Cox Regression Analysis

Introducing Cox Regression

Cox regression (Cox proportional-hazards model) tests the effects of several factors (predictors) on survival time. Predictors that lower the probability of survival at a given time are called risk factors; predictors that increase the probability of survival at a given time are called protective factors. The Cox proportional-hazards model are similar to a multiple logistic regression that considers time-to-event rather than simply whether an event occurred or not.

In this tutorial, we will use Cox Regression to test the effects of tumor gene expression on survival time while accounting for tumor size.

Performing Cox Regression Analysis

To begin, you should have the Survival Tutorial data set open in Partek Genomics Suite as shown.

- Select **Stat** from the main toolbar
- Select **Survival Analysis** then **Cox Regression** from the *Stat* menu (Figure 1)

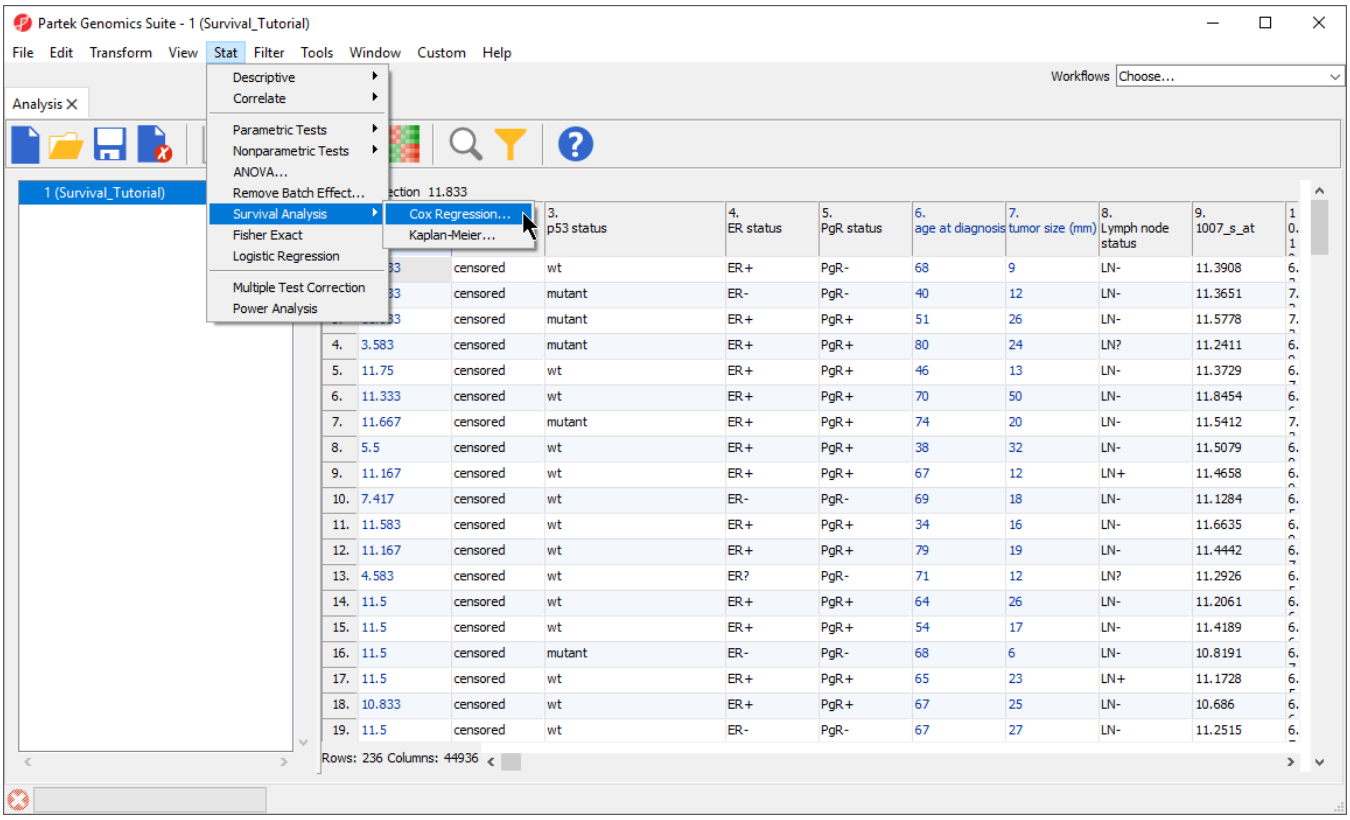


Figure 9. Invoking Cox Regression

The Cox Regression dialog will open. Please note that in this tutorial data set, column *1. Survival (years)* indicates the survival time of each patient in years and column *2. Event* indicates the event status for each patient, *death* or *censored.*

- Set *Time Variable* to **1. Survival (years)** using the drop-down menu
- Set *Event Variable* to **2. Event** using the drop-down menu

Only numeric data are displayed in the *Time Variable* drop-down list and only categorical data with two categories are displayed in *Event Variable*.

- Set *Event Status* to **death** using the drop-down menu (Figure 2)

Event Status should be set to the primary event outcome. *All Response Variables* will be automatically selected for *Predictor*. This means that Cox Regression will test every probe set for association with the survival (time-to-event).

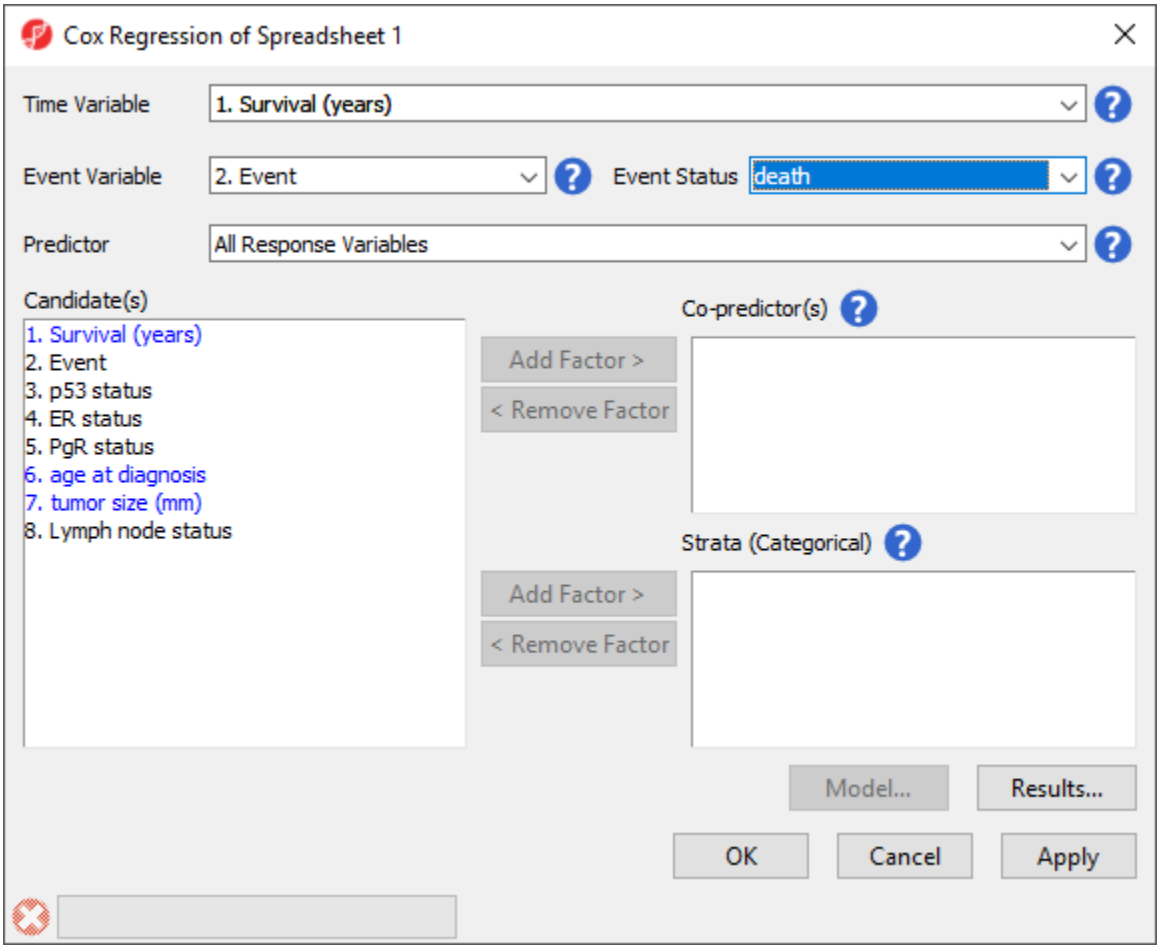


Figure 10. Configuring the Cox Regression dialog

Co-predictors are numeric or categorical factors that will be included in the regression model. To evaluate the association between tumor size and gene expression, we can add tumor size to the co-predictors list.

- Select **7. tumor size (mm)** from the *Candidate(s)* panel
- Select **Add Factor >** to add it to the *Co-predictor(s)* panel

Advanced options such as the inclusion of interactions between predictors and co-predictors can be accessed by selecting *Model...* (Figure 3) and the *Results...* button invokes a dialog (Figure 4) with additional output options for the results spreadsheet. We do not need to adjust any of the advanced model or output options for this tutorial.

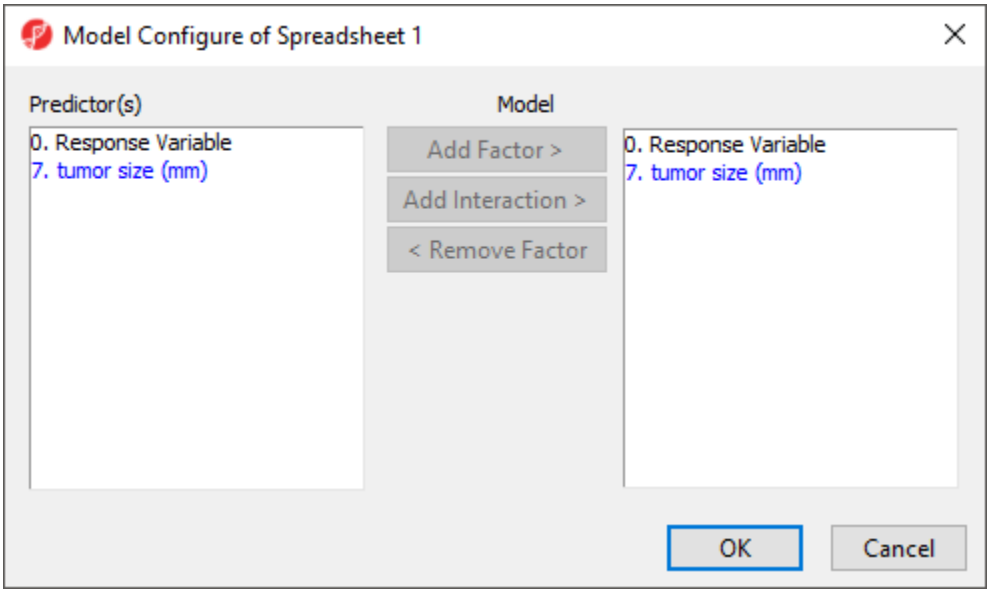


Figure 11. Configuring advanced options for Cox Regression

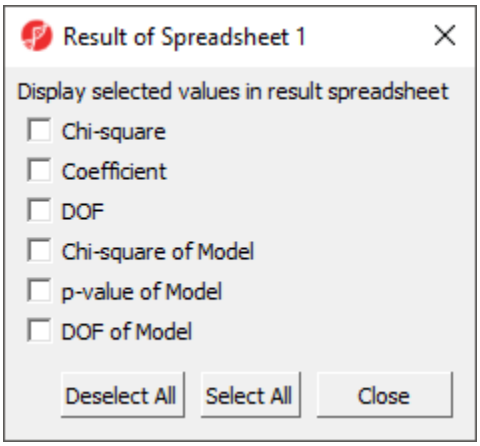


Figure 12. Configuring output options for Cox Regression

- Select **OK** to run Cox Regression (Figure 5)

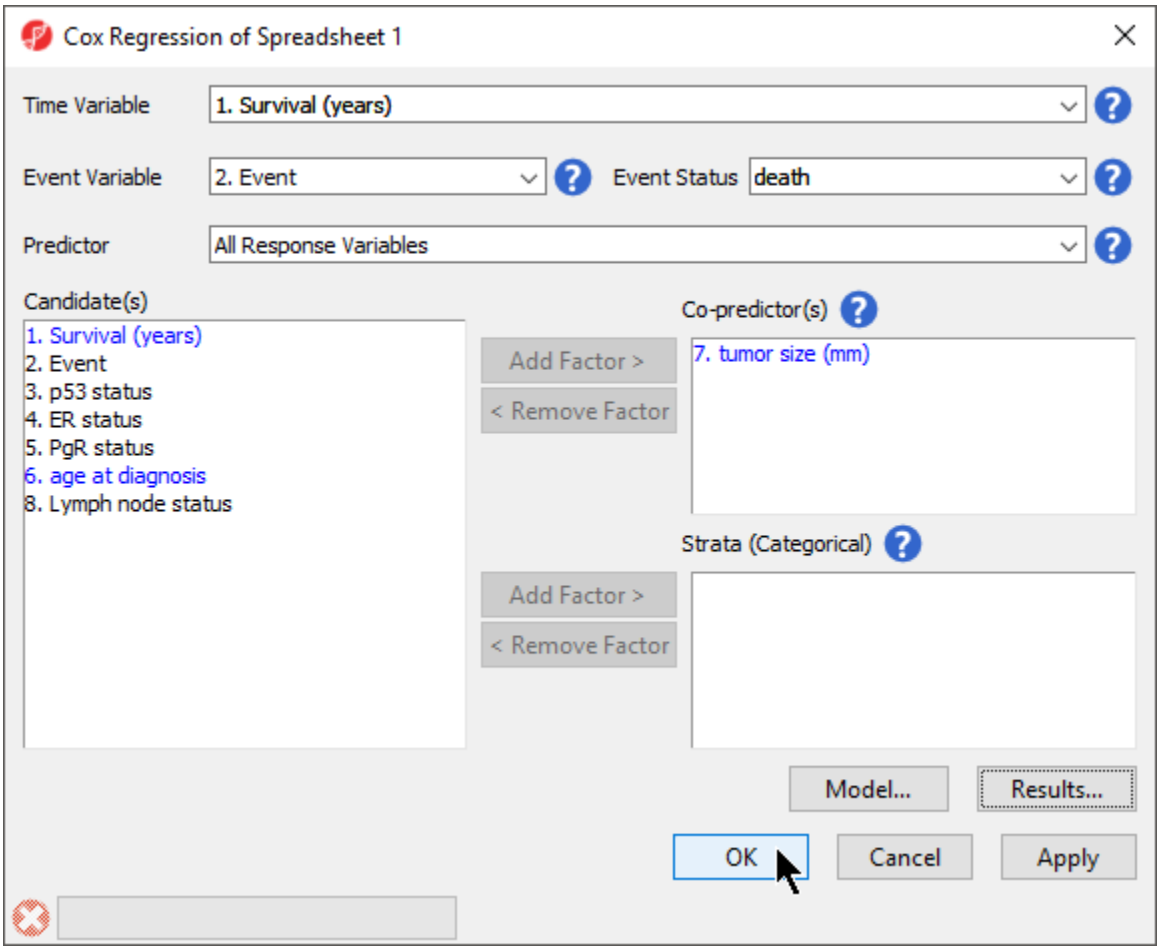


Figure 13. Configuring Cox Regression to assess the effect of gene expression and tumor size on survival

The spreadsheet generated by Cox Regression (Figure 6) includes a row for each probe set; the columns provide the following information:

1. Column # - Column number of probe set in probe intensities spreadsheet

2. Probest ID - ID of probe set in probe intensities spreadsheet

3. HRatio(gene) - Hazard ratio for the probe set

4. LowCI(gene) - lower 95% confidence boundary of the hazard ratio for the probe set

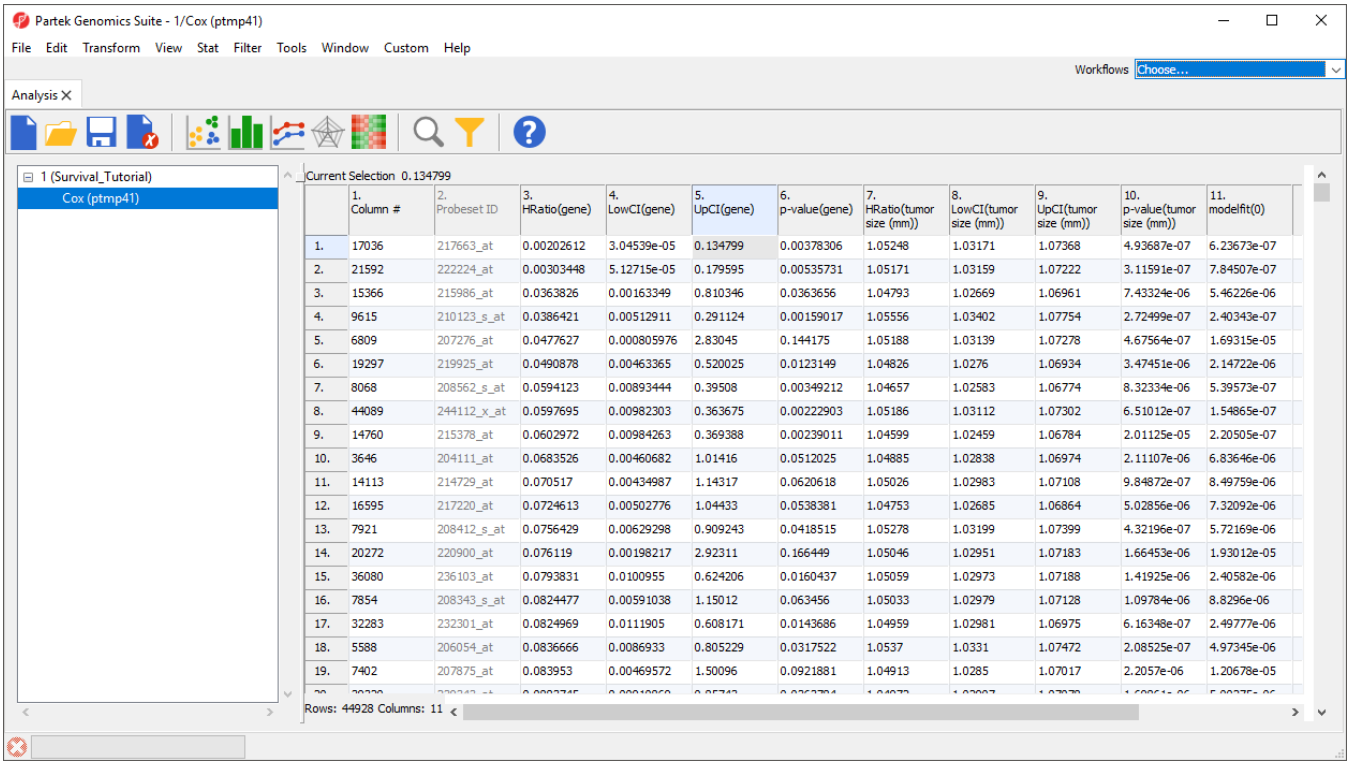
5. UpCI(gene) - upper 95% confidence boundary of the hazard ratio for the probe set

6. p-value(gene) - P-value of the corresponding Chi-squared test. A low value indicates that the predictor (probe set) poses a large hazard or is associated with shortened surivival time

7. to 10. - Effects of the co-predictor on survival time; for each co-predictor, a similar set of columns is added

11. modelfit(0) - P-value of the test assessing the overall model fit, i.e., the relationship between survival time, the predictor, and co-predictors in the model. A modelfit value of > 0.05 indicates a low association between the predictor and/or co-predictors with survival time.

Please note that the Cox Regression results spreadsheet is a temporary file. If you would like to be able to view the spreadsheet again after closing Partek Genomics Suite, be sure to save it by selecting the *Save Active Spreadsheet* icon ( ).



	1. Column #	2. Probeset ID	3. HRatio(gene)	4. LowCI(gene)	5. UpCI(gene)	6. p-value(gene)	7. HRatio(tumor size (mm))	8. LowCI(tumor size (mm))	9. UpCI(tumor size (mm))	10. p-value(tumor size (mm))	11. modelfit(0)
1.	17036	217663_at	0.00202612	3.04539e-05	0.134799	0.00378306	1.05248	1.03171	1.07368	4.93687e-07	6.23673e-07
2.	21592	222224_at	0.00303448	5.12715e-05	0.179595	0.00535731	1.05171	1.03159	1.07222	3.11591e-07	7.84507e-07
3.	15366	215986_at	0.0363826	0.00163349	0.810346	0.0363656	1.04793	1.02669	1.06961	7.43324e-06	5.46226e-06
4.	9615	210123_s_at	0.0386421	0.00512911	0.291124	0.00159017	1.05556	1.03402	1.07754	2.72499e-07	2.40343e-07
5.	6809	207276_at	0.0477627	0.000805976	2.83045	0.144175	1.05188	1.03139	1.07278	4.67564e-07	1.69315e-05
6.	19297	219925_at	0.0490878	0.00463365	0.520025	0.0123149	1.04826	1.0276	1.06934	3.47451e-06	2.14722e-06
7.	8068	208562_s_at	0.0594123	0.00893444	0.39508	0.00349212	1.04657	1.02583	1.06774	8.32334e-06	5.39573e-07
8.	44089	244112_x_at	0.0597695	0.00982303	0.363675	0.00222903	1.05186	1.03112	1.07302	6.51012e-07	1.54865e-07
9.	14760	215378_at	0.0602972	0.00984263	0.369388	0.00239011	1.04599	1.02459	1.06784	2.01125e-05	2.20505e-07
10.	3646	204111_at	0.0683526	0.00460682	1.01416	0.0512025	1.04885	1.02838	1.06974	2.11107e-06	6.83646e-06
11.	14113	214729_at	0.070517	0.00434987	1.14317	0.0620618	1.05026	1.02983	1.07108	9.84872e-07	8.49759e-06
12.	16595	217220_at	0.0724613	0.00502776	1.04433	0.0538381	1.04753	1.02685	1.06864	5.02856e-06	7.32092e-06
13.	7921	208412_s_at	0.0756429	0.00629298	0.909243	0.0418515	1.05278	1.03199	1.07399	4.32196e-07	5.72169e-06
14.	20272	220900_at	0.076119	0.00198217	2.92311	0.166449	1.05046	1.02951	1.07183	1.66453e-06	1.93012e-05
15.	36080	236103_at	0.0793831	0.0100955	0.624206	0.0160437	1.05059	1.02973	1.07188	1.41925e-06	2.40582e-06
16.	7854	208343_s_at	0.0824477	0.00591038	1.15012	0.063456	1.05033	1.02979	1.07128	1.09784e-06	8.8296e-06
17.	32283	232301_at	0.0824969	0.0111905	0.608171	0.0143686	1.04959	1.02981	1.06975	6.16348e-07	2.49777e-06
18.	5588	206054_at	0.0836666	0.0086933	0.805229	0.0317522	1.0537	1.0331	1.07472	2.08525e-07	4.97345e-06
19.	7402	207875_at	0.083953	0.00469572	1.50096	0.0921881	1.04913	1.0285	1.07017	2.2057e-06	1.20678e-05

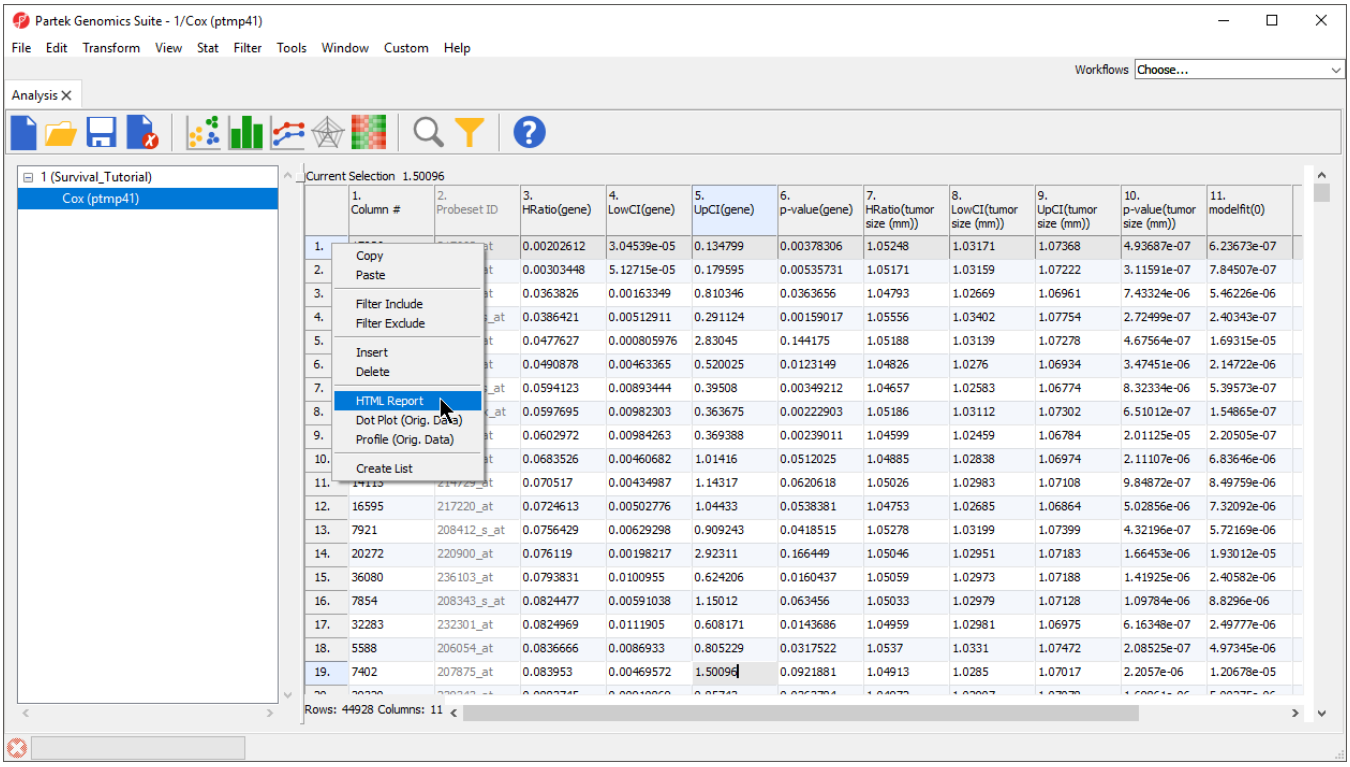
Figure 14. Cox Regression results spreadsheet

The hazard ratio is an effect size measure used to assess the direction and magnitude of the effect of a predictor variable on the relative likelihood of the event occurring at any given point in time, controlling for other predictors in the model.

For continuous predictors, such as gene expression values and tumor size, the hazard ratio is the predicted change in the hazard for a unit increase in the predictor. A hazard ratio greater than 1 indicates that the predictor is associated with shorter time-to-event, hazard ratio less than 1 indicates that the predictor is associated with greater time-to-event, and a hazard ratio of 1 indicates that the predictor has no effect on time-to-event. For categorical predictors, the hazard ratio is relative to the reference category.

For any probe set, we can view a detailed HTML report.

- Right-click the row header for row 1
- Select **HTML Report** from the pop-up menu (Figure 7)



	1. Column #	2. Probeset ID	3. HRatio(gene)	4. LowCI(gene)	5. UpCI(gene)	6. p-value(gene)	7. HRatio(tumor size (mm))	8. LowCI(tumor size (mm))	9. UpCI(tumor size (mm))	10. p-value(tumor size (mm))	11. modelfit(0)
1.			0.00202612	3.04539e-05	0.134799	0.00378306	1.05248	1.03171	1.07368	4.93687e-07	6.23673e-07
2.			0.00303448	5.12715e-05	0.179595	0.00535731	1.05171	1.03159	1.07222	3.11591e-07	7.84507e-07
3.			0.0363826	0.00163349	0.810346	0.0363656	1.04793	1.02669	1.06961	7.43324e-06	5.46226e-06
4.			0.0386421	0.00512911	0.291124	0.00159017	1.05556	1.03402	1.07754	2.72499e-07	2.40343e-07
5.			0.0477627	0.000805976	2.83045	0.144175	1.05188	1.03139	1.07278	4.67564e-07	1.69315e-05
6.			0.0490878	0.00463365	0.520025	0.0123149	1.04826	1.0276	1.06934	3.47451e-06	2.14722e-06
7.			0.0594123	0.00893444	0.39508	0.00349212	1.04657	1.02583	1.06774	8.32334e-06	5.39573e-07
8.			0.0597695	0.00982303	0.363675	0.00222903	1.05186	1.03112	1.07302	6.51012e-07	1.54865e-07
9.			0.0602972	0.00984263	0.369388	0.00239011	1.04599	1.02459	1.06784	2.01125e-05	2.20505e-07
10.			0.0683526	0.00460682	1.01416	0.0512025	1.04885	1.02838	1.06974	2.11107e-06	6.83646e-06
11.			0.070517	0.00434987	1.14317	0.0620618	1.05026	1.02983	1.07108	9.84872e-07	8.49759e-06
12.	16595	217220_at	0.0724613	0.00502776	1.04433	0.0538381	1.04753	1.02685	1.06864	5.02856e-06	7.32092e-06
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16.	7854	208343_s_at	0.0824477	0.00591038	1.15012	0.063456	1.05033	1.02979	1.07128	1.09784e-06	8.8296e-06
17.	32283	232301_at	0.0824969	0.0111905	0.608171	0.0143686	1.04959	1.02981	1.06975	6.16348e-07	2.49777e-06
18.	5588	206054_at	0.0836666	0.0086933	0.805229	0.0317522	1.0537	1.0331	1.07472	2.08525e-07	4.97345e-06
19.	7402	207875_at	0.083953	0.00469572	1.50096	0.0921881	1.04913	1.0285	1.07017	2.2057e-06	1.20678e-05

Figure 15. Invoking an HTML report for a probe set

The HTML report (Figure 8) will open in your default web browser.

Cox Regression Result of 217663_at

Produced by Partek Genomics Suite

Model Information go to top

Test	Chi Square	DF	p-value
Likelihood Ratio	28.575278	2	6.23673e-07
Wald	31.412603	2	1.50952e-07
Score	32.678824	2	8.01463e-08

Coefficient Information go to top

Name	DF	Estimate	Std Error	W (Wald Chi Square)	p-value (W)	Hazard Ratio	LowCI	UpCI
217663_at	1	-6.201632	2.141665	8.385116	0.00378306	0.00202612	3.04539e-05	0.134799
tumor size (mm)	1	0.0511531	0.0101721	25.288328	4.93687e-07	1.052484	1.031708	1.073678

Model Fit Statistics go to top

	Without Predictor(s)	With Predictor(s)
-2logL	570.209215	541.633937
AIC	570.209215	545.633937
SBC	570.209215	549.648603

Figure 16. Cox Regression HTML report

Additional Assistance

If you need additional assistance, please visit our support page to submit a help ticket or find phone numbers for regional support.

Your Rating: Results: 34 rates