Construction and analysis of the biological interaction network for BCL2

Seok Jong Yu*, Jaesoo Yoo**
*KISTI, Korea, **Chungbuk Nat'l Univ., Korea
E-mail : seokjongyu@gmail.com*, yjs@chungbuk.ac.kr**

1. Introduction

A number of studies for apoptosis, which is the process of programmed cell death have shed light for 2 decades. The amount of apoptosis that occurs in developing and adult animal tissues can be astonishing. After finding the relation between apoptosis and cancer, many proteins have been identified, including p53, to understand the mechanism that can stimulate tumour-pathogenesis. Bcl2 protein have been reported as one of regulator of apoptosis and novel front-line anticancer agents[1]. Even though the role of Bcl2 is essential for oncogenesis, there are a few systematic analysis based on text-mining analysis for Bcl2 and apoptosis process.

In this paper, we have constructed a Bcl2 signaling pathway network by using Bioknowldege viewer, which is a text-mining system to analyze and identify a new biological model of Bcl2.

2. Text-mining system and BCL2 analysis

We designed client software that can launch a Pubmed query, download the Pubmed data, submit the text-mining job to a server, and manage the mining results in graph databases (Neo4J). We also implement several perspective modes, including monitoring the job, curating the text-mining results, and navigating the network. The BioKnowledge Viewer is an integrated system for constructing the biological networks, creating the biological models based on the text-mining results, and navigating the complex biological networks

We used Pubmed database to download the papers for BCL2. After downloading the papers, we analyze it with MKEM model[2], Stanford parser and Abner[3] for tagging biological concepts. Constructing the BCL2 network is done by using graph database (Neo4J)[5]. The main network of BCL2 and main hub protein was identified with graph searching algorithm implemented in Neo4J.

[Table 1] The major proteins in the BCL2 network

Protein name	Number of connection
BCL2	158
p53	41
Bax	39
PP2A	12
STAT3	12
MMP-2	9
JNK	8
Bad	8
MAPK3	6
BH3	5

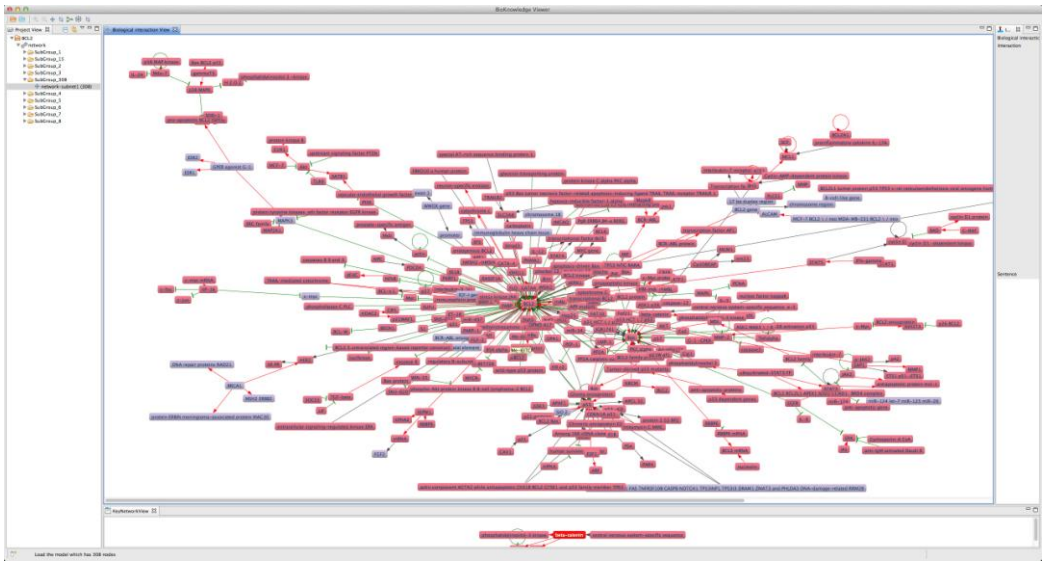

Figure 1. A signal transduction pathway network for BCL2

3. Results and Discussion

We select 4375 papers in Pubmed and analyze the abstract of the papers with BioKnowledge Viewer. Total 677 interactions of biological relation for Bcl2 are identified and the main biological network is consisted with 308 nodes (Figure 1). In the network analysis, we found the major hub proteins, which are BCL2, p53, Bax, PP2A, and STAT3 protein (Table1). The major hub proteins are tightly connected each other to regulate a function of each protein. We also found that the relation between BCL2 and Bax that is not defined in the previous signal transduction database (KEGG)[4]. With the text-mining results, we construct a new Boolean network to propose the regulation process between Bax and BCL2. It could be a novel apoptosis model for understanding the mechanism of BCL2.

[1] T. Oltersdorf, S. W. Elmore, A. R. Shoemaker, R. C. Armstrong, D. J. Augeri, B. A. Belli, M. Bruncko, T. L. Deckwerth, J. Dinges, P. J. Hajduk, M. K. Joseph, S. Kitada, S. J. Korsmeyer, A. R. Kunzer, A. Letai, C. Li, M. J. Mitten, D. G. Nettesheim, S. Ng, P. M. Nimmer, J. M. O'Connor, A. Oleksijew, A. M. Petros, J. C. Reed, W. Shen, S. K. Tahir, C. B. Thompson, K. J. Tomaselli, B. Wang, M. D. Wendt, H. Zhang, S. W. Fesik, and S. H. Rosenberg, “An inhibitor of Bcl-2 family proteins induces regression of solid tumours.,” Nature, vol. 435, no. 7042, pp. 677–681, Jun. 2005.

[2] M. S. D. L. Ali Z Ijaz, “MKEM: a Multi-level Knowledge Emergence Model for mining undiscovered public knowledge,” BMC Bioinformatics, vol. 11, no. 2, p. S3, 2010.

[3] B. Settles, “ABNER: an open source tool for automatically tagging genes, proteins and other entity names in text.,” Bioinformatics, vol. 21, no. 14, pp. 3191–3192, Jul. 2005.

[4] H. Ogata, S. Goto, K. Sato, W. Fujibuchi, H. Bono, and M. Kanehisa, “KEGG: Kyoto Encyclopedia of Genes and Genomes.,” Nucleic Acids Research, vol. 27, no. 1, pp. 29–34, Jan. 1999.

[5] Neo4J http://www.neo4j.org