

Workshop Argentina-Japan

“Bioscience and Biotechnology for the Promotion of  
Agriculture and Food Production”

-August 3rd to 7th 2009-

# Omics-Based Science of Food and Nutrition in Japan

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Organization for Interdisciplinary Research Projects

The University of Tokyo



Japan 日本

# Life Expectancy at Birth

(2008, by the Japanese Ministry of Health, Labor, and Welfare)

Female: 86.05 years (the longest in the world)

Male: 79.29 years (the 4<sup>th</sup> in the world)



# Japanese

Blessed with a Variety of  
Healthy Traditional Foods

Abundant Experience on  
Functional Food Factors



Accumulated research data  
and experience will help health  
promotion of other countries!!

# Japan explores the boundary between food and medicine

**Tokyo & London.** Japan's leading cosmetics manufacturer Shiseido is now marketing rice as a health product. This is the first step by Japanese industry to create a new market for foods engineered to have special medical benefits.

Last month, Shiseido became the first company in Japan to win approval from the Ministry of Health and Welfare to sell a "physiologically functional food", defined by new legislation introduced last September. Shiseido's product consists of rice from which the protein globulin has been removed for the benefit of those allergic to it.

For unexplained reasons, allergy to rice has become common in Japan, afflicting thousands of people young and old. The allergy causes unsightly red lesions on the skin covering large areas of the body. The present cure, the avoidance of rice and its products (including *sake*) in the diet is not welcomed by the Japanese.

Shiseido's engineered rice is one of many products being developed by hundreds of companies expecting to create a new niche in Japan's huge food market. Basic research in the field by university researchers is being supported by a large grant from the

phosphate milk, produced by Morinaga Milk Company for patients with chronic kidney disorders. Thirteen others are in the final stages of the eight-step approval process (see figure), including oligosaccharide-based foods for regulating intestinal flora, peptide-based foods for regulating mineral absorption and a material based on soya bean protein for regulating blood cholesterol.

According to Seichi Arai of Tokyo University's Department of Agricultural Chemistry, who is a member of one of the *ad hoc* committees set up by the Ministry of Health and Welfare, "at least 200 companies" are involved in the research and development of physiologically functional foods. Arai says that companies such as Nestlé are also involved. He is surprised that there seems to be less activity in the United States.

Although it is not illegal in Japan to sell products such as these as food, approval allows companies to claim medical benefits on their labels. Critics are worried that the approval process, which takes one to two years, will not be strict enough, but Shiseido's rice was tested on about 2,000 patients before approval.

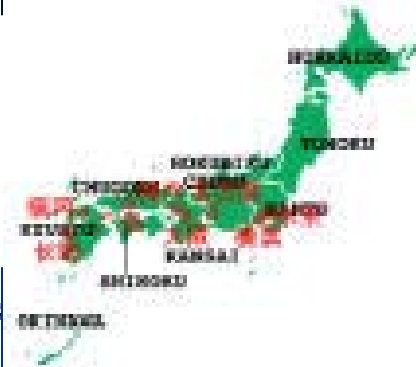
The interest of the MFSC is unusual

## Fish add benefit

**Tokyo.** Japan's interest in fish as health foods is illustrated by the sale of a fatty fish oil, itself the product of a fishmonger and a researcher.

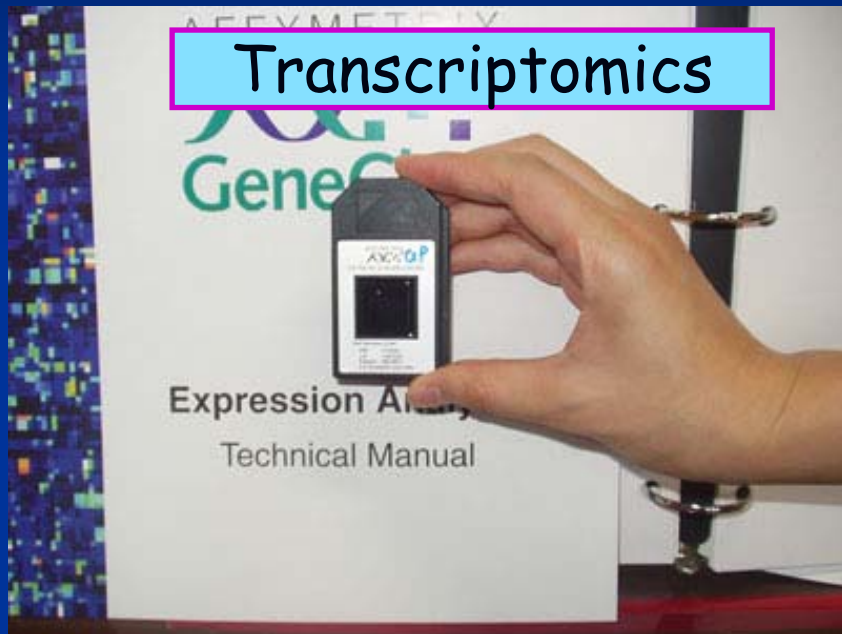
Kiyoshi Kuroda of the National Research Center for Health Sciences has suggested that soya bean oil, which has been shown to stimulate resistance to disease, and, in particular, docosahexaenoic acid, has been shown to reduce blood pressure and blood cholesterol.

But the findings were not conclusive. When a happy owner asked Kuroda to test the oil at the centre, vasa was considered. The results showed that the oil from tuna was more effective than these tissues are.

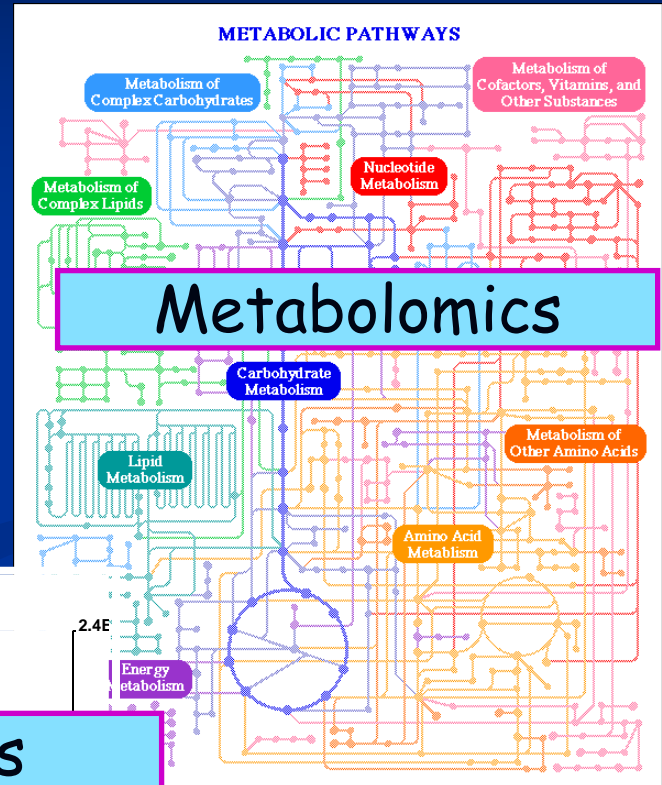


# Omics Analyses in Food and Nutrition Science

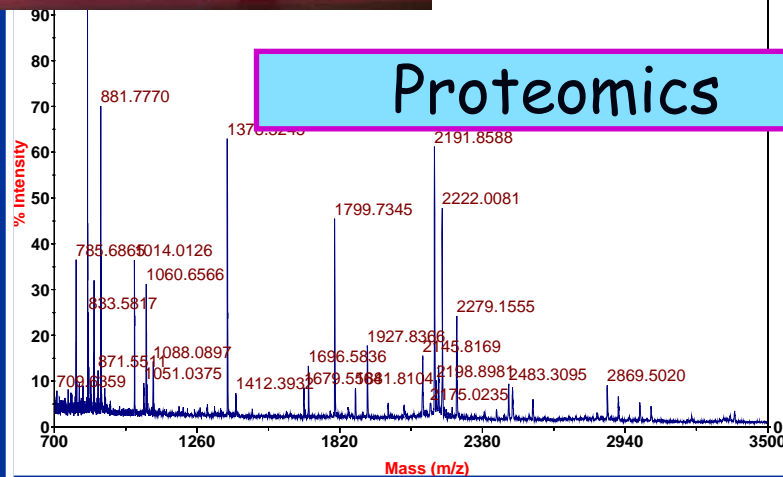
## Transcriptomics



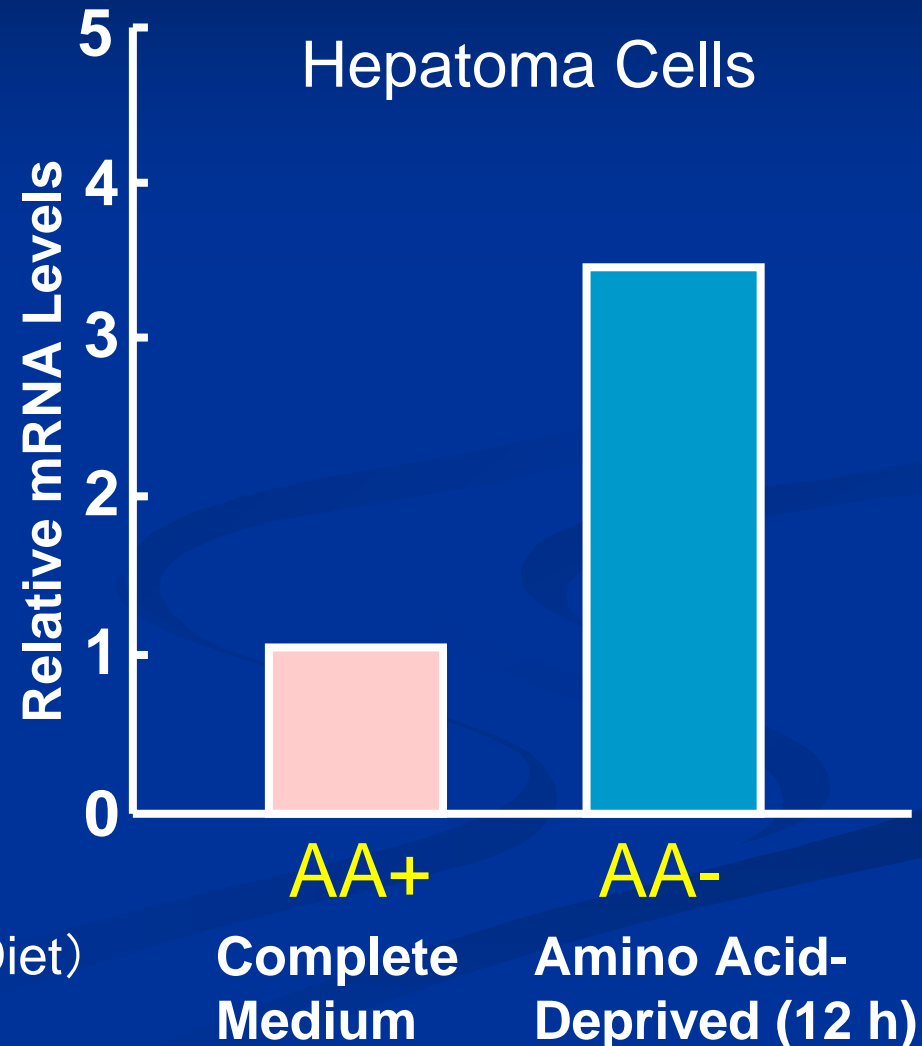
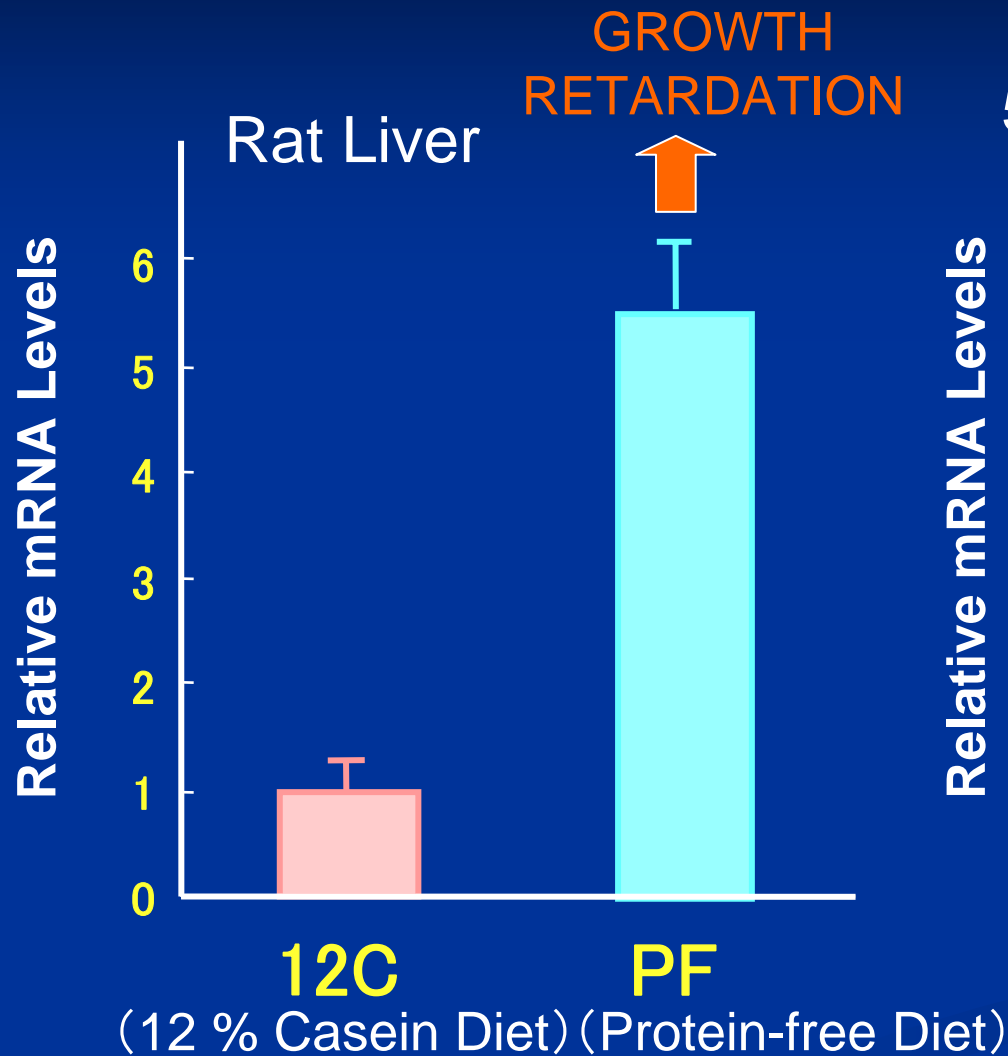
## Metabolomics



## Proteomics

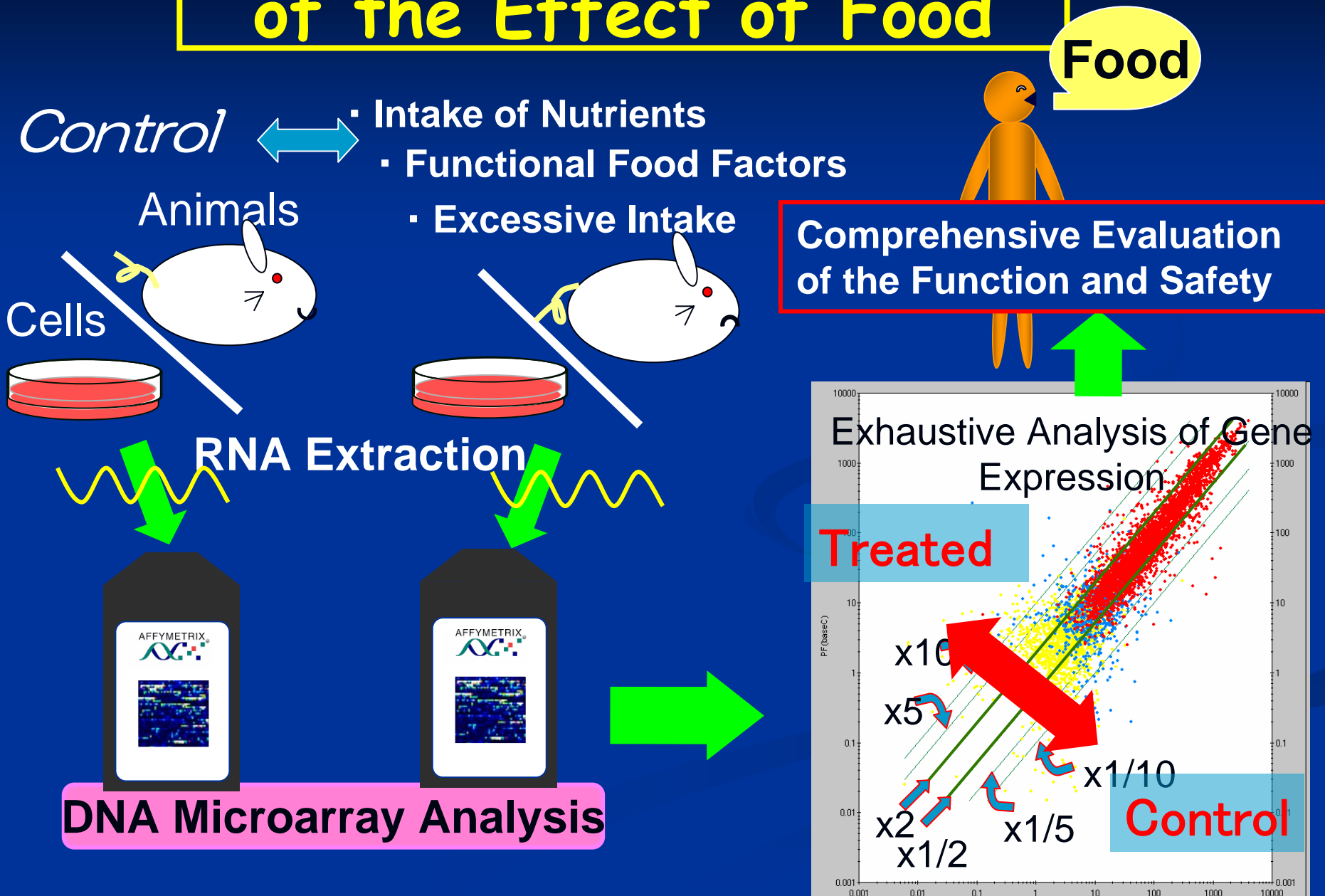


# Effects of Dietary Protein Deprivation and Amino Acid Deprivation on mRNA Levels of IGFBP-1 Gene





# Transcriptome Analysis of the Effect of Food



# The World of OMICS

Target	Omics Discipline	Nutritional Omics
Genes	Genomics	Nutrigenomics (narrow sense)
Transcripts	Transcriptomics	Nutritranscriptomics
Proteins	Proteomics	Nutriproteomics
Metabolites	Metabolomics	Nutrimetabolomics
⋮	⋮	⋮
		Nutrigenomics
		Nutriomics



# Other OMICS

Epigenomics (Chromatin Modification)

Interactomics (Protein-Protein Interaction)

Toponomics (Cellular Localization)  
(Localizomics)

Fluxomics (Cellular Flux of Metabolites)

Lipidomics (Lipids)

Glycomics (Sugars)

⋮

**CAUTION: Economics and Comics Do NOT  
Belong to the Omics Family**

# Use of DNA Microarray

## 1. Nutritional Intervention

## 2. Known Function of a Food Factor

## 3. A Food Material or Component of Interest

DNA Microarray and Other Omics Analyses

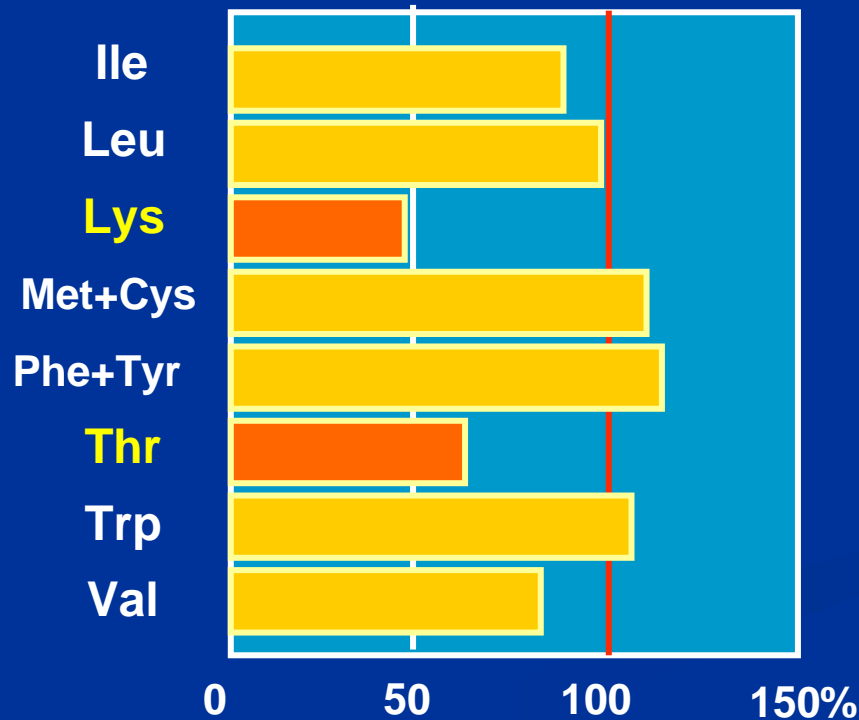
Understanding  
Whole Response

Understanding  
Mechanisms

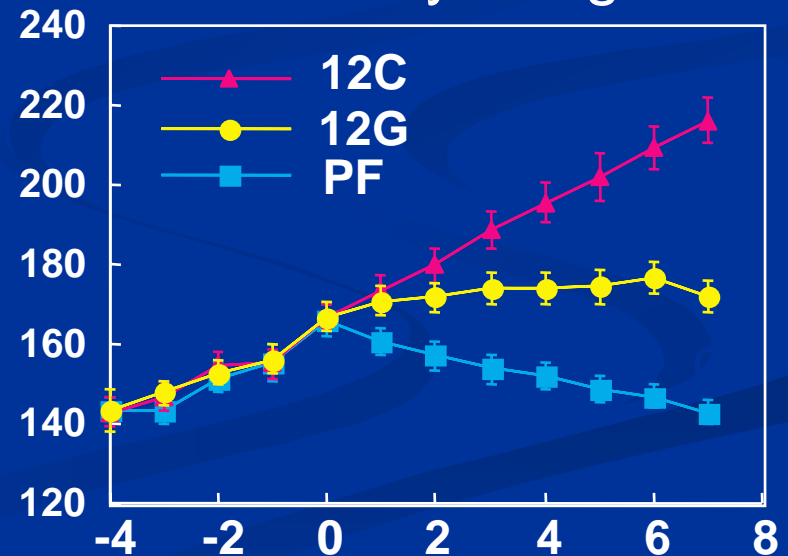
Unknown Functionality

	12% Casein (12C)	12% Gluten (12G)	Protein Free (PF)
Casein	140 (+Met 2)	0	0
Gluten	0	150	0
Cornstarch	656	648	798
Mineral Mix	50	50	50
Vitamin Mix	40	40	40
Vitamin Mix	10	10	10
Cellulose	100	100	100
Choline chloride	2	2	2

## Essential Amino Acid Pattern of Gluten



## Rat Body Weight

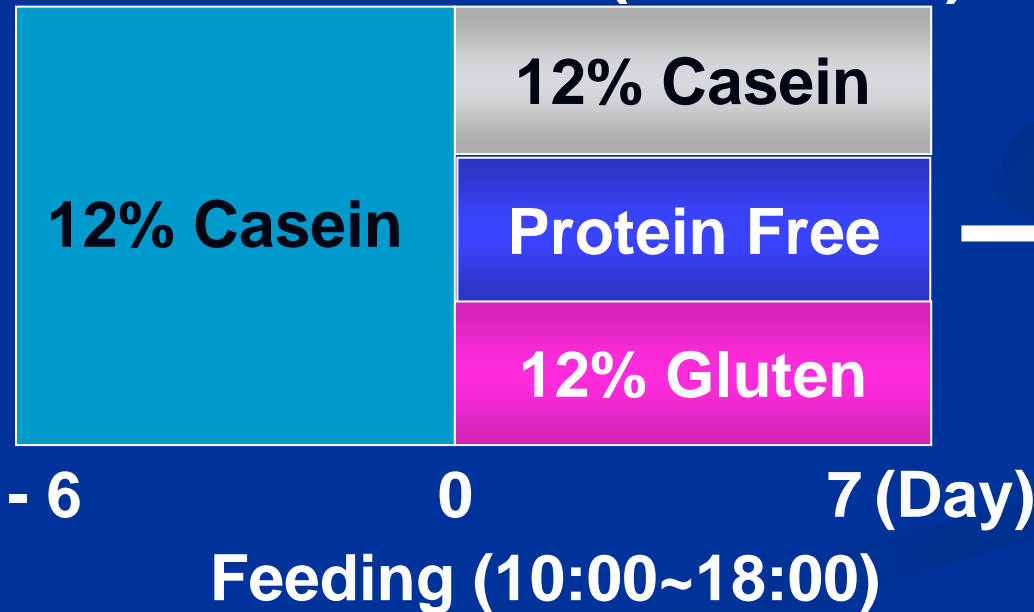


# Object

To obtain a comprehensive view of the changes in gene expression in response to the alteration of protein nutrition

# Method

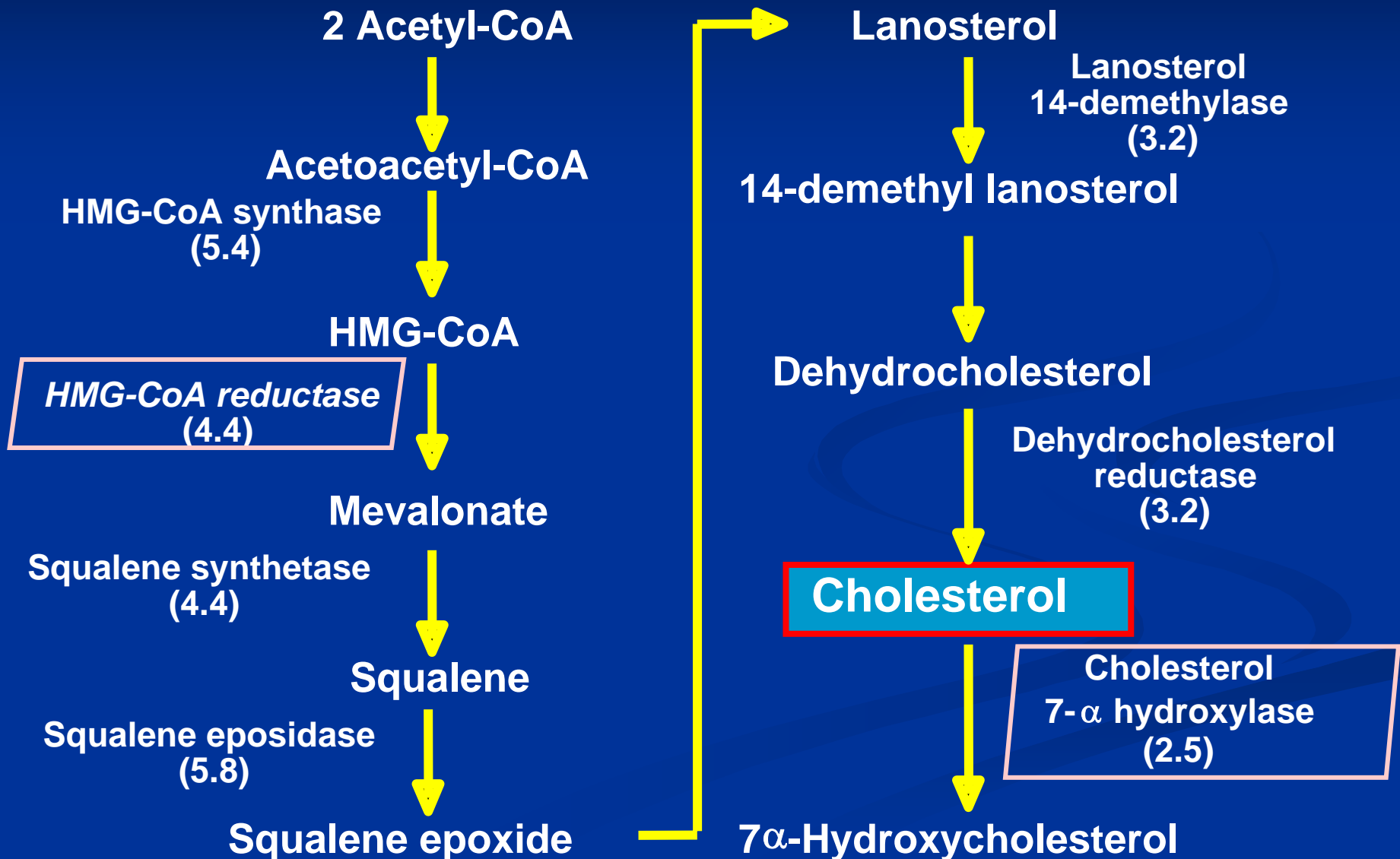
Male Wistar rats ( 5 wk old)



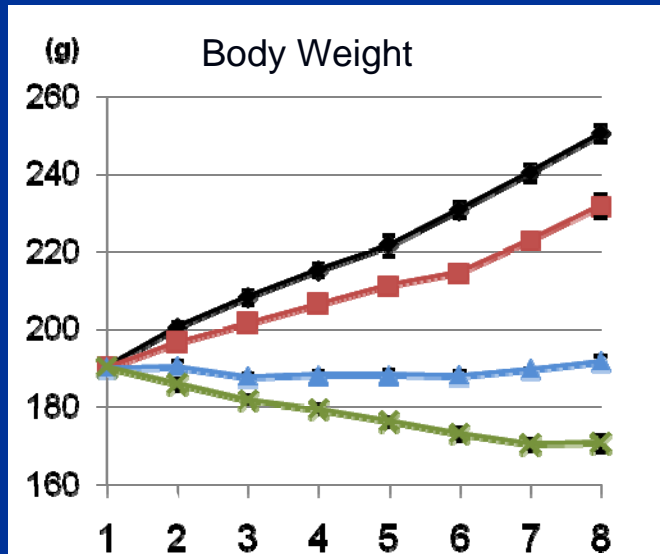
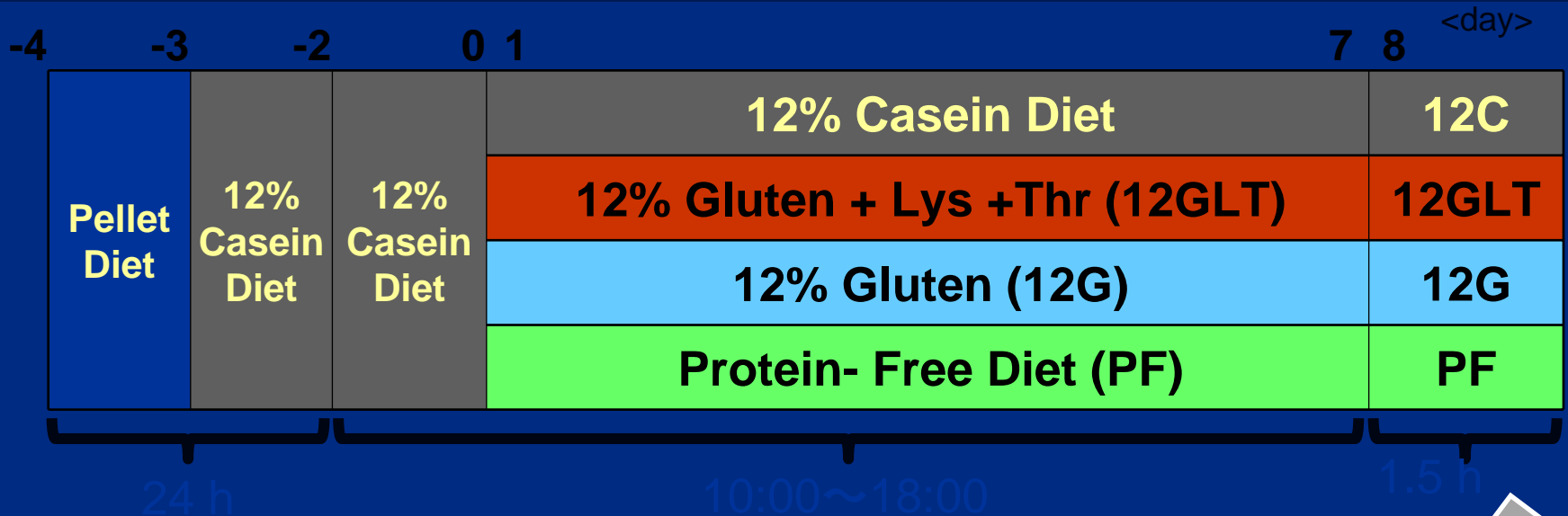
RNA extraction  
(Liver, Muscle,,)

Rat U34A Genome  
Array (Affymetrix)

# Ingestion of Gluten Up-regulates Genes for Both Synthesis and Catabolism of Cholesterol



# Protein Nutrition and Skin Gene Expression



Excision of Skin

DNA Microarray  
(n=4)



# Professional Program for Agricultural Bioinformatics (Tokyo Univ.)



Professional Programme for Agricultural Bioinformatics

農学生命情報科学大学院教育研究ユニット

## アグリバイオインフォマティクス 人材養成プログラム

東京大学大学院農学生命科学研究科

**ホーム**

**本ユニットについて**

**各講義のページ**

**受講手続き**

### Outline of the Agricultural Bioinformatics Unit

The Agricultural Bioinformatics Unit was established in 2004 with support from MEXT (Ministry of Education, Culture, Sports, Science, and Technology) to conduct education and research on bioinformatics for graduate students who are studying agricultural and life sciences. The unit's educational programs include lectures, practice, and seminars in foundations, methodologies, and advanced topics of bioinformatics and their agricultural research of master and doctoral students linked directly to each research topic. The unit also promotes cooperation for experimental and industry-university cooperation.



### Educational Program

**Fundamentals**

- Bioinformatics Literacy I
- Bioinformatics Literacy II
- Introduction to Biostatistics
- Basic Practice of Bioinformatics

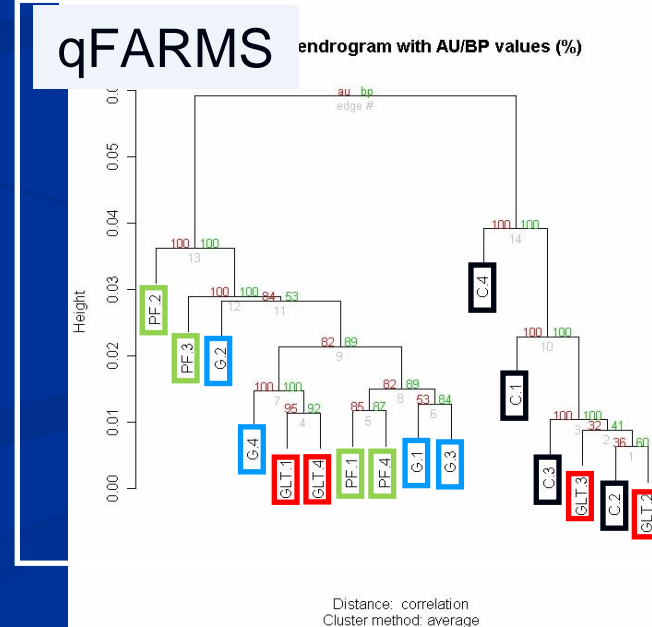
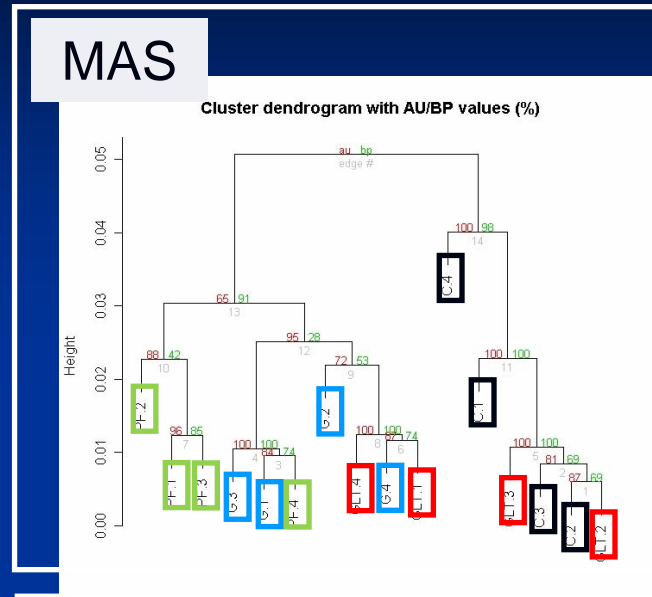
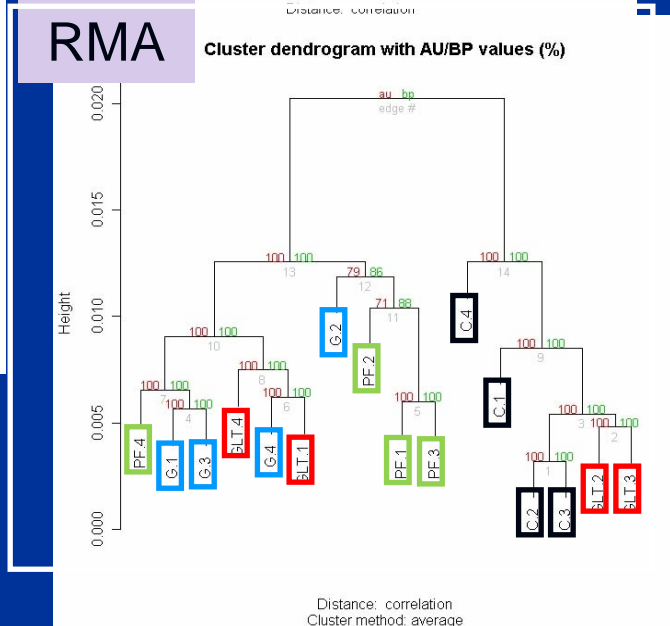
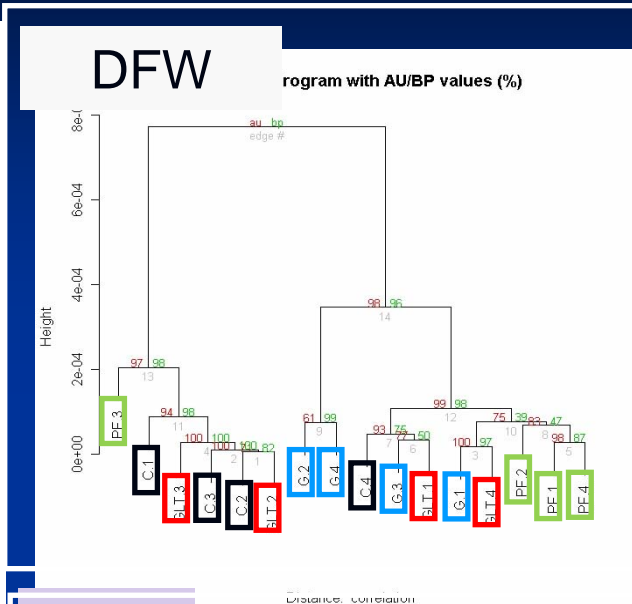
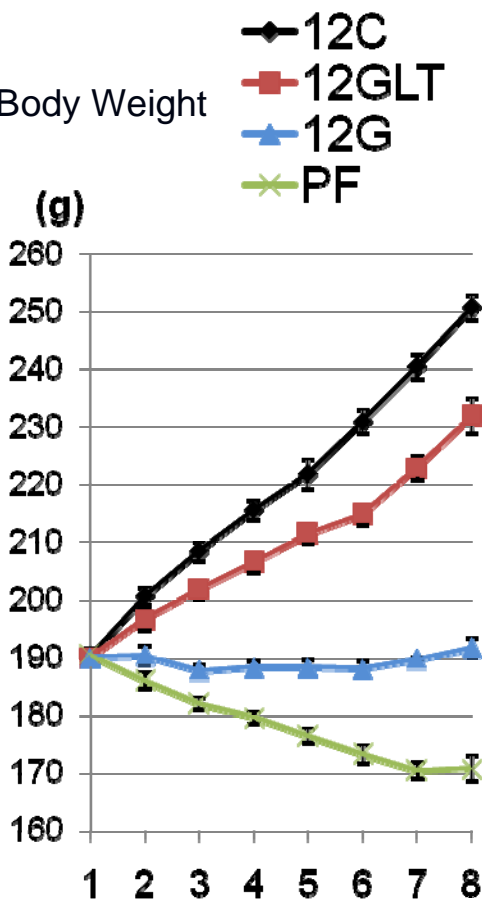
**Methodology**

**English**

**アンケート**

東京大学  
The University of Tokyo

# Choice of Normalization Method



# Other Ongoing Projects (transcriptomics)

Deficiency and Excess of Amino Acids

Specific Proteins and Peptides

Protein Intake Levels at Various Life Stage

Effect of Dietary Factor on Longevity, Diabetes, Hypertension

Effect of Biological Rhythm and Exercise on Gene Expression

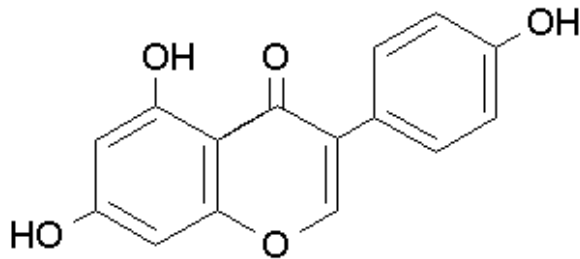
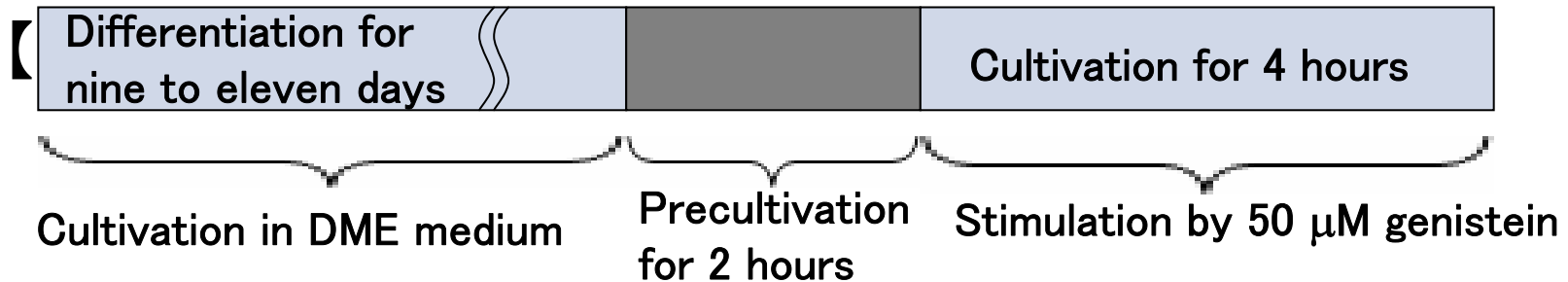
Insulin-mimetic Activity of Soy Isoflavone

Hypocholesterolemic Effect of Sulfur-Containing Amino Acid

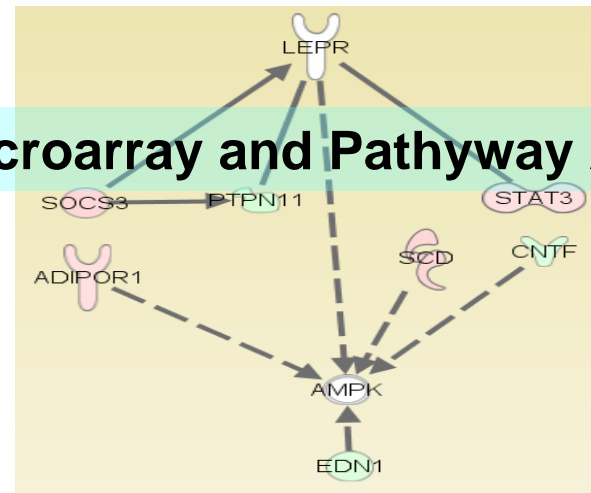
Anti-obesity Effect of Dietary Amino Acid Supplementation

# Stimulation of Glucose Uptake by a Soy Isoflavone, Genistein, in L6 Myotubes

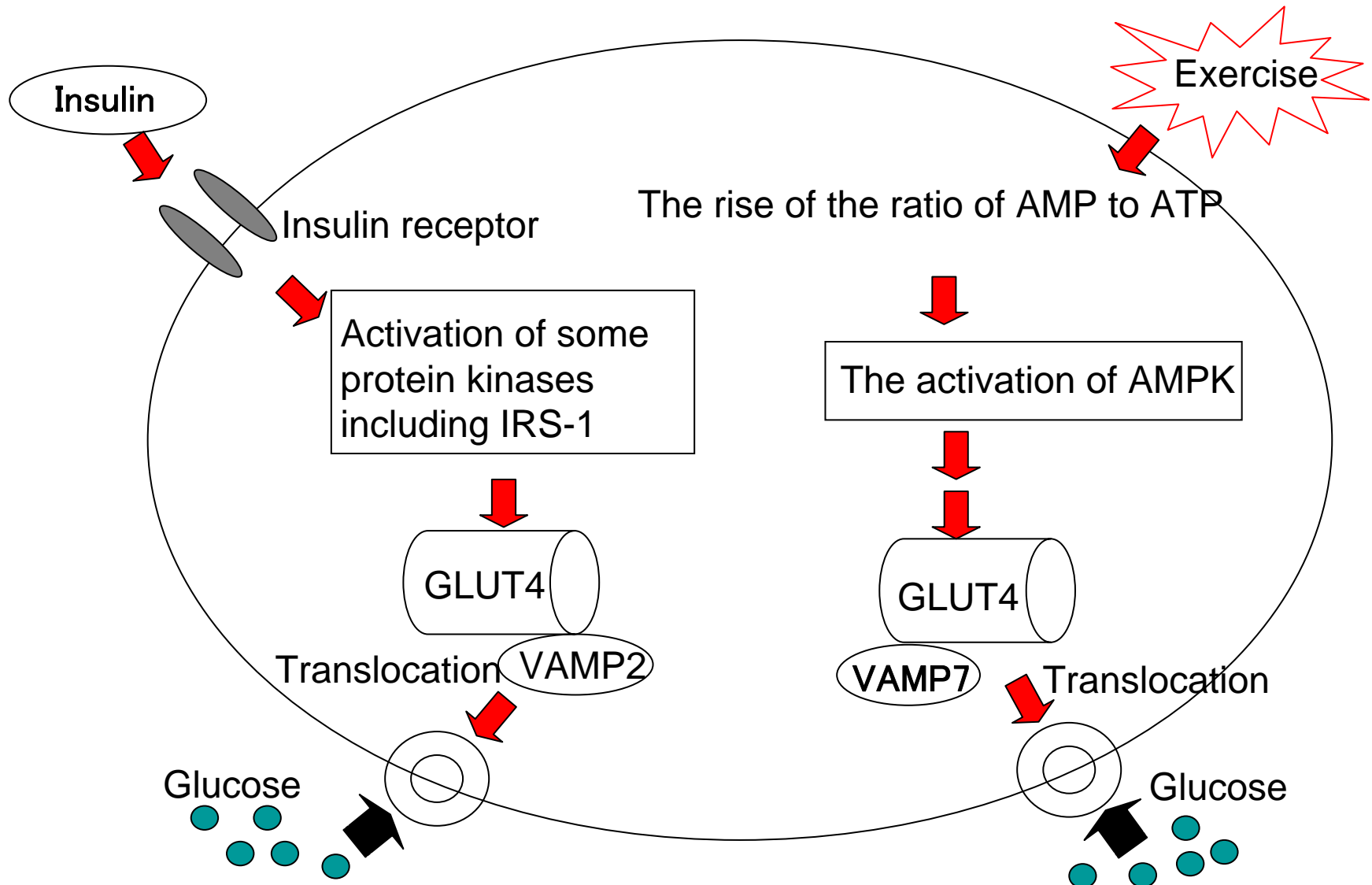
【Cells】 L6 myotubes (from rattus)



## DNA Microarray and Pathway Analysis



# Genistein Seems to Activate Two Pathways Leading to GLUT4 Translocation



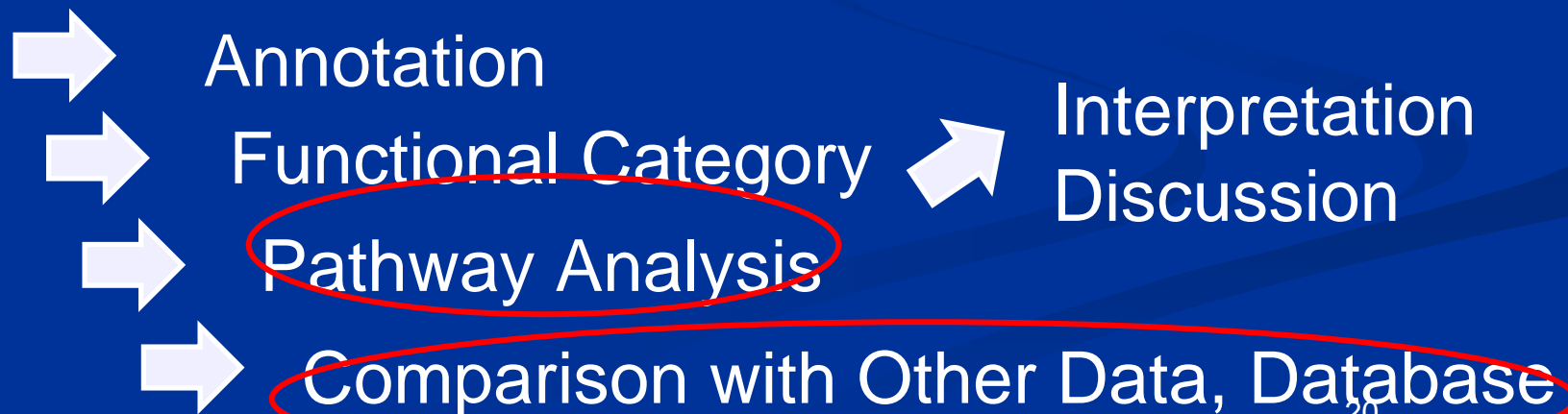
# A Typical Flow of DNA Microarray Data Analysis for Food and Nutrition Science

Raw Data → Normalization → Filtering



Cluster Analysis, Principal Component Analysis, etc.  
(Tendency, Extraction of Marker Genes)

Each Responder Genes  
(Rank Analysis, Statistical, Fold change...)





# Nutrigenomics Database

ABOUT PUBLICATION ARRAYDATA CONTACT/SUBMIT LINK LOGIN

## Nutrigenomics Database

### ABOUT

Nutrigenomics database was designed for effective storage, management, analysis and sharing of gene expression data to nutritional scientists involved in the microarray experiment. Currently, there are more than **500** publications and several expression data sets available for any user. This database offers a solution for scientists who need advanced search for microarray data related to nutrition. Although this database is still under testing and construction, please try out and send us any comments or suggestions.

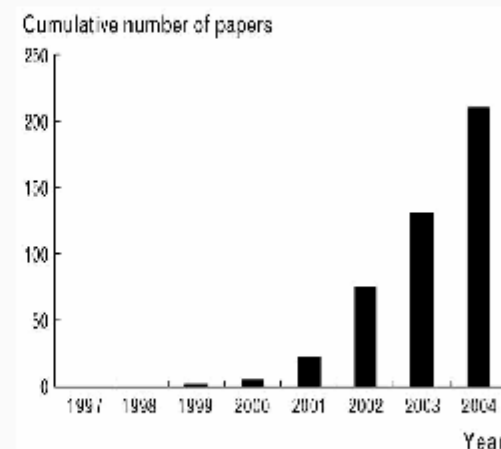
Administrator of this web site  
K. Saito

### FEATURES

- **Simple pull-down search**  
-The search engine enables you to access, easily and intuitively to all the information from published nutrigenomics studies and associated gene expression data by the carefully selected nutrition-related keywords in the search menu.

### CURRENT STATUS

Total number of publications : 507  
Total number of arraydata registered  
-Experiments : 43  
-Hybridizations : 126  
**Last Update 2007 Dec 1**



The numbers of papers relating to dietary conditions, nutrients, food factors and pertinent disorders