

Open Flow Biological Network Initiative:

Pathway map building, standards, simulation, and knowledge sharing

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- 1st Generation
 - Isolated DB, domain specific models
 - KEGG, Panther Pathway DB, Reactome, etc.
- 2nd Generation
 - Repository, Standard Formation (SBML, SBGN, MIRIAM..) such as Biomodels.net, Panther Community
- 3rd Generation
 - Integration, Web 2.0, Open Flow
 - Payao, Next Generation Pathway DB Suite
- 4th Generation
 - Integration simulation, Plug-in Scalable System
- 5th Generation
 - Integrate with original resource banks

SBI Pathway Map Building Infrastructure





PAYAO platform for sharing models

"PAYAO"

Community Tagging System to SBML models

- A community tool to work on the same pathway models simultaneously, insert tags to the specific parts of the model, exchange comments, record the discussions and eventually update the models accurately and concurrently.
- Reads SBML models, display them with CellDesigner

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SB PAYAO: SBML Models Tagging System





PAYAO - Tags



SBI The Systems PAYAO – Tags expanded

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PAYAO-PATHTEXT

PAYAO – PathTEXT (1)

PathText

SB The Systems Biology

Search results for Model: oda_nfkappab

Node: re1 : HETERODIMER_ASSOCIATION



PAYAO – PathTEXT (2)

SB The Systems Biology Institute





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Node ID="sa2" Type="species">	
Link PMID="16404725" Type="textmining" Source="medie" MedlineDate="20070201"> Link PMID="17009976" Type="annotation" Source="koda" MedlineDate="20060901">	
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A user then logs in to the Payao community tagging system and selects a pathway model.

When a model is selected, a request is sent to the PathText Web Service for publications matching any node in the selected model.

The Pathtext Web Service then returns an xml result containing the matching publications.



Payao then displays document icons on the matching nodes.

Note: This process will begin either automatically and/or when the "Automatic Search-Search" button is clicked.

The document icons are hyperlinks that when selected, open a PathText Results Page in a new tab of the user's browser.

PathText

Search Results for Model: NFkB for PathText Project

Sort by: Publication Date | Publication Ranking | Author

Positive and negative regulation of IkappaB kinase activity through IKKbeta subunit phosphorylation.

In mammalian cells, phosphorylation of two sites at the activation loop of IKKb was essential for activation of IKK by tumor necrosis factor and interleukin-1. View Annotation

Whereas the Ser177-> Ala177 (S177A) mutation in IKKb slightly decreased cytokine responsiveness, the S181A mutation had a more severe effect, and the replacement of both sites abolished IKK activation altogether. View Annotation

Science, 1999 Apr 9, 284(5412):309-13, PMID: 10195894 Delhase M, Hayakawa M, Chen Y, Karin M. Laboratory of Gene Regulation and Signal Transduction, Department of Pharmacology, University of California, San Diego, 9500 Gilman Drive, La Jolla, CA 92093-0636, USA. Annotation by K. Oda

TAK1 is a ubiquitin-dependent kinase of MKK and IKK

Significantly, the TAK1 kinase once activated by Ubc13-Uev1A-mediated ubiquitination was able to phosphorylate IKKb specifically at S177 and S181. Thus, TAK1 is a ubiquitin-dependent kinase of IKKb. View Annotation

Nature, 2001 Jul 19, 412(6844):346-51, PMID: 11460167 Wang C, Deng L, Hong M, Akkaraju GR, Inoue J, Chen ZJ Department of Molecular Biology, University of Texas Southwestern Medical Center, Dallas, Texas 75390-9148, USA Annotation by K. Oda

Mammalian TAK1 activates Snf1 protein kinase in yeast and phosphorylates AMP-activated protein kinase in vitro.

Mammalian <u>TAK1</u> activates Snf1 protein kinase in yeast and phosphorylates AMP-activated protein kinase in vitro

The Journal of biological chemistry, 2006 Sep 1, 281(35):25336-43. Epub 2006 Jul 11, PMID: 16835226 Momcilovic M, Hong SP, Carlson M. Search Term(s): s:TAK1 v:Phosphorylate

View Publication | Create Annotation | Mark "Not Relevant"

Constitutive activation of <mark>TAK1</mark> by HTLV-1 tax-dependent overexpression of TAB2 induces activation of JNK-ATF2 but not <mark>IKK</mark>-NF-kappaB.

... Transforming growth factor-beta-activated kinase 1 (TAK1) has been shown to play a critical role in these transcription factors. Here, we found that TAK1 was constitutively activated in Tax-positive HTLV-1-transformed T cells. Tax induced persistent overespression of TAK1-binding protein 2 (TAB2), but not TAB3, which is essential for TAK1 activation. Surprisingly, TAK1 was not involved in thye activation of NF-kappaB. On the other

The PathText Results Page displays the results matching the selected node in Payao from both the PathText Annotation Tool and text mining queries.

View Publication | Create Annotation | Mark "Not Relevant"



In "Manual Search" Mode, a search for Co-Occurrences will take place.

(Note: This is essentially the same as the current prototype and will use the current web service)

A user selects one or more nodes and/or reactions and clicks the Search button.

FACTA

p105 p50

Search MEDLINE

✔ Gene/Protein ✔ Disease ✔ Symptom ✔ Drug ✔ Compound All Clear

Lipopolysaccharide from Salmonella enterica activates NF-kappaB through both classical and alternative pathways in primary B Lymphocytes.

... In addition, we observed that LPS triggered the processing of NF-kappaB **p105** to **p50** and that of NF-kappaB p100 to p52 in parallel with nuclear translocation of active **p50** and p52, as NF-kappaBp50/RelA and NF-kappaBp52/RelB heterodimers, respectively. ... PMID:17698569 Infect. Immun. 2007 Oct

Increased cyclooxygenase-2 expression in hypothalamic paraventricular nucleus in rats with heart failure: role of nuclear factor kappaB.

... In the PVN, NF-kappaB **p50** precursor **p105** mRNA increased, and mRNA for its inhibitor, IkappaB, decreased (P<0.05). ... Both pyrrolidine dithiocarbamate and eplerenone reduced (P<0.05) **p105** mRNA and increased IkappaB mRNA in PVN. ... PMID:17242297 Hypertension 2007 Mar

Adenine nucleotides inhibit proliferation of the human lung adenocarcinoma cell line LXF-289 by activation of nuclear factor kappaB1 and mitogen-activated protein kinase pathways.

... Western blot analysis revealed transient activation of p38 mitogen-activated protein kinase, extracellular signal-related kinase 1/2, and nuclear factor kappaB1 and possibly new formation of **p50** from its precursor **p105**. ATP-induced attenuation of LXF-289 cell proliferation was

The results are displayed in Facta, allowing the user to then continue on with other searches using the Facta system.



PubMed ID Link



Pathway Curation Suite: Open Flow Model





Public DB Integration Panther, Reactome, Pathway Commons, etc.

Open Yeast

Extensive Mapping and Annotation for Budding Yeast





- High-precision comprehensive budding yeast
 - Molecular-based computational model that can predict physiological responses of budding yeast against genetic mutations and drugs perturbations at more than 90% of accuracy.
- Medical implications as well
 - Histon regulation system is highly homologous to human
 - Sir2 discovered in yeast, now important in human aging

Open Yeast Initiative

- Open collaboration initiative to uncover molecular interactions
- Evolving DB and models

Systems Biology

 Hot Plug-in and Play simulation platform (in future)

SBI Budding Yeast Cell Cycle and Signaling





Genome-wide in vivo robustness profile





Multi-scale heterogeneous models





SBI Biology Proof-of-Concept Project



Positions Available for Systems Biology in Okinawa

Open Biology Project



Software-related Research and Development Digital Yeast / Open Yeast Project

Location: Okinawa Institute for Science and Technology

Launch of the project conditional on agreement of contract details.

Acknowledgement

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Systems Biology

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