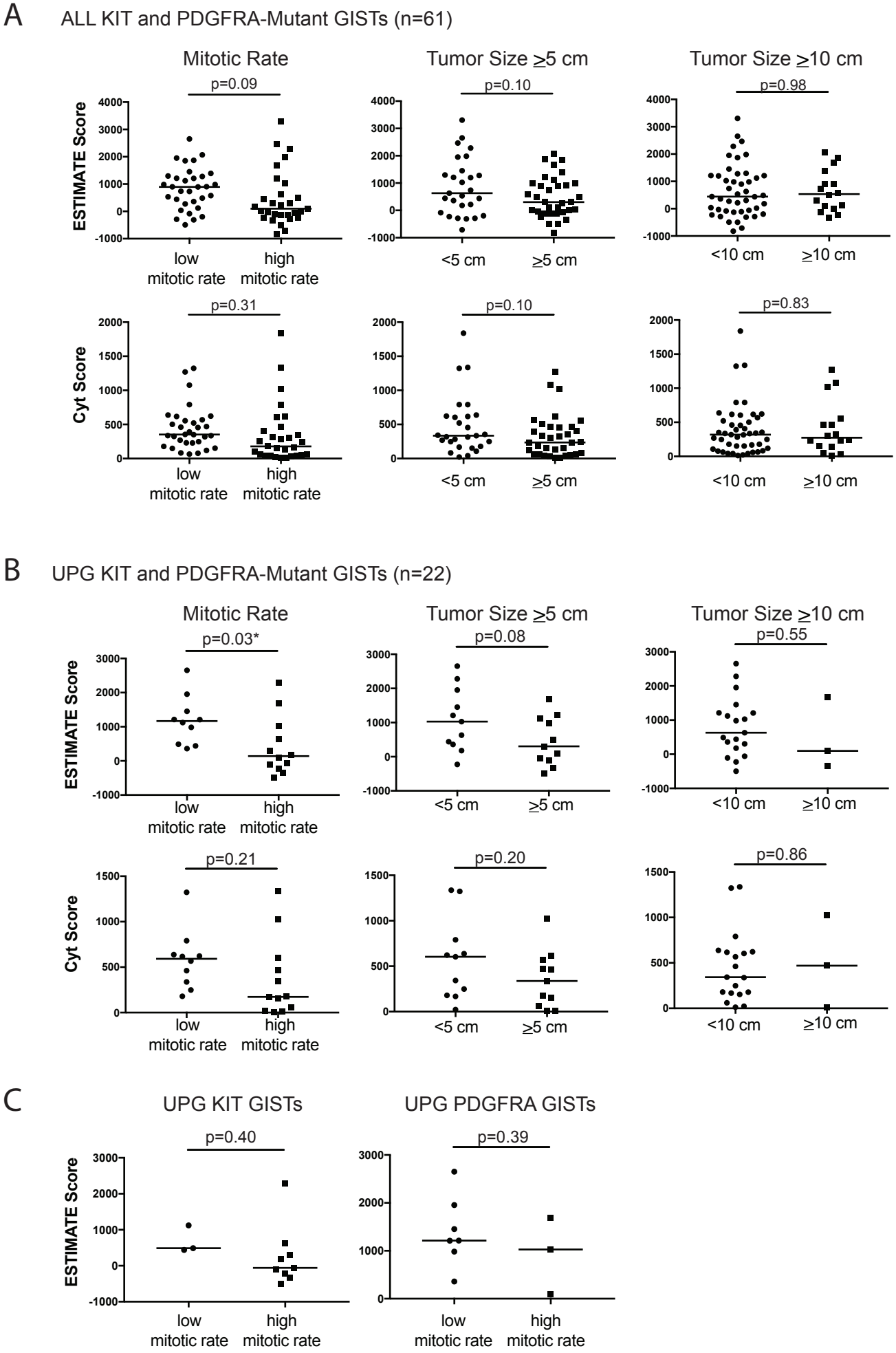
Supplemental Figure 1



Only KIT, PDGFRA, and SDH shown for clarity



Supplemental Figure 2



Supplemental Figure 3

A

Increasing Model Performance with Fewer Model Features
(Prevention of Overfitting)

117 Feature Model

Testing Set Actual

Predicted	ALL KIT	ALL PDGFRA
ALL KIT	7	3
ALL PDGFRA	0	1

Accuracy: 72.7%
95% CI: [39.7-94.0]
NIR = 63.6%
p-value [Acc > NIR] : 0.39
Sensitivity: 25%
Specificity: 100%

10 Feature Model

Testing Set Actual

Predicted	ALL KIT	ALL PDGFRA
ALL KIT	5	1
ALL PDGFRA	2	3

Accuracy: 72.7%
95% CI: [39.7-94.0]
NIR = 63.6%
p-value [Acc > NIR]: 0.39
Sensitivity: 75%
Specificity: 71.4%

8 Feature Model

Testing Set Actual

Predicted	ALL KIT	ALL PDGFRA
ALL KIT	6	1
ALL PDGFRA	1	3

Accuracy: 81.8%
95% CI: [48.2-97.7]
NIR = 63.6%
p-value [Acc > NIR] : 0.18
Sensitivity: 75%
Specificity: 85.7%

6 Feature Model

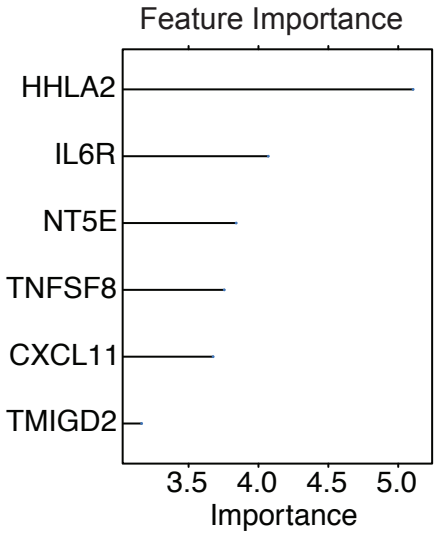
Testing Set Actual

Predicted	ALL KIT	ALL PDGFRA
ALL KIT	6	0
ALL PDGFRA	1	4

Accuracy: 90.9%
95% CI: [58.7-99.8]
NIR = 63.6%
p-value [Acc > NIR]: 0.05
Sensitivity: 100%
Specificity: 85.7%

B

Retrained All KIT vs. All PDGFRA Model with Top 6 Features Excluded



Predicted

Actual	ALL KIT	ALL PDGFRA
ALL KIT	26	4
ALL PDGFRA	7	13

OOB Estimate of Error: 22%

Predictive Capacity

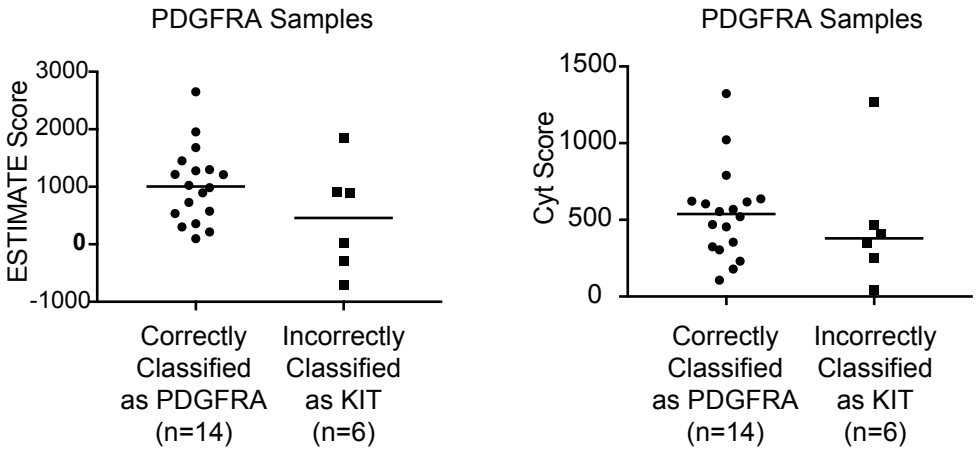
Testing Set Actual

Predicted	ALL KIT	ALL PDGFRA
ALL KIT	6	2
ALL PDGFRA	1	2

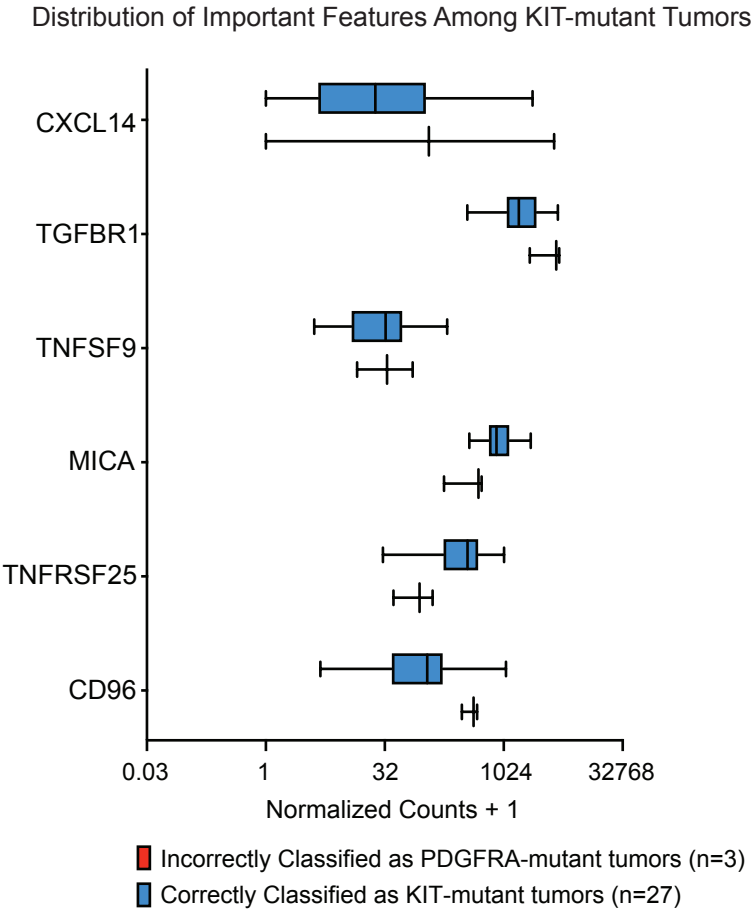
Accuracy: 72.7%
95% CI: [39.0-94.0]
NIR = 63.6%
p-value [Acc > NIR] : 0.39
Sensitivity: 50%
Specificity: 85.7%

Supplemental Figure 4

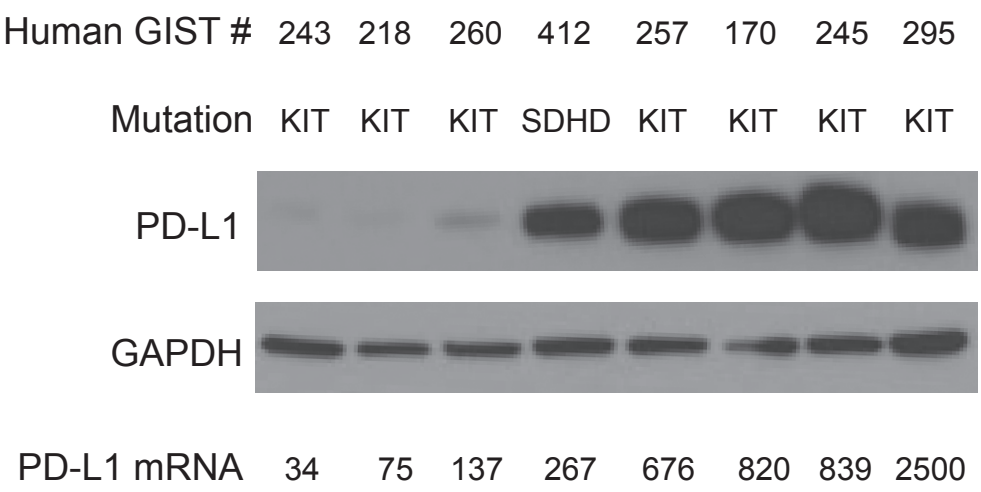
A

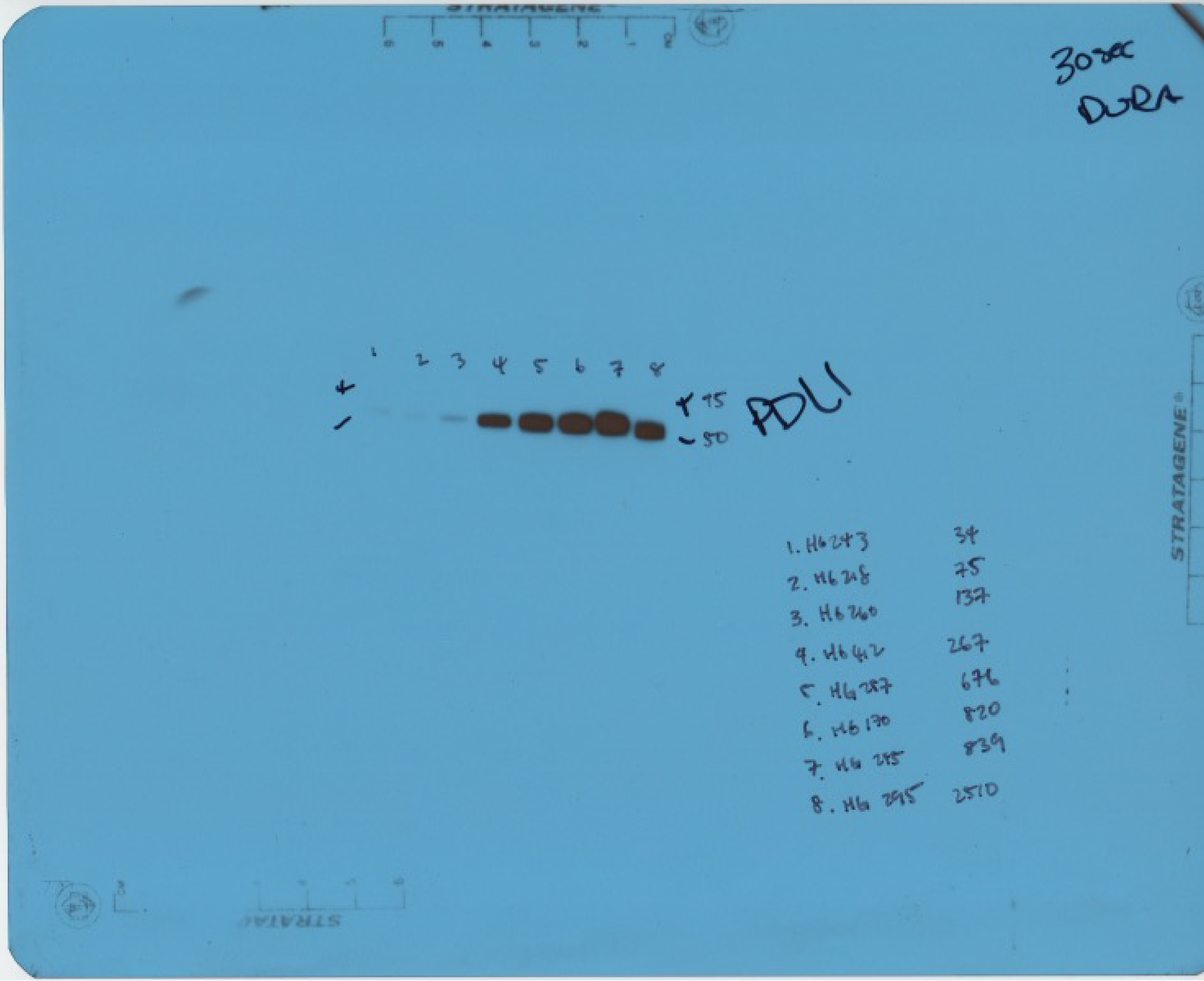


B



Supplemental Figure 5

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DURA
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75
50
PDI1
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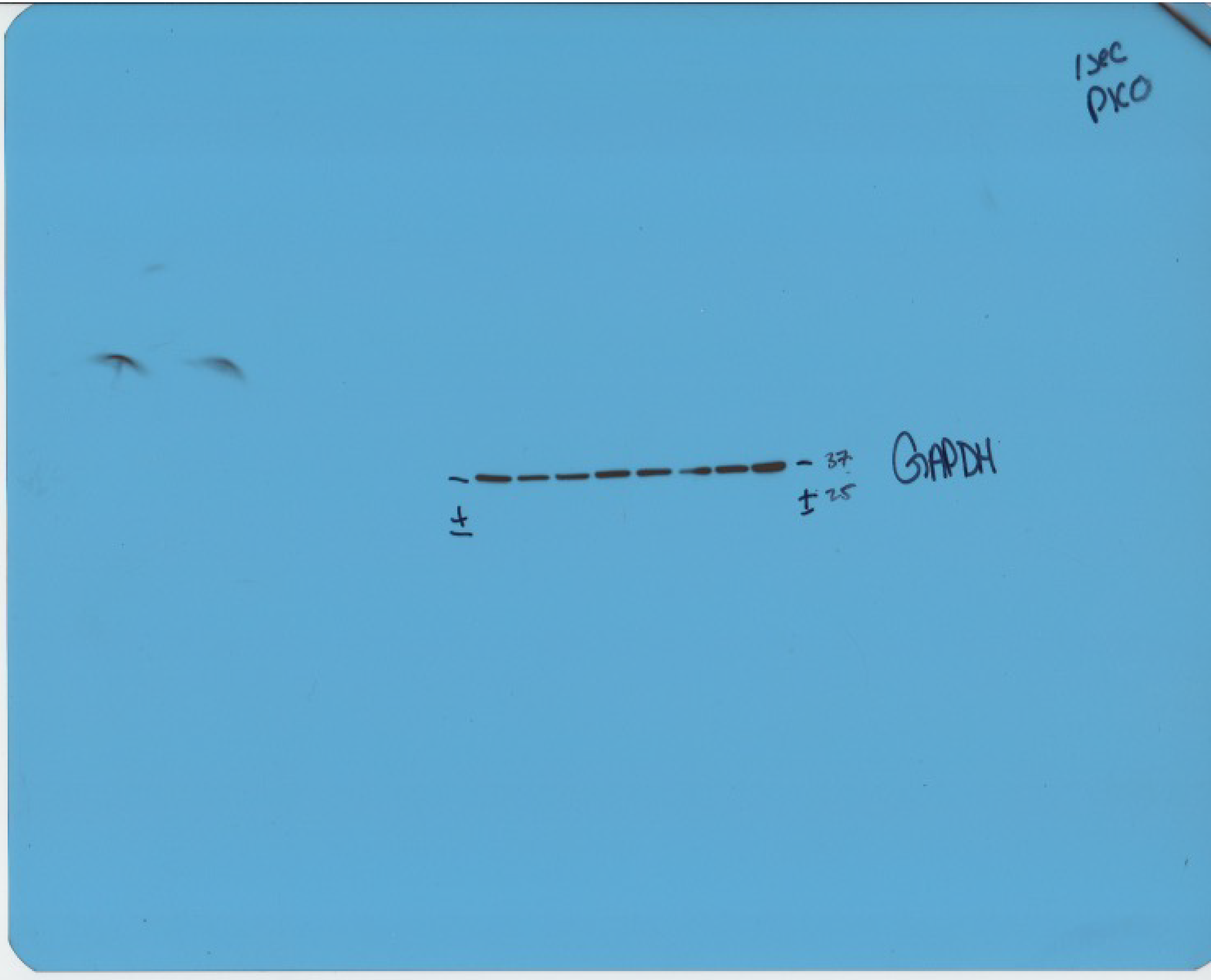
2. H6248 75
3. H6260 137
4. H6412 267
5. H6287 676
6. H6170 820
7. H6 285 839
8. H6 295 2510
STRATAGENE


1sec
pico
GAPDH
37
25