

# RLIMS-P Website Help Document

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**URL:** [http://annotation.dbi.udel.edu/text\\_mining/rlimsp2/](http://annotation.dbi.udel.edu/text_mining/rlimsp2/)

## Introduction

**RLIMS-P** (Figure 1) is a rule-based text-mining program specifically designed to extract protein phosphorylation information on protein kinases, substrates and phosphorylation sites from biomedical literature (Hu *et al.*, 2005). **RLIMS-P** currently works on PubMed abstracts, but it will be extended to open access full text articles soon. **RLIMS-P** allows users to quickly find the relevant literature for phosphorylated proteins and their kinases, thereby facilitating the study of kinase-substrate networks.

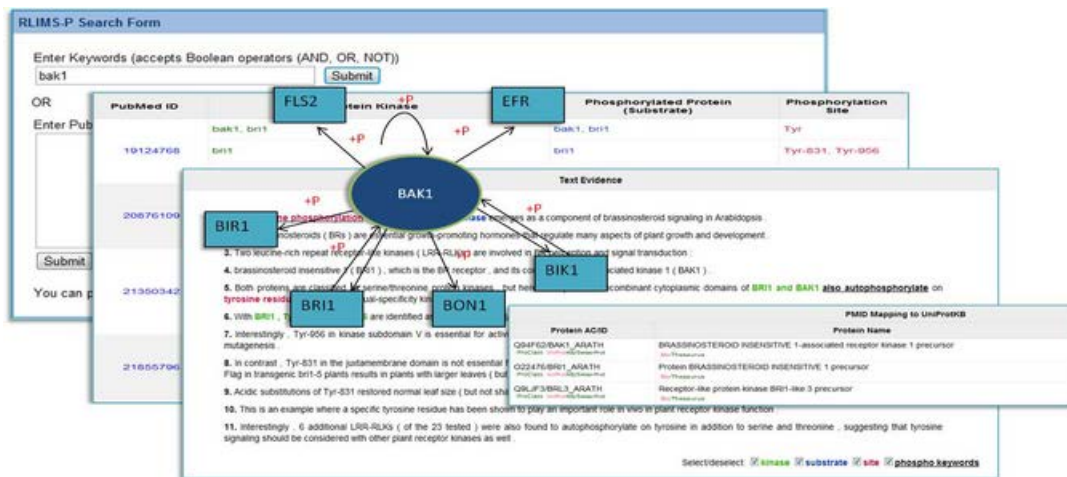


Figure 1: RLIMS-P overview.

## RLIMS-P architecture

The RLIMS-P website consists of two parts: **1**) a back-end database and **2**) a web interface (Figure 1). Phosphorylation information is first extracted from Medline abstracts by RLIMS-P version 2.0, and then processed and stored in the database for easy and fast later retrieval. The web interface enables users to search for phosphorylation information using keywords or a list of PMIDs. The results (kinase, substrate, site) are displayed in sortable tables, which are downloadable for further research.

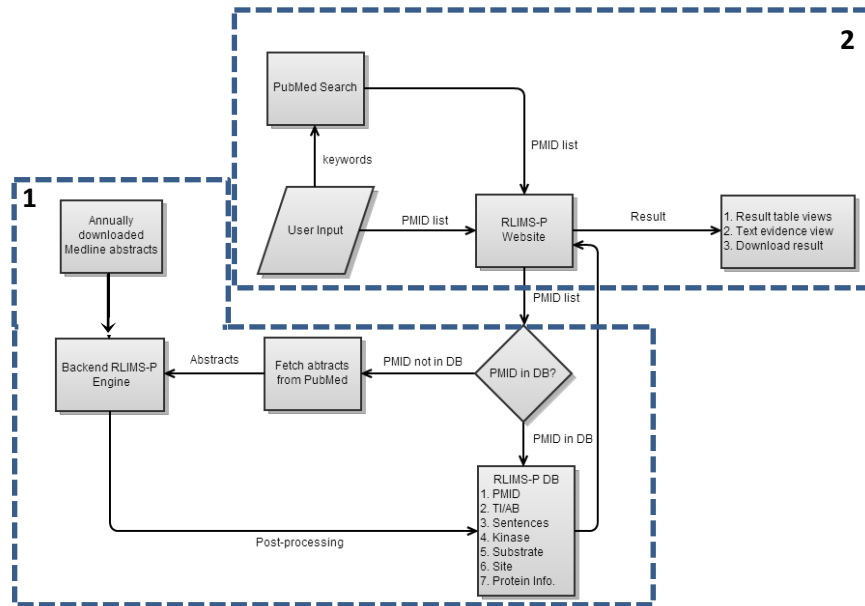


Figure 2: RLIMS-P system architecture

## RLIMS-P interface

### Login

To edit and export curated RLIMS-P results, users need to login (Figure 3, **1**). In order to login for the first time, users need to sign up (Figure 3, **2**) by entering their e-mail, name and affiliation (Figure 3, **3**). Once logged in, the heading will appear as in Figure 4.

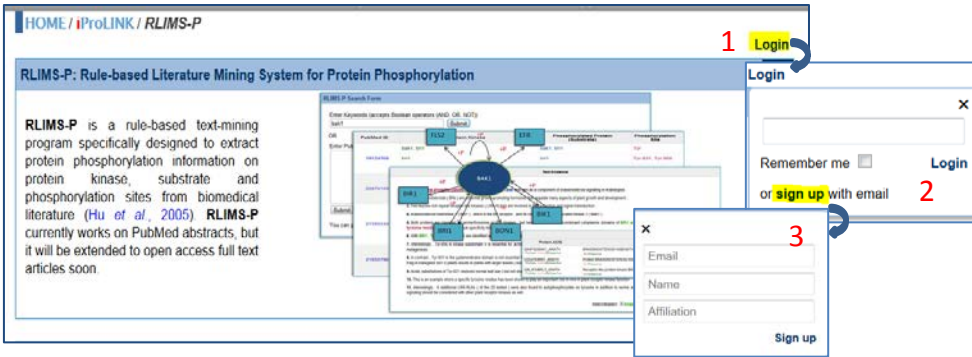


Figure 3: Login screen

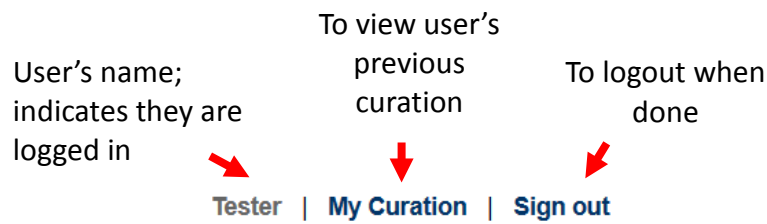


Figure 4: Appearance of heading after login

## Input page

**In short**  
**Input: Keywords or Pubmed IDs (IDs)**

The new website allows the input of keywords or phrases (Figure 5, 1) that can be combined using Boolean operators. This input is used to query PubMed documents, and relevant documents are retrieved for processing by RLIMS-P. Alternatively a list of PMIDs (Figure 5, 2), delimited by comma, space, or new line can be entered. Users can enter up to 200 PMIDs per run. In both cases, clicking on **Submit Query** will retrieve the results, and clicking on **Reset** will empty the query box, so that a different query can be entered.

**RLIMS-P Search Form**

1 Enter Keywords (accepts Boolean operators (AND, OR, NOT))

OR

2 Enter PubMed IDs (PMIDs) delimited by "," or space, e.g., 2108025, 16436437.

23412089

23406730

23400998

23397032

23396981

23396967

You can process up to 200 PMIDs per run. [Sample output](#)

Figure 5: RLIMS-P input interface

## Results Page

**In short**  
**RLIMS-P Results: statistics, summary table with different views (kinase, substrate, PMID), access to text evidence, and table saving**

**Return links**

[Previous Page](#) | [RLIMSP Home](#)

[Tester](#) | [My Curation](#) | [Sign out](#)

The latest **200** of **629** documents with potential phosphorylation are processed. [Save PMIDs](#)  
 Documents RLIMS-P positive=**178** where Kinase=**42**, Substrate=**164** and Site=**39**  
 Click [here](#) to see full results. Note the processing time may be long due to the big amount of PMIDs.

**Statistics**
**View options**
**Save**

**Summary** View by Summary ▾ Save Table

Show Selected	Results Table	Protein Kinase	Phosphorylated Protein (Substrate)	No. of Sentences	Text Evidence
<input type="checkbox"/>	22126602	flt3/itd-related, flt3/itd, flt3	<a href="#">beta-catenin</a>	7	<a href="#">Text Evidence</a>
<input type="checkbox"/>	22369945	p21-activated kinase 1 ( pak1 ), protein kinase a, pak1 k299r	<a href="#">beta-catenin</a>	7	<a href="#">Text Evidence</a>
<input type="checkbox"/>	22511927	kinase d1 ( pkd1 )	<a href="#">beta-catenin</a> <a href="#">beta-catenin</a>	5	<a href="#">Text Evidence</a>
<input type="checkbox"/>	22025562	ck1alpha	<b>RLIMS-P annotation</b>	3	<a href="#">Text Evidence</a>
<input type="checkbox"/>	22515442	pkm2, c-src, y333 beta-catenin	<a href="#">beta-catenin</a> , <a href="#">pkm2</a>	2	<a href="#">Text Evidence</a>

**Link to PubMed**
**Links to text evidence and curation interface**

Figure 6: Overview of the results page

**Overview:** The results page contains the search statistics and the results table (Figure 6). Users can customize their view of the information in the table and download their results from this page.

**RLIMS-P Statistics:** The new RLIMS-P results page presents detailed statistics on the documents with potential phosphorylation information (those containing a phosphorylation-related trigger word) and those with phosphorylation information according to RLIMS-P processing (Figure 7). For convenience, only the results for the latest 200 PMIDs are shown for a keyword search, but the user can choose to access the full result set.

[← Previous Page](#)
[RLIMSP Home](#)

The latest **200** of **629** documents with potential phosphorylation are processed. [Save PMIDs](#)
➔ Total PMIDs processed; link to save PMIDs  
 Documents RLIMS-P positive=**178** where Kinase=**42**, Substrate=**154** and Site=**39**
➔ Statistics for processed PMIDs  
 Click [here](#) to see full results. Note the processing time may be long due to the big amount of PMIDs.

➔ [Link to full results](#)

**Figure 7: RLIMS-P Statistics**

**Results table:**

**(i) Columns in the results table:** The results table contains the following columns. Note that the order and appearance of these columns will vary depending on a variety of user-settable options (see below).

**Show Selected:** Allows the user to select which annotation lines to display. Annotation lines are selected by clicking on the corresponding check boxes and then on “Show Selected” (Figure 8). annotation lines by clicking on the corresponding check boxes and then on Show Selected.

Show Selected	PubMed ID	Protein Kinase	Phosphorylated Protein (Substrate)	Phosphorylation Site	No. of Sentences	Text Evidence
<input type="checkbox"/>		ckiepsilon	ror2	Ser, Thr	1	E2 <sup>o</sup>
<input type="checkbox"/>		ckiepsilon	ckiepsilon	Ser, Thr	1	E2 <sup>o</sup>
<input checked="" type="checkbox"/>	15375164	ror2	ror2	Tyr	1	E2 <sup>o</sup>
<input type="checkbox"/>		g protein-coupled receptor kinase 2		Tyr	1	E2 <sup>o</sup>
<input type="checkbox"/>		ror2		Ser, Thr, Tyr	1	E2 <sup>o</sup>
<input checked="" type="checkbox"/>		gsk-3beta	beta-catenin	Ser-45	1	E2 <sup>o</sup>
<input type="checkbox"/>		ck1	beta-catenin	Ser-45	1	E2 <sup>o</sup>
<input checked="" type="checkbox"/>	12051714	gsk-3	beta-catenin	Ser-45	1	E2 <sup>o</sup>
<input type="checkbox"/>			beta-catenin	Ser-33, Ser-37, Thr-41	1	E2 <sup>o</sup>
<input type="checkbox"/>			wnt	Ser, Thr	1	E2 <sup>o</sup>
<input type="checkbox"/>			beta-catenin	Ser, Thr	1	E2 <sup>o</sup>
			beta-catenin	Ser-33, Ser-37, Thr-41, Ser-45	1	E2 <sup>o</sup>

**Figure 8: Displaying desired annotation lines using the Show Selected column**

**PubMed ID:** Displays the PubMed ID of each RLIMS-P positive document. Clicking on the ID will link to the PubMed abstract.

**Protein Kinase:** Kinases identified by RLIMS-P are shown in green.

Last updated 08/28/2013

**Phosphorylated Protein (Substrate):** Proteins determined by RLIMS-P to be phosphorylated substrates are shown in blue.

**Phosphorylation Site:** Phosphorylation sites identified by RLIMS-P are shown in red. This column is not included in the Summary view (see below).

**No. of Sentences:** Indicates the number of sentences from the document that contain evidence for that line of annotation. Clicking on the number links to the Text Evidence/Curation page for that line of annotation (Figure 9).

**View by Substrate** Show all annotations

Show Selected	Phosphorylated Protein (Substrate)	PubMed ID	Protein Kinase	Phosphorylation Site	No. of Sentences	Text Evidence
<input type="checkbox"/>	beta-catenin	22126602	flt3/itd-related	Tyr	1	
<input type="checkbox"/>	beta-catenin	22369945	p21-activated kinase 1 ( pak1 ), protein kinase a	Ser-675	1	
<input type="checkbox"/>	beta-catenin	22369945	pak1 k299r	Thr-423	1	
<input type="checkbox"/>	beta-catenin	22515442	pkm2, c-src	Tyr-333	1	
<input type="checkbox"/>	beta-catenin	22126602	flt3/itd	Tyr-654	1	
<input type="checkbox"/>	beta-catenin	22369945	p21-activated kinase 1 ( pak1 )	Ser-663	2	
<input type="checkbox"/>	beta-catenin	22126602	flt3	Tyr-654	1	

**Text Evidence**

PubMed Information  
 22369945 2012 Mar 16 Park MH, Kim DJ, You ST, Lee CS, Kim H... Biochem Biophys Res Commun Full Text

RLIMS-P Annotation

No.	Kinase	Substrate	Site	Sentence	Comment	Validation
1	p21-activated kinase 1 ( pak1 )	beta-catenin	Ser-663	6, 9		<input type="checkbox"/> <input type="checkbox"/>

Add Annotation

Gene Normalization

Protein	Name	UniProtKB AC	Add UniProtKB AC	Annotation No.
Kinase	pak1	Not normalized	<input type="text"/>	1
Substrate	beta-catenin	Not normalized	<input type="text"/>	1

Add Gene Normalization

PMID Mapping to UniProtKB

Protein AC/ID	Protein Name	Organism Name
Q13153/PAK1_HUMAN <small>ProClass: /M/S/Se/Pr/</small>	Serine/threonine-protein kinase PAK 1	Homo sapiens (Human)
Q8WYA6/CTBL1_HUMAN <small>ProClass: /M/S/Se/Pr/</small>	Beta-catenin-like protein 1	Homo sapiens (Human)

Text Evidence

6 Mutagenesis followed by a kinase assay revealed that PAK1 phosphorylated S663 in addition to S675, and an anti-phospho-beta-catenin (S663) antibody detected the phosphorylation of S663 downstream of PAK1 in various human colon cancer cells.

9 Taken together, these results provide evidence that PAK1 specifically phosphorylates beta-catenin at S663 and that this phosphorylation is essential for the PAK1-mediated transcriptional activation of beta-catenin.

Select/deselect:  kinase  substrate  site  phospho keywords

**Figure 9: Clicking on the number of sentences displays the Text Evidence page for that line of annotation**

**Text Evidence/Curation:** Clicking on the icon provides access to the RLIMS-P text evidence and editing/curation page for the entire title and abstract of the document indicated on that line of annotation (see Text Evidence/Curation section below).

**(ii) Column sorting:** Each column in the results table can be sorted based on ascending or descending numerical or alphabetical by clicking on the arrows next to the column headings (Figure 10).

Show Selected	PubMed ID	Protein Kinase	Phosphorylated Protein (Substrate)
---------------	-----------	----------------	------------------------------------

**Figure 10: Arrows next to the column headings can be used to sort the results**

**(iii) View Options:** Users can organize the display in the results table according to their interests using the “View by” menu (Figure 6, [View options](#)).

**View by Summary:** The default view of the RLIMS-P results table is the Summary view, in which all of the kinases and phosphorylated substrates identified in a particular document are summarized in a single line of annotation (Figure 11). Documents containing kinase, substrate and site information are listed first. Phosphorylation site information is not presented in this view.

[Previous Page](#) [RLIMSP Home](#)

[Tester](#) | [My Curation](#) | [Sign out](#)

The latest 200 of 629 documents with potential phosphorylation are processed. [Save PMIDs](#)  
 Documents RLIMS-P positive=178 where Kinase=42, Substrate=154 and Site=39  
 Click [here](#) to see full results. Note the processing time may be long due to the big amount of PMIDs.

**Summary** View by Summary ▾ Save Table

Show Selected	PubMed ID	Protein Kinase	Phosphorylated Protein (Substrate)	No. of Sentences	Text Evidence
<input type="checkbox"/>	22126602	flt3/itd-related, flt3/itd, flt3	beta-catenin	7	EQ*
<input type="checkbox"/>	22369945	p21-activated kinase 1 ( pak1 ), protein kinase a, pak1 k299r	beta-catenin	7	EQ*
<input type="checkbox"/>	22511927	kinase d1 ( pkd1 )	beta-catenin, t120 beta-catenin	5	EQ*
<input type="checkbox"/>	22025562	ck1alpha	c-myc, beta-catenin	3	EQ*
<input type="checkbox"/>	22515442	pkm2, c-src, y333 beta-catenin	beta-catenin, pkm2	2	EQ*

**Figure 11: View by Summary**

**View by PMID:** This view is document-centric, grouping together all of the annotation lines for a particular document (Figure 12). Unlike the Summary view, each line of annotation in the PMID view consists of a single kinase, its substrate, and the corresponding phosphorylation site(s). Columns are left blank if kinase, substrate, and/or site information was not obtained from the document.

**View by PMID** [Show all annotations](#) View by PMID ▾ Save Table

Show Selected	PubMed ID	Protein Kinase	Phosphorylated Protein (Substrate)	Phosphorylation Site#	No. of Sentences	Text Evidence
<input type="checkbox"/>	22126602	flt3/itd-related	beta-catenin	Tyr	1	EQ*
<input type="checkbox"/>		flt3/itd	beta-catenin	Tyr-654	1	EQ*
<input type="checkbox"/>		flt3	beta-catenin	Tyr-654	1	EQ*
<input type="checkbox"/>	22369945	p21-activated kinase 1 ( pak1 ), protein kinase a	beta-catenin	Ser-675	1	EQ*
<input type="checkbox"/>		pak1 k299r	beta-catenin	Thr-423	1	EQ*
<input type="checkbox"/>		p21-activated kinase 1 ( pak1 )	beta-catenin	Ser-663	2	EQ*

**Figure 12: View by PMID**

**View by Kinase:** The view is kinase-centric, grouping together information for each unique kinase mentioned in the document set (Figure 13). Note that we are still working on improving the standardization of protein names, and therefore in some cases, if a kinase is referred to by multiple names, all mentions of the kinase will not be collected into a single group. Within a group, each line of annotation shows an individual substrate of the kinase, the phosphorylation site(s), and the PMID for the document containing the evidence for that annotation. Substrate and/or site columns will be left blank if that information was not obtained from a particular document.

**View by Kinase** Show all annotations View by Kinase Save Table

Show Selected	Protein Kinase	PubMed ID	Phosphorylated Protein (Substrate)	Phosphorylation Site	No. of Sentences	Text Evidence
<input type="checkbox"/>	kinase d1 ( pkd1 )	22511927	beta catenin	Thr-120	2	E3 <sup>a</sup>
		22511927	t120 beta-catenin	Thr-120	1	E3 <sup>a</sup>
<input type="checkbox"/>	ck1alpha	22025562	c-myc	Ser-252	1	E3 <sup>a</sup>
		22025562	beta-catenin		1	E3 <sup>a</sup>
<input type="checkbox"/>	gsk-3beta	21496192	beta-catenin	Ser-45	1	E3 <sup>a</sup>
		21837368	beta-catenin		1	E3 <sup>a</sup>


**Figure 13: View by Kinase**

*View By Substrate:* This view is substrate-centric, grouping together information for each unique substrate mentioned the document set (Figure 14). Note that we are still working on improving the standardization of protein names, and therefore in some cases, if a substrate is referred to by multiple names, all mentions of the substrate will not be collected into a single group. Within a group, each line of annotation shows an individual kinase for the substrate, the phosphorylation site(s), and the PMID for the document containing the evidence for that annotation. Kinase and/or site columns will be left blank if that information was not obtained from a particular document.



**View by Substrate** Show all annotations View by Substrate Save Table

Show Selected	Phosphorylated Protein (Substrate)	PubMed ID	Protein Kinase	Phosphorylation Site	No. of Sentences	Text Evidence
<input type="checkbox"/>	beta-catenin	22126602	flt3/itd-related	Tyr	1	E3 <sup>a</sup>
		22369945	p21-activated kinase 1 ( pak1 ), protein kinase a	Ser-675	1	E3 <sup>a</sup>
		22369945	pak1 k299r	Thr-423	1	E3 <sup>a</sup>
		22515442	pkm2, c-src	Tyr-333	1	E3 <sup>a</sup>
		22126602	flt3/itd	Tyr-654	1	E3 <sup>a</sup>
		22369945	p21-activated kinase 1 ( pak1 )	Ser-663	2	E3 <sup>a</sup>
		22126602	flt3	Tyr-654	1	E3 <sup>a</sup>
		22173096	pak4	Ser-675	1	E3 <sup>a</sup>
		23076981	glycogen synthase kinase-3beta ( gsk-3beta ), kinase casein kinase 1alpha ( ck1alpha )	Ser-33, Ser-37, Thr-41, Ser-45	1	E3 <sup>a</sup>

**Figure 14: View by Substrate**

**(iv) Expanded RLIMS-P results:** Clicking on the  icon will expand the table to show the full RLIMS-P results, including information that is partially redundant (as is the case for the annotation in the dashed box in Figure 15). This option is available for all of the table arrangements described in the previous section.



Show all annotations   Click to show expanded annotation


<input type="checkbox"/>	22946057	ck1	wnt3a	Ser, Thr	1	E3"
		fyn, src	wnt3a	Tyr	1	E3"

<input type="checkbox"/>	22946057	fyn, src	wnt3a	Tyr	1	E3"
		ck1	wnt3a	Ser, Thr	1	E3"
		ck1	wnt3a		1	E3"

Figure 15: Expanded annotation

(v) *Downloading the results table:* Clicking on the Download button will create a comma-delimited file containing the PMID, kinase, substrate, and site information and the associated evidence sentences (Figure 16). The order of the information in the file will vary depending on the view from which it was downloaded.


View by PMID  View by PMID Download

Show Selected	PubMed ID	Protein Kinase	Phosphorylated Protein (Substrate)	Phosphorylation Site	No. of Sentences	Text Evidence/Curation
<input type="checkbox"/>	22126602	flt3/itd-related	beta-catenin	Tyr	1	#s
		flt3/itd				
		flt3				
		p21-activate kinase a				
<input type="checkbox"/>	22369945	pak1 k299r	beta-catenin	Tyr		
			beta-catenin	Tyr		
			beta-catenin	Tyr-654		
			beta-catenin	Tyr-654		
			beta-catenin	Tyr-654		
		p21-activate	beta-catenin	Ser-675		
		pak1 k299r	beta-catenin	Thr-423		
		p21-activate	beta-catenin	Ser-663		
		p21-activate	beta-catenin	Ser-663		
			beta-catenin	Ser-663		
			beta-catenin	Ser-663		
		p21-activated kinase 1 ( pak1 ),protein	beta-catenin			
			beta-catenin			


Figure 16: Downloading the results table

Text Evidence/Curation Page

**In short**  
**RLIMS-P Text Evidence/Curation page: statistics, text evidence, curation interface (including PubMed information, RLIMS-P annotation, gene normalization, and PMID mapping to UniProtKB), and download options**

**Accessing the Text Evidence/Curation Page:** Clicking on the  icon in the results table provides access to the RLIMS-P text evidence and editing/curation page for the entire title and abstract of the document indicated on that line of annotation (Figure 6). Clicking on the number in the “No. of Sentences” column of the results table provides access to the text evidence and editing/curation page for that line of annotation only (Figure 6, Figure 9).

**Returning to the results table:** From the Text Evidence/Curation page, users can return to the Results page by choosing a viewing option (Summary, PMID, Kinase, or Substrate) from the Back to Views menu (Figure 17).



**Text Evidence**

**PubMed Information**

22126602 2012 Apr Kajiguchi T, Katsumi A, Tanizaki R, Kiyoi H, Naoe T Eur J Haematol

**RLIMS-P Annotation**

No.	Kinase	Substrate	Site	Sentence	Comment	Validation
1	flt3/itd-related	beta-catenin	Tyr	1		✓ X
2	flt3/itd	beta-catenin	Tyr-654	5		✓ X
3	flt3	beta-catenin	Tyr-654	7		✓ X

**Summary**

PMID

1 TI - Y654 of beta-cate Kinase for FLT3/ITD-related tyrosine phosphorylation and nuclea -catenin .

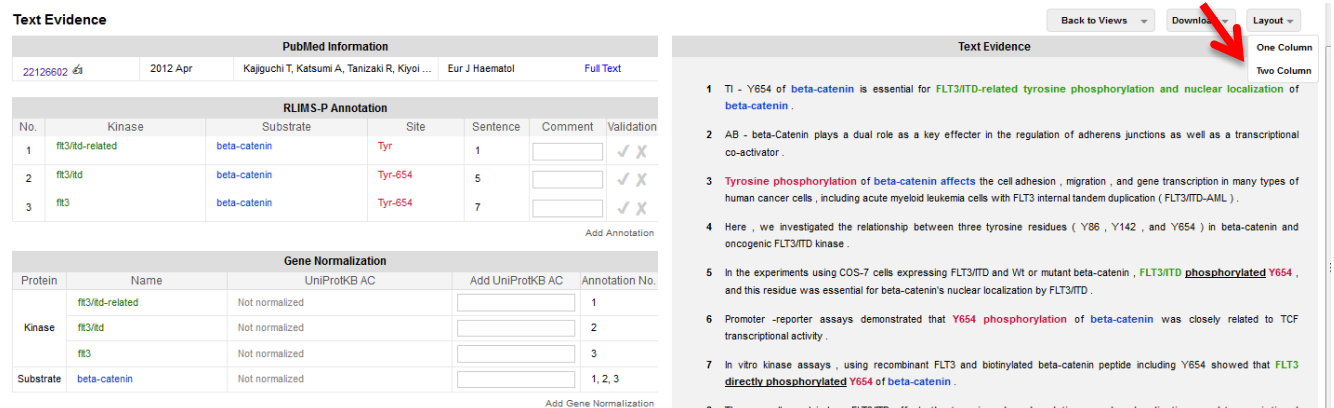
2 AB - beta-Catenin plays a dual role as a key effector in the regulation of adherens junctions as well as a transcriptional co-activator .

3 Tyrosine phosphorylation of beta-catenin affects the cell adhesion , migration , and gene transcription in many types of human cancer cells , including acute myeloid

Figure 17: The Back to Views menu on the Text Evidence/Curation page

**RLIMS-P Statistics:** Like the Results page, the Text Evidence/Curation page displays the RLIMS-P statistics for the current query (Figure 7).

**Layout:** Using the Layout menu, users can switch between a two-column (Figure 18) and one-column (Figure 19) layout of the Text Evidence/Curation page.



**Text Evidence**

**PubMed Information**

22126602 2012 Apr Kajiguchi T, Katsumi A, Tanizaki R, Kiyoi ... Eur J Haematol Full Text

**RLIMS-P Annotation**

No.	Kinase	Substrate	Site	Sentence	Comment	Validation
1	flt3/itd-related	beta-catenin	Tyr	1		✓ X
2	flt3/itd	beta-catenin	Tyr-654	5		✓ X
3	flt3	beta-catenin	Tyr-654	7		✓ X

Add Annotation

**Gene Normalization**

Protein	Name	UniProtKB AC	Add UniProtKB AC	Annotation No.
Kinase	flt3/itd-related	Not normalized		1
	flt3/itd	Not normalized		2
	flt3	Not normalized		3
Substrate	beta-catenin	Not normalized		1, 2, 3

Add Gene Normalization

**Text Evidence**

1 TI - Y654 of beta-catenin is essential for FLT3/ITD-related tyrosine phosphorylation and nuclear localization of beta-catenin .

2 AB - beta-Catenin plays a dual role as a key effector in the regulation of adherens junctions as well as a transcriptional co-activator .

3 Tyrosine phosphorylation of beta-catenin affects the cell adhesion , migration , and gene transcription in many types of human cancer cells , including acute myeloid leukemia cells with FLT3 internal tandem duplication ( FLT3/ITD-AML ) .

4 Here , we investigated the relationship between three tyrosine residues ( Y86 , Y142 , and Y654 ) in beta-catenin and oncogenic FLT3/ITD kinase .


5 In the experiments using COS-7 cells expressing FLT3/ITD and Wt or mutant beta-catenin , FLT3/ITD phosphorylated Y654 , and this residue was essential for beta-catenin's nuclear localization by FLT3/ITD .


6 Promoter -reporter assays demonstrated that Y654 phosphorylation of beta-catenin was closely related to TCF transcriptional activity .

7 In vitro kinase assays , using recombinant FLT3 and biotinylated beta-catenin peptide including Y654 showed that FLT3 directly phosphorylated Y654 of beta-catenin .

8 These results explain how FLT3/ITD affects the tyrosine phosphorylation , nuclear localization , and transcriptional

Figure 18: Two-column layout of the Text Evidence/Curation page

**Text Evidence** Back to Views ▾ Download  Layout ▾

PubMed Information						One Column
22126602 	2012 Apr	Kajiguchi T, Katsumi A, Tanizaki R, Kiyoi ...	Eur J Haematol	<a href="#">Full Text</a>		Two Column

RLIMS-P Annotation						
No.	Kinase	Substrate	Site	Sentence	Comment	Validation
1	<a href="#">flt3/itd-related</a>	<a href="#">beta-catenin</a>	<a href="#">Tyr</a>	1	<input type="text"/>	<input checked="" type="checkbox"/> <input type="checkbox"/>
2	<a href="#">flt3/itd</a>	<a href="#">beta-catenin</a>	<a href="#">Tyr-654</a>	5	<input type="text"/>	<input checked="" type="checkbox"/> <input type="checkbox"/>
3	<a href="#">flt3</a>	<a href="#">beta-catenin</a>	<a href="#">Tyr-654</a>	7	<input type="text"/>	<input checked="" type="checkbox"/> <input type="checkbox"/>

Add Annotation

Gene Normalization				
Protein	Name	UniProtKB AC	Add UniProtKB AC	Annotation No.
Kinase	<a href="#">flt3/itd-related</a>	Not normalized	<input type="text"/>	1
	<a href="#">flt3/itd</a>	Not normalized	<input type="text"/>	2
	<a href="#">flt3</a>	Not normalized	<input type="text"/>	3
Substrate	<a href="#">beta-catenin</a>	Not normalized	<input type="text"/>	1, 2, 3


Add Gene Normalization

**Text Evidence**

- 1 TI - Y654 of [beta-catenin](#) is essential for [FLT3/ITD-related tyrosine phosphorylation and nuclear localization of beta-catenin](#) .
- 2 AB - beta-Catenin plays a dual role as a key effector in the regulation of adherens junctions as well as a transcriptional co-activator .
- 3 [Tyrosine phosphorylation of beta-catenin affects](#) the cell adhesion , migration , and gene transcription in many types of human cancer cells , including acute myeloid leukemia cells with FLT3 internal tandem duplication ( FLT3/ITD-AML ) .

**Figure 19: One-column layout of the Text Evidence/Curation page**

**Text Evidence:** When accessed via the  icon in the results table, the Text Evidence section displays each sentence of the title and abstract with phosphorylation-related information highlighted. By default, kinase (green), substrate (blue), site (red), and phospho-keyword (black, underlined) evidence is highlighted (Figure 20). Users can customize the highlighting using the check boxes provided. When accessed via the number in the No. of Sentences column in the results table, the Text Evidence section will display only the sentences containing evidence for that line of annotation (Figure 9).

**Text Evidence**

- 1 TI - Y654 of [beta-catenin](#) is essential for [FLT3/ITD-related tyrosine phosphorylation and nuclear localization of beta-catenin](#) .
- 2 AB - beta-Catenin plays a dual role as a key effector in the regulation of adherens junctions as well as a transcriptional co-activator .
- 3 [Tyrosine phosphorylation of beta-catenin affects](#) the cell adhesion , migration , and gene transcription in many types of human cancer cells , including acute myeloid leukemia cells with FLT3 internal tandem duplication ( FLT3/ITD-AML ) .
- 4 Here , we investigated the relationship between three tyrosine residues ( Y86 , Y142 , and Y654 ) in beta-catenin and oncogenic FLT3/ITD kinase .
- 5 In the experiments using COS-7 cells expressing FLT3/ITD and Wt or mutant beta-catenin , [FLT3/ITD phosphorylated Y654](#) , and this residue was essential for beta-catenin's nuclear localization by FLT3/ITD .
- 6 Promoter -reporter assays demonstrated that [Y654 phosphorylation of beta-catenin](#) was closely related to TCF transcriptional activity .
- 7 In vitro kinase assays , using recombinant FLT3 and biotinylated beta-catenin peptide including Y654 showed that [FLT3 directly phosphorylated Y654 of beta-catenin](#) .
- 8 These results explain how FLT3/ITD affects [the tyrosine phosphorylation , nuclear localization , and transcriptional activity of beta-catenin](#) .
- 9 Targeting [Y654 phosphorylation](#) may lead to the development of novel approaches to therapy for FLT3/ITD-AML .
- 10 > (c) 2012 John Wiley & ; Sons A/S. < /CopyrightInformation>NNP

Select/deselect:  kinase  substrate  site  phospho keywords

**Figure 20: Text Evidence display**

**Curation Interface:** The curation interface portion of the Text Evidence/Curation page allows the user to validate the RLIMS-P phosphorylation annotation and gene normalization. If there are any errors or omissions, the user can enter the correct information. The interface is divided into four sections: PubMed Information, RLIMS-P Annotation, Gene Normalization, and PMID Mapping to UniProt KB.

**(i) PubMed Information:** The PubMed information section displays the PMID, publication date, authors, and journal for the annotated document. Clicking on the PMID links to the PubMed record for the document (Figure 21A). For open access articles, the link to Full Text is also available (Figure 21B)

A

PubMed Information					
22357623	2012 Apr	Li P, Goto H, Kasahara K, Matsuyama M...	Mol Biol Cell	Full Text	



PubMed  
US National Library of Medicine  
National Institutes of Health

PubMed  [Advanced](#)

Display Settings:  Abstract [Send to:](#)

Mol Biol Cell, 2012 Apr;23(8):1582-92. doi: 10.1091/mbc.E11-10-0883. Epub 2012 Feb 22.

**P90 RSK arranges Chk1 in the nucleus for monitoring of genomic integrity during cell proliferation.**  
L.P. Goto H, Kasahara K, Matsuyama M, Wang Z, Yatabe Y, Kiyono T, Inagaki M.  
Division of Biochemistry, Aichi Cancer Center Research Institute, 1-1 Kanokoden, Chikusa-Ku, Nagoya, Aichi 464-8681, Japan.

**Abstract**  
The ataxia telangiectasia mutated- and rad3-related kinase (ATR)/Chk1 pathway is a sentinel of cell cycle progression. On the other hand, the Ras/mitogen-activated protein kinase/90-kDa ribosomal S6 kinase (p90 RSK) pathway is a central node in cell signaling downstream of growth factors. These pathways are closely correlated in cell proliferation, but their interaction is largely unknown. Here we show that Chk1 is phosphorylated predominantly at Ser-280 and translocated from cytoplasm to nucleus in response to serum stimulation. Nonphosphorylated Chk1-Ser-280 mutation attenuates nuclear Chk1 accumulation, whereas the phosphomimic mutation has a reverse effect on the localization. Treatment with p90 RSK inhibitor impairs Chk1 phosphorylation at Ser-280 and accumulation at the nucleus after serum stimulation, whereas these two phenomena are induced by the expression of the constitutively active mutant of p90 RSK in serum-starved cells. In vitro analyses indicate that p90 RSK stoichiometrically phosphorylates Ser-280 on Chk1. Together

B

PubMed Information					
22357623	2012 Apr	Li P, Goto H, Kasahara K, Matsuyama M...	Mol Biol Cell	Full Text	

PMC  [Save search](#) [Journal List](#) [Limits](#) [Advanced](#)

Display Settings:  Summary [Send to:](#)  **Filter your result**

[P90 RSK arranges Chk1 in the nucleus for monitoring of genomic integrity during cell proliferation](#)  
Ping Li, Hidemasa Goto, Kousuke Kasahara, Makoto Matsuyama, Zhonghua Wang, Yasushi Yatabe, Tohru Kiyono, Masaki Inagaki  
Mol Biol Cell. 2012 April 15; 23(8): 1582–1592. doi: 10.1091/mbc.E11-10-0883  
PMCID: PMC3327324  
[Article](#) [PubReader](#) [PDF-5.5M](#) [Supplementary Material](#)

**Related inform**  
Cited Articles



Figure 21: PubMed Information section of the curation interface

**(ii) RLIMS-P Annotation:** This section displays a table of the RLIMS-P phosphorylation annotation lines. The first five columns—No. (line number), Kinase, Substrate, Site, and Sentence (sentence numbers from which evidence was obtained)—present the same information as in the results table and are not modifiable by the user. The last two columns—Comment and Validation—accept user input. In the Validation column, the user can click the check mark (turns green when clicked) if the RLIMS-P annotation on that line is correct and the X (turns red when clicked) if the annotation is incorrect (Figure 22). In the Comment column, the user can enter free-text comments; for example, if the annotation is incorrect, the user can provide a brief explanation of what is wrong (Figure 23). Clicking on Add Annotation at the bottom of the table creates a User Added Annotation section, which allows the user to enter additional kinase, substrate, site, and/or text evidence information (Figure 24).

RLIMS-P Annotation						
No.	Kinase	Substrate	Site	Sentence	Comment	Validation
1	p90 rsk	chk1	Ser-280	7, 8, 11	<input type="text"/>	<input checked="" type="checkbox"/> <input type="checkbox"/>
2	atr	chk1	Ser-280	9	<input type="text"/>	<input type="checkbox"/> <input checked="" type="checkbox"/>
3	chk1	chk1	Ser-296	9	<input type="text"/>	<input checked="" type="checkbox"/> <input type="checkbox"/>
4	atr	chk1	Ser-345	9	<input type="text"/>	<input checked="" type="checkbox"/> <input type="checkbox"/>
5		chk1	Ser-296, Ser-345	10	<input type="text"/>	<input checked="" type="checkbox"/> <input type="checkbox"/>

Add Annotation


Figure 22: RLIMS-P Annotation section of the curation interface showing user validation

RLIMS-P Annotation						
No.	Kinase	Substrate	Site	Sentence	Comment	Validation
1	p90 rsk	chk1	Ser-280	7, 8, 11	<input type="text"/>	<input checked="" type="checkbox"/> <input type="checkbox"/>
2	atr	chk1	Ser-280	9	Kinase should be p90 rsk	<input type="checkbox"/> <input checked="" type="checkbox"/>
3	chk1	chk1	Ser-296	9	<input type="text"/>	<input type="checkbox"/> <input checked="" type="checkbox"/>
4	atr	chk1	Ser-345	9	<input type="text"/>	<input type="checkbox"/> <input checked="" type="checkbox"/>
5		chk1	Ser-296, Ser-345	10	<input type="text"/>	<input checked="" type="checkbox"/> <input type="checkbox"/>

Figure 23: RLIMS-P Annotation section of the curation interface showing a user-entered comment

RLIMS-P Annotation						
No.	Kinase	Substrate	Site	Sentence	Comment	Validation
1	p90 rsk	chk1	Ser-280	7, 8, 11	<input type="text"/>	<input checked="" type="checkbox"/> <input type="checkbox"/>
2	atr	chk1	Ser-280	9	<input type="text"/>	<input type="checkbox"/> <input checked="" type="checkbox"/>
3	chk1	chk1	Ser-296	9	<input type="text"/>	<input checked="" type="checkbox"/> <input type="checkbox"/>
4	atr	chk1	Ser-345	9	<input type="text"/>	<input checked="" type="checkbox"/> <input type="checkbox"/>
5		chk1	Ser-296, Ser-345	10	<input type="text"/>	<input checked="" type="checkbox"/> <input type="checkbox"/>

Add Annotation



User Added Annotation						
No.	Kinase	Substrate	Site	Sentence	Comment	Delete
7	<input type="text" value="Kinase"/>	<input type="text" value="Substrate"/>	<input type="text" value="Site"/>	<input type="text" value="Sentence"/>	<input type="text" value="Commen"/>	<input type="button" value="🗑"/>

Add Annotation

**Figure 24: Clicking on the Add Annotation link below the RLIMS-P Annotation table allows users to enter new lines of annotation**

**(iii) Gene Normalization:** The Gene Normalization section displays suggested UniProtKB accession numbers (UniProtKB ACs) for the kinase and substrate proteins mentioned in the RLIMS-P annotation (Figure 24). This normalization is done using the cross-species gene normalization tool, GenNorm (<http://ikmbio.csie.ncku.edu.tw/GN/>). Clicking on the UniProtKB AC links to the UniProtKB record. Users can indicate that the mapping is correct by clicking on the check mark in the UniProtKB AC box (turns the box green) or incorrect by clicking on the 'X' (turns the box red). Mousing-over any line in the table causes a search UniProt icon to appear. Clicking on this icon queries UniProtKB using the protein name as it appeared in the text. If the user identifies a UniProtKB AC that corresponds to the protein name, it can be entered in the Add UniProtKB AC column.

Gene Normalization				
Protein	Name	UniProtKB AC	Add UniProtKB AC	Annotation No.
Kinase	atr	Q13535 ✓ x	<input type="text"/>	2, 4
	chk1	O14757 ✓ x B4DT73 ✓ x	<input type="text"/>	3
	p90 rsk	Q UniProt Not normalized	<input type="text"/>	
Substrate	chk1	O14757 ✓ x	<input type="text"/>	1, 2, 3, 4, 5

Search UniProtKB for protein name

Display UniProtKB record

Figure 24: Gene Normalization section of the curation interface

**(iv) PMID Mapping to UniProt KB:** The section displays a table with suggested UniProtKB ACs for the kinases and substrates obtained using a bibliography mapping service provided by the Protein Information Resource (pir.georgetown.edu). The information in this section can be used to assist in assigning UniProt KB ACs to the proteins mentioned in the RLIMS-P annotation and addition of these to the Gene normalization table. Each line provides the UniProtKB AC and ID (with links to the UniProtKB and iProClass records for the protein), the name of the protein as it appears in the UniProtKB record (with a link to Biothesaurus), and the organism name (Figure 25).

PMID Mapping to UniProtKB		
Protein AC/ID	Protein Name	Organism Name
B4DDD0/B4DDD0_HUMAN <a href="#">/ProClass</a> <a href="#">UniProtKB/Swiss-Prot</a>	cDNA FLJ59449, highly similar to Serine/threonine-protein kinase Chk1 ... <a href="#">BioThesaurus</a>	Homo sapiens (Human)
B4DT73/B4DT73_HUMAN <a href="#">/ProClass</a> <a href="#">UniProtKB/Swiss-Prot</a>	cDNA FLJ56409, highly similar to Serine/threonine-protein kinase Chk1 ... <a href="#">BioThesaurus</a>	Homo sapiens (Human)
F5H7S4/F5H7S4_HUMAN <a href="#">/ProClass</a> <a href="#">UniProtKB/Swiss-Prot</a>	Serine/threonine-protein kinase Chk1 <a href="#">BioThesaurus</a>	Homo sapiens (Human)
O14757/CHK1_HUMAN <a href="#">/ProClass</a> <a href="#">UniProtKB/Swiss-Prot</a>	Serine/threonine-protein kinase Chk1 <a href="#">BioThesaurus</a>	Homo sapiens (Human)
Q15418/KS6A1_HUMAN <a href="#">/ProClass</a> <a href="#">UniProtKB/Swiss-Prot</a>	Ribosomal protein S6 kinase alpha-1 <a href="#">BioThesaurus</a>	Homo sapiens (Human)

Figure 25: PMID Mapping to UniProtKB section of the curation interface

**Downloading Text Evidence/Curation:** Selecting Text Evidence from the Download menu will create a comma-delimited file containing all of the information on the Text Evidence/Curation page including user-added validation and comments (Figure 26). Selecting RLIMS-P Result in BioC from the Download menu will create a file containing the RLIMS-P annotation in BioCreative format (Figure 27).

Back to Views ▾   Download ▾   Layout ▾

**Text Evidence**

Text Evidence

RLIMS-P Result in BioC

- 1 TI - P90 RSK arranges Chk1 in the nucleus for monitoring of genomic integrity during cell proliferation .
- 2 AB - The ataxia telangiectasia mutated - and rad3-related kinase ( ATR )/Chk1 pathway

	A	B	C	D	E	F	G	H	I	J
1	###Text Evidence###									
2	#PubMed Information									
3	22357623	2012 Apr	Li P, Goto H,	Mol Biol Cell						
4	#RLIMS-P Annotation									
5	No.	Kinase	Substrate	Site	Comment	Validation	Sentence			
6	1	p90 rsk	chk1	Ser-280		Agree	Treatment with p90 RSK inhibitor impairs Chk1 phospho			
7	1	p90 rsk	chk1	Ser-280		Agree	In vitro analyses indicate that p90 RSK stoichiometrically			
8	1	p90 rsk	chk1	Ser-280		Agree	These results suggest that p90 RSK facilitates nuclear Chl			
9	2	chk1	chk1	Ser-296		Agree	Together with Chk1 phosphorylation at Ser-345 by ATR a			
10	3	atr	chk1	Ser-345		Agree	Together with Chk1 phosphorylation at Ser-345 by ATR a			
11	4	atr	chk1	Ser-280	Kinase should be p90 rsk	Disagree	Together with Chk1 phosphorylation at Ser-345 by ATR a			
12	5	N/A	chk1	Ser-280		N/A	Here we show that Chk1 is phosphorylated predominant			
13	6	N/A	chk1	Ser-296,Ser-345		Agree	In addition , Chk1 phosphorylation at Ser-345 and Ser-29			
14	#User Add Annotation									
15	Kinase	Substrate	Site	Comment	Sentence					
16	#Gene Normalization									
17	Protein	Name	UniProtKB At	Annotation	Comment	Validation				
18	Kinase	atr	Q13535	3,4		Agree				
19	Kinase	chk1	O14757	2		Agree				
20	Kinase	chk1	B4DT73	2		N/A				
21	Substrate	chk1	O14757	1,2,3,4,5,6		Agree				
22	Substrate	chk1	B4DT73	1,2,3,4,5,6		N/A				
23	#PMID Mapping to UniProtKB									
24	Protein AC/ID	Protein Nam	Organism Name							
25	B4DDD0/B4I	cDNA FLJ594	Homo sapiens (Human)							
26	B4DT73/B4I	cDNA FLJ564	Homo sapiens (Human)							
27	FSH754/FSH	Serine/threo	Homo sapiens (Human)							
28	O14757/CHK	Serine/threo	Homo sapiens (Human)							
29	Q15418/KS6	Ribosomal pi	Homo sapiens (Human)							
30										
31										

Figure 26: Downloading RLIMS-P annotation as a comma-delimited file



Back to Views ▾
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Layout ▾

Text Evidence	Text Evidence
1 TI - P90 RSK arranges Chk1 in the nucleus for monitoring of genomic integrity during cell proliferation .	RLIMS-P Result in BioC
2 AB - The ataxia telangiectasia mutated - and rad3 related kinase ( ATR )/Chk1 pathway	

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    PMID - 22357623 TI - P90 RSK arranges Chk1 in the nucleus for monitoring of genomic integrity during cell proliferation . AB - The ataxia telangiectasia mutated - and rad3-related kinase ( ATR )/Chk1 pathway is a sentinel of cell cycle progression . On the other hand, the Ras/mitogen -activated protein kinase/90-kDa ribosomal S6 kinase ( p90 RSK ) pathway is a central node in cell signaling downstream of growth factors . These pathways are closely correlated in cell proliferation , but their interaction is largely unknown . Here we show that Chk1 is phosphorylated predominantly at Ser-280 and translocated from cytoplasm to nucleus in response to serum stimulation . Nonphosphorylated Chk1-Ser-280 mutation attenuates nuclear Chk1 accumulation , whereas the phosphomimic mutation has a reverse effect on the localization . Treatment with p90 RSK inhibitor impairs Chk1 phosphorylation at Ser-280 and accumulation at the nucleus after serum stimulation , whereas these two phenomena are induced by the expression of the constitutively active mutant of p90 RSK in serum-starved cells . In vitro analyses indicate that p90 RSK stoichiometrically phosphorylates Ser-280 on Chk1 . Together with Chk1 phosphorylation at Ser-345 by ATR and its autophosphorylation at Ser-296 , which are critical for checkpoint signaling , Chk1-Ser-280 phosphorylation is elevated in a p90 RSK -dependent manner after UV irradiation . In addition , Chk1 phosphorylation at Ser-345 and Ser-296 after UV irradiation is also attenuated by the treatment with p90 RSK inhibitor or by Ser-280 mutation to Ala . These results suggest that p90 RSK facilitates nuclear Chk1 accumulation through Chk1-Ser-280 phosphorylation and that this pathway plays an important role in the preparation for monitoring genetic stability during cell proliferation .
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  </annotation>
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    <infun key="rlims_internal_representation">Chk1</infun>
    <location offset="549" length="4"/>
    <text>Chk1</text>
  </annotation>
  . . .
  
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Figure 27: Downloading RLIMS-P annotation in BioC format