

cBioPortal Tutorial #7: Pathways

Explore genomics data in the context of pathways

Tutorial Objectives

- Motivate viewing cancer genomics data in context of pathways
- Locate cBioPortal Pathways tabs in **Results** or **Patient** views
- Introduce pathway view components
- Detail pathway view toolbar operations
 - Save as static images
 - Perform layout
 - Expand query genes [Results view only]
 - Edit pathway with PathwayMapper editor [Results view only]
 - Get help on notation
- Walk through different pathway ranking options [Results view only]
- List technology behind the component

Motivation for Pathways View

- Genomic alterations in cancer often affect a relatively small number of signaling pathways involved in cell proliferation, cell growth, apoptosis and DNA repair, among others [1]
- The Cancer Genome Atlas (TCGA), an effort to comprehensively characterize genomic alterations in more than 20 tumor types, produced a number of publications with hand-drawn pathways summarizing such alterations [2]
- Pathways tabs in cBioPortal overlay alteration data from your **study** or **patient of interest** on TCGA pathways while highlighting your genes of interest.
- The Pathways tab is available in *Results view* and *Patient view*

[1] Bahceci et al. "[PathwayMapper: a collaborative visual web editor for cancer pathways and genomic data](#)", Bioinformatics, 2017

[2] [The Cancer Genome Atlas Program](#)

Pathways Tab in Results View

- One may be interested in viewing genetic alterations in a particular *study* in the context of pathways
- Start with Results view in *TP53* and *MDM2/4* alterations in “Glioblastoma (TCGA, Nature 2008)” as an example

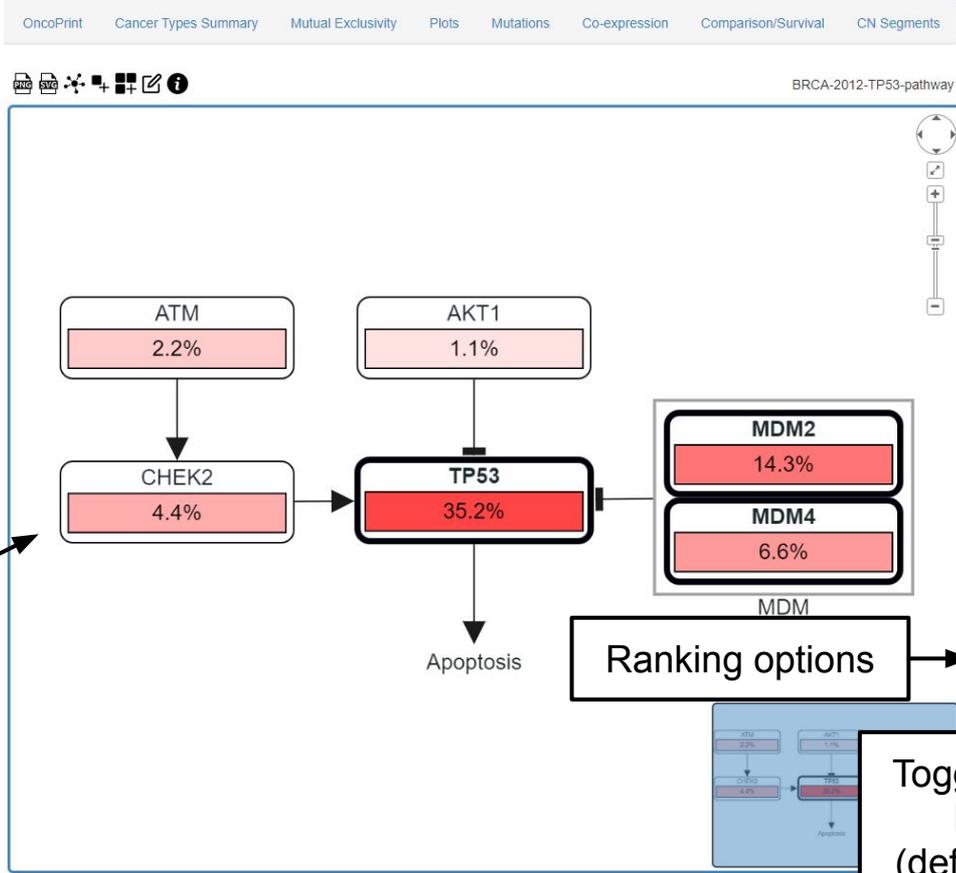
Not sure how to run a query to get to Results View? Review [Tutorial #2: Single Study Query](#)

Pathways Tab in Results View

Pathways tab

TCGA pathways table, sorted by score using current ranking scheme

Toolbar for pathway operations



Pathway with alteration frequencies of selected genetic profiles of the chosen study overlaid

Ranking options

Pathway name	Score	Genes matched
<input checked="" type="radio"/> BRCA-2012-TP53-pathw...	3.00	TP53 MDM2 MDM4
<input type="radio"/> TP53	3.00	TP53 MDM2 MDM4
<input type="radio"/> GBM-2008-TP53-pathwa...	3.00	TP53 MDM2 MDM4
<input checked="" type="radio"/> GBM-2013-TP53-pathwa...	3.00	TP53 MDM2 MDM4
<input type="radio"/> SKCM-2015-TP53-pathw...	2.00	TP53 MDM2
<input type="radio"/> ACC-2016-TP53-RB-p8t...	2.00	TP53 MDM2
<input type="radio"/> BLCA-2014-TP53-RB-p8...	2.00	TP53 MDM2
<input type="radio"/> Cell Cycle	2.00	TP53 MDM2
<input type="radio"/> LUAD-2014-TP53-pathw...	2.00	TP53 MDM2
<input type="radio"/> COADREAD-2012-TP53-p...	1.00	TP53

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Show TCGA PanCancer Atlas pathways only

Ranking options

Match count

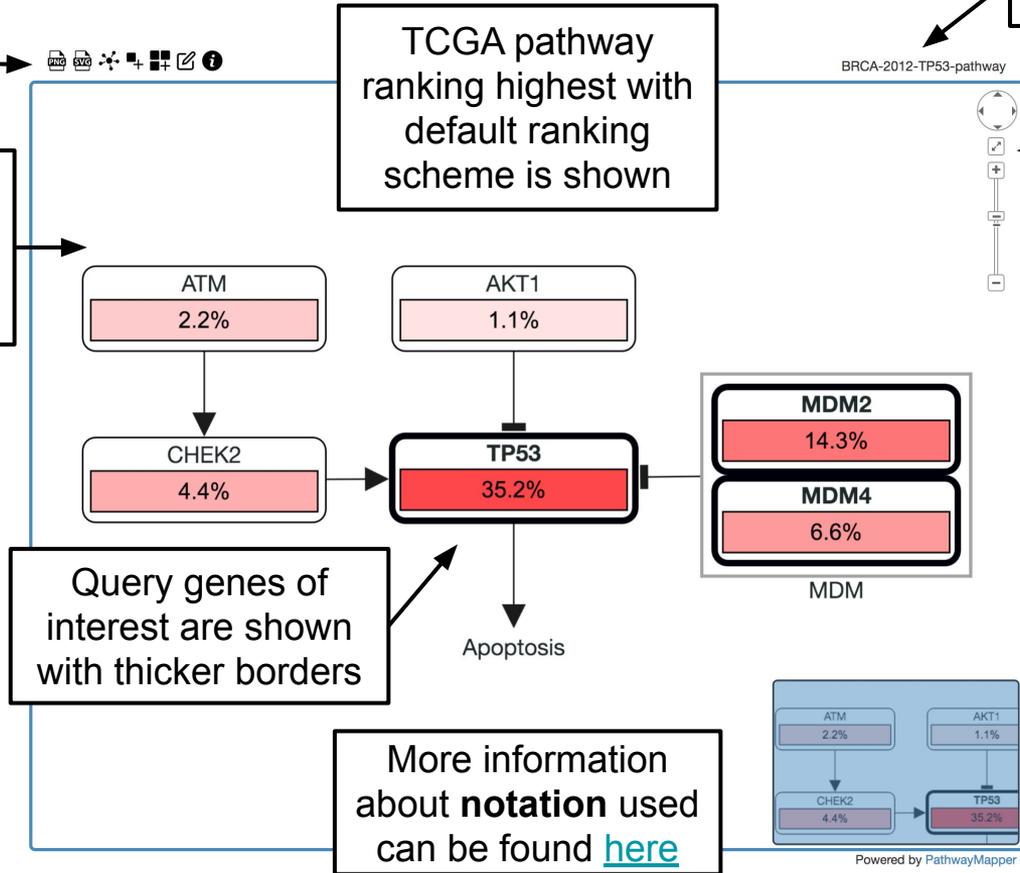
Consider alteration frequency

Toggle between pathways defined by [TCGA PanCancer Atlas](#) (default), or all TCGA publications

Results Pathways View

Toolbar for pathway operations

Resulting pathway tab from example query "TP53 and MDM2/4 alterations in GBM"



Name of TCGA pathway currently shown

Pan-zoom controls

Overview window (useful for navigating large pathways)

Results Pathways View Toolbar

Buttons on the toolbar provide useful operations



Save current pathway as PNG



Save current pathway as SVG



Perform incremental layout, respecting current positions



Add selected genes to query



Add all valid genes in this pathway to query



Edit pathway with [PathwayMapper](#) editor



Quick help with a link to [detailed documentation](#)

Results Pathways Table & Ranking Options

BRCA-2012-TP53-pathway

TCGA pathway currently selected / shown

Score of each TCGA pathway using current ranking scheme

Search pathway by name

Toggle between pathways defined by [TCGA PanCancer Atlas](#) (default), or all TCGA publications

Genes in current pathway matching those in query genes

Consider **alteration frequency**: whether we should take each matching gene with a count of 1 or with a weight of its alteration frequency in scoring

Match count vs **percentage**: whether we should score pathways by the number of genes matched or by the percentage of genes matched

Pathway name	Score	Genes matched
<input checked="" type="radio"/> BRCA-2012-TP53-pathw...	3.00	TP53 MDM2 MDM4
<input type="radio"/> TP53	3.00	TP53 MDM2 MDM4
<input type="radio"/> GBM-2008-TP53-pathwa...	3.00	TP53 MDM2 MDM4
<input type="radio"/> GBM-2013-TP53-pathwa...	2.00	TP53 MDM2 MDM4
<input type="radio"/> SKCM-2015-TP53-pathw...	2.00	TP53 MDM2
<input type="radio"/> ACC-2016-TP53-RB-pat...	2.00	TP53 MDM2
<input type="radio"/> BLCA-2014-TP53-RB-pa...	2.00	TP53 MDM2
<input type="radio"/> Cell Cycle	2.00	TP53 MDM2
<input type="radio"/> LUAD-2014-TP53-pathw...	2.00	TP53 MDM2
<input type="radio"/> COADREAD-2012-TP53-p...	1.00	TP53

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Show TCGA PanCancer Atlas pathways only

Ranking options

Match count

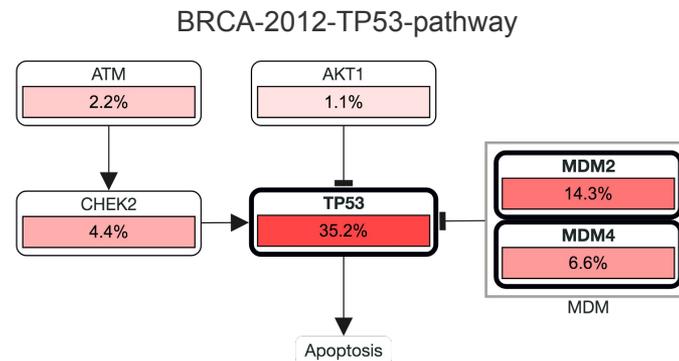
Consider alteration frequency

MDM2
14.3%

MDM4

Results Pathways View Ranking Options

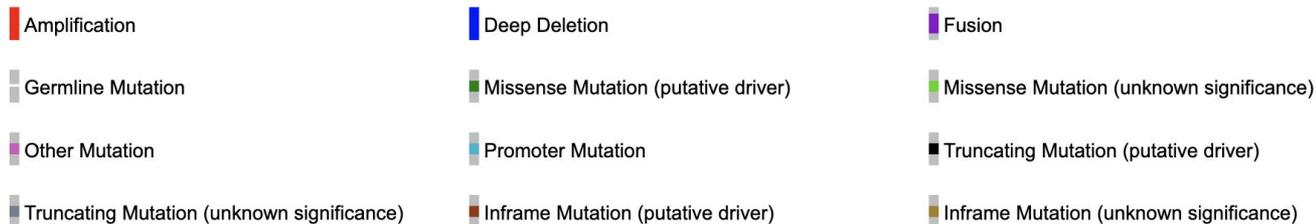
- When a query gene is in a particular pathway, we consider it “matching”.
- Example:
 - Query genes: TP53, MDM2, MDM4
 - Pathway: BRCA-2012-TP53-pathway (see on the right)



- Match count vs percentage:
 - Count the query genes matching and rank pathways based on this count. The score in our example is **3** as all three genes are in the pathway.
 - Take the ratio of query genes matching to total number of genes in the pathway. The score in our example is $3 / 6 = \mathbf{50\%}$.
- Consider alteration frequency:
 - When checked, each matching gene will not contribute to the score as 1 unit but with its alteration frequency of that gene. The score in our example is $35.2 + 14.3 + 6.6 = \mathbf{56.1}$.

Pathways Tab in Patient View

- One may be interested in viewing following types of genetic alterations of a *patient* in the context of pathways



Putative driver and unknown significance annotations are based on data from OncoKB and CancerHotspots.org.

- Start with “Patient view of an endometrial cancer case (TCGA, Nature 2013)” as an example

Patient: [TCGA-BK-A0CC](#), Female, 69 years old, Endometrial Cancer (Uterine Serous Carcinoma/Uterine Papillary Serous Carcinoma), [Uterine Corpus Endometrial Carcinoma \(TCGA, Nature 2013\)](#)
[LIVING](#) (10 months), [DiseaseFree](#) (10 months)

Samples: 1 [TCGA-BK-A0CC-01](#), Primary, Stage III

Not sure how to get to patient view? Review [Tutorial #3: Patient View](#)

Patient Pathways View

The screenshot displays the 'Patient Pathways View' interface. At the top, there is a navigation bar with tabs: 'Summary', 'Pathways', 'Clinical Data', 'Pathology Report', and 'Tissue Image'. The 'Pathways' tab is selected. Below the navigation bar is a toolbar with icons for print, download, share, and help. The main content area shows a pathway diagram for 'ACC-2016-TP53-RB-pathway'. The diagram is a flowchart starting with CDKN2A at the top, which branches into CDK4 and MDM2. CDK4 leads to RB1, and MDM2 leads to TP53. Genetic alterations are indicated by red bars: a red bar under CCNE1 (with a note 'TCGA-BK-A0CC-01 CNA: CCNE1 AMPLIFIED') and a red bar under TP53. A text box points to the diagram with the text 'More information about notation used can be found here'. Another text box points to the CCNE1 node with the text 'Pathway with genetic alterations of the patient'. A third text box points to the pathway list on the right with the text 'TCGA pathways table, where altered pathways are shown before non-altered ones by default'. The pathway list on the right has columns for 'Pathway name', 'Pathway altered', and 'Genes matched'. The first three pathways are selected (radio button checked): 'ACC-2016-TP53-RB-pat...', 'BLCA-2014-TP53-RB-pa...', and 'Cell Cycle'. Below the list is a 'Showing 1-10 of 55' indicator and a 'Show more' button.

Pathways tab

Summary Pathways Clinical Data Pathology Report Tissue Image

Toolbar for pathway operations

More information about notation used can be found [here](#)

Pathway with genetic alterations of the patient

TCGA pathways table, where altered pathways are shown before non-altered ones by default

ACC-2016-TP53-RB-pathway

Pathway name	Pathway altered	Genes matched
<input checked="" type="radio"/> ACC-2016-TP53-RB-pat...	Yes	TP53 CCNE1
<input type="radio"/> BLCA-2014-TP53-RB-pa...	Yes	TP53 CCNE1
<input type="radio"/> Cell Cycle	Yes	TP53 CCNE1
<input type="radio"/> BRCA-2012-Cell-cycle...		
<input type="radio"/> BRCA-2012-RTK-RAS-Pl...		
<input type="radio"/> ESAD-2017-RTK-RAS-Pl...		
<input type="radio"/> LUAD-2014-Cell-cycle...		
<input type="radio"/> ESAD-2017-Cell-cycle...		
<input type="radio"/> KIRC-2013-RTK-RAS-Pl...		
<input type="radio"/> HNSC-2015-RTK-RAS-Pl...	Yes	EGFR

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Patient Pathways View

Summary Pathways Clinical Data Pathology Report Tissue Image

ACC-2016-TP53-RB-pathway

Pathways tab from example "Patient view of an endometrial cancer case"

Pan-zoom controls

Name of TCGA pathway currently shown

CDKN2A

CDK4

MDM2

CCNE1

RB1

TP53

TCGA-BK-A0CC-01
CNA: CCNE1 AMPLIFIED

Mouse over to see alteration details

Altered genes are shown with thicker borders

Pathway name	Pathway altered	Genes matched
<input checked="" type="radio"/> ACC-2016-TP53-RB-pat...	Yes	TP53 CCNE1
<input type="radio"/> BLCA-2014-TP53-RB-pa...	Yes	TP53 CCNE1
<input type="radio"/> Cell Cycle	Yes	TP53 CCNE1
<input type="radio"/> BRCA-2012-Cell-cycle...	Yes	CCNE1
<input type="radio"/> BRCA-2012-RTK-RAS-Pl...	Yes	EGFR
<input type="radio"/> ESAD-2017-RTK-RAS-Pl...	Yes	EGFR
<input type="radio"/> LUAD-2014-Cell-cycle...	Yes	CCNE1
<input type="radio"/> ESAD-2017-Cell-cycle...	Yes	CCNE1
<input type="radio"/> KIRC-2013-RTK-RAS-Pl...	Yes	EGFR
<input type="radio"/> HNSC-2015-RTK-RAS-Pl...	Yes	EGFR

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Patient Pathways View

Buttons on the toolbar
provide useful operations



Save current pathway as PNG



Save current pathway as SVG



Perform incremental layout, respecting current positions



Quick help with a link to [detailed documentation](#)

Pathways tabs in cBioPortal were built using a *viewer only edition* of [PathwayMapper](#), which in turn was based on [Cytoscape.js](#), a fully featured graph library in pure JavaScript.

Questions?

Check out our other tutorials
or email us at:

cbioportal@googlegroups.com