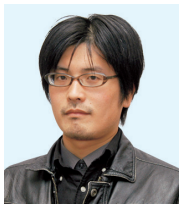
Bioinformatics Center
– Chemical Life Science –

http://cls.kuicr.kyoto-u.ac.jp/

Prof
KANEHISA, Minoru
(D Sc)

Assoc Prof
GOTO, Susumu
(D Eng)

Program-Specific Assist Prof
TOKIMATSU, Toshiaki
(D Agr)



Program-Specific Assist Prof
KOTERA, Masaaki
(D Sc)

Program-Specific Res
RUIZ, Diego Deiz
(Ph D)

Guest Res Assoc
KIRWAN, Gemma May
(Ph D)

Guest Res Assoc
JOANNIN, Nicolas
(Ph D)

PD
TAKARABE, Masataka
(D Pharm Sc)

Researchers

MORIYA, Yuki
NAKAGAWA, Zenichi

Students

MUTO, Ai (D3)
SHIMIZU, Yugo (D3)
DONG, Hong Ju (D3)
MIZUTANI, Sayaka (D3)
HIRANUKA, Kazushi (D3)
NISHIMURA, Yosuke (D2)
FUJITA, Megumi (D3)
MIHARA, Tomoko (D2)
JIN, Zhao (D1)
KONG, Xiang Shuo (M2)
CHEN, Zhang (M1)

Visitor

Dr TSAI, Yu-Shuen National Yang-Ming University, Taiwan, 7 October 2011–30 April 2012

Scope of Research

Genomes encode proteins and RNAs responsible for biosynthesis, biodegradation, and transport of additional molecules, such as small metabolites, lipids and glycans. This fact may indicate that the genomic DNA sequence specify all cellular functions. In practice, however, inferring higher-level systemic functions of a cell or organism needs more than solely the genomic information. We are developing bioinformatics methods to integrate different types of data and knowledge on various aspects of the biological systems towards basic understanding of life as a molecular interaction/reaction system and also toward practical applications in medical and pharmaceutical sciences.

KEYWORDS

KEGG
(Meta)genomics
Pathway
Bioinformatics
Metabolomics

Selected Publications

Takarabe, M.; Shigemizu, D.; Kotera, M.; Goto, S.; Kanehisa, M., Network-based Analysis and Characterization of Adverse Drug-drug Interactions, *J. Chem. Inf. Model*, **51,** 2977-2985 (2011).

Kotera, M.; Tokimatsu, T.; Kanehisa, M.; Goto, S., MUCHA: Multiple Chemical Alignment Algorithm to Obtain Building Block Substructures of Orphan Metabolites, *BMC Bioinformatics*, **12(Suppl 14),** S1 (2011).

Kirwan, G. M.; Diez, D.; Haeggstrom, J. Z.; Goto, S.; Wheelock, C. E., Systems Biology Approaches for Investigating the Relationships between Lipids and Cardiovascular Disease, *Curr. Cardiovasc. Risk Rep.*, **5,** 52-61 (2011).

Moriya, Y.; Shigemizu, D.; Hattori, M.; Tokimatsu, T.; Kotera, M.; Goto, S.; Kanehisa, M., PathPred: an Enzyme-catalyzed Metabolic Pathway Prediction Server, *Nucleic Acids Res.*, **38,** W138-W143 (2010).

Kanehisa, M.; Goto, S.; Furumichi, M.; Tanabe, M.; Hirakawa, M., KEGG for Representation and Analysis of Molecular Networks Involving Diseases and Drugs, *Nucleic Acids Res.*, **38,** D355-D360 (2010).

KEGG MEDICUS for Translational Bioinformatics

KEGG MEDICUS is a new resource for diseases, drugs and environmental substances, aiming to bring the genomic revolution to society. In KEGG, diseases are perturbed states in the molecular system and drugs are perturbants to the molecular system. Our knowledge on perturbed molecular system (network) is captured and presented as disease pathway maps in KEGG PATHWAY database. Other disease related knowledge on genetic and environmental perturbation is stored in KEGG DISEASE, listing known genetic factors (disease genes), environmental factors, diagnostic markers, and therapeutic drugs. All the marketed drugs in Japan, the OTC dugs as well as the prescription drugs, are fully represented in KEGG DRUG based on the chemical structures and/or the chemical components associated with target, metabolizing enzyme and other molecular network information. They are also integrated with the package insert information (labels information) that is applied to the adverse drug-drug interaction analysis described below. Health promoting and damaging substances such as crude drugs, essential oils, and other chemical substances are also collected and stored in KEGG ENVIRON with chemical component, efficacy and source species information whenever applicable. KEGG MEDICUS integrates the information in KEGG DISEASE, KEGG DRUG, KEGG ENVIRON, as well as other KEGG and outside databases in terms of genome-based biological systems (molecular network) information. As an attempt to integrate with outside resources, somatic mutation data obtained from Sanger Institute's COSMIC (Catalog Of Somatic Mutation In Cancer) database are mapped against KEGG cancer pathway and visualized in 3D map viewer (Figure 1).

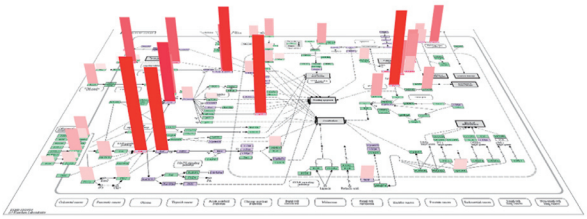
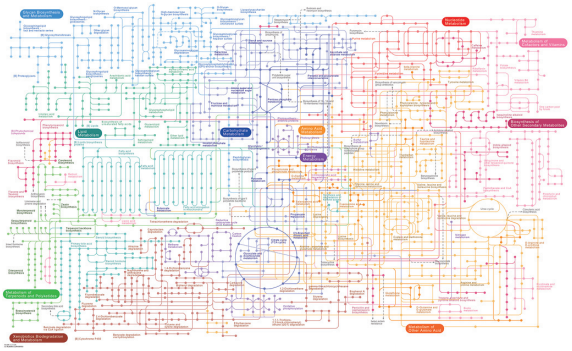


Figure 1. Cancer pathway map with somatic mutation frequency observed in colorectal cancer. The green boxes correspond to genes and the height or color-shading of the bar associated with each gene corresponds to the mutation frequency.



System Wide Analysis of Adverse Drug-drug Interactions

Co-administration of multiple drugs can cause adverse effects. It is becoming more important to provide a comprehensive view of drug-drug interactions among all the drugs in use, as well as a computational method to identify potential interactions. We extracted 1,306,565 known drug-drug interactions from all the package inserts of prescription drugs marketed in Japan. They were reduced to 45,180 interactions involving 1352 drugs (active ingredients) identified by the D numbers in the KEGG DRUG database, of which 14,441 interactions involving 735 drugs were linked to the same drug-metabolizing enzymes and/or overlapping drug targets. The interactions with shared targets were classified into three types: acting on the same target, acting on different but similar targets in the same protein family, and acting on different targets assigned to the same pathway. For the rest of the extracted interaction data, we attempted to characterize interaction patterns using drug group information. The drug groups were defined by the Anatomical Therapeutic Chemical (ATC) classification system, where the high-resolution network at the D number level is progressively reduced to a low-resolution global network. Based on this study we have developed a drug-drug interaction retrieval system in the KEGG DRUG database, which may be used for both searching against known drug-drug interactions and predicting potential interactions.

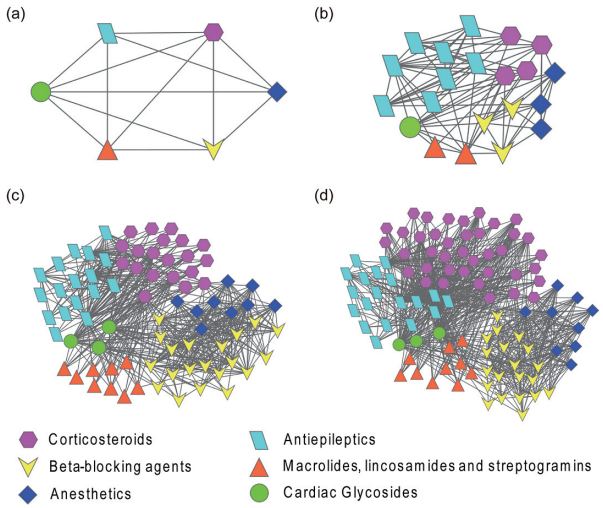


Figure 2. Drug interaction networks in the drug hierarchy.