A Signal Transduction Database

K. Suzuki
suzuken@kuicr.kyoto-u.ac.jp
S. Goto
goto@kuicr.kyoto-u.ac.jp
Y. Akiyama
akiyama@kuicr.kyoto-u.ac.jp
M. Kanehisa
kanehisa@kuicr.kyoto-u.ac.jp

Institute for Chemical Research, Kyoto University
Gokasho, Uji, Kyoto 611 Japan

Abstract

We are developing a signal transduction database which represents molecular interactions involved in the signaling pathways in a cell from the activation of cell surface receptors by external signals to the activation of transcription factors in the nucleus. The database is linked to the Medline literature, the SWISS-PROT and PIR protein sequence database, the PDB protein 3-D structural database, the LIGAND chemical database for enzyme reactions, and the OMIM database on genetic diseases. We provide a graphical user interface of the World Wide Web (WWW) to access this database.

The signal transduction from extracellular signals to gene expression is one of the significant cellular events that are beginning to be unraveled in molecular details. The event starts at the cell surface receptor accepting an external signal. The signal is transmitted inside the cell to key signaling molecules such as Ras and G-protein. The activation of these molecules is often followed by a cascade of protein phosphorylation events which results in the activation of specific transcription factors in the cell nucleus. Such an overall picture is derived from numerous experiments on molecular interactions, i.e., data on one molecule affecting other molecules either directly or indirectly. Our long-term objective is to automatically construct such an overall picture from pieces of data stored in the database. Toward that end we have started collecting data on molecular interactions that play parts in the signal transduction pathways and experimenting various representations and manipulations of those data.

Our short-term objective is to provide a browser of different types of data in an integrated environment. Thus, the molecular interaction data are linked to consensus views of the transduction pathways, as well as to other databases including bibliographic data (Medline), protein sequences (SWISS-PROT and PIR), protein 3-D strctures (PDB), chemical compounds

鈴木健二、五斗進、秋山泰、金久實：京都大学化学研究所、〒611 京都府宇治市五ヶ庄

in enzyme reactions (LIGAND), and genetic diseases (OMIM). Table 1 shows a description of molecular interactions in the Ras pathway, where the basic element is a pair of interacting molecules or molecular complexes, called a donor and an acceptor, together with the description of molecular events.

The interface to access our signal transduction database is implemented using Mosaic in the World Wide Web (WWW) system, since Mosaic has an easy-to-use graphical user interface and also since we already have an integrated retrieval system called WebDBget linking fifteen databases in molecular biology (Y. Akiyama and M. Kanehisa, unpublished). Data items in Table 1 can be clickable by mouse operations to retrieve related information.

Acknowledgement

This work was supported by the Grant-in-Aid for Scientific Research on the Priority Area 'Genome Informatics' from the Ministry of Education, Science and Culture of Japan.

Table 1: A sample of data entry

Donor	*Acceptor*	*Signal*	*Interaction*	*Events*
GF	RTK	+	binding	GF binding to RTK leads to RTK dimerization & autophosphorylation
RTK	GRB2	+	binding	Phosphorylated RTK interacts with SH2 domain of GRB2
GRB2	Sos	+	complex	Signal transmitted through SH3 domain of GRB2 in GRB2/Sos complex
GRB2/Sos	Ras	+	binding	GRB2/Sos complex binding to Ras Ras-GDP changes to Ras-GTP
Ras	Raf	+	translocation	Ras-GTP binding to Raf and recruitment to the plasma membrane
Raf	MEK	+	phosphorylation	
MEK	MAPK	+	phosphorylation	
MAPK	Myc	+	phosphorylation	
Myc	DNA	+	binding	Transcription
MAPK	Jun	+	phosphorylation	
Jun	Fos	+	dimerization	Leucine zipper dimerization
Jun/Fos	DNA	+	binding	Transcription