

SUPPLEMENTAL FIGURE LEDENDS

Figure S1. Model generation of protein location (related to Figure 1A). i) Generation of static single protein features (S). Nine kinds of S_i (AA , $diAA$, $gapAA$, three kinds of $chemAA$, $pseuAA$, $Motif$, and GO) are generated for each protein P_i based on its sequence, chemical properties, motifs and functions. ii) Generation of network features N^D and L^D for model generation using known interactions ($D=1,2$). Each N^D is generated using the S features of proteins within network distance D of the target, with all edges having the same weight (here, denoted by the Representative Network I^R). Each L^D is generated using weighted locations of network neighbors using pair-location conditional probabilities (**Methods**). iii) Model generation for each location. The best combination of S , N and L features is selected for each location based on a forward approach with the DC-kNN classifier.

Figure S2. Effectiveness of network neighbors in location prediction. (A–D) The performance of subcellular location prediction using the static features N^D using **Motif** (A), **dAA** (B) and **pAA** (C) or locations L^D (D) of distance D neighbors, respectively. Performance (y-axis) is calculated based on accuracy. Three cases are considered using i) only protein-protein interaction (PPI) partners, ii) only partners that have high Gene Expression (GE) correlation, and iii) those features together. The x-axis is the radius of the network neighborhood D ; $D=0$ means only static single protein features were used. A DCKNN classifier was used.

Figure S3. Result of forward feature set selection using a DCKNN in model generation. Regardless of condition, we selected feasible feature sets for location prediction using a DCKNN classifier. The mapped 5252 known locations of proteins based on gene ontology (GO) terms were used as a gold-standard positive training set for finding a feasible feature set of each location. As a negative training set, the 54159 remaining locations for these same annotated proteins were used. We selected the feature set showing the highest AUC value for each location. The selected feature sets were also used for the prediction of condition-dependent location without rerunning in order to reduce over-fitting. AUC: Area Under the ROC curve.

Figure S4. Principal component analysis (PCA) of gene expressions across the three conditions including normal brain (black) and low-grade (red) and high-grade (blue) gliomas. The numbers begin with GSE and GPL are the identifications of previous studies or microarray platforms, respectively. In this analysis only fully filled expressions across the conditions are used. The result of PCA with PC1 vs. PC1 (A), PC1 vs. PC3 (B), and PC2 vs. PC3 (C). PC: Principal Component.

Figure S5. Distribution of possibility degrees on positive and negative training locations. To assess the significance of all predicted condition-specific locations (**Table S1**), we used the 5252 known locations of proteins in gene ontology (GO) terms as a gold-standard positive training set. As a negative training set, we used the 54159 remaining locations for these same annotated proteins. Proteins with no annotations in GO did not contribute to the positive or

negative sets. Here, x-axis is a possibility degree and y-axis is the number of locations predicted as “present”.

Figure S6. Cell images of SMAD4 using confocal microscopy. (A) Conditional Location Map (CML) of SMAD4. By prediction, SMAD4 has the high signal at nucleus only in normal brain (the second column), and low (the third) and high (the fourth) grades of glioma, not others including cytosol, even though previously known locations of SMAD4 are both nucleus and cytosol (the filled white squares in the first column). The color of the heatmaps indicates predicted possibility degree and “H” indicates the location with the highest degree of possibility degree within each condition. The first column marks in white all previously known subcellular locations as recorded in the gene ontology cellular component database. (B) Confocal images of SMAD4 using two different location markers for nucleus (NU; blue) and cytosol (CY; red) in normal brain tissues. The cyan color indicates high overlap between SMAD4 and the nucleus. (C) The distribution of locations of the first network neighbors of SMAD4. For protein interactions we used previously reported protein-protein interactions performed under any kind of condition. The number of neighbors annotated with each distinct location is shown in parentheses. The widths of each link are proportional to the summed expression coherence score. Here, only location-mapped neighbours of SMAD4 were used. AT: actin, CC: cell cortex, CT: centrosome, CY: cytosol, ER: endoplasmic reticulum, GL: Golgi apparatus, LS: lysosome, MT: mitochondrion, NO: nucleolus, NU: nucleus, PX: peroxisome, PM: plasma membrane, VO: vacuole. Scale bar, 5µm.

Figure S7. Specificity validation of antibodies for location markers. (A) The western blot experiments for the specificity test of antibodies for the five locations tested in this study were performed. The antibodies labeled specifically to the corresponding locations. (B) The specificity tests for individual cellular locations were performed in normal brain primary cells. The markers for different fractionation were shown specifically on each cellular sub-fractionation (β-actin: beta actin for cytosol, SPA: sodium potassium ATPase for plasma membrane, CAL: calreticulin for endoplasmic reticulum, and RPII: RNA polymerase II for nucleus). CY: cytoplasm, PM: plasma membrane, ER: endoplasmic reticulum, and NU: nucleus.

Figure S8. Specificity validation of antibodies for proteins. The western blot experiments for the specificity validation of antibodies for the proteins used in this study were performed using normal or glioma primary cells. The tested antibodies labeled specifically to the corresponding antigens.

Figure S9. Cell images of NKX2-2 using confocal microscopy in low and high grades of glioma tissues. Confocal images of NKX2-2 using two different location markers for endoplasmic reticulum (ER; red) and nucleus (NU; blue) in low (A) and high (B) grades of glioma tissues. The yellow color indicates high overlap between NKX2-2 and the ER markers. Scale bar, 5µm.

Figure S10. Result of cellular sub-fractionation and western blot for the nucleus location of GSK3B in glioma (low-grade) primary cells. B-A: beta actin for a cytosol marker, RPII: RNA polymerase II for nucleus.

Figure S11. Performance of validated 100 condition-specific locations for each compartment. The performance of the validated 100 locations in brain normal and low and high grades of glioma (shown in **Figure 3I**) was calculated using several different kinds of measure for each compartment. CY: cytosol; ER: endoplasmic reticulum; GL: Golgi apparatus; NU: nucleus; PM: plasma membrane.

Figure S12. Comparison of the performance of 100 validated condition-specific locations with 10,000 random guesses. To assess the significance of predicted condition-specific locations, we compared the performance of the 100 validated locations shown in **Figure 3I** with 10,000 random guesses. For each random guess, we selected the same numbers of positive locations (i.e. 22) as the predicted locations. The distributions of the 10,000 random guesses are shown with different colors corresponding to three kinds of performance measures (precision: green, recall: blue and accuracy: black). Here, precision (also described as positive predictive value) is the fraction of predicted locations that are true, while recall (also referred to as sensitivity) is the fraction of true locations that are predicted. Accuracy is the proportion of true results (both true positive locations and true negative locations) in the 100 locations. Arrows indicate the performance of our method using the 100 validated predicted condition-specific locations (from **Figure 3I**).

Figure S13. Performance comparison between real and permuted expressions in glioma-specific location prediction. To check how sensitive the predicted condition-specific location to expressions, we predicted the condition-specific locations using 50 permuted expression sets. The performance was shown in black. For the expressions we used the real ones used here. Blue means the performance of predicted locations with real expression profiles. For the golden-data set we used the 100 validated locations shown in **Figure 3I**.

Figure S14. Performance comparison between different kinds of cross-validation in condition-specific location prediction. Four different kinds of cross-validation approach (leave-two-out in red, 3-fold in brown, 5-fold in blue, and 10-fold in black) were shown. For the golden-data set we used the 100 validated locations shown in **Figure 3I**.

Figure S15. Null distribution for computing significance of protein mislocation. To assess the significance of the predicted mislocations, we calculated the significance of the difference of possibility degrees between normal brain and glioma based on random chance. To randomize the data, the set of possibility degrees assigned to each (condition, protein) pair was permuted and mapped back to the intact (non-randomized) protein-protein interaction network. These permuted values were then used to generate differences in possibility degrees for each (protein, location) pair. These differences were aggregated over 1000 permuted data sets to generate the probability distribution function as shown.

Figure S16. Brighter tissue images of the mislocation of KIF13A. The confocal images of KIF13A using two different location markers for Golgi apparatus (GL; red) and for nucleus (NU; blue) in normal brain (*Normal*) and glioma (*Glioma*) tissues. Here, green color is used for KIF13A. Yellow means overlap between KIF13A and the GL and cyan means between KIF13A and the nucleus. Scale bar, 50µm.

Figure S17. Confocal images for the mislocation of KIF13A using the three kinds of primary cells. (A–C) The confocal images of KIF13A using two different location markers for Golgi apparatus (GL; red) and for nucleus (NU; blue) in the three conditions including normal brain (*Normal*; A), and low-grade (*Low*; B), and high-grade (*High*; C) glioma primary cells. Here, green color is used for KIF13A. Yellow means overlap between KIF13A and the GL and cyan means between KIF13A and the nucleus. Scale bar, 5µm.

Figure S18. Brighter tissue images of the mislocation of RNF138. The confocal images of RNF138 using two different location markers for endoplasmic reticulum (ER; red) and for nucleus (NU; blue) in normal brain (*Normal*) and glioma (*Glioma*) tissues. Here, green color is used for RNF138. Yellow means overlap between RNF138 and the ER and cyan means between RNF138 and the nucleus. Scale bar, 50µm.

Figure S19. Validation of RNF138 mislocation using the three kinds of tissue. (A–F) The confocal images for RNF138 are shown versus endoplasmic reticulum (ER) or nucleus (NU) location markers (rows) using the three kinds of tissue (columns; *Normal* brain, and *Low* and *High* grade of glioma). Here, green color is used for RNF138, red is for ER, and blue is for NU. Yellow in (A) means overlap between RNF138 and the ER marker. Cyan in (D) and (F) means overlap between RNF138 and the NU markers. ‘o’ denotes a high overlap between the protein and location markers and ‘×’ denotes lack of overlap. Scale bar, 5µm.

Figure S20. Brighter tissue images of the mislocation of TLX3. The confocal images of TLX3 using two different location markers for nucleus (NU; blue) and for endoplasmic reticulum (ER; red) in normal brain (*Normal*) and glioma (*Glioma*) tissues. Here, green color is used for TLX3. Yellow means overlap between TLX3 and the ER and cyan means between TLX3 and the nucleus. Scale bar, 50µm.

Figure S21. Validation of TLX3 mislocation using the three kinds of tissue. (A–F) The confocal images for TLX3 are shown versus nucleus (NU) or endoplasmic reticulum (ER) location markers (rows) using the three kinds of tissue (columns; *Normal* brain, and *Low* and *High* grade of glioma). Here, green color is used for TLX3, red is for ER, and blue is for NU. Cyan in (A) means overlap between TLX3 and the NU markers. Yellow in (D) and (F) means overlap between TLX3 and the ER marker. ‘o’ denotes a high overlap between the protein and location markers and ‘×’ denotes lack of overlap. Scale bar, 5µm.

Figure S22. Validation of ATIC mislocation. (A) By prediction, ATIC has the highest signal in the cytosol (CY) under *Normal* brain, but nucleus (NU) in gliomas. The color of the heatmaps indicates predicted possibility degree and “H” indicates the location with the highest degree of possibility degree within each condition. (B–G) The confocal images for ATIC are shown versus CY or NU location markers (rows) using the three kinds of tissue (columns). Here, green color is used for ATIC, red is for CY, and blue is for NU. Yellow in (B) means overlap between ATIC and the CY marker. Cyan in (E) and (G) means overlap between ATIC and the NU markers. In the bottom right of each panel in the third column, ‘o’ denotes an observed overlap between the protein and location markers and ‘x’ denotes lack of overlap. Scale bar, 5µm. (H–W) The multiple cell images for ATIC are shown versus CY or NU location markers (rows) using normal brain (upper two rows) and glioma (lower two rows) tissues. The last column ‘*Magnified*’ is for the 14X magnification of the original images of single cells which are indicated by the red rectangles in the first three columns. Yellow in (J) and (K) means overlap between ATIC and the CY marker. Cyan in (V) and (W) means overlap between ATIC and the NU marker. Scale bar, 100µm. (X) The fraction of co-localized cells using >50,000 normal brain and glioma primary cells with CY and NU markers. Samples from four normal and five glioma subjects were used. The fraction numbers were automatically counted by using a high content screening method (Thermo Fisher Scientific Inc.). (Y) The result of cellular sub-fractionation and western blot for the mislocation of ATIC using normal brain or glioma primary cells. AT: actin, CC: cell cortex, CT: centrosome, CY: cytosol, ER: endoplasmic reticulum, GL: Golgi apparatus, LS: lysosome, MT: mitochondrion, NO: nucleolus, NU: nucleus, PX: peroxisome, PM: plasma membrane, VO: vacuole. B–A: beta actin for a cytosol marker, RPII: RNA polymerase II for nucleus.

Figure S23. Validation of DIP2A mislocation. (A) By prediction, DIP2A has the highest signal in the nucleus (NU) under *Normal* brain, but endoplasmic reticulum (ER) in *Low-* and *High-*grade gliomas. The color of the heatmaps indicates predicted possibility degree and “H” indicates the location with the highest degree of possibility degree within each condition. (B–G) The confocal images for DIP2A are shown versus NU or ER location markers (rows) using the three kinds of tissue (columns). Here, green color is used for DIP2A, red is for ER, and blue is for NU. Cyan in (B) means overlap between DIP2A and the NU marker. Yellow in (E) and (G) means overlap between DIP2A and the ER markers. In the bottom right of each panel in the third column, ‘o’ denotes an observed overlap between the protein and location markers and ‘x’ denotes lack of overlap. Scale bar, 5µm. (H–W) The multiple cell images for DIP2A are shown versus NU or ER location markers (rows) using normal brain (upper two rows) and glioma (lower two rows) tissues. The last column ‘*Magnified*’ is for the 14X magnification of the original images of single cells which are indicated by the red rectangles in the first three columns. Cyan in (J) and (K) means overlap between DIP2A and the NU marker. Yellow in (V) and (W) means overlap between DIP2A and the ER marker. Scale bar, 100µm. (X) The fraction of co-localized cells using >50,000 normal brain and glioma primary cells with NU and ER markers. Samples from four normal and five glioma subjects were used. The fraction numbers were automatically counted by using a high content screening method (Thermo Fisher Scientific Inc.). (Y) The result of cellular sub-fractionation and western blot for the mislocation of DIP2A using normal brain or glioma primary cells.

AT: actin, CC: cell cortex, CT: centrosome, CY: cytosol, ER: endoplasmic reticulum, GL: Golgi apparatus, LS: lysosome, MT: mitochondrion, NO: nucleolus, NU: nucleus, PX: peroxisome, PM: plasma membrane, VO: vacuole. CRT: calreticulin for endoplasmic reticulum and RPII: RNA polymerase II for nucleus.

Figure S24. Validation of DLX2 mislocation. (A) By prediction, DLX2 has the highest signal in the endoplasmic reticulum (ER) under *Normal* brain, but nucleus (NU) in *Low-* and *High-grade* gliomas. The color of the heatmaps indicates predicted possibility degree and “H” indicates the location with the highest degree of possibility degree within each condition. (B–G) The confocal images for DLX2 are shown versus ER or NU location markers (rows) using the three kinds of tissue (columns). Here, green color is used for DLX2, red is for ER, and blue is for NU. Yellow in (B) means overlap between DLX2 and the ER marker. Cyan in (E) and (G) means overlap between DLX2 and the NU markers. In the bottom right of each panel in the third column, ‘o’ denotes an observed overlap between the protein and location markers and ‘x’ denotes lack of overlap. Scale bar, 5µm. (H–W) The multiple cell images for DLX2 are shown versus ER or NU location markers (rows) using normal brain (upper two rows) and glioma (lower two rows) tissues. The last column ‘*Magnified*’ is for the 14X magnification of the original images of single cells which are indicated by the red rectangles in the first three columns. Yellow in (J) and (K) means overlap between DLX2 and the ER marker. Cyan in (V) and (W) means overlap between DLX2 and the NU marker. Scale bar, 100µm. (X) The fraction of co-localized cells using >50,000 normal brain and glioma primary cells with ER and NU markers. Samples from four normal and five glioma subjects were used. The fraction numbers were automatically counted by using a high content screening method (Thermo Fisher Scientific Inc.). (Y) The result of cellular sub-fractionation and western blot for the mislocation of DLX2 using normal brain or glioma primary cells. AT: actin, CC: cell cortex, CT: centrosome, CY: cytosol, ER: endoplasmic reticulum, GL: Golgi apparatus, LS: lysosome, MT: mitochondrion, NO: nucleolus, NU: nucleus, PX: peroxisome, PM: plasma membrane, VO: vacuole. CRT: calreticulin for endoplasmic reticulum and RPII: RNA polymerase II for nucleus.

Figure S25. Validation of TBX19 mislocation. (A) By prediction, TBX19 has the highest signal in the endoplasmic reticulum (ER) under *Normal* brain, but nucleus (NU) in *Low-* and *High-grade* gliomas. The color of the heatmaps indicates predicted possibility degree and “H” indicates the location with the highest degree of possibility degree within each condition. (B–G) The confocal images for TBX19 are shown versus ER or NU location markers (rows) using the three kinds of tissue (columns). Here, green color is used for TBX19, red is for ER, and blue is for NU. Yellow in (B) means overlap between TBX19 and the ER markers. Cyan in (E) and (G) means overlap between TBX19 and the NU markers. In the bottom right of each panel in the third column, ‘o’ denotes an observed overlap between the protein and location markers and ‘x’ denotes lack of overlap. Scale bar, 5µm. (H–W) The multiple cell images for TBX19 are shown versus ER or NU location markers (rows) using normal brain (upper two rows) and glioma (lower two rows) tissues. The last column ‘*Magnified*’ is for the 14X magnification of the original images of single cells which are indicated by the red rectangles in the first three columns. Yellow in (J) and (K) means overlap between TBX19 and the ER marker. Cyan in (V) and (W) means overlap between TBX19 and the NU marker. Scale bar, 100µm. (X) The fraction of co-localized cells using >50,000 normal brain and

glioma primary cells with ER and NU markers. Samples from four normal and five glioma subjects were used. The fraction numbers were automatically counted by using a high content screening method (Thermo Fisher Scientific Inc.). (Y) The result of cellular sub-fractionation and western blot for the mislocation of TBX19 using normal brain or glioma primary cells. AT: actin, CC: cell cortex, CT: centrosome, CY: cytosol, ER: endoplasmic reticulum, GL: Golgi apparatus, LS: lysosome, MT: mitochondrion, NO: nucleolus, NU: nucleus, PX: peroxisome, PM: plasma membrane, VO: vacuole. CRT: calrecitulin for endoplasmic reticulum and RPII: RNA polymerase II for nucleus.

Figure S26. Validation of HPS5 location. (A) By prediction, HPS5 has the highest signal at the plasma membrane (PM) under brain *Normal*, but endoplasmic reticulum (ER) under *Low*- and *High*-grade gliomas. The color of the heatmaps indicates predicted possibility degree and “H” indicates the location with the highest degree of possibility degree within each condition. (B–Q) The multiple cell images for HPS5 are shown versus PM or ER location markers (rows) using normal brain (upper two rows) and glioma (lower two rows) tissues. The last column ‘*Magnified*’ is for the 14X magnification of the original images of single cells which are indicated by the red rectangles in the first three columns. Yellow in (D–E, L–M) or (H–I, P–Q) means overlap between HPS5 and the PM or the ER markers, respectively. Scale bar, 100µm. (R) The fraction of co-localized cells using >50,000 normal brain and glioma primary cells with two different location markers. Samples from four normal and five glioma subjects were used. The fraction numbers were automatically counted by using a high content screening method (Thermo Fisher Scientific Inc.). (S) The result of cellular sub-fractionation and western blot for the location of HPS5 using normal brain or glioma primary cells. AT: actin, CC: cell cortex, CT: centrosome, CY: cytosol, ER: endoplasmic reticulum, GL: Golgi apparatus, LS: lysosome, MT: mitochondrion, NO: nucleolus, NU: nucleus, PX: peroxisome, PM: plasma membrane, VO: vacuole. SPA: sodium potassium ATPase for plasma membrane and CRT: calrecitulin for endoplasmic reticulum.

Figure S27. Validation of negatives for mislocation in glioma. (A) The Conditional Location Maps of CDH2 (plasma membrane: PM), HSF1 (nucleus: NU), MAGED1 (cytosol: CY) and PAX6 (nucleus: NU). These proteins were predicted to reside at the same locations regardless of glioma outbreak. The color of the heatmaps indicates predicted possibility degree and “H” indicates the location with the highest degree of possibility degree within each condition. (B–E) The confocal images for CDH2 (with PM markers using *Normal* brain and *Low*- and *High*-grade glioma tissues), HSF1 (with NUs), MAGED1 (with CYs) and PAX6 (with NUs) are shown. Here, green color is used for the proteins, red for the PM or CY markers, and blue for the NU markers. Yellow in the third rows in (B) and (D) means high overlap between CDH2 and the PM markers (B) or between MAGED1 and the CY markers (D) in normal brain and low- and high-grade glioma tissues, respectively. Cyan in the third rows in (C) and (E) means high overlap between HSF1 and the NU markers (C) or between PAX6 and the NU markers (E) in normal brain and low- and high-grade glioma tissues, respectively. Scale bar, 10µm. (F) The result of cellular sub-fractionation and western blot for the location of CDH2, HSF1, MAGED1 and PAX6 using normal brain or glioma primary cells. Red: predicted locations.

Figure S28. Validation of STAT3 mislocation. (A) By prediction, STAT3 has the highest signal in nucleus (NU) across all the three conditions including *Normal* brain and *Low-* and *High-*grade gliomas. The color of the heatmaps indicates predicted possibility degree and “H” indicates the location with the highest degree of possibility degree within each condition. (B–Q) The multiple cell images for STAT3 are shown versus plasma membrane (PM) or NU location markers (rows) using normal brain (upper two rows) and glioma (lower two rows) tissues. The last column ‘*Magnified*’ is for the 14X magnification of the original images of single cells which are indicated by the red rectangles in the first three columns. Yellow in (D) and (E) means overlap between STAT3 and the PM marker. Cyan in (P) and (Q) means overlap between STAT3 and the NU marker. Scale bar, 100µm. (R) The fraction of co-localized cells using >50,000 normal brain and glioma primary cells with PM and NU markers. Samples from four normal and five glioma subjects were used. The fraction numbers were automatically counted by using a high content screening method (Thermo Fisher Scientific Inc.). (S) The confocal images for STAT3 are shown versus PM or NU location markers (column) using the three kinds of tissue. Here, green color is used for STAT3, red is for PM, and blue is for NU. Yellow means overlap between STAT3 and the PM marker. Cyan means overlap between STAT3 and the nucleus marker. Scale bar, 10µm. (T) The result of cellular sub-fractionation and western blot for the mislocation of STAT3 using normal brain or glioma primary cells. AT: actin, CC: cell cortex, CT: centrosome, CY: cytosol, ER: endoplasmic reticulum, GL: Golgi apparatus, LS: lysosome, MT: mitochondrion, NO: nucleolus, NU: nucleus, PX: peroxisome, PM: plasma membrane, VO: vacuole. SPA: sodium potassium ATPase for plasma membrane and RPII: RNA polymerase II for nucleus.

Figure S29. Validation of AGAP1 mislocation. (A) By prediction, AGAP1 has the highest signal in the cytosol (CY) under *Normal* brain, but Golgi apparatus (GL) in *Low-* and *High-*grade gliomas. The color of the heatmaps indicates predicted possibility degree and “H” indicates the location with the highest degree of possibility degree within each condition. (B–G) The confocal images for AGAP1 are shown versus CY or GL location markers (rows) using the three kinds of tissue (columns). Here, green color is used for AGAP1, red is for CY or GL. Yellow in (B) means overlap between AGAP1 and the CY marker. Yellow in (E) and (G) means overlap between AGAP1 and the GL marker. In the bottom right of each panel in the third column, ‘o’ denotes an observed overlap between the protein and location markers and ‘x’ denotes lack of overlap. Scale bar, 5µm. (H–W) The multiple cell images for AGAP1 are shown versus CY or GL location markers (rows) using normal brain (upper two rows) and glioma (lower two rows) tissues. The last column ‘*Magnified*’ is for the 14X magnification of the original images of single cells which are indicated by the red rectangles in the first three columns. Yellow in (J) and (K) means overlap between AGAP1 and the CY marker. Yellow in (V) and (W) means overlap between AGAP1 and the GL marker. Scale bar, 100µm. (X) The fraction of co-localized cells using >50,000 normal brain and glioma primary cells with CY and GL markers. Samples from four normal and five glioma subjects were used. The fraction numbers were automatically counted by using a high content screening method (Thermo Fisher Scientific Inc.).

Figure S30. Validation of CPB1 mislocation. (A) By prediction, CPB1 has the highest signal in the cytosol (CY) under *Normal* brain, but endoplasmic reticulum (ER) in *Low-* and *High-grade* gliomas. The color of the heatmaps indicates predicted possibility degree and “H” indicates the location with the highest degree of possibility degree within each condition. (B–G) The confocal images for CPB1 are shown versus CY or ER location markers (rows) using the three kinds of tissue (columns). Here, green color is used for CPB1 and red is for CY or ER. Yellow means overlap between CPB1 and the CY (in B) or CPB1 and the ER (in E or G), respectively. In the bottom right of each panel in the third column, ‘o’ denotes an observed overlap between the protein and location markers and ‘x’ denotes lack of overlap. Scale bar, 5µm. (H–W) The multiple cell images for CPB1 are shown versus CY or ER location markers (rows) using normal brain (upper two rows) and glioma (lower two rows) tissues. The last column ‘*Magnified*’ is for the 14X magnification of the original images of single cells which are indicated by the red rectangles in the first three columns. Yellow in (J) and (K) means overlap between CPB1 and the CY marker. Yellow in (V) and (W) means overlap between CPB1 and the ER marker. Scale bar, 100µm. (X) The fraction of co-localized cells using >50,000 normal brain and glioma primary cells with CY and ER markers. Samples from four normal and five glioma subjects were used. The fraction numbers were automatically counted by using a high content screening method (Thermo Fisher Scientific Inc.). (Y) The result of cellular sub-fractionation and western blot for the mislocation of CPB1 using normal brain or glioma primary cells. β-actin: beta actin for cytosol and CRT: calreticulin for endoplasmic reticulum.

Figure S31. Validation of NFRKB mislocation. (A) By prediction, NFRKB has the highest signal in the endoplasmic reticulum (ER) under *Normal* brain, but nucleus (NU) in *Low-* and *High-grade* gliomas. The color of the heatmaps indicates predicted possibility degree and “H” indicates the location with the highest degree of possibility degree within each condition. (B–G) The confocal images for NFRKB are shown versus ER or NU location markers (rows) using the three kinds of tissue (columns). Here, green color is used for NFRKB, red is for ER, and blue is for NU. Yellow in (B) means overlap between NFRKB and the ER marker. Cyan in (E) and (G) means overlap between NFRKB and the NU markers. In the bottom right of each panel in the third column, ‘o’ denotes an observed overlap between the protein and location markers and ‘x’ denotes lack of overlap. Scale bar, 5µm. (H–W) The multiple cell images for NFRKB are shown versus ER or NU location markers (rows) using normal brain (upper two rows) and glioma (lower two rows) tissues. The last column ‘*Magnified*’ is for the 14X magnification of the original images of single cells which are indicated by the red rectangles in the first three columns. Yellow in (J) and (K) means overlap between NFRKB and the ER marker. Cyan in (V) and (W) means overlap between NFRKB and the NU marker. Scale bar, 100µm. (X) The fraction of co-localized cells using >50,000 normal brain and glioma primary cells with ER and NU markers. Samples from four normal and five glioma subjects were used. The fraction numbers were automatically counted by using a high content screening method (Thermo Fisher Scientific Inc.). (Y) The result of cellular sub-fractionation and western blot for the mislocation of NFRKB using normal brain or glioma primary cells. CRT: calreticulin for endoplasmic reticulum and RPII: RNA polymerase II for nucleus.

Figure S32. Validation of ARHGEF15 mislocation. (A) By prediction, ARHGEF15 has the highest signal in the endoplasmic reticulum (ER) under *Normal* brain, but plasma membrane (PM) in *Low*- and *High*-grade gliomas. The color of the heatmaps indicates predicted possibility degree and “H” indicates the location with the highest degree of possibility degree within each condition. (B–G) The confocal images for ARHGEF15 are shown versus ER or PM location markers (rows) using the three kinds of tissue (columns). Here, green color is used for ARHGEF15 and red is for ER or PM. Yellow in (B) means overlap between ARHGEF15 and the ER marker. Yellow in (E) and (G) means overlap between ARHGEF15 and the PM markers. In the bottom right of each panel in the third column, ‘o’ denotes an observed overlap between the protein and location markers and ‘x’ denotes lack of overlap. Scale bar, 5 μ m. (H–W) The multiple cell images for ARHGEF15 are shown versus ER or PM location markers (rows) using normal brain (upper two rows) and glioma (lower two rows) tissues. The last column ‘*Magnified*’ is for the 14X magnification of the original images of single cells which are indicated by the red rectangles in the first three columns. Yellow in (J) and (K) means overlap between ARHGEF15 and the ER marker. Yellow in (V) and (W) means overlap between ARHGEF15 and the PM marker. Scale bar, 100 μ m. (X) The fraction of co-localized cells using >50,000 normal brain and glioma primary cells with ER and PM markers. Samples from four normal and five glioma subjects were used. The fraction numbers were automatically counted by using a high content screening method (Thermo Fisher Scientific Inc.). (Y) The result of cellular sub-fractionation and western blot for the mislocation of ARHGEF15 using normal brain or glioma primary cells. SPA: sodium potassium ATPase for plasma membrane and CRT: calreticulin for endoplasmic reticulum.

Figure S33. Validation of CLK2 mislocation. (A) By prediction, CLK2 has the highest signal in the endoplasmic reticulum (ER) under *Normal* brain, but nucleus (NU) in *Low*- and *High*-grade gliomas. The color of the heatmaps indicates predicted possibility degree and “H” indicates the location with the highest degree of possibility degree within each condition. (B–G) The confocal images for CLK2 are shown versus ER or NU location markers (rows) using the three kinds of tissue (columns). Here, green color is used for CLK2, red is for ER, and blue is for NU. Yellow in (B) means overlap between CLK2 and the ER marker. Cyan in (E) and (G) means overlap between CLK2 and the NU markers. In the bottom right of each panel in the third column, ‘o’ denotes an observed overlap between the protein and location markers and ‘x’ denotes lack of overlap. Scale bar, 5 μ m. (H–W) The multiple cell images for CLK2 are shown versus ER or NU location markers (rows) using normal brain (upper two rows) and glioma (lower two rows) tissues. The last column ‘*Magnified*’ is for the 14X magnification of the original images of single cells which are indicated by the red rectangles in the first three columns. Yellow in (J) and (K) means overlap between CLK2 and the ER marker. Cyan in (V) and (W) means overlap between CLK2 and the NU marker. Scale bar, 100 μ m. (X) The fraction of co-localized cells using >50,000 normal brain and glioma primary cells with ER and NU markers. Samples from four normal and five glioma subjects were used. The fraction numbers were automatically counted by using a high content screening method (Thermo Fisher Scientific Inc.). (Y) The result of cellular sub-fractionation and western blot for the mislocation of CLK2 using normal brain or glioma primary cells. CRT: calreticulin for endoplasmic reticulum and RPII: RNA polymerase II for nucleus.

Figure S34. Validation of SYT9 mislocation. (A) By prediction, SYT9 has the highest signal in the Golgi apparatus (GL) under *Normal* brain, but nucleus (NU) in *Low*- and *High*-grade gliomas. The color of the heatmaps indicates predicted possibility degree and “H” indicates the location with the highest degree of possibility degree within each condition. (B–G) The confocal images for SYT9 are shown versus GL or NU location markers (rows) using the three kinds of tissue (columns). Here, green color is used for SYT9, red is for GL, and blue is for NU. Yellow in (B) means overlap between SYT9 and the GL marker. Cyan in (E) and (G) means overlap between SYT9 and the NU markers. In the bottom right of each panel in the third column, ‘o’ denotes an observed overlap between the protein and location markers and ‘x’ denotes lack of overlap. Scale bar, 5µm. (H–W) The multiple cell images for SYT9 are shown versus GL or NU location markers (rows) using normal brain (upper two rows) and glioma (lower two rows) tissues. The last column ‘*Magnified*’ is for the 14X magnification of the original images of single cells which are indicated by the red rectangles in the first three columns. Yellow in (J) and (K) means overlap between SYT9 and the GL marker. Cyan in (V) and (W) means overlap between SYT9 and the NU marker. Scale bar, 100µm. (X) The fraction of co-localized cells using >50,000 normal brain and glioma primary cells with GL and NU markers. Samples from four normal and five glioma subjects were used. The fraction numbers were automatically counted by using a high content screening method (Thermo Fisher Scientific Inc.).

Figure S35. Distribution of predicted mislocations using wild-type expression data. (A–B) Distributions of predicted mislocations using 50 expression sets (A) and correctly predicted mislocations (B). Sixteen validated mislocations were used as controls. For wild-type expression, we used GSE7307 (>500 normal samples). Random was obtained by permutation of actual expression. Arrows indicate the results of real expression sets.

Figure S36. Confocal images of RET/PSPN/GFRA4 using primary cells. (A–C) The multiple cell merged images of GFRA4 (A), PSPN (B), or RET (C) are shown versus two location markers (PM and ER) in *Normal* brain or *Glioma* (high-grade) tissues. Here, green color is used for proteins (GFRA4, PSPN and RET) and red is for PM or ER. Yellow means overlap between proteins and the corresponding location markers. Scale bar, 100µm.

Figure S37. Number of blobs (or interactions) per cell between RET, PSPN and GFRA4 in brain normal, low- and high-grade of glioma tissues. Average number of “blobs” (spots or interactions) per cell for RET:PSPN, RET:GFRA4, or GFRA4:PSPN under the three conditions showing that the numbers of interacting pairs between RET:PSPN or RET:GFRA4 decreased dramatically, but that of GFRA4:PSPN increased during glioma progression. *Normal*: normal brain, *Low*: low-grade glioma, and *High*: high-grade glioma.

Figure S38. Protein expressions of RET, GFRA4, and PSPN in normal brain and glioma primary cells. High-grade glioma cells were used.

Figure S39. Confocal images of pSTAT3 using primary cells. The multiple cell images of pSTAT3 are shown with DAPI in *Normal* brain and high-grade *Glioma* primary cells with ('*siGFRA4*') or without *GFRA4* ('glioma') silencing. 'FKBP-FRB' indicates the redirection of GFRA4 to plasma membrane using a rapamycin technique. Here, green is for the pSTAT3 protein, blue is DAPI for a nucleus marker. Cyan indicates overlap between pSTAT3 and the nucleus marker. Scale bar, 100µm.

Figure S1

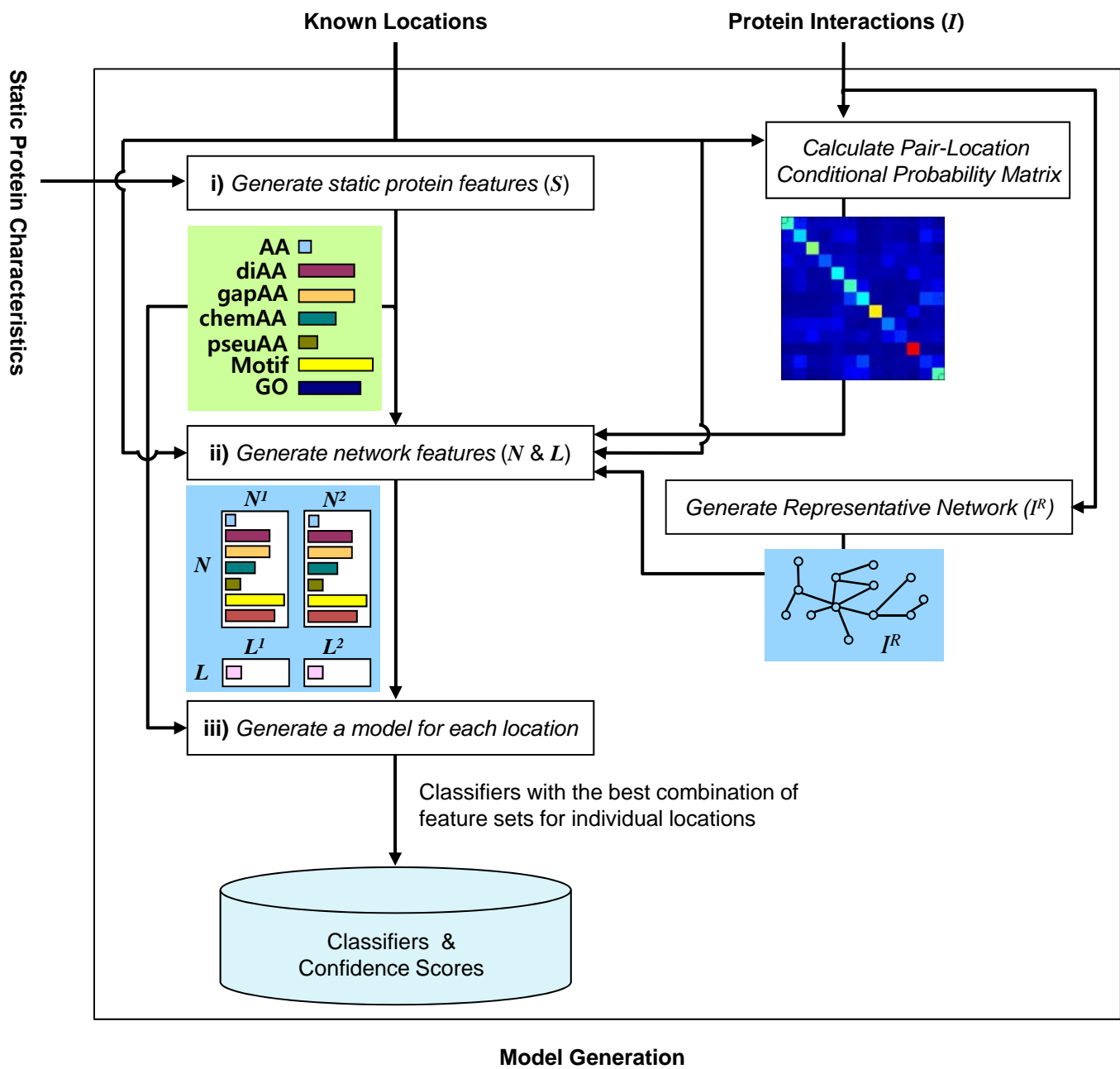


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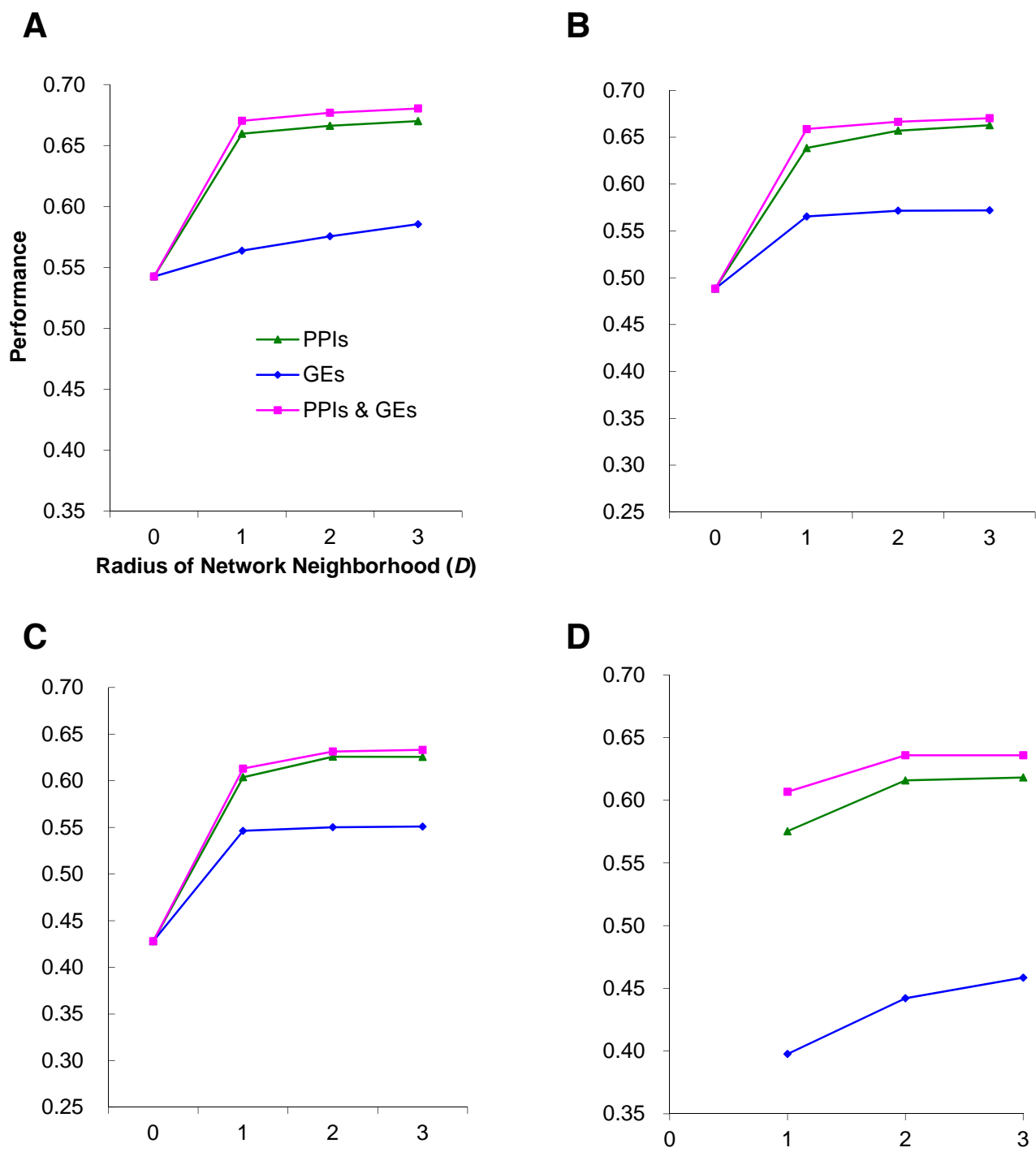


Figure S3

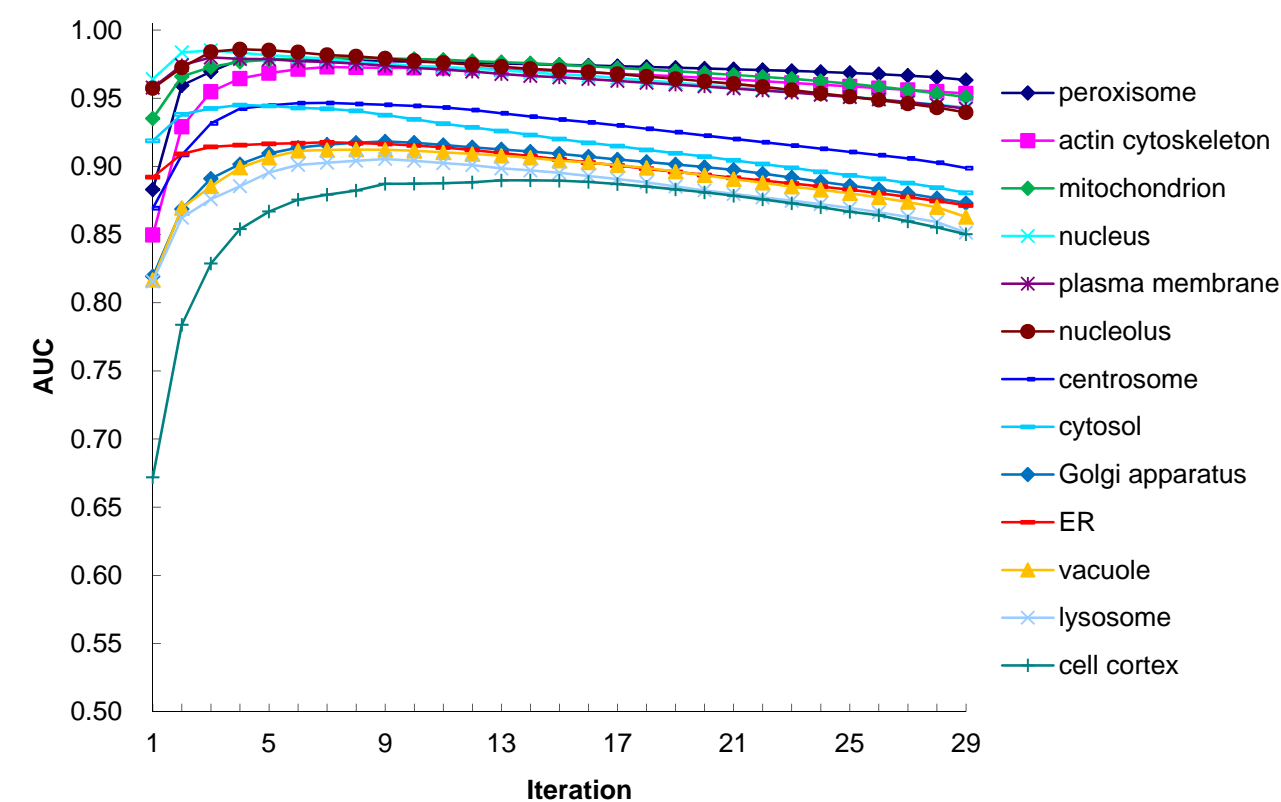


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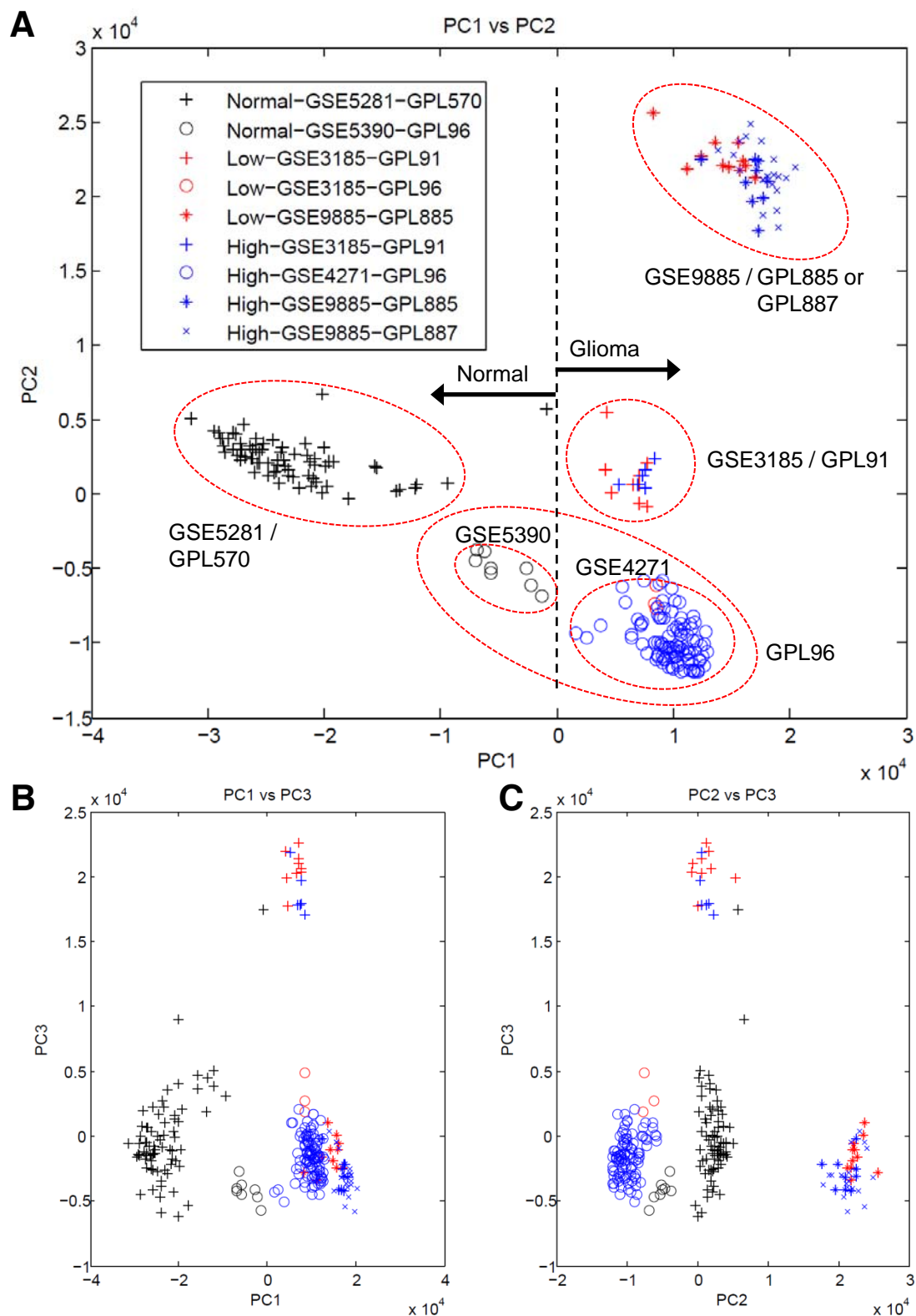


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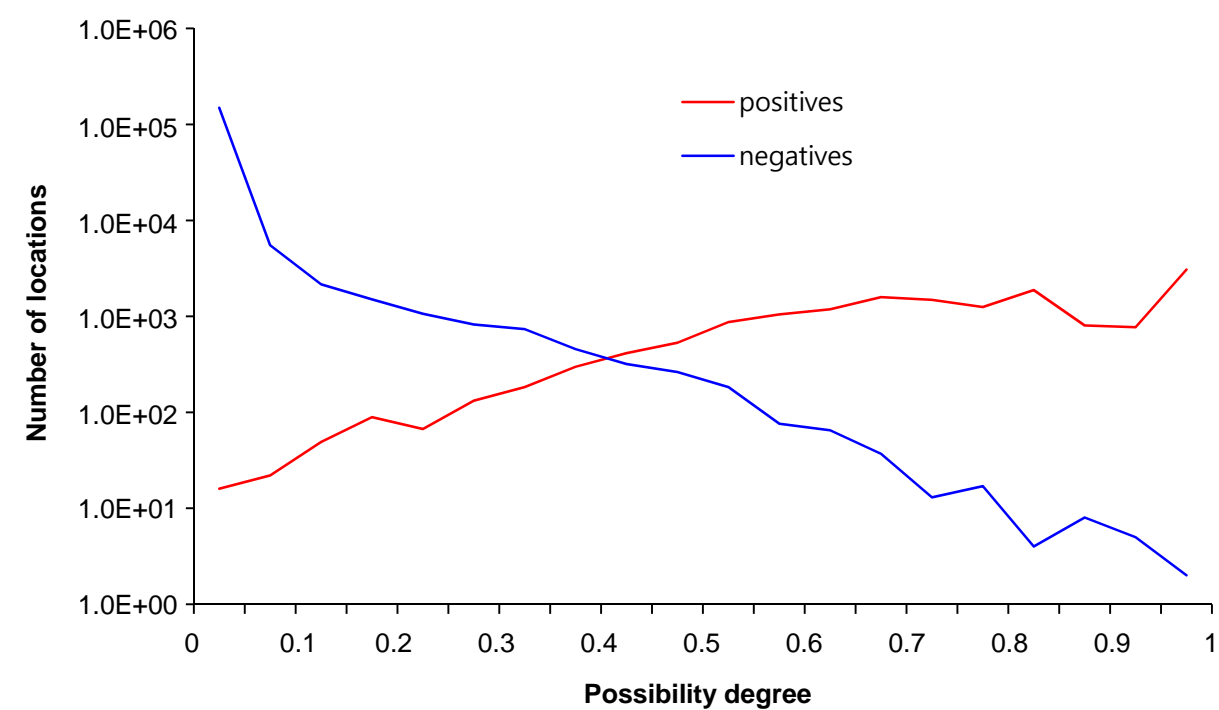


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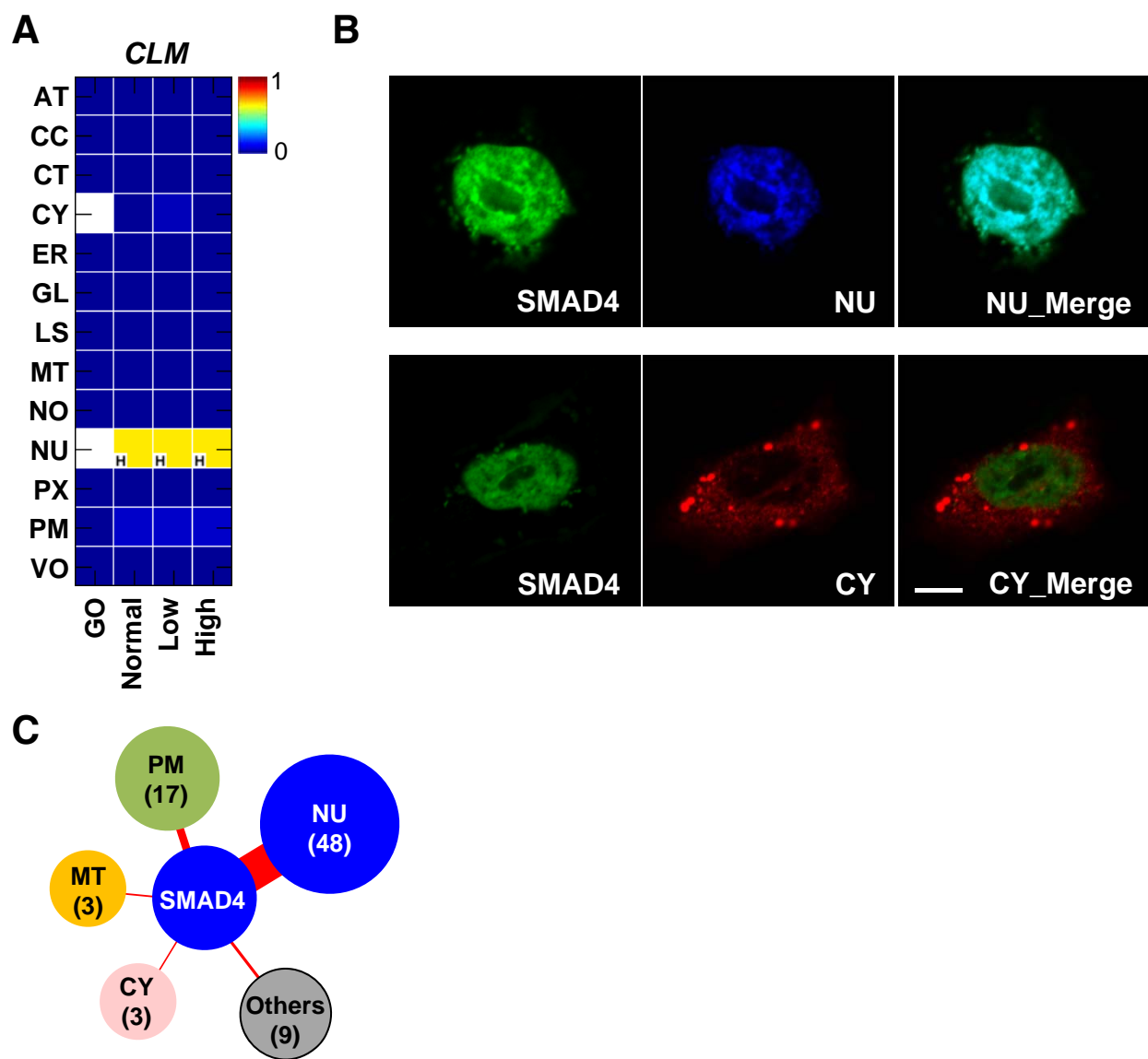


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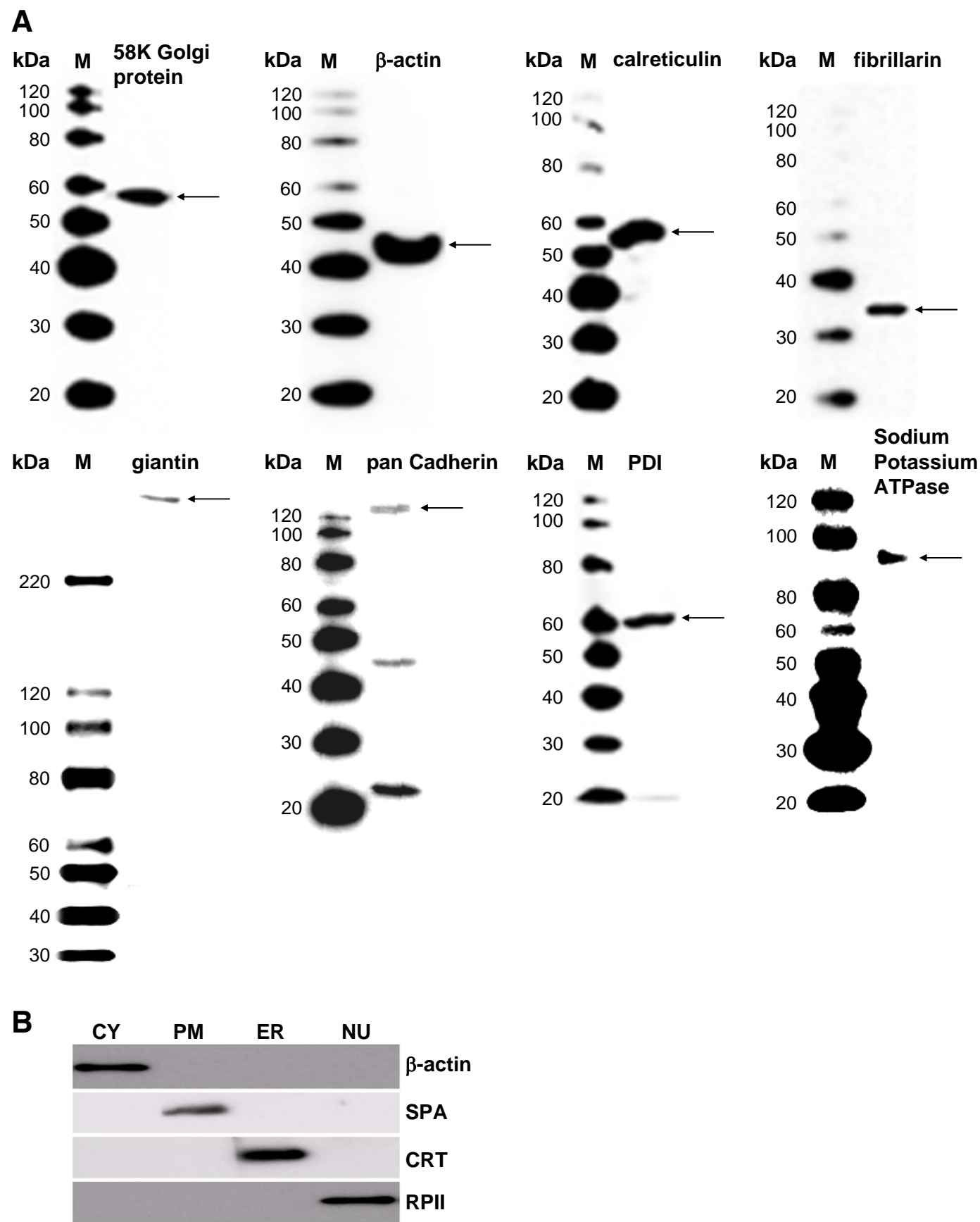


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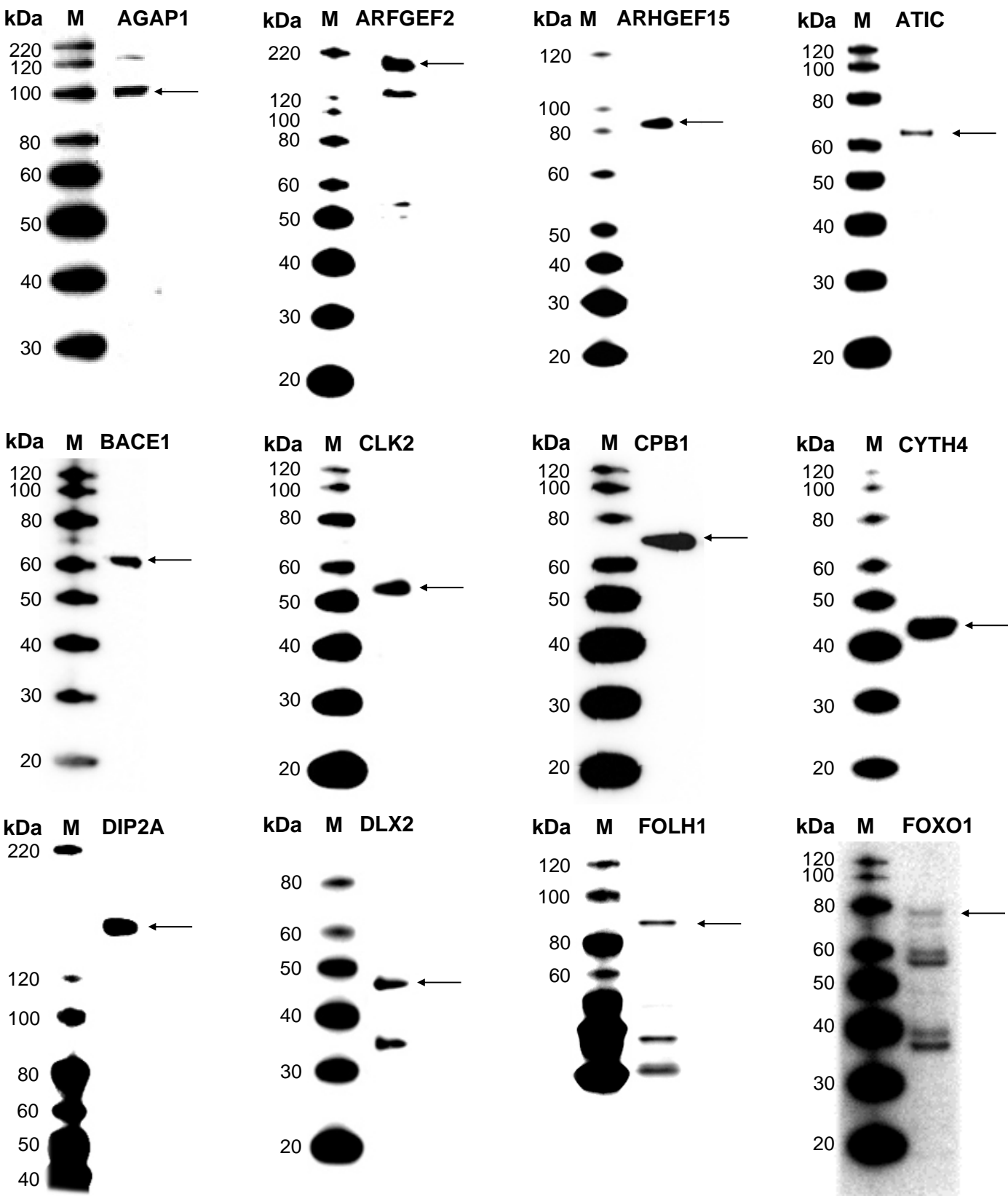


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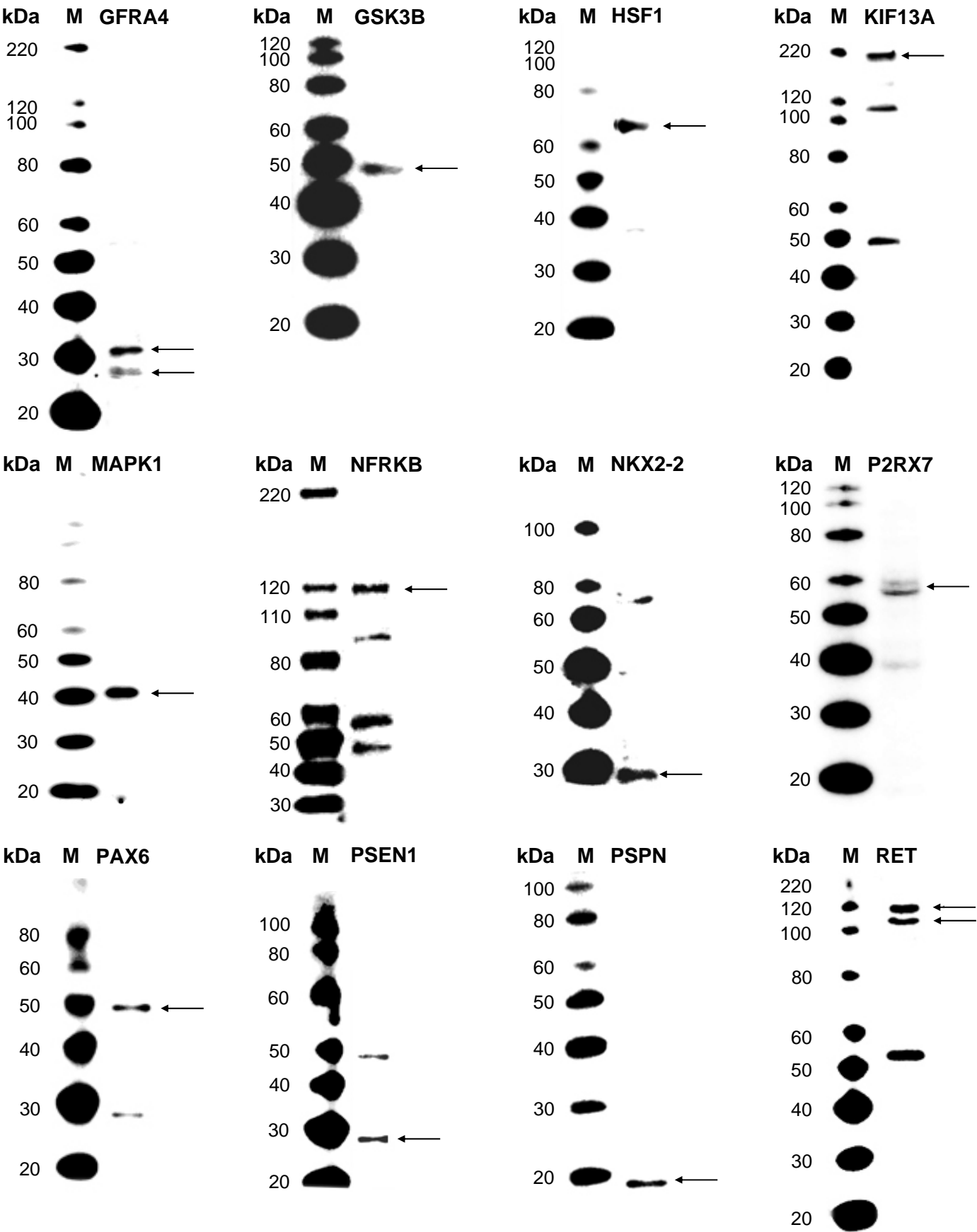


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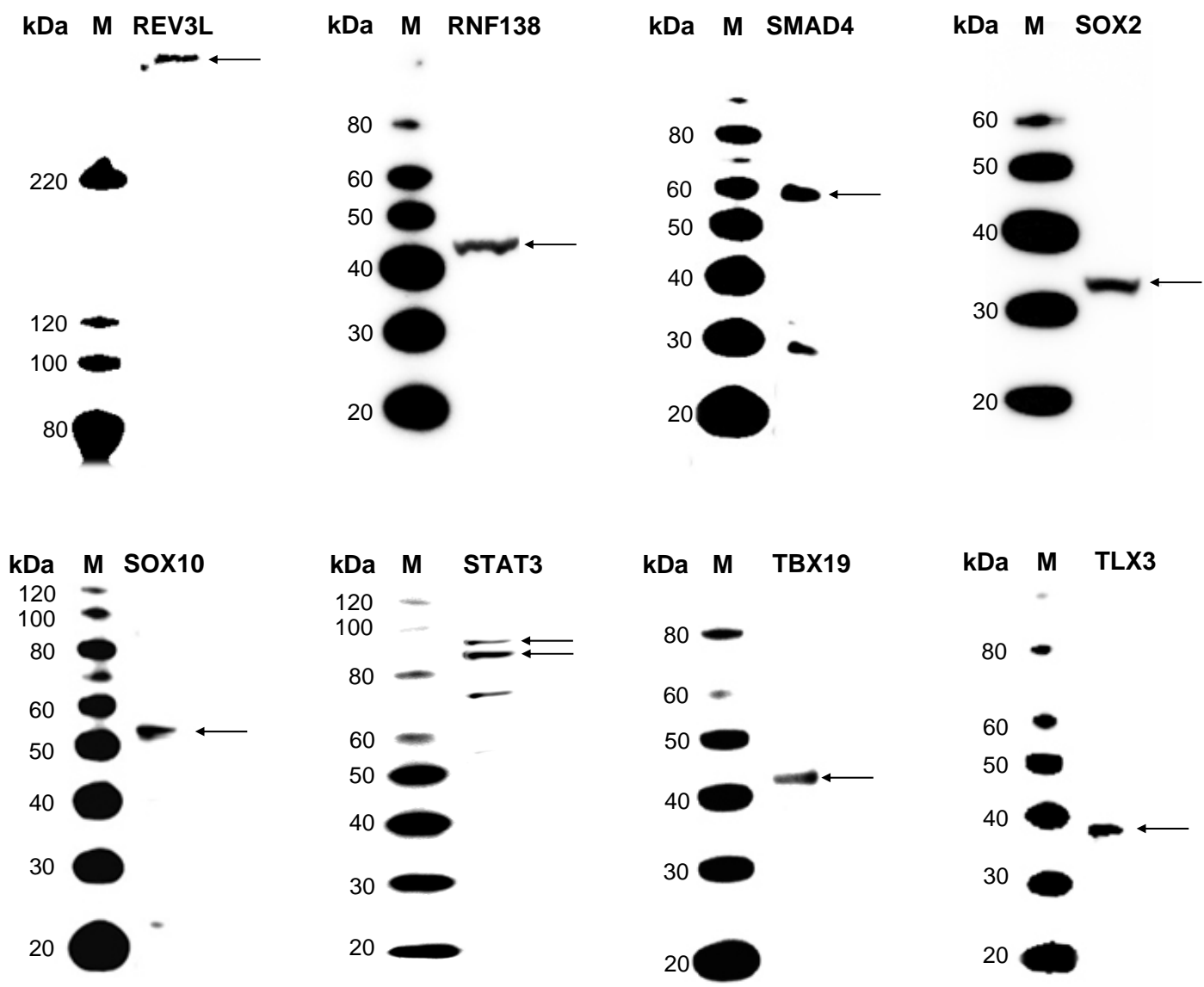


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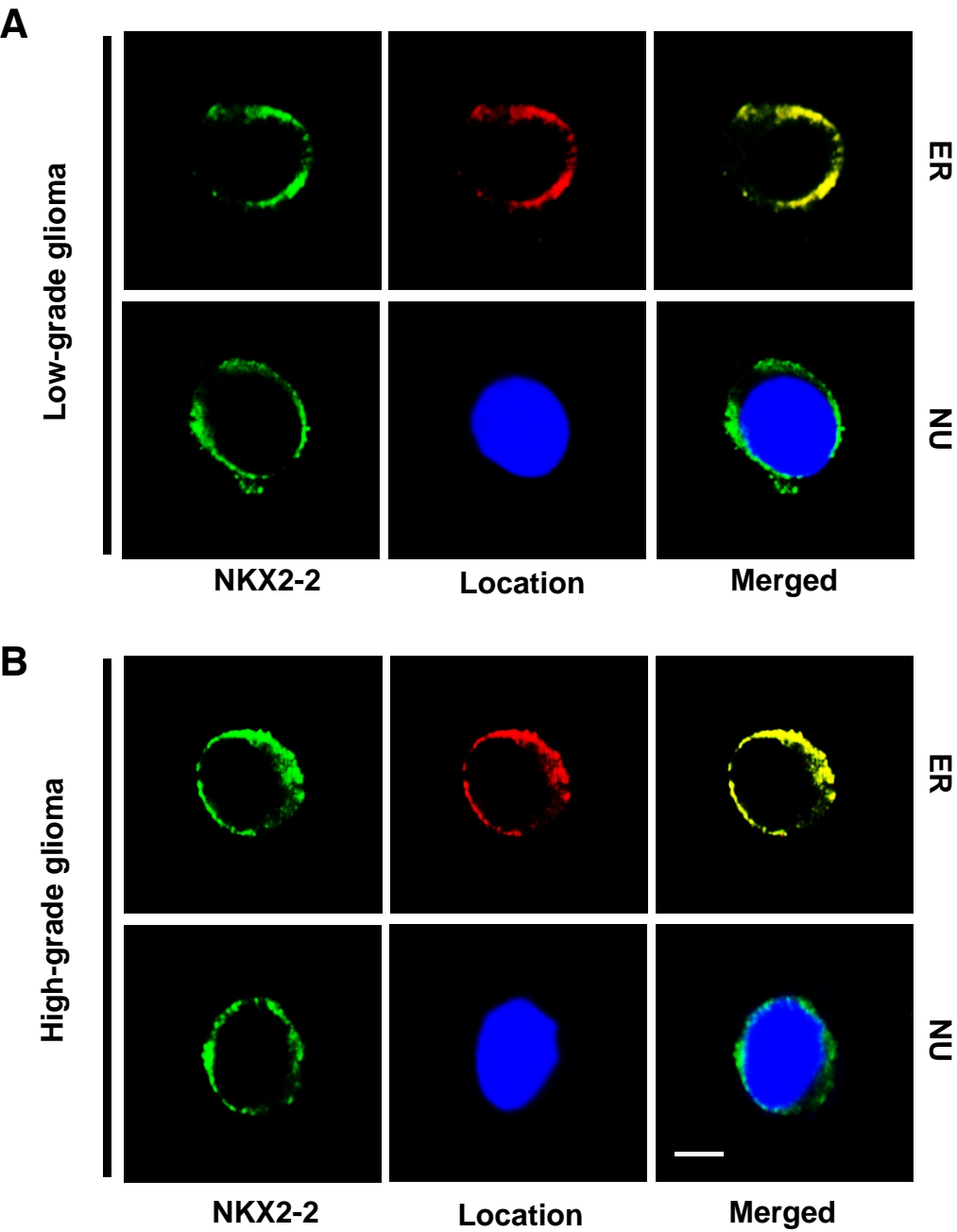


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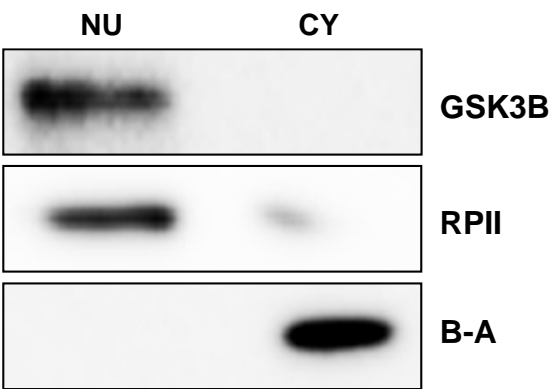


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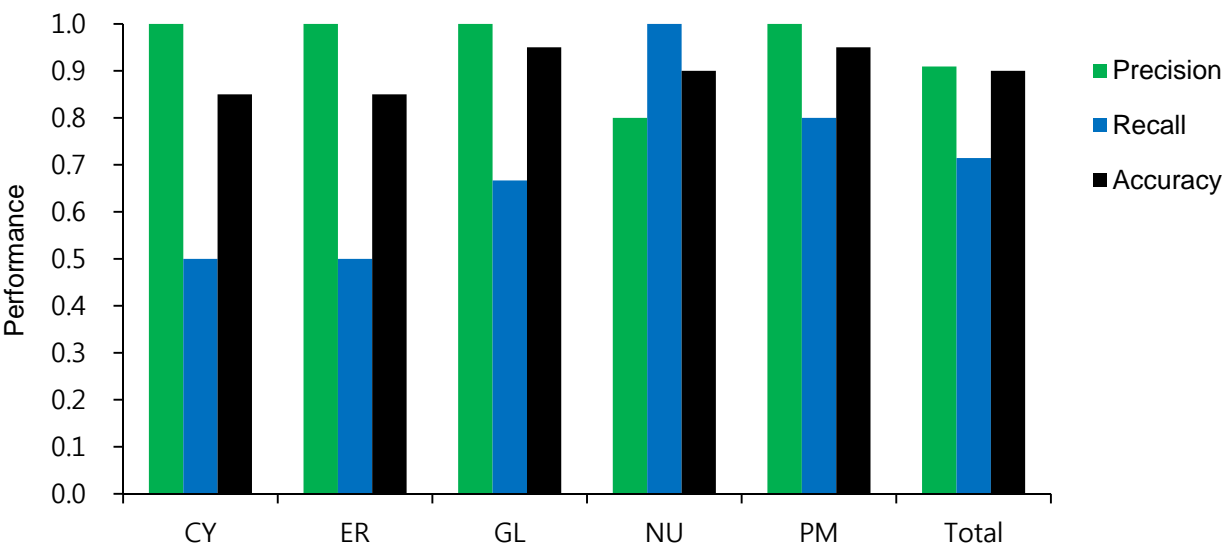


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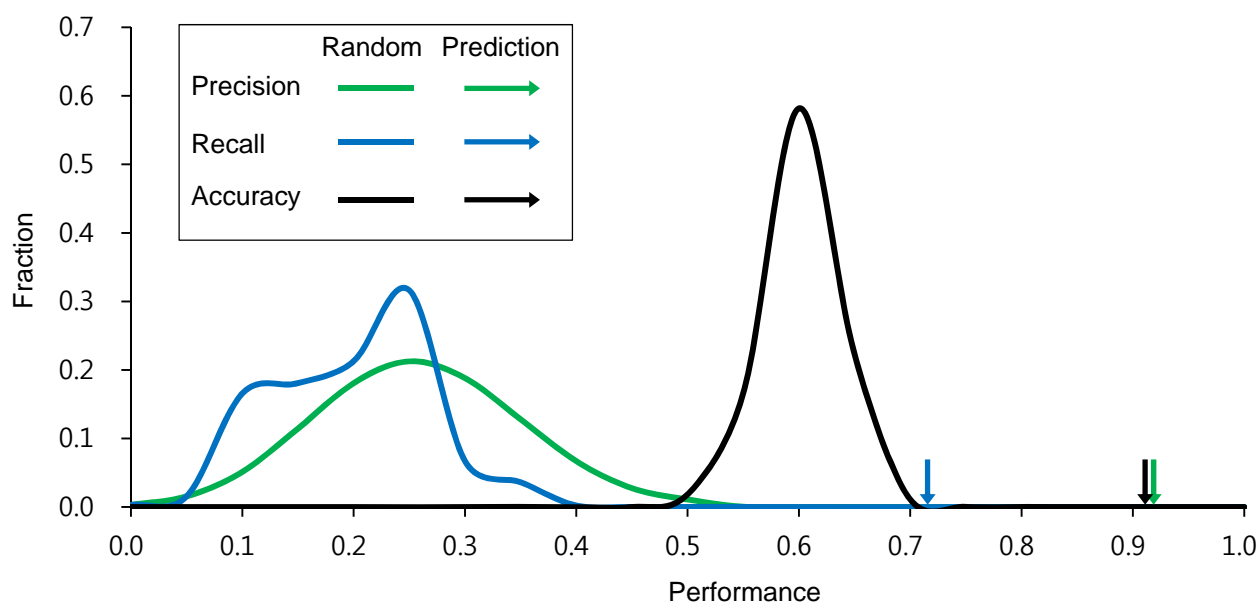


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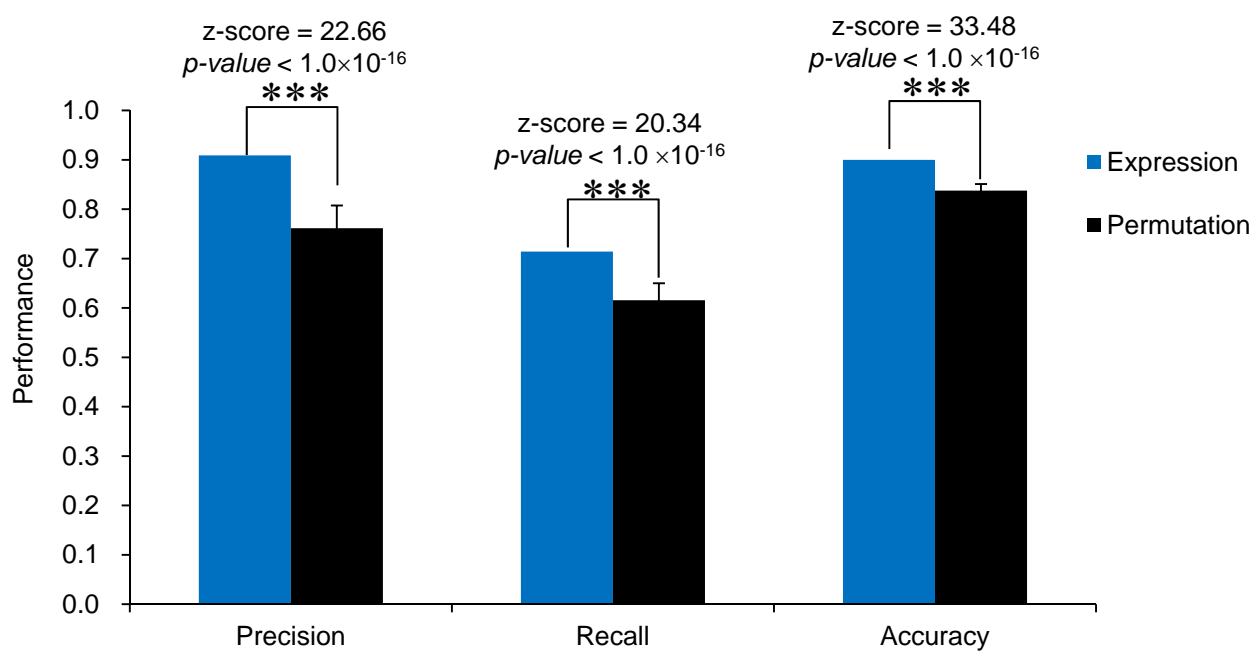


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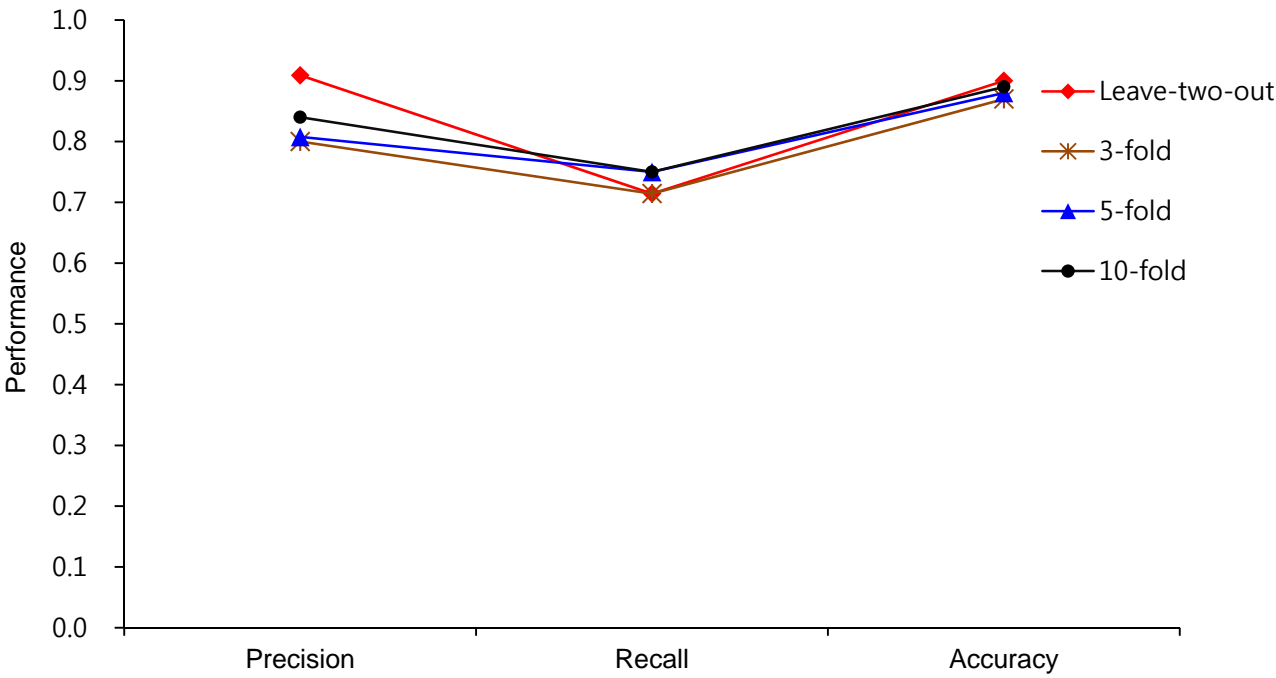


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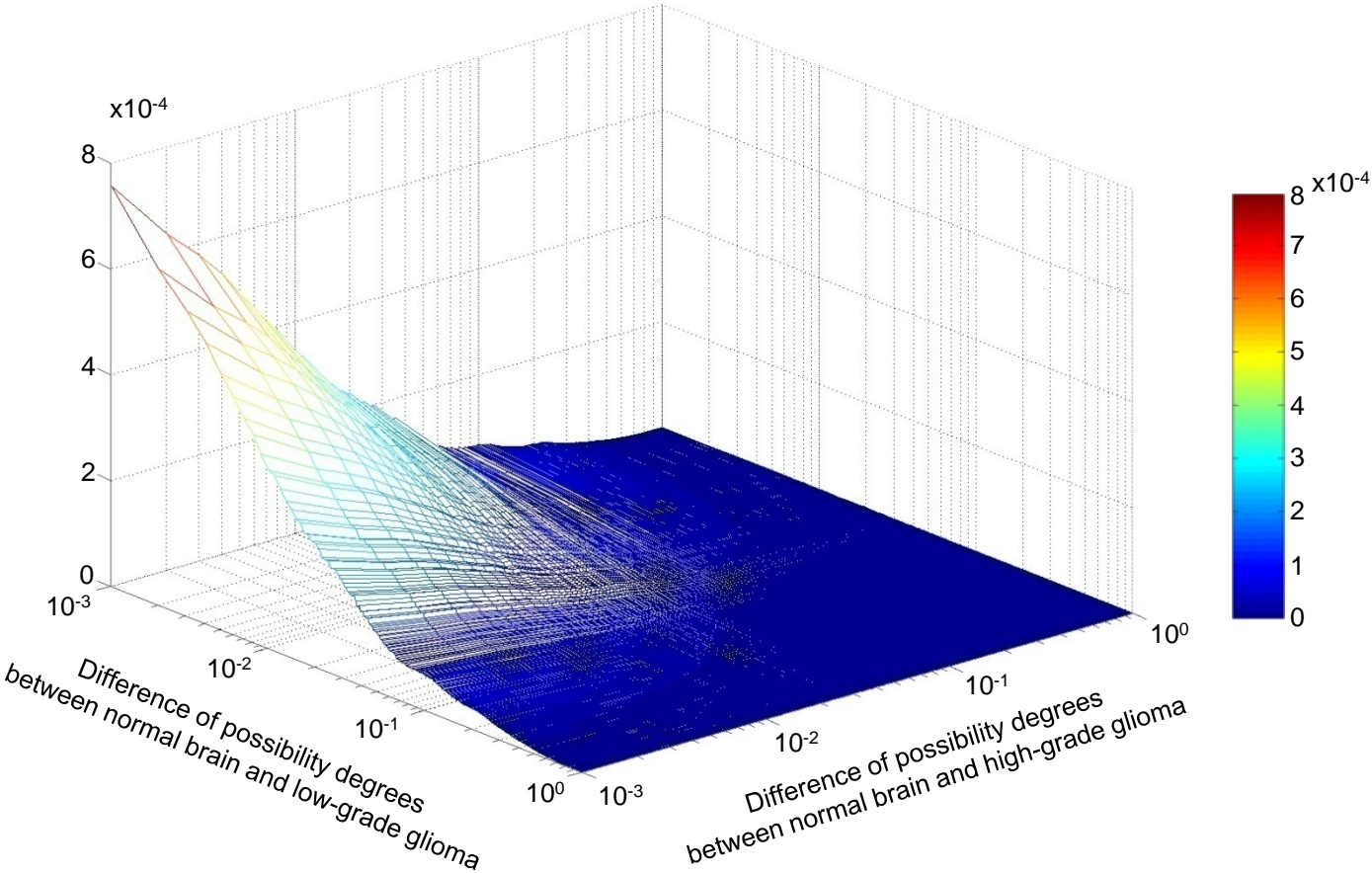


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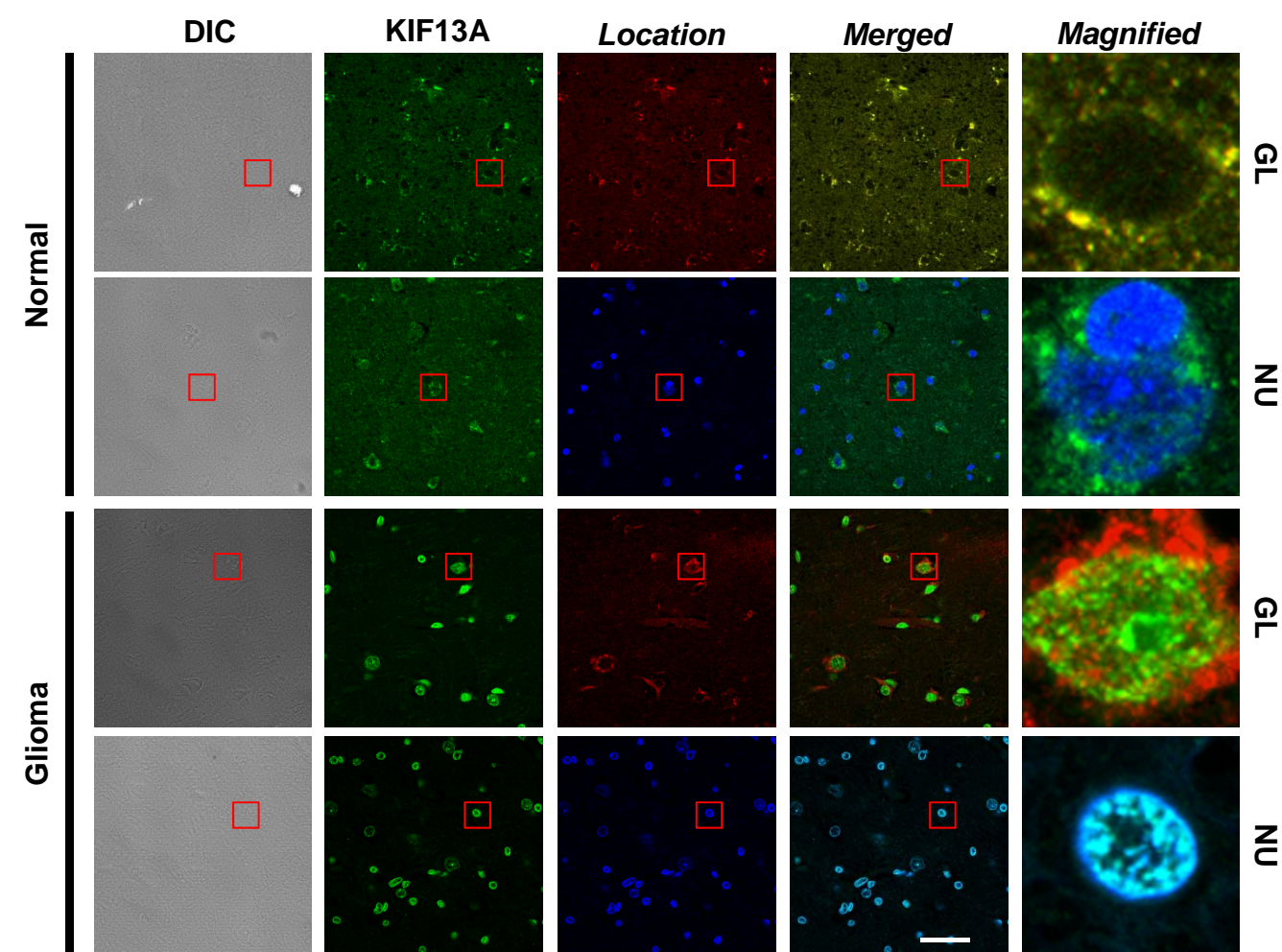


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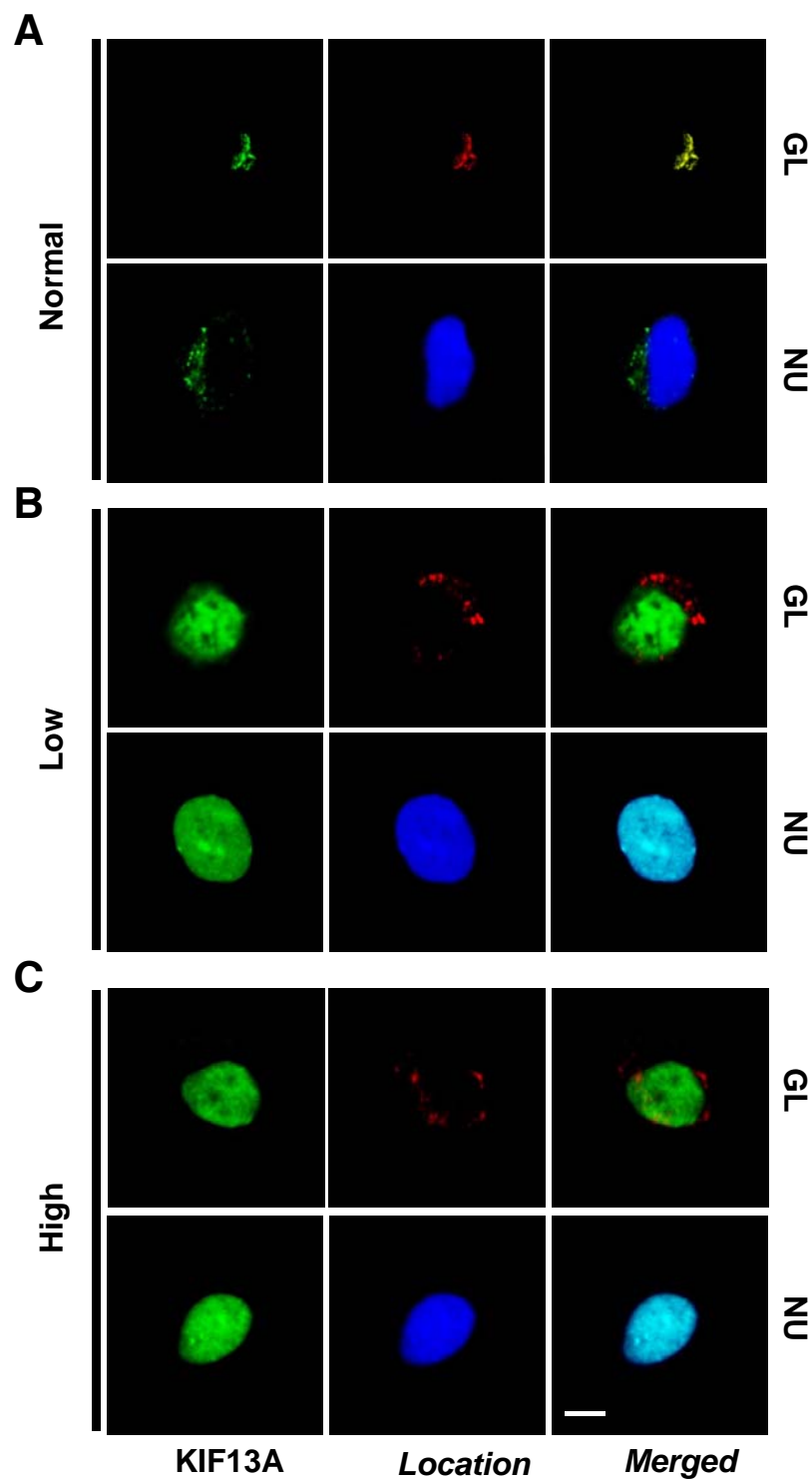


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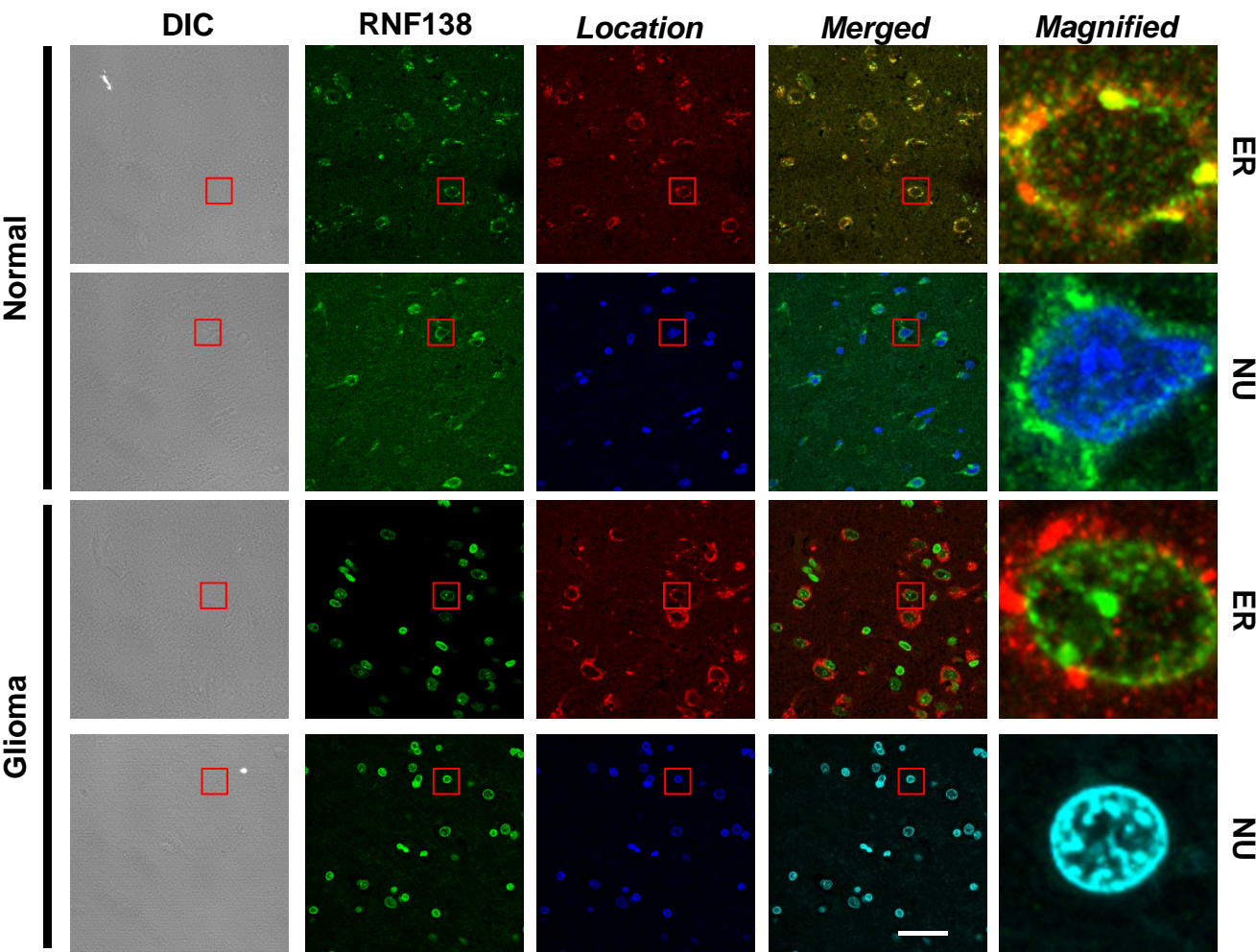


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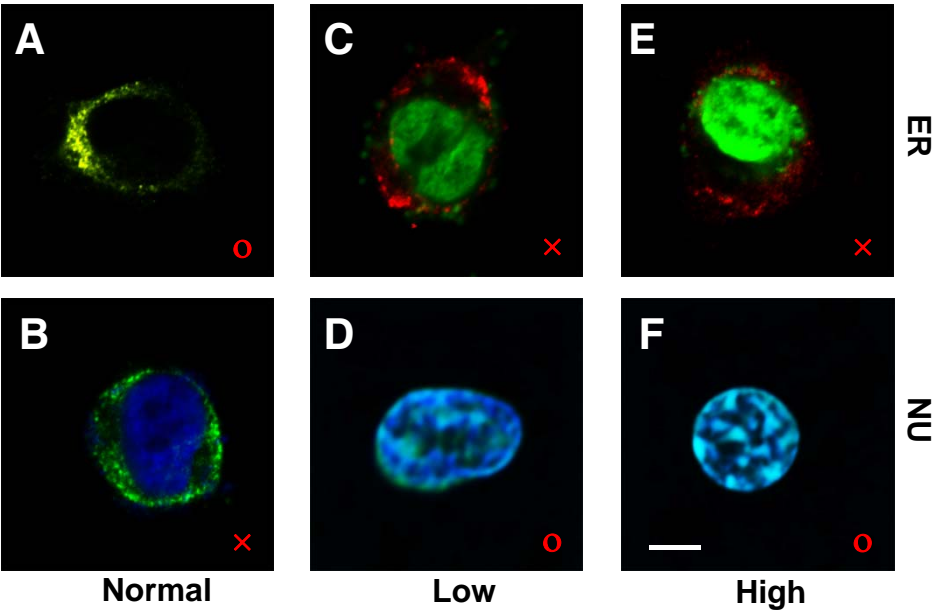


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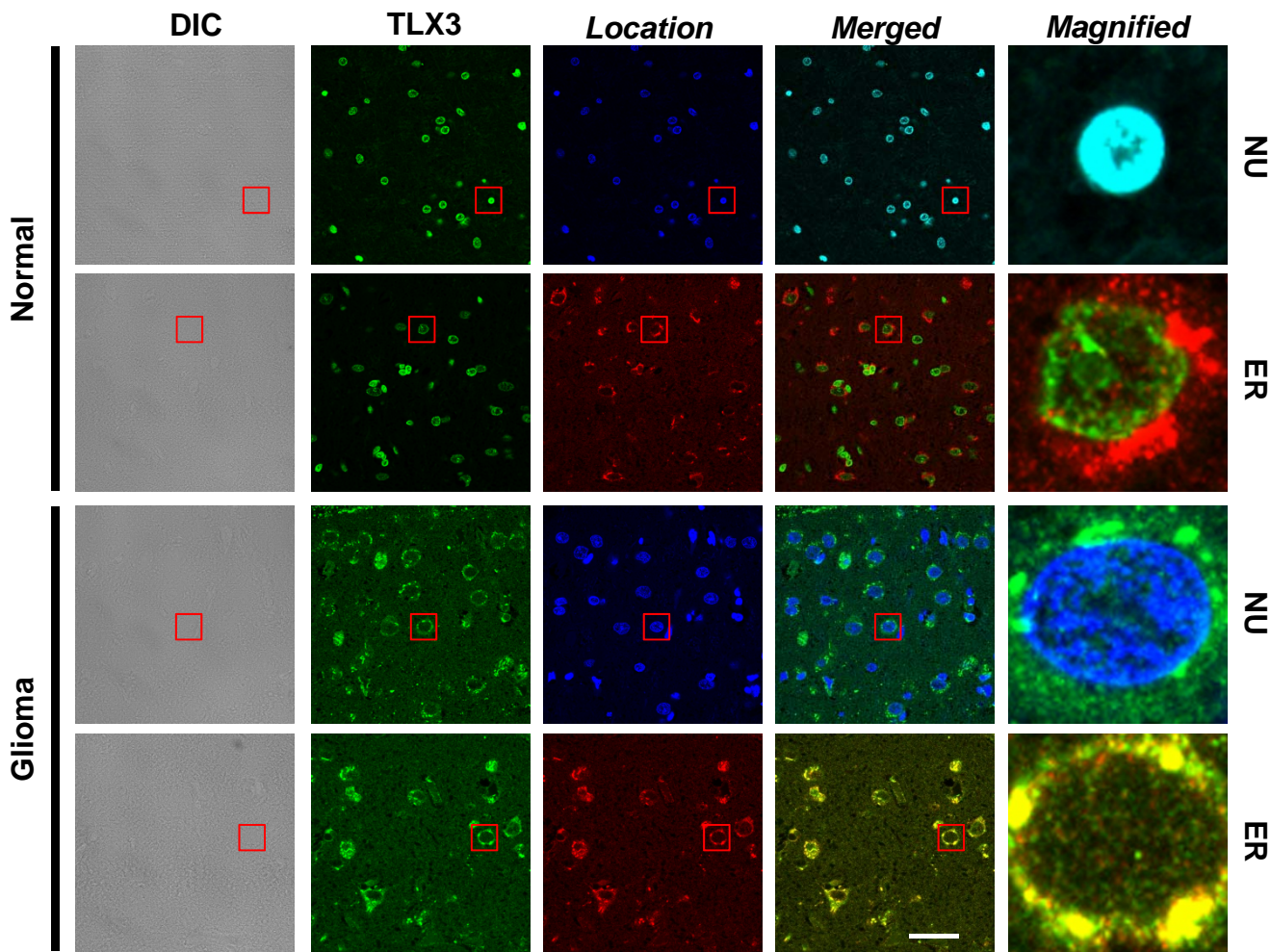


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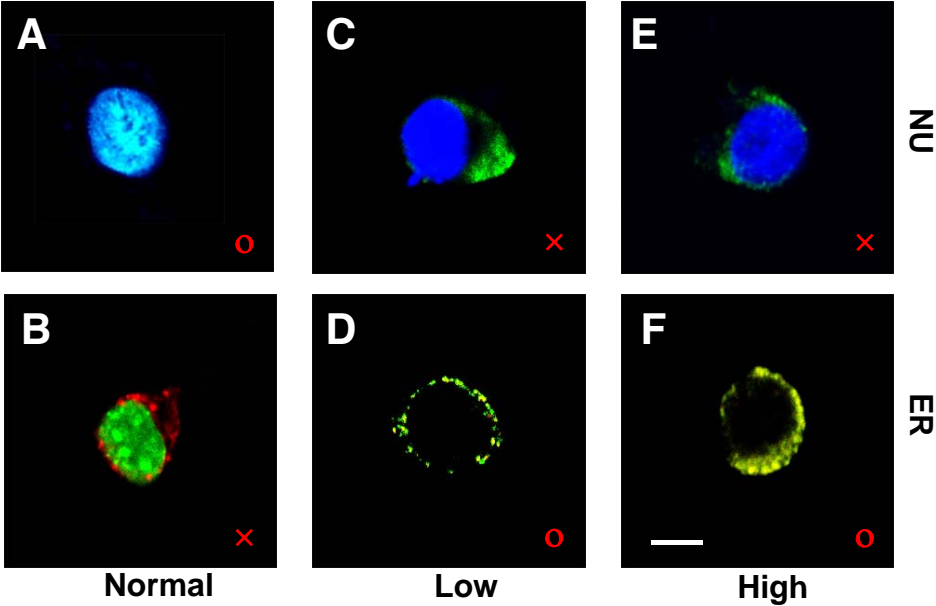


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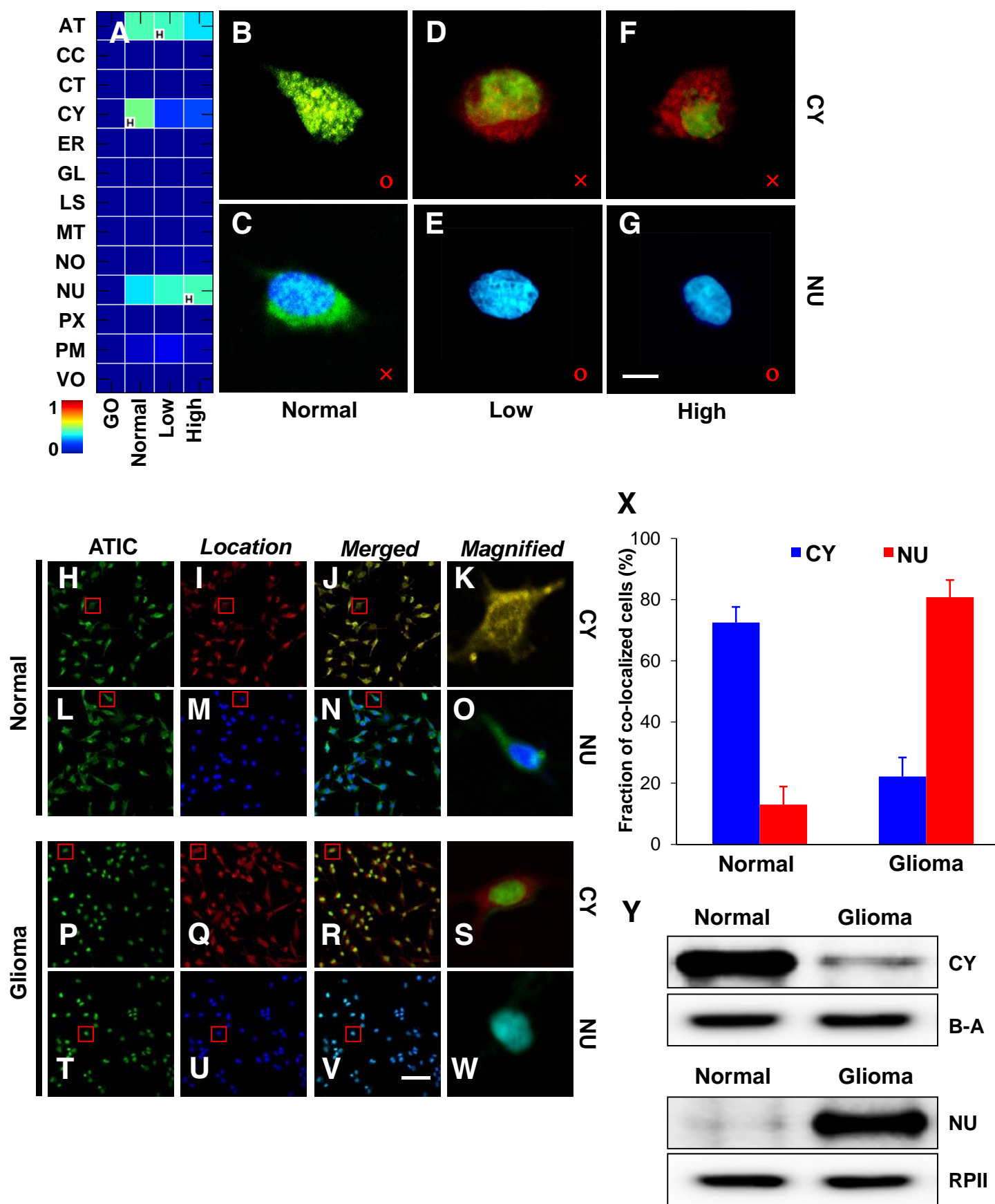


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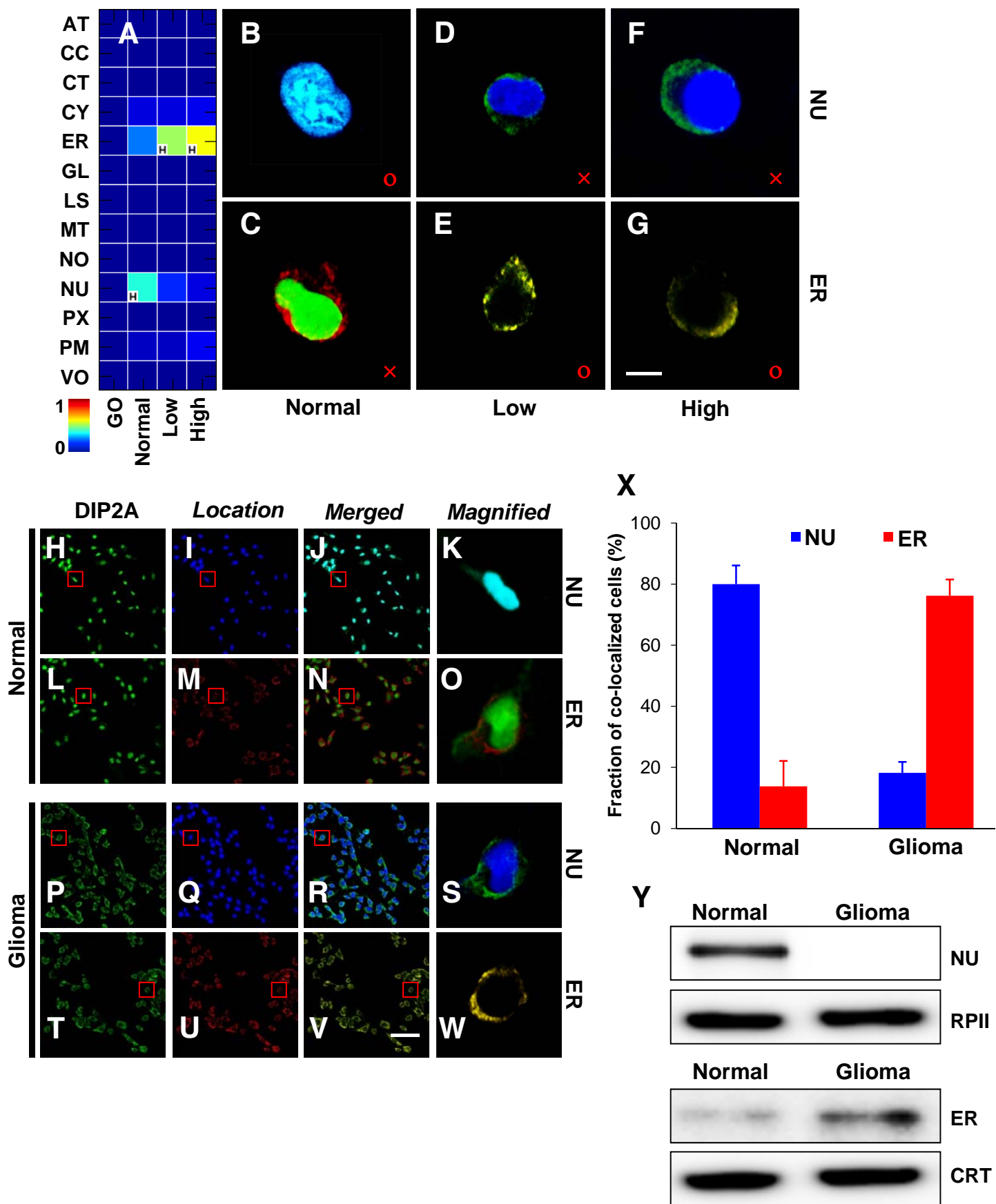


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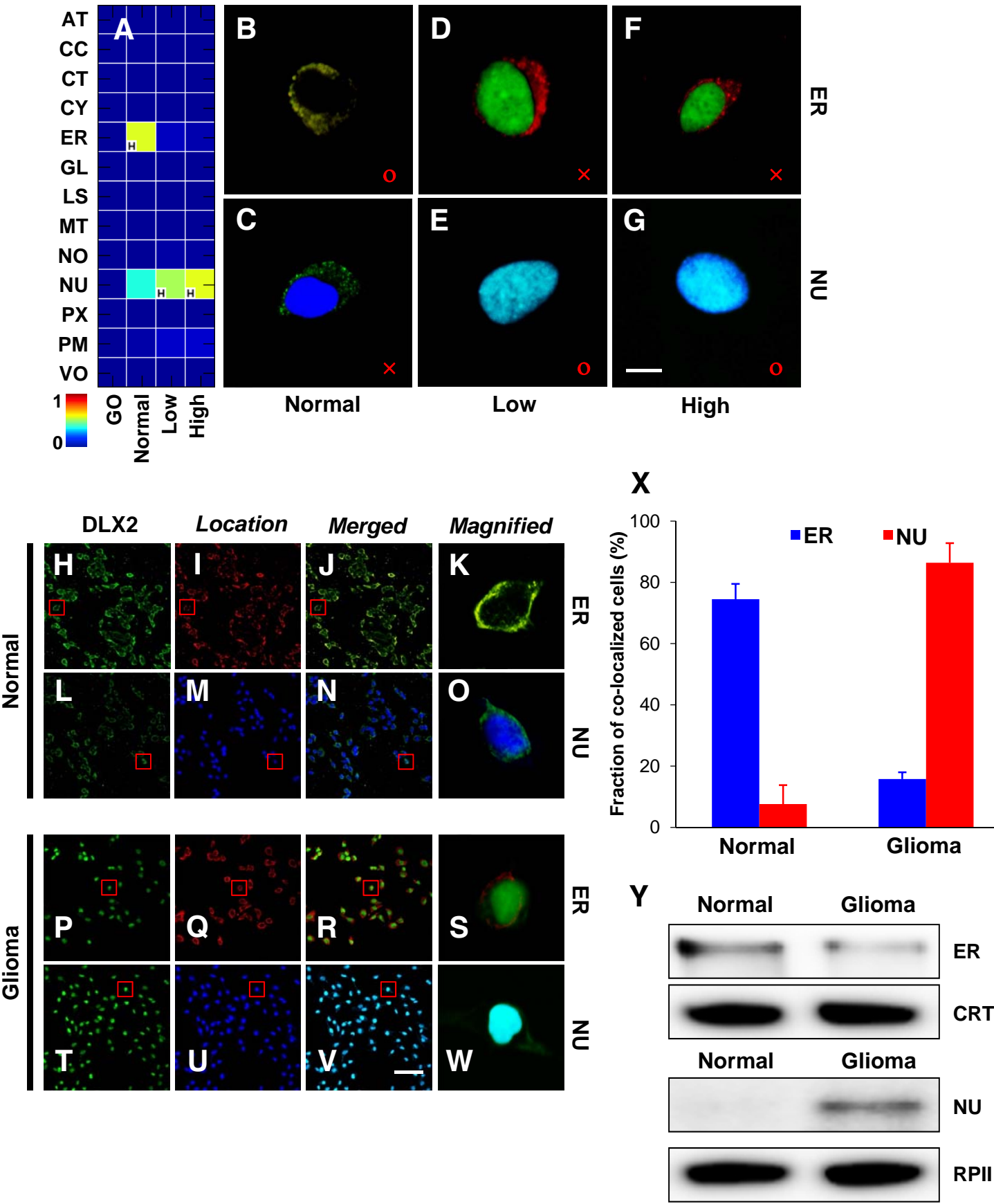


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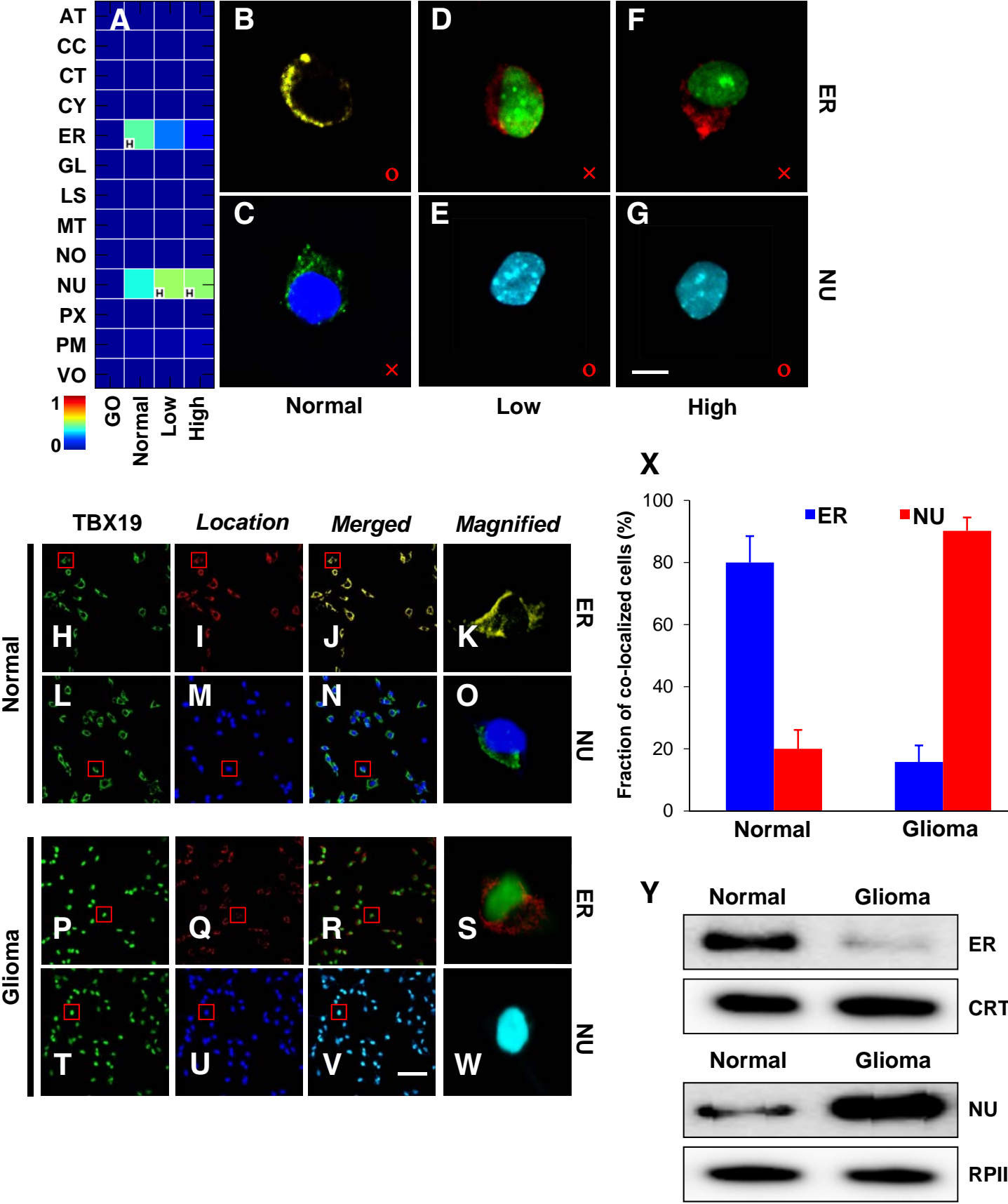


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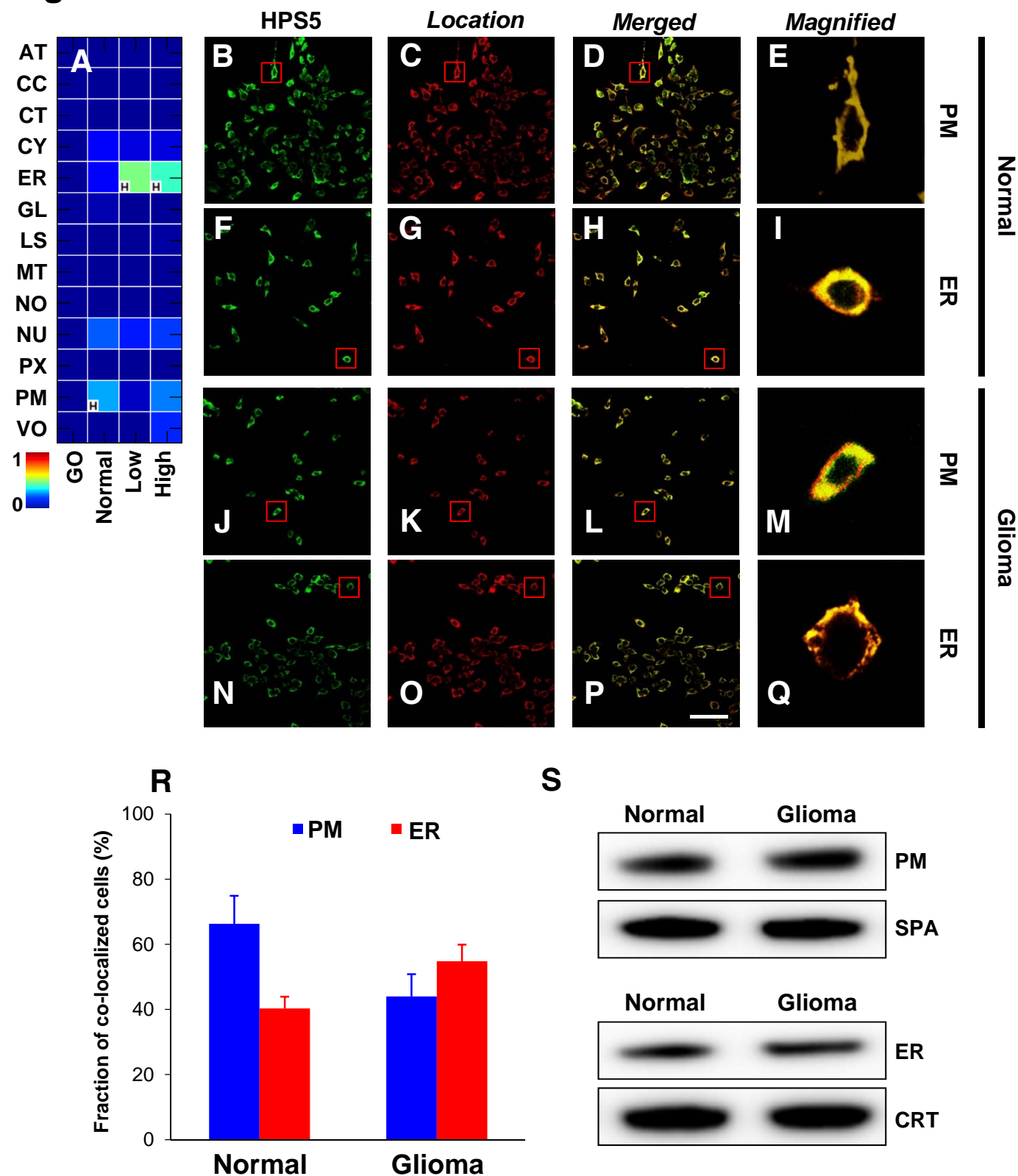


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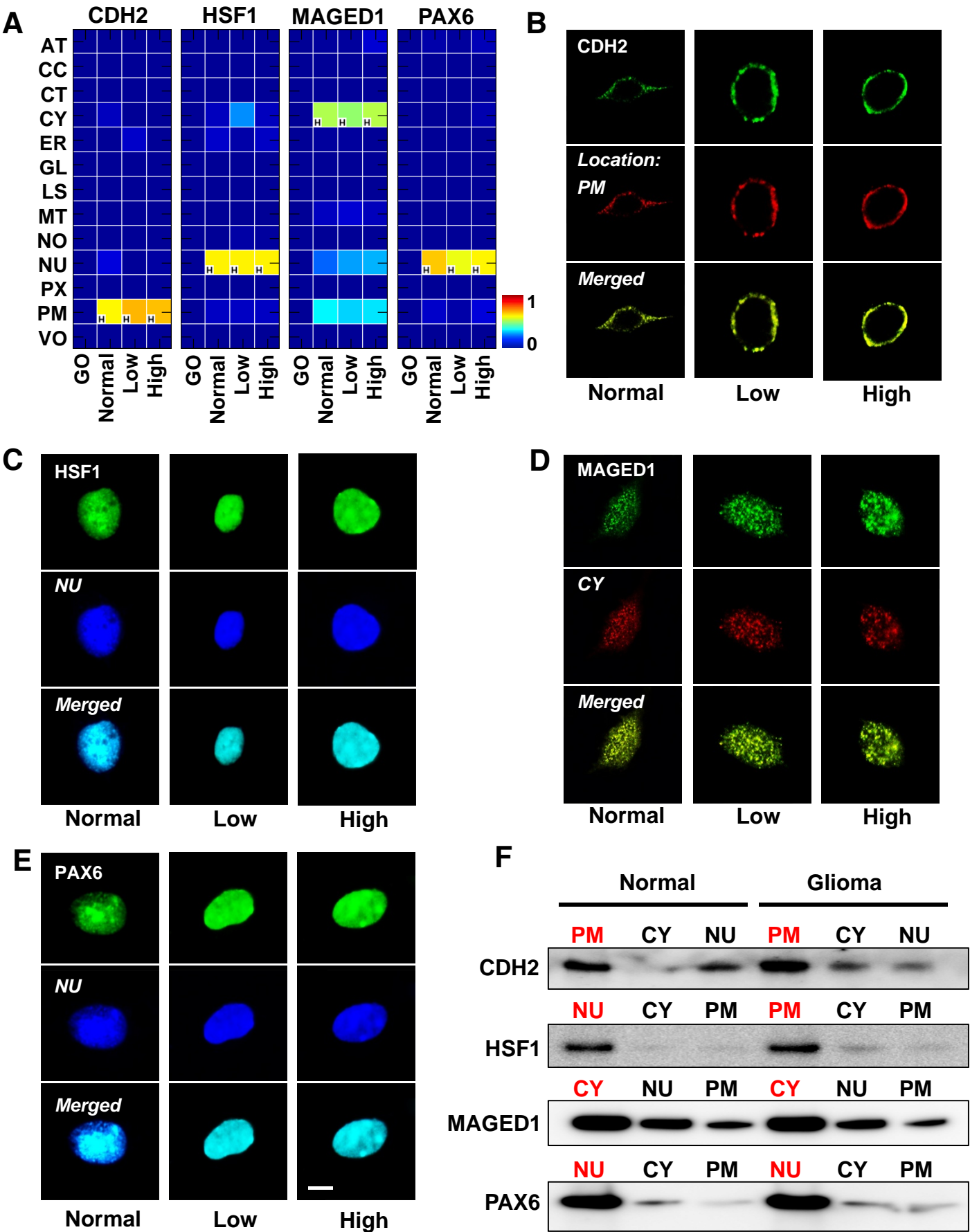


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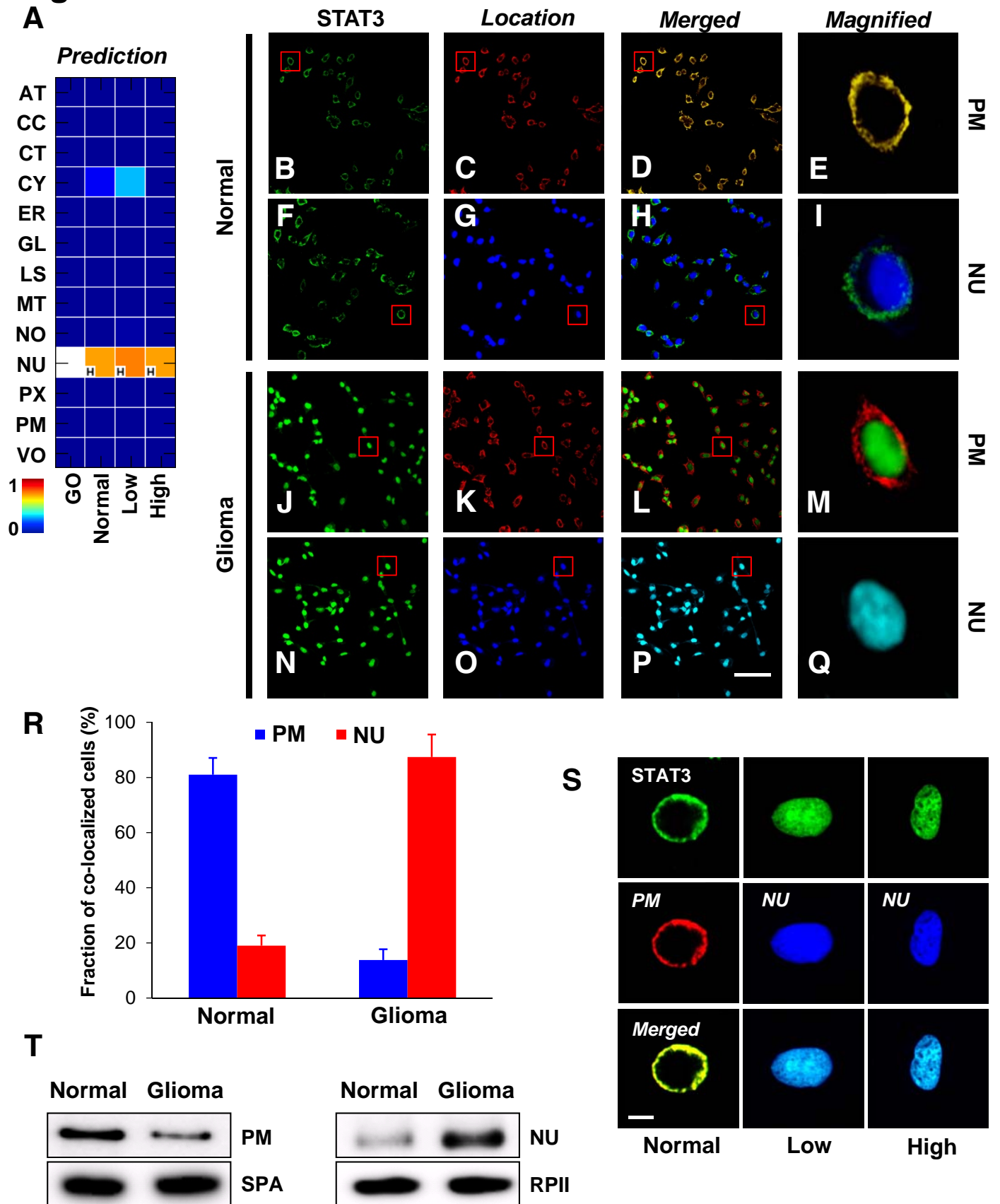


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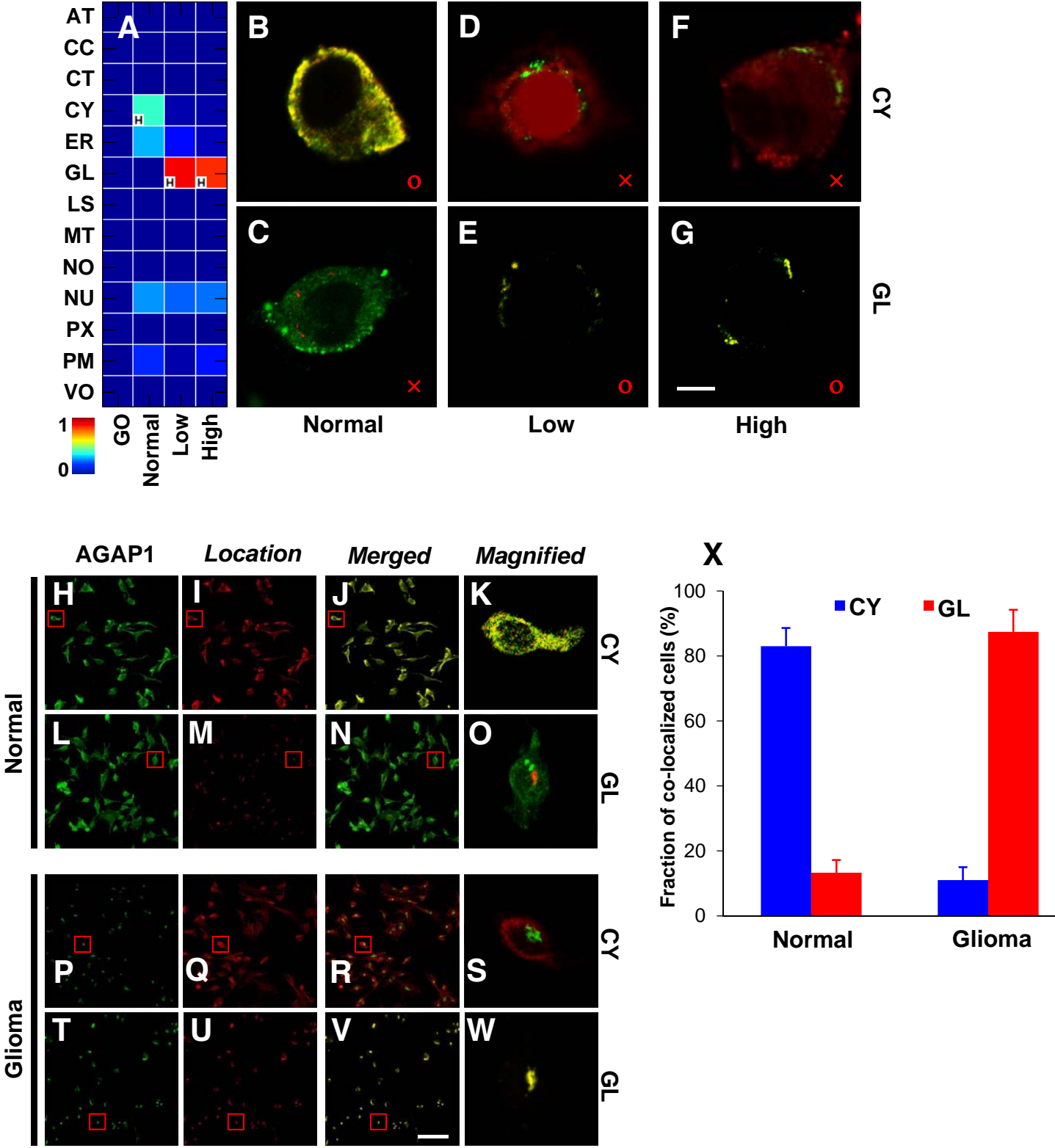


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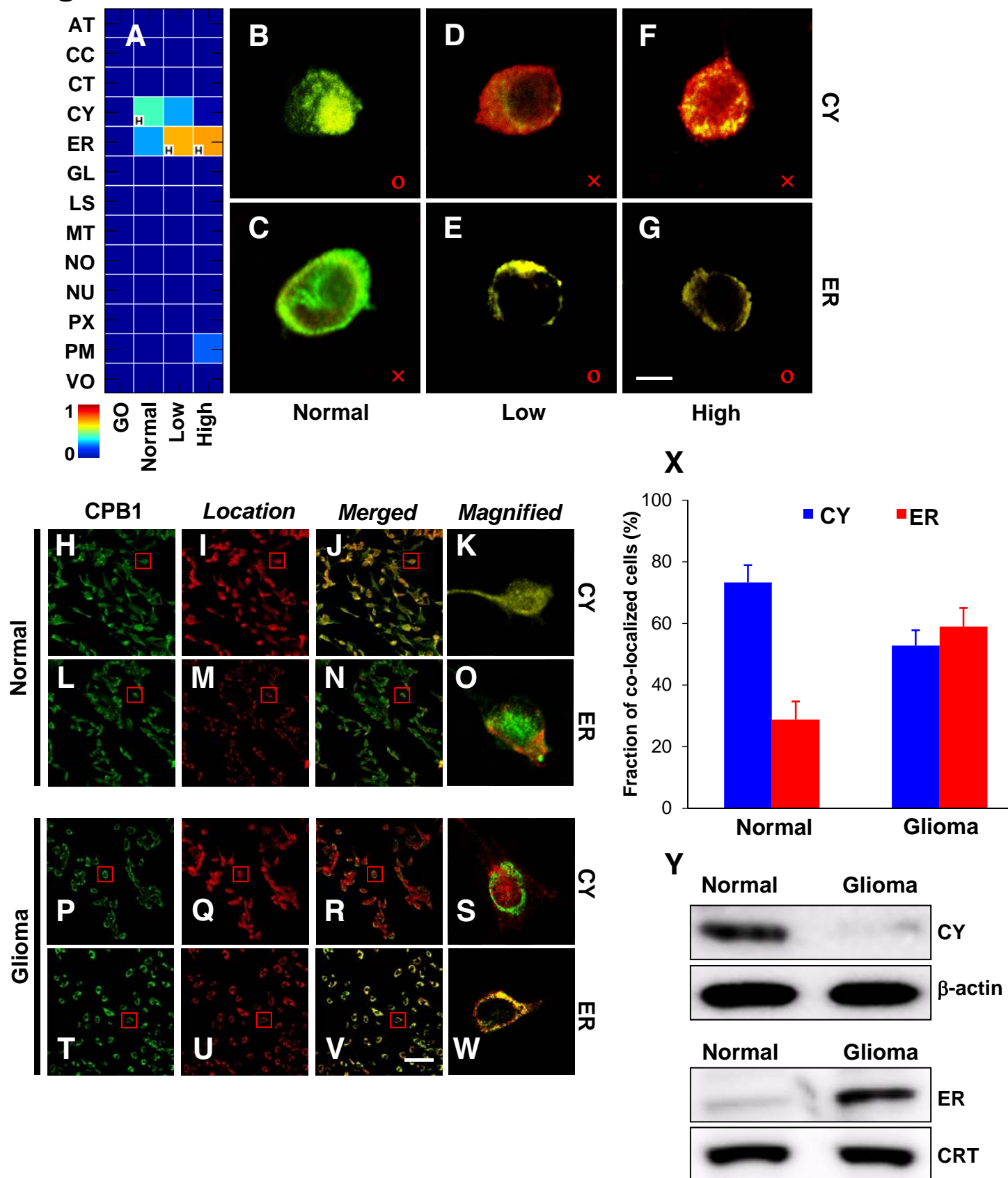


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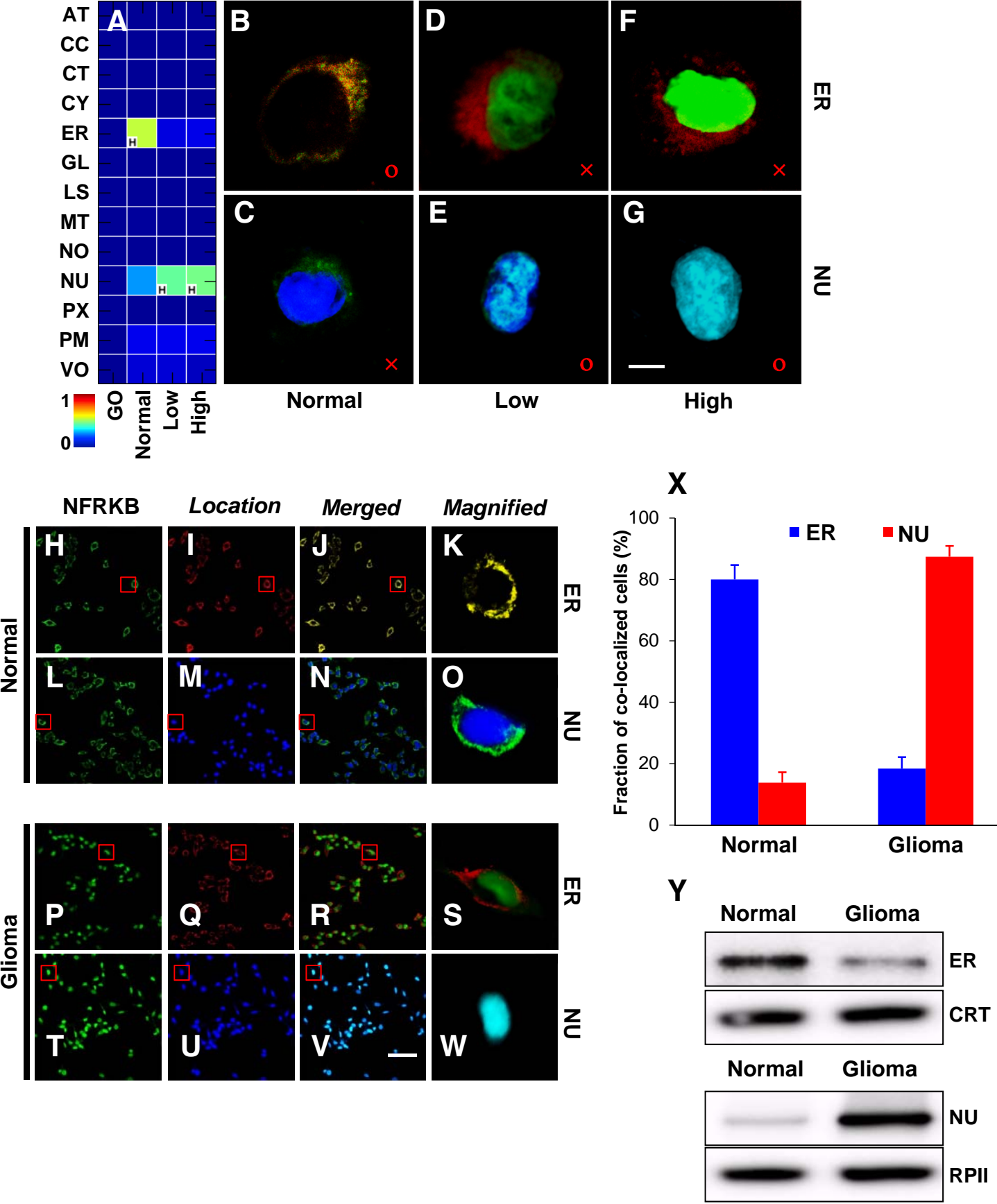


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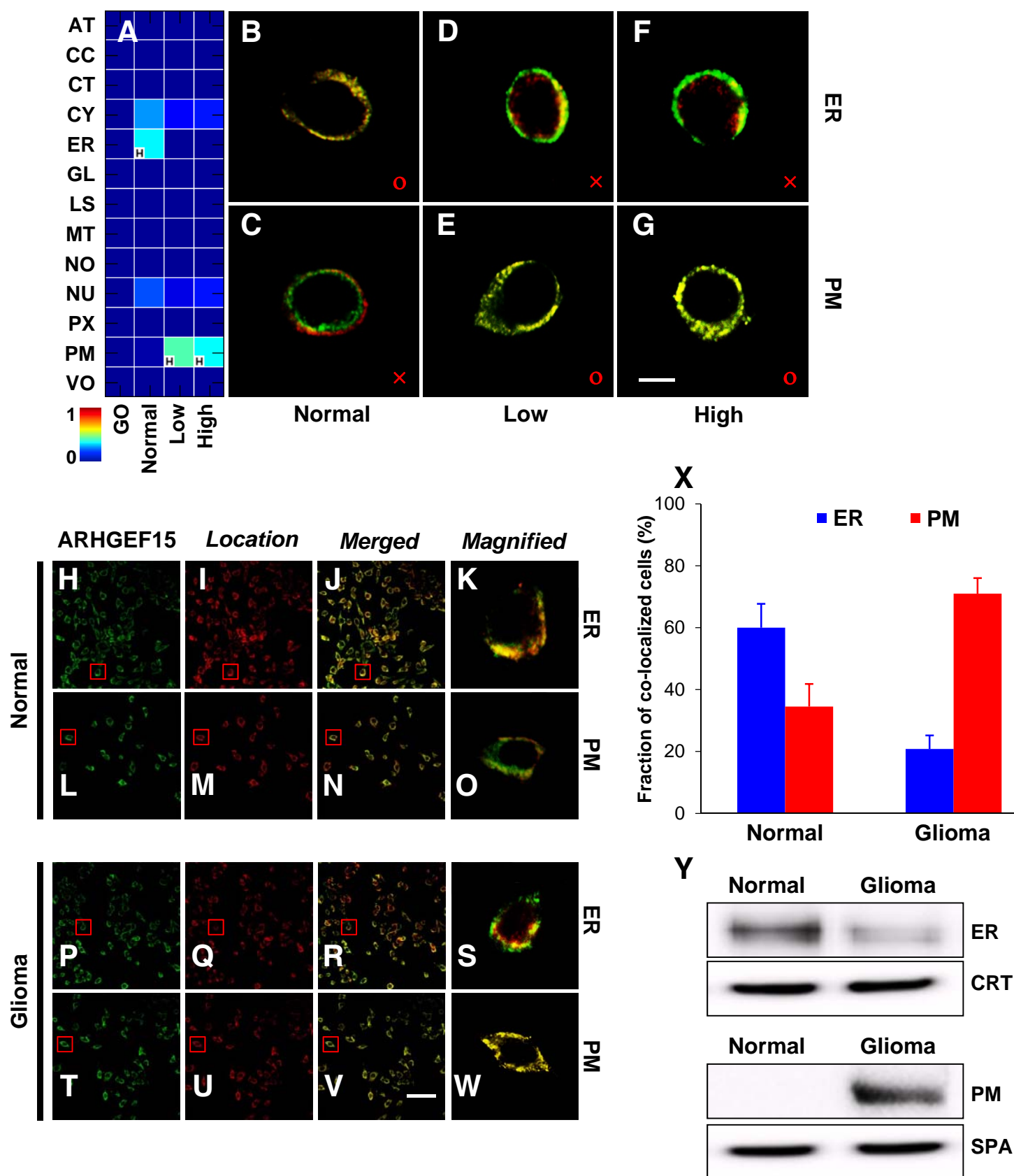


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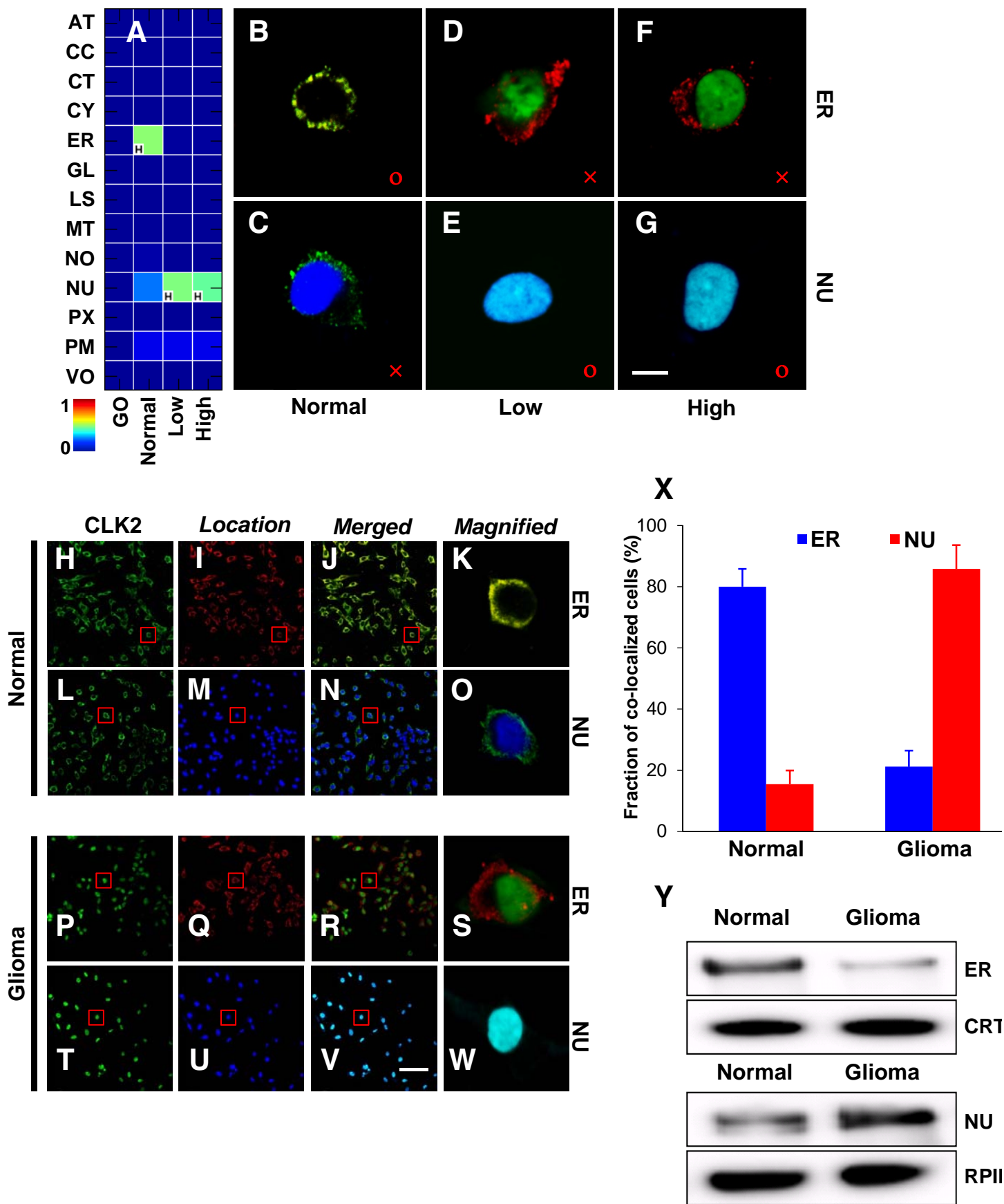


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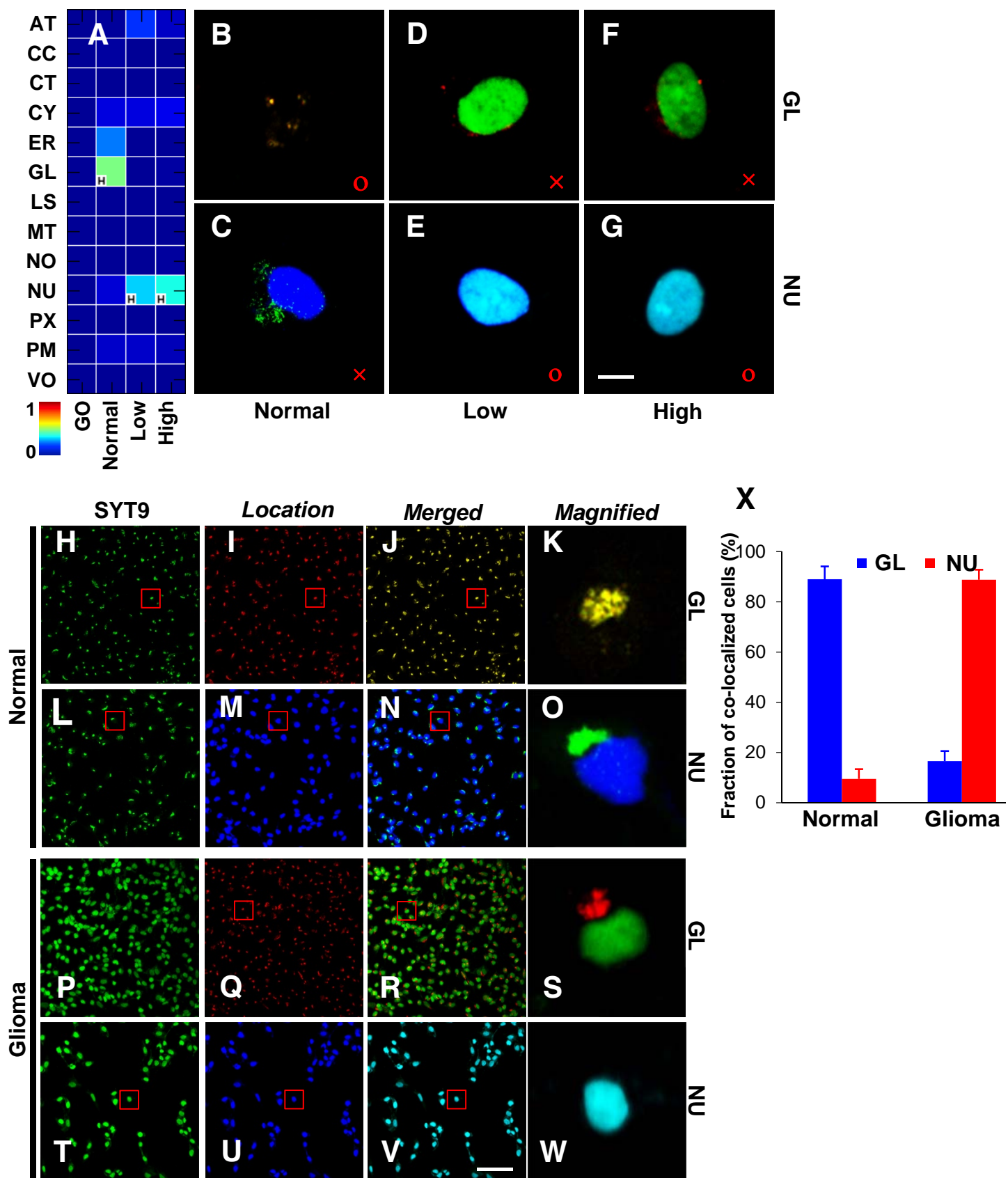


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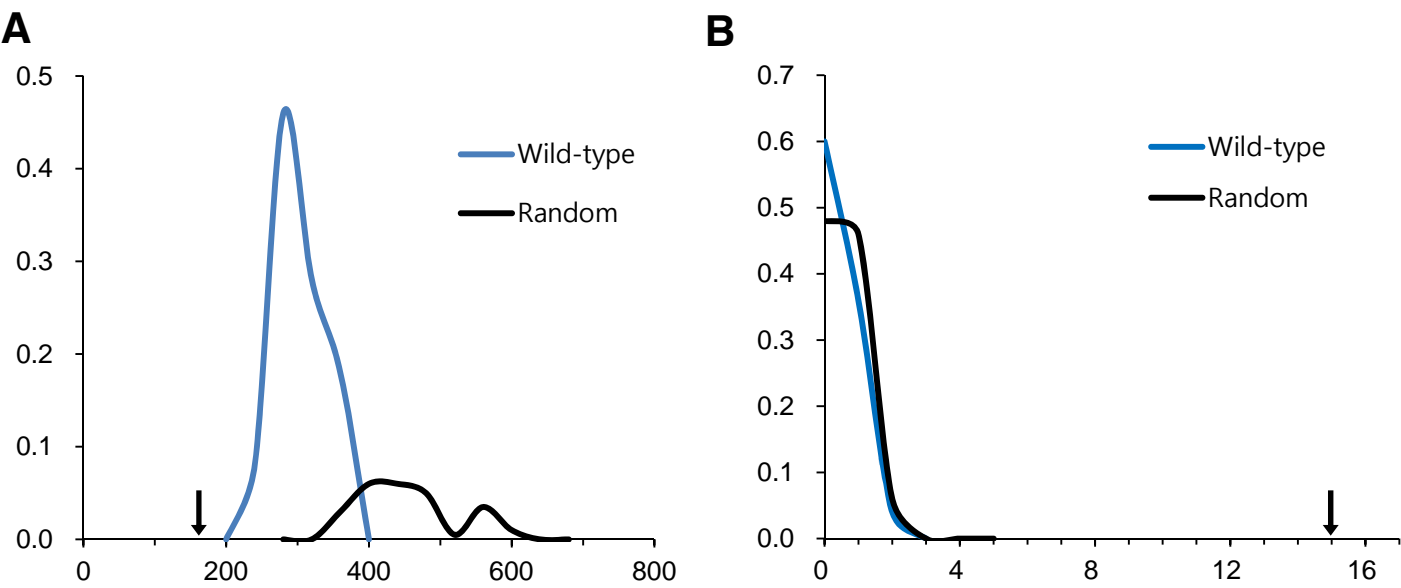


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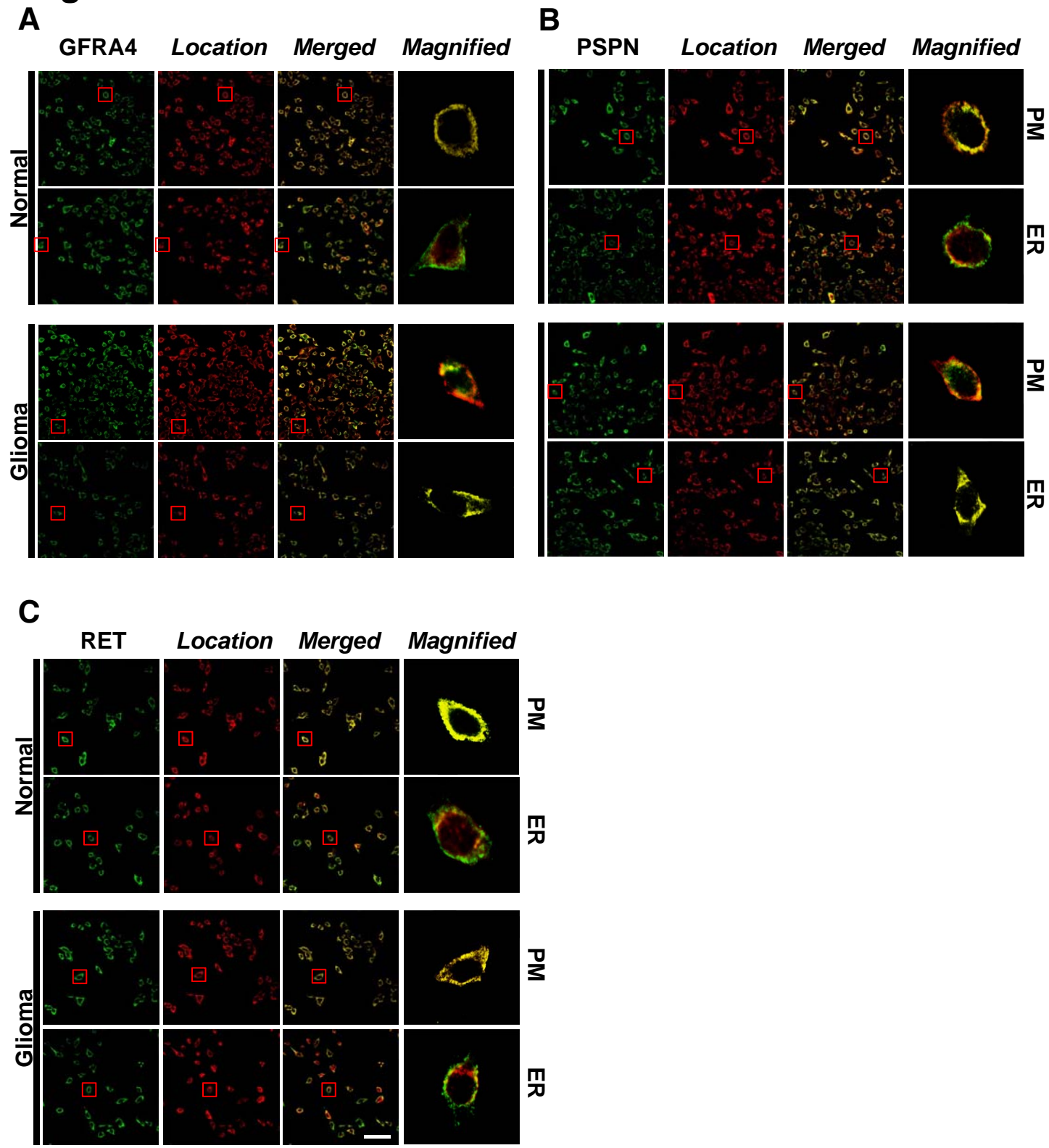


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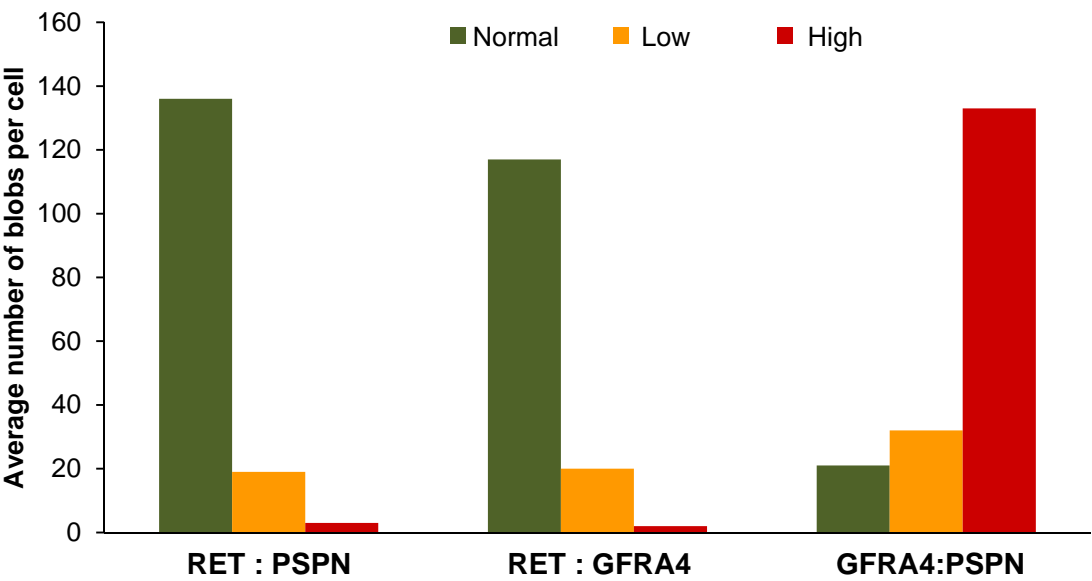


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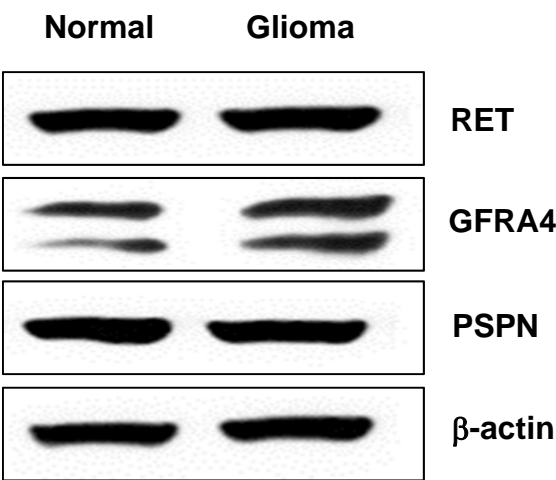


Figure S39

