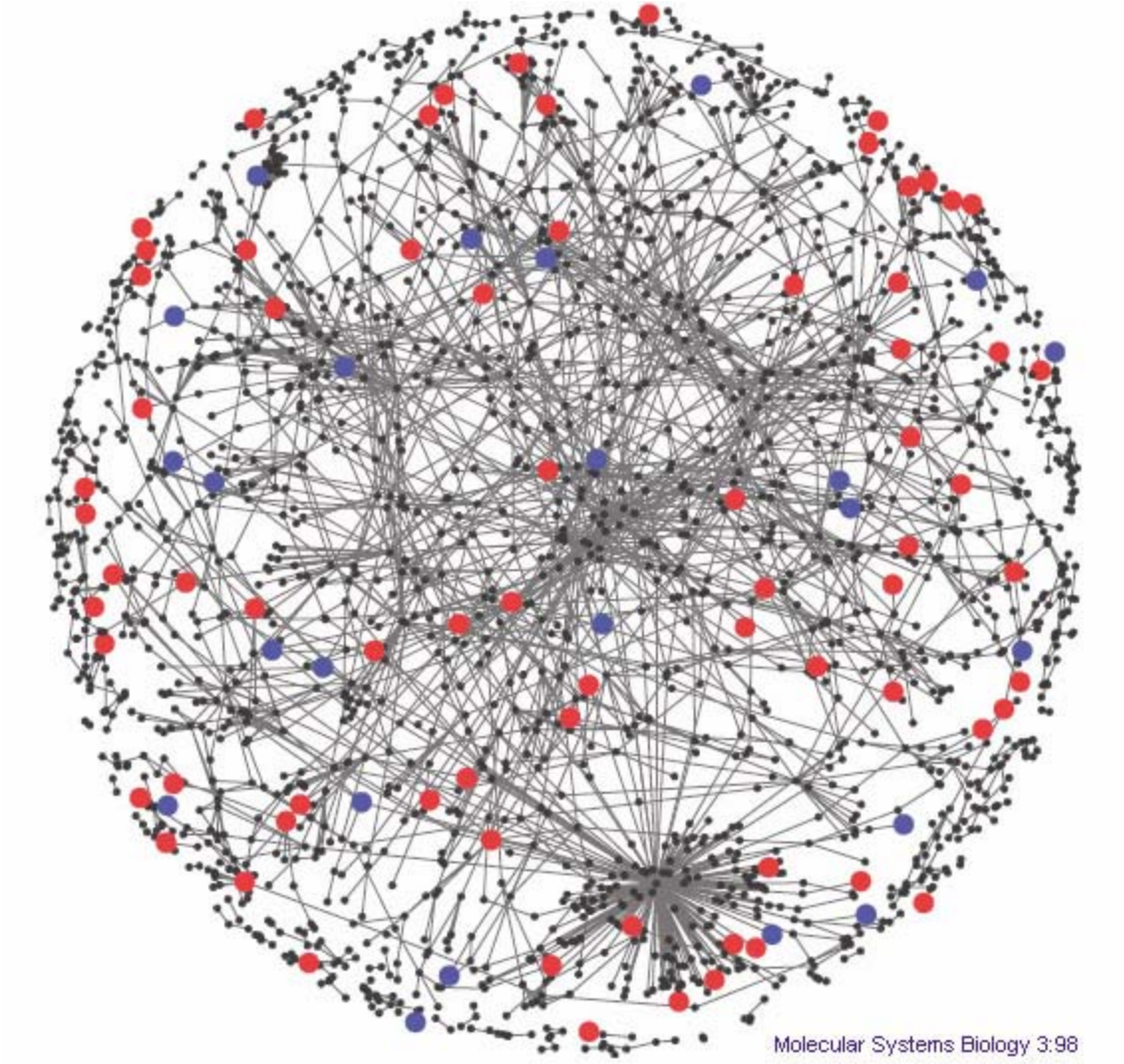
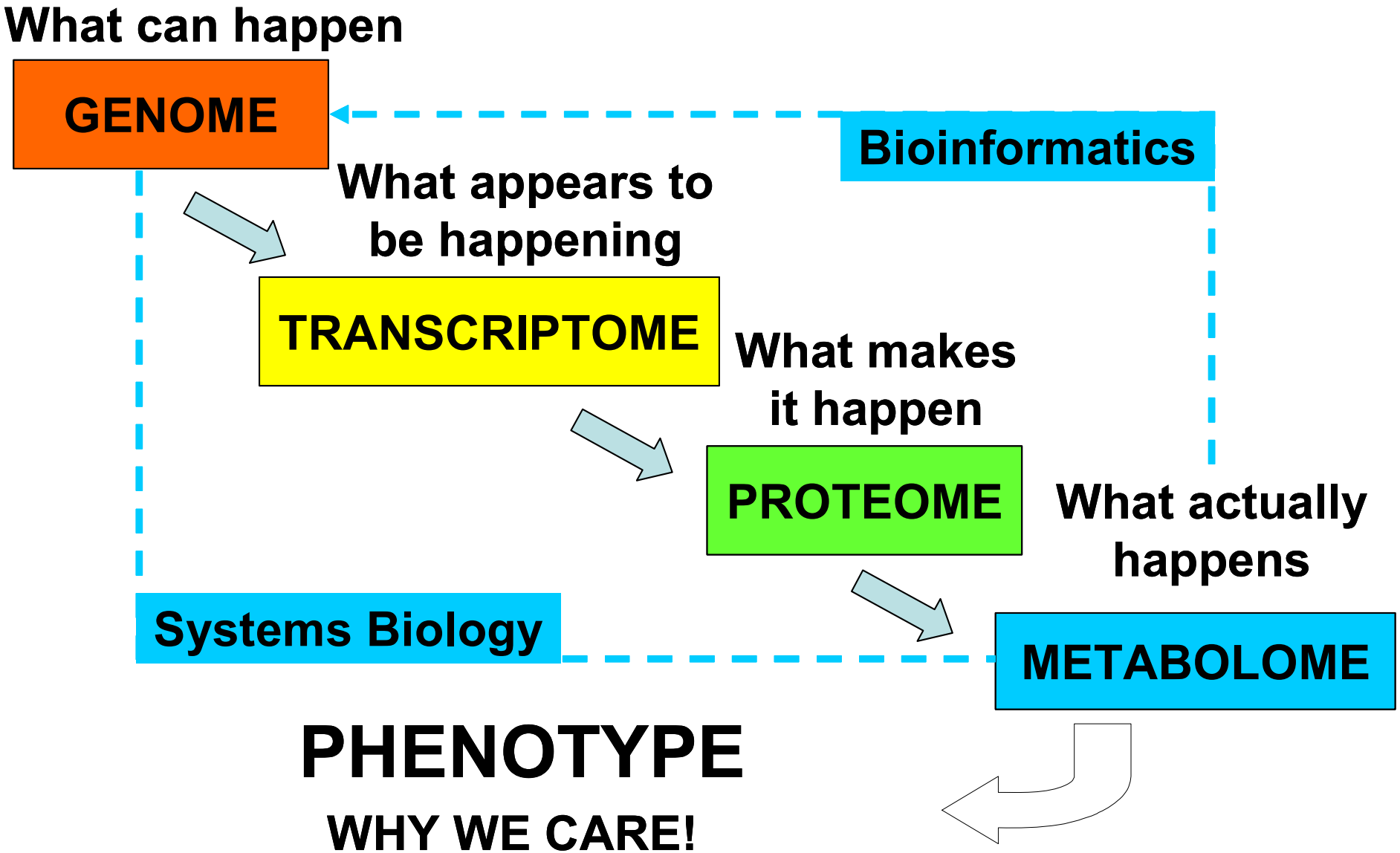


Systems Biology and the Omics Cascade
June 9-13th, 2008

The Omics-Cascade



Day 1 June 9th

- **Omics overview. Basic concepts of omics-approach to research, systems biology & theory behind large-scale data acquisition**

- **<u>Morning (Loben, Thoraxhuset, plan 6)</u>**
- **9:00-9:30 Introduction – (Craig Wheelock, KI)**
- **9:30-10:15 Overview of "omics cascade" (Åsa Wheelock, KI)**
- **10:15-10:30 coffee break**
- **10:30-11:15 Proteomics (Åsa Wheelock, KI)**
- **11:15-12:00 Transcriptomics (Peter Nilsson, KTH)**
- **12:00-13:00 Lunch**

- **<u>Afternoon (Loben, Thoraxhuset, plan 6)</u>**
- **13:00-13:45 Metabolomics (Craig Wheelock, KI)**
- **13:45-14:45 "Chemometrics for omics" (Torbjörn Lundstedt, UU)**
- **14:45-15:00 coffee break**
- **15:00-16:00 "Personalized Medicine" (Torbjörn Lundstedt, AcurePharma)**

Day 2 June 10th

- **Introduction to KEGG pathways (Kyoto Encyclopedia of Genes and Genomes)**

- **<u>Morning (MBB, Stora Seminarierummet located at A2 319)</u>**
- **What is KEGG and how can it be used? (Susumu Goto and Masahiro Hattori)**
- **9:00-10:15 Lecture (Susumu Goto, Kyoto University)**
- **10:15-10:30 coffee break**
- **10:30-12:00 Lecture (Masahiro Hattori, Kyoto University)**
- **12:00-13:00 Lunch**

- **<u>Afternoon (Datorsal Space, BZ plan2, in Utopia)</u>**
- **Computer laboratory-based work with KEGG**
- **13:00-14:30 Lab (Kyoto University Bioinformatics Center)**
- **14:30-14:45 coffee break**
- **14:45-16:00 Lab (Kyoto University Bioinformatics Center)**

Day 3 June 11th

- **Genome Informatics. Introduction to available on-line databases and biological pathways**

- **<u>Morning (MBB, Stora Seminarierummet located at A2 319)</u>**
- **availability and potential application of on-line database resources. (Kiyoko Aoki-Kinoshita)**
- **9:00-10:15 Lecture (Kiyoko Aoki-Kinoshita, Soka University)**
- **10:15-10:30 coffee break**
- **10:30-11:45 Lecture (Kiyoko Aoki-Kinoshita, Soka University)**
- **11:45-13:00 Lunch**

- **<u>Afternoon (Datorsal Space, BZ plan2, in Utopia)</u>**
- **Computer laboratory-based work using on-line databases.**
- **13:00-14:30 Lab (Kiyoko Aoki-Kinoshita, Soka University)**
- **14:30-14:45 coffee break**
- **14:45-16:00 Lab (Kiyoko Aoki-Kinoshita, Soka University)**

Day 4 June 12th

- Computer programming languages and algorithms

- Morning (Loben, Thoraxhuset, plan 6)
- Overview of various high-level programming concepts, with focus upon Perl (David Leangen, Diego Diez)
- 09:00-09:45 Programming concepts (David Leangen, Bioscene)
- 09:45-10:00 coffee break
- 10:00-10:45 Programming concepts (David Leangen, Bioscene)
- 10:45-11:00 Break
- 11:00-12:00 Programming Perl (Diego Diez, Kyoto University)
- 12:00-13:00 Lunch

- Afternoon (Loben, Thoraxhuset, plan 6)
- Overview of algorithms. (Kiyoko Aoki-Kinoshita, Soka University)
- 13:00-14:15 Lecture (Kiyoko Aoki-Kinoshita, Soka University)
- 14:15-14:30 coffee break
- 14:30-16:00 Lecture (Kiyoko Aoki-Kinoshita, Soka University)

Day 5 June 13th

- **Systems biology – putting it all together**

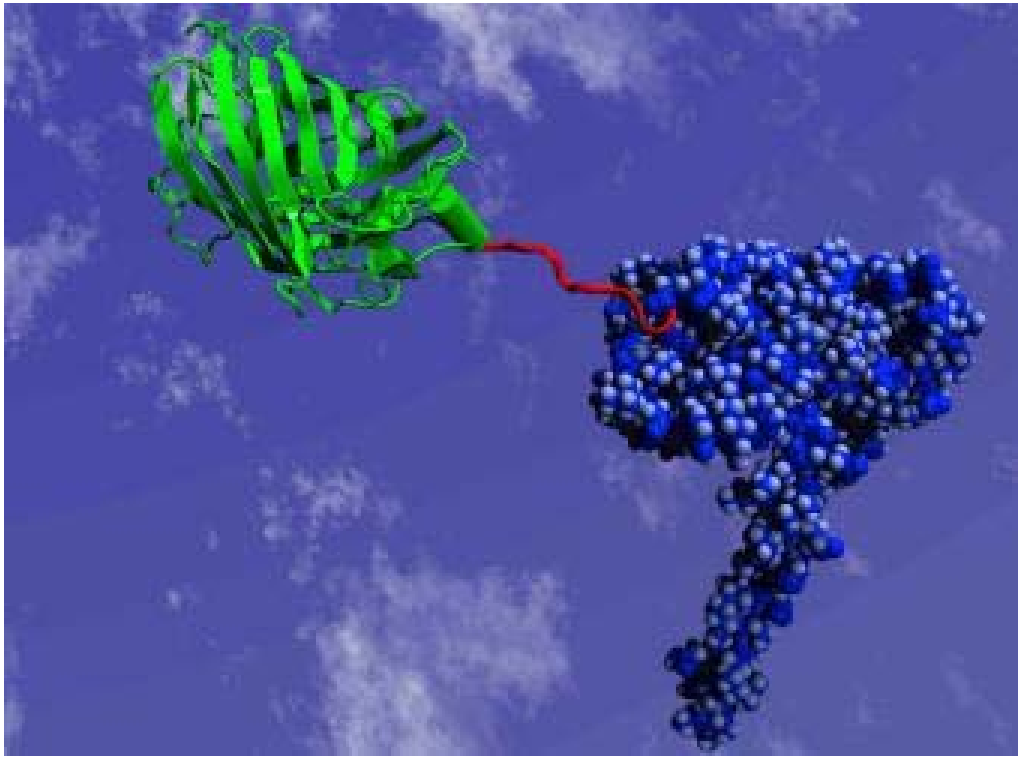
- **<u>Morning (Datorsal Space, BZ plan2, in Utopia)</u>**
- **BioPerl-based computational tasks (Kiyoko Aoki-Kinoshita)**
- **9:00-10:15 Lab (Kiyoko Aoki-Kinoshita, Soka University)**
- **10:15-10:30 coffee break**
- **10:30-12:00 Lab (Kiyoko Aoki-Kinoshita, Soka University)**
- **12:00-13:00 Lunch**

- **<u>Afternoon (MBB, Stora Seminarierummet located at A2 319)</u>**
- **13:00-13:50 Research seminar (Peter Nilsson, KTH)**
- **13:50-14:05 coffee break**
- **14:05-14:55 Research seminar (Serhiy Souchelnytskyi, KBC, KI)**
- **14:55-15:10 coffee break**
- **15:10-16:00 Research seminar (Matej Orešič, VTT, Technical Research Centre of Finland)**
- **16:00-16:15 Course summary (Craig Wheelock, KI)**

Course examination

- no course examine
- research report on an aspect of systems biology
- choose your own subject, but needs my approval
- maximum 3 pages including references
- submit by June 30th (via email)
- use journal articles & concepts discussed in course
- ideally report relates to systems biology applications in your own research area
- if report is unsatisfactory, one additional week to re-write and resubmit
- attendance at all laboratory sessions is required

the omics cascade . . .



What are “omics” sciences?

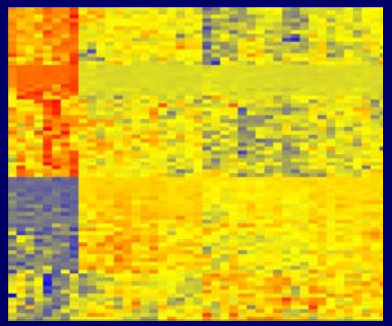
- **The suffix “*ome*” comes from “genome”, which was formed after “chromosome”**
- **The word “chromosome” comes from the Greek stems “color” and “body”**
- **Omics implies an integration of biology with information science**
- **Omics conveys a systems approach**
- **Large scale biology**
- **Significant data acquisition**

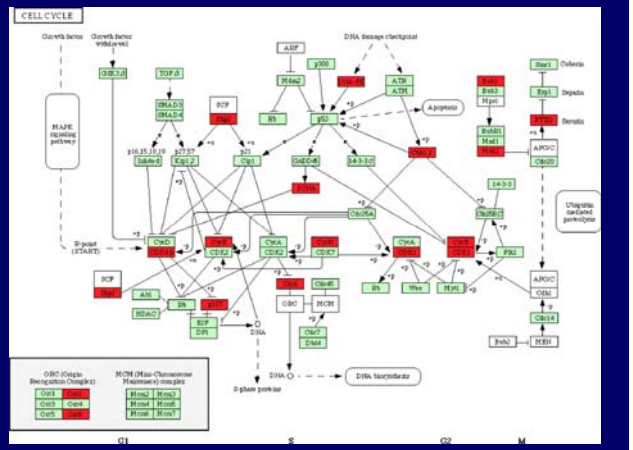
What is Omics good for?

Discovery Science

”Fishing trip”

Hypothesis-generating





What is systems biology?

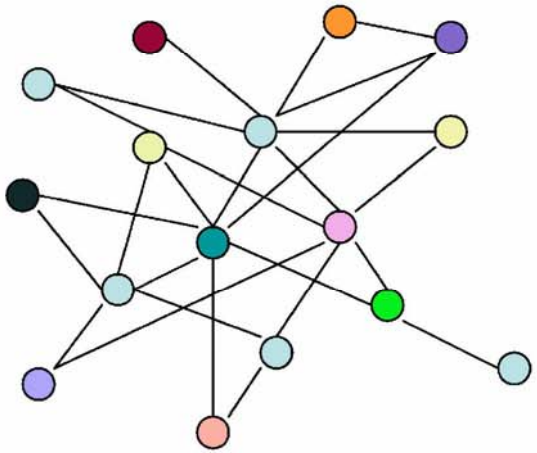
“Organisms function in an integrated manner - our senses, our muscles, our metabolism and our mind work together seamlessly. But biologists have historically studied organisms part by part and celebrated the modern ability to study them molecule by molecule, gene by gene. Systems biology is devoted to a new science, a critical science of the future that seeks to understand the integration of the pieces to form biological systems.”

-David Baltimore, Nobel Laureate

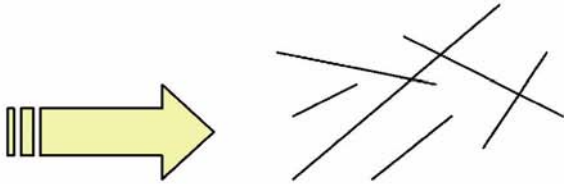
Reductionism

Components

Time
Space
Context



Systems Science



Interrelationships,
Dynamics

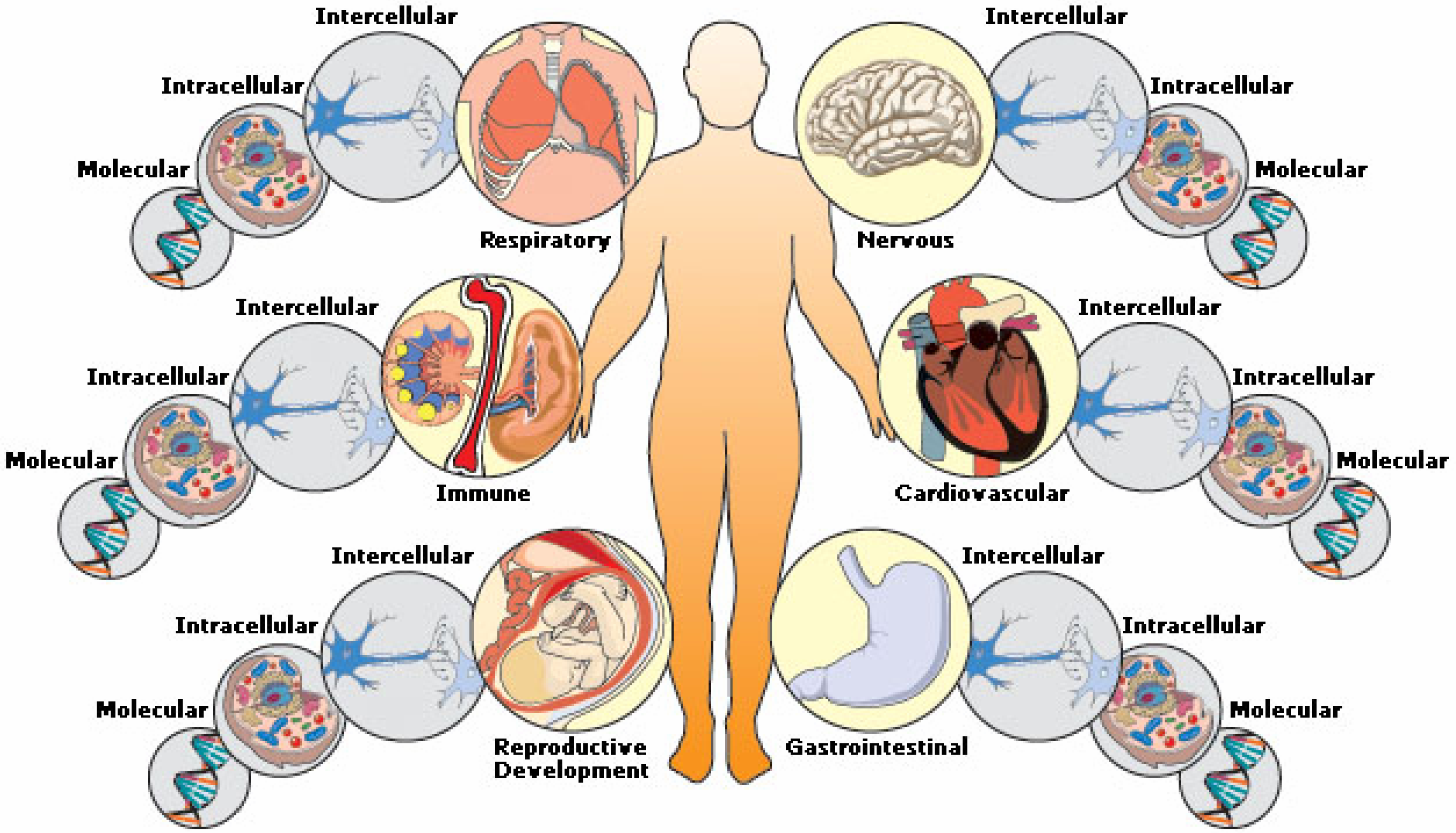
Medical Treatments

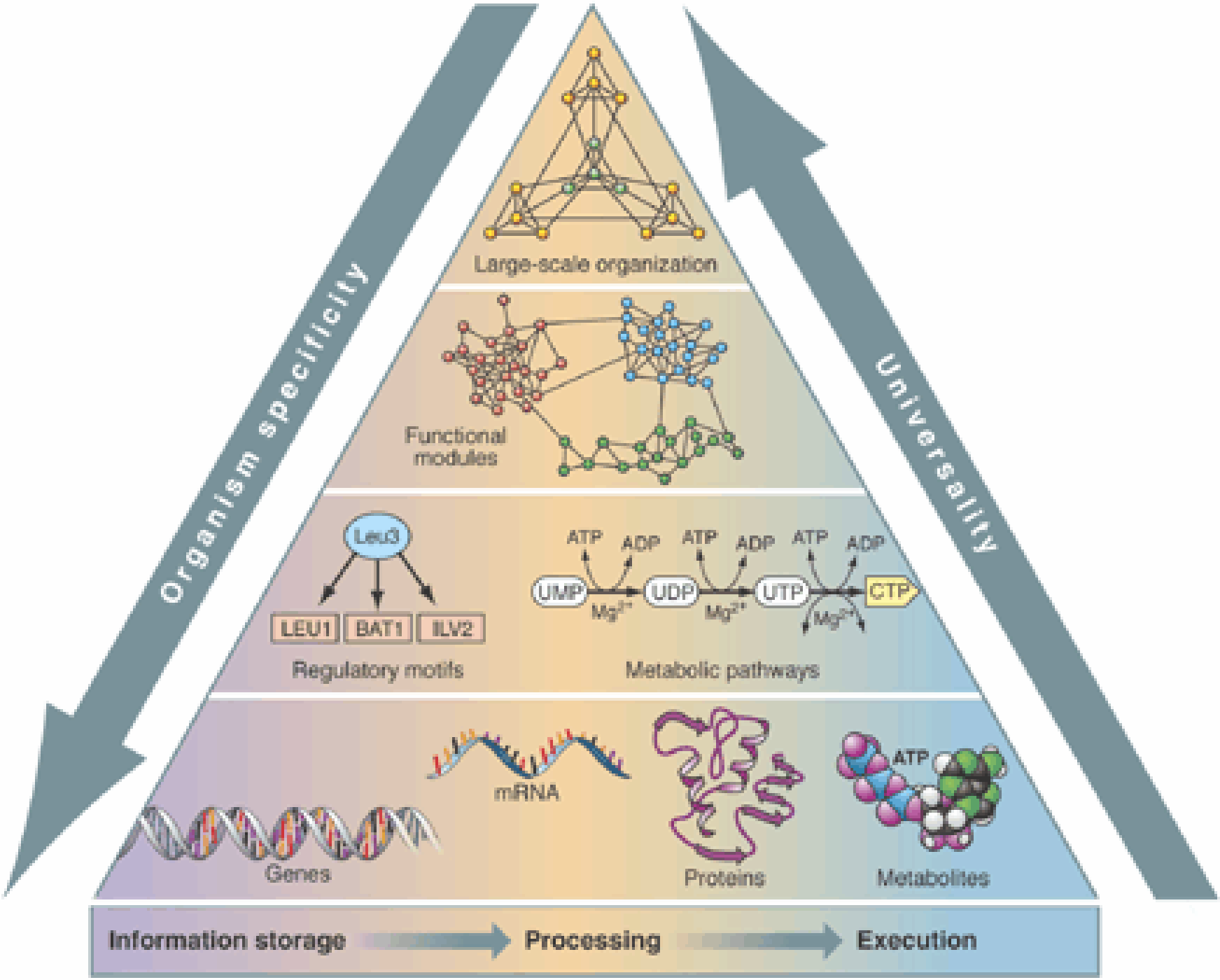
Disease-driven
Aimed for normalcy (normal range)
Additive

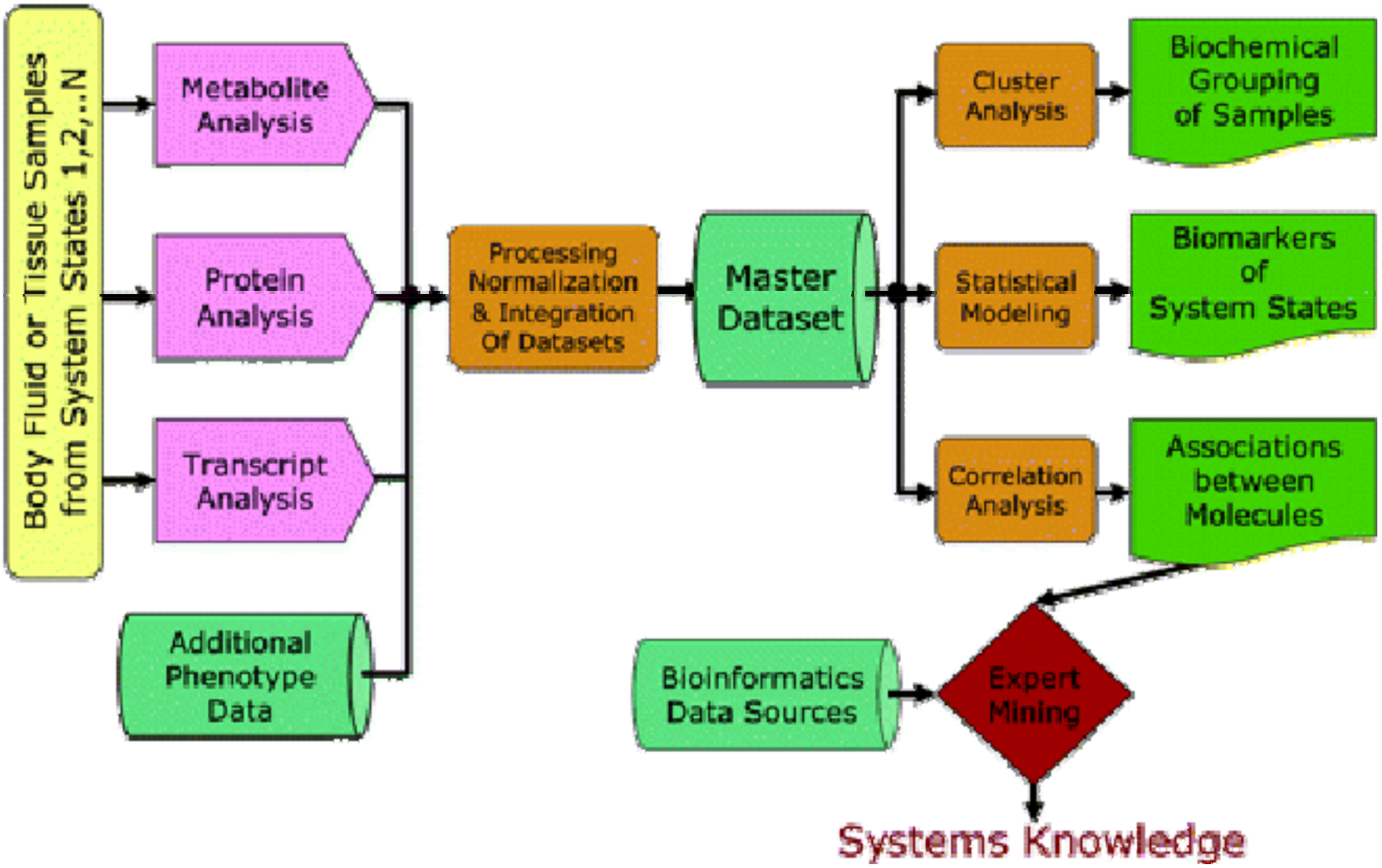
Medical Treatments

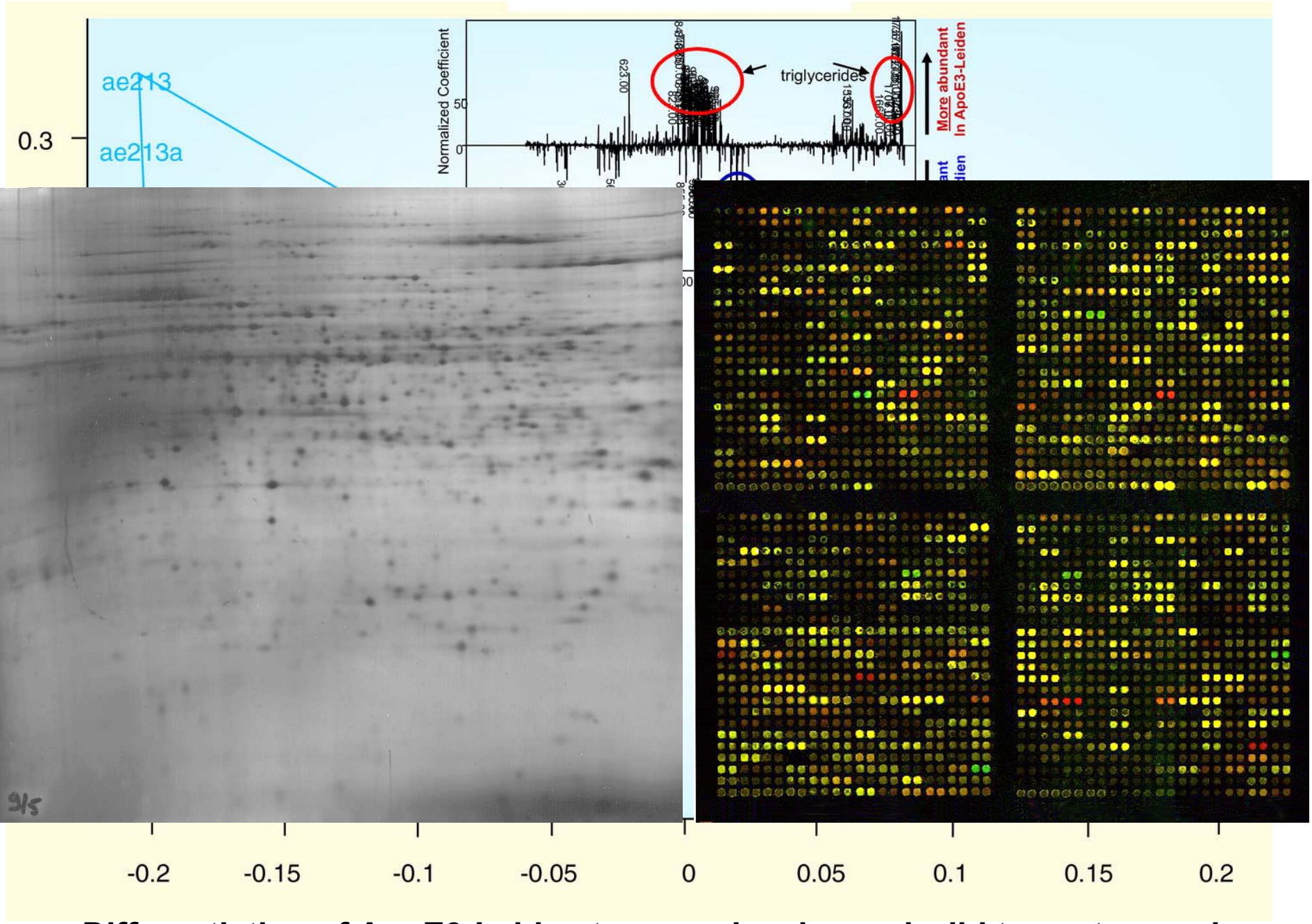
Individualized
Multidimensional use of drugs
Time-sensitive
Space-sensitive
Synergistic

Ahn et al. PLoS Med. 2006.e209.


Intercellular
Intracellular
Molecular
Respiratory
Nervous
Immune
Cardiovascular
Reproductive
Development
Gastrointestinal

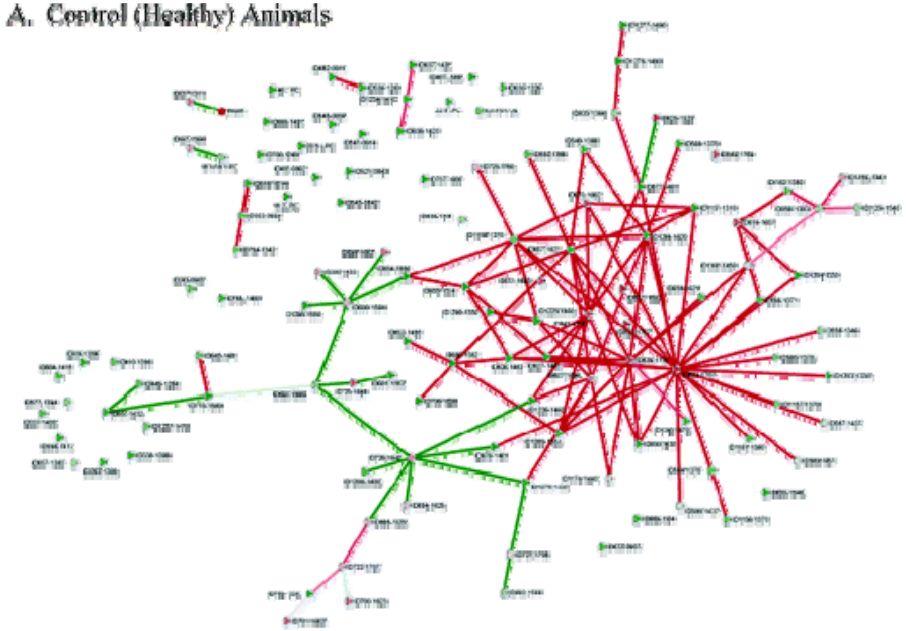

Organism specificity
Universality
Large-scale organization
Functional modules
Leu3
LEU1
BAT1
ILV2
Regulatory motifs
ATP
ADP
UMP
UDP
UTP
CTP
Metabolic pathways
mRNA
Genes
Proteins
ATP
Metabolites
Information storage
Processing
Execution


Body Fluid or Tissue Samples from System States 1,2,..N
Metabolite Analysis
Protein Analysis
Transcript Analysis
Additional Phenotype Data
Processing Normalization & Integration Of Datasets
Master Dataset
Cluster Analysis
Statistical Modeling
Correlation Analysis
Biochemical Grouping of Samples
Biomarkers of System States
Associations between Molecules
Bioinformatics Data Sources
Expert Mining
Systems Knowledge

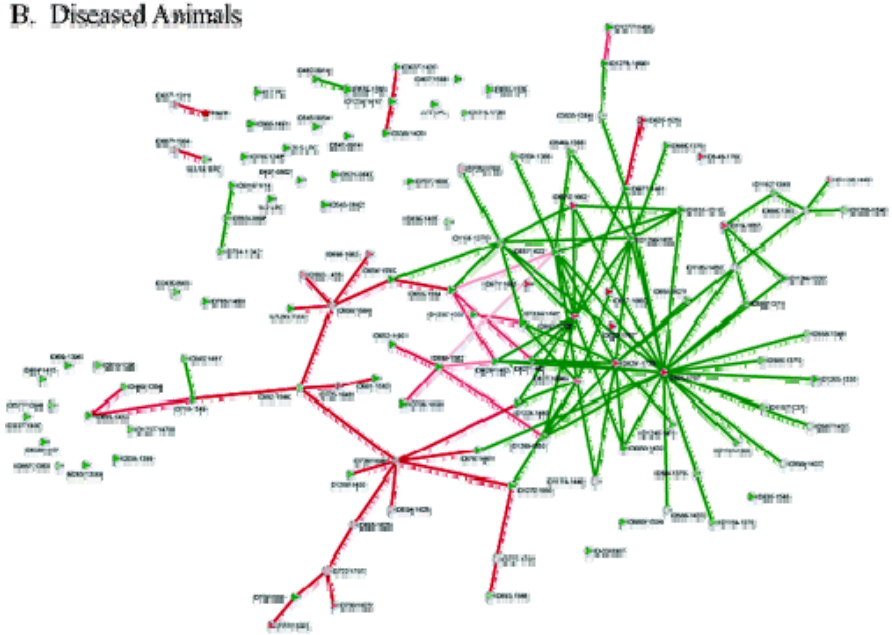


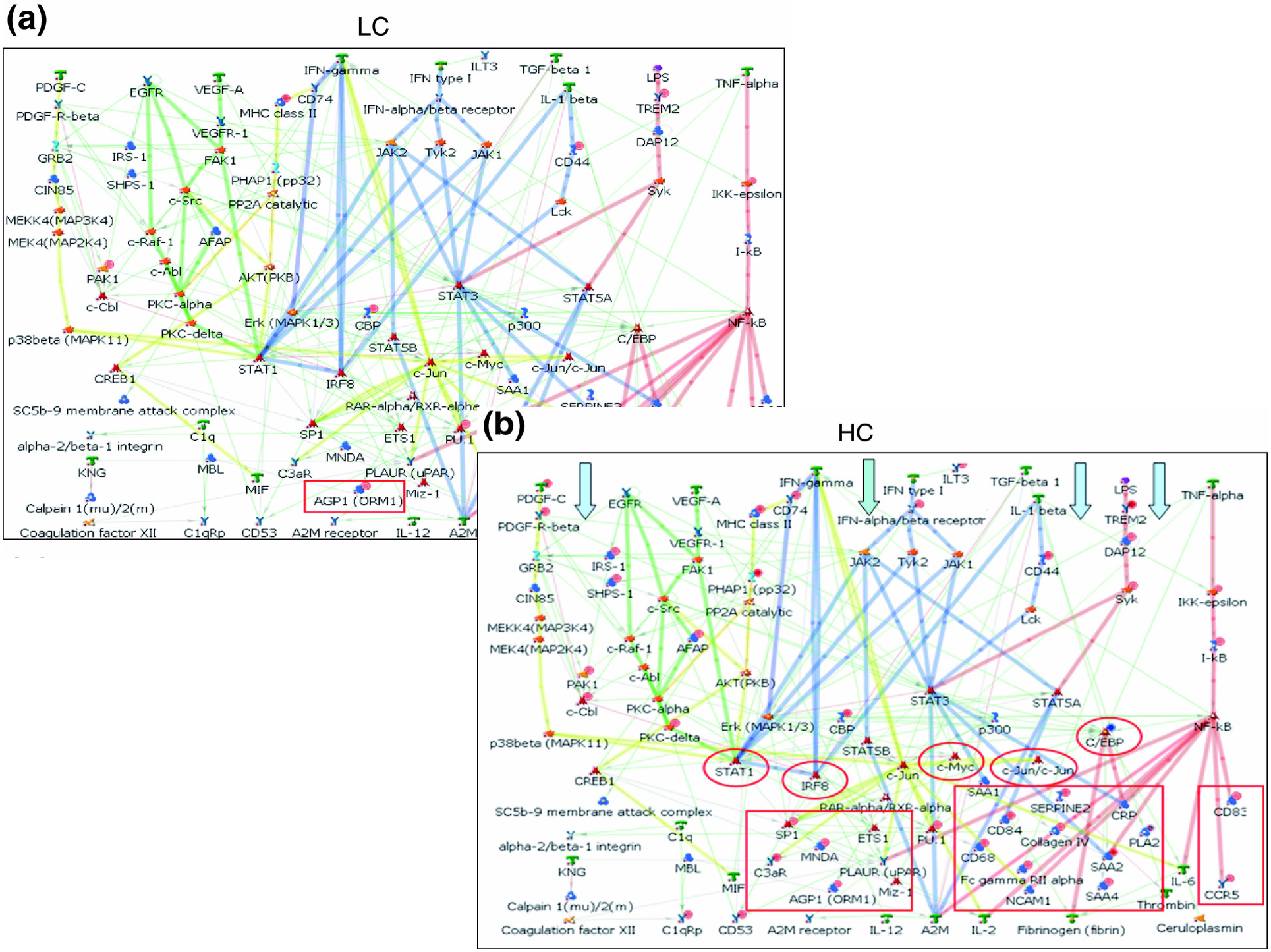
Differentiation of ApoE3-Leiden transgenic mice and wild type at an early stage of development.

A. Control (Healthy) Animals

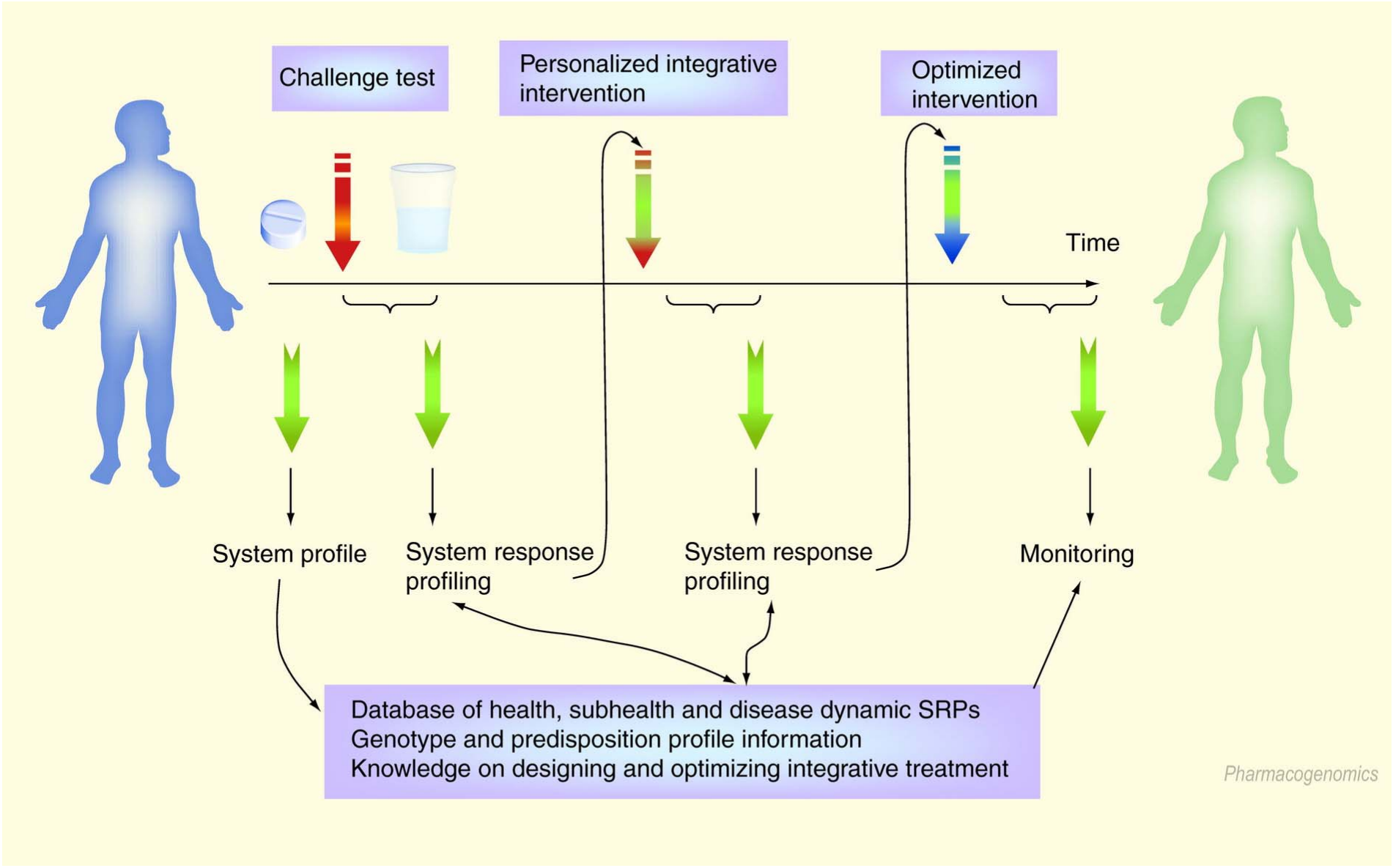


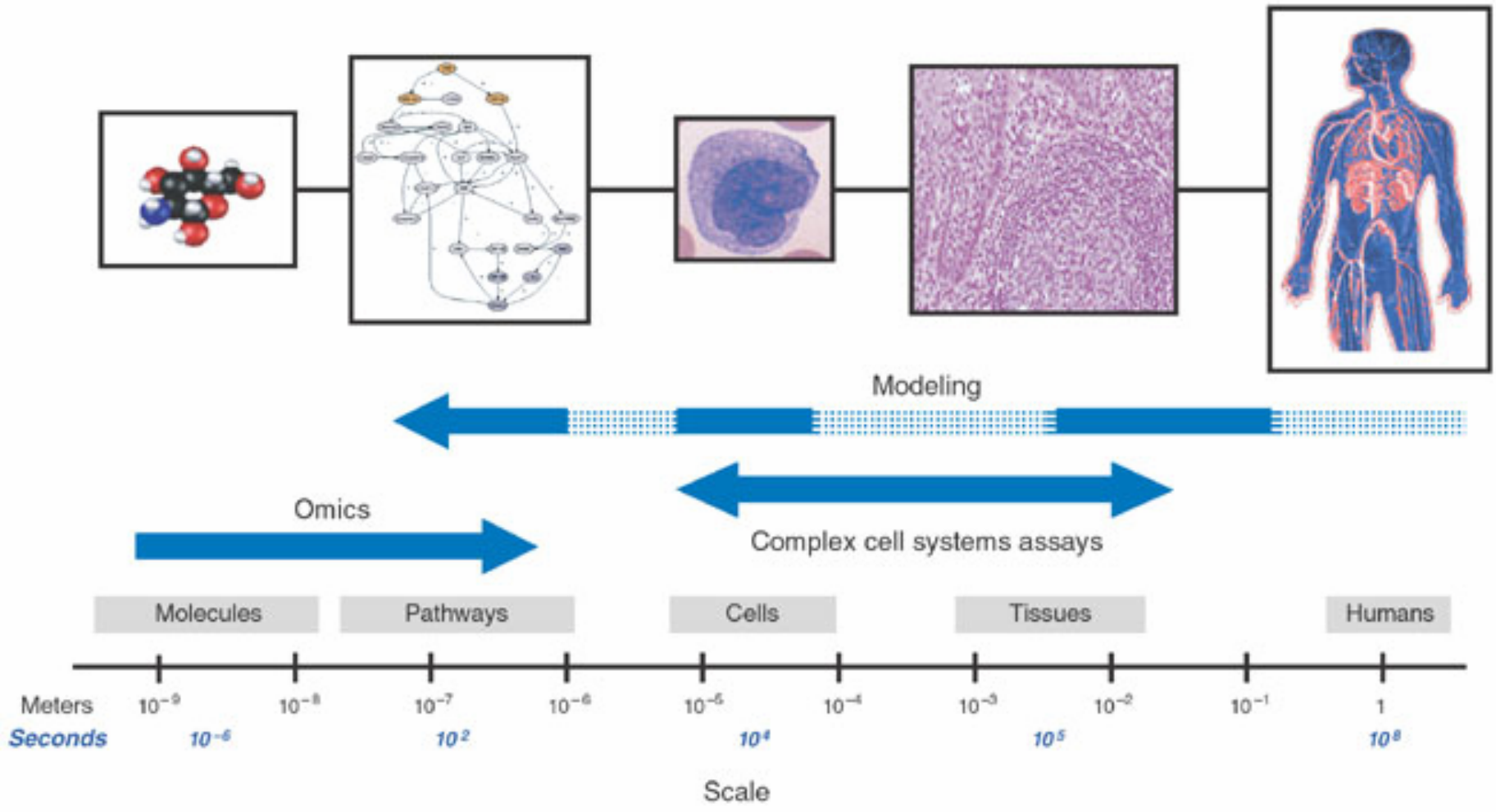
B. Diseased Animals



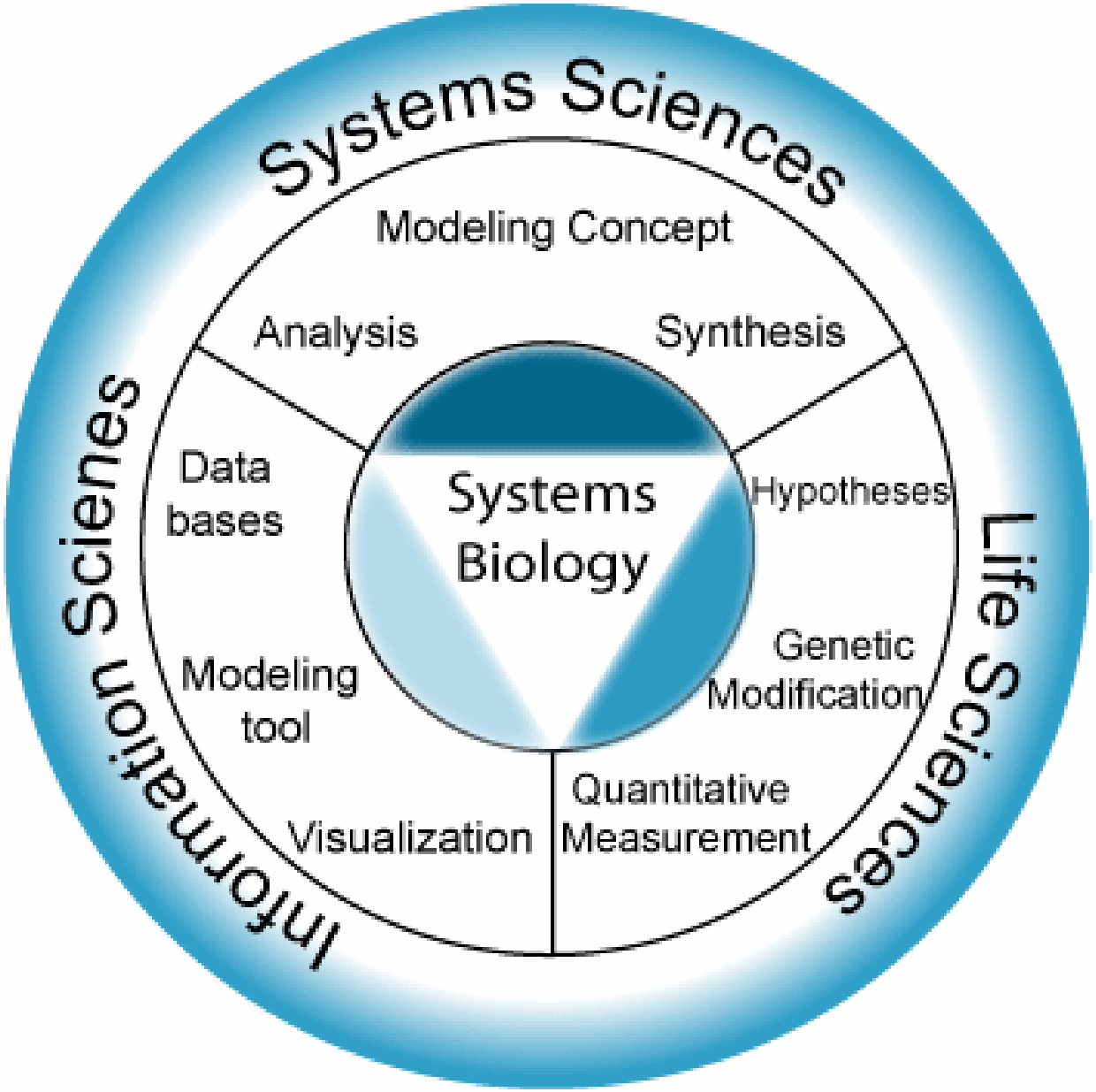

(a)
LC
PDGF-C
EGFR
VEGF-A
IFN-gamma
CD74
MHC class II
IFN type I
ILT3
IFN-alpha/beta receptor
TGF-beta 1
IL-1 beta
LPS
TREM2
DAP12
TNF-alpha
PDGF-R-beta
VEGFR-1
GRB2
IRS-1
FAK1
JAK2
Tyk2
JAK1
CD44
Syk
IKK-epsilon
CIN85
SHPS-1
c-Src
PHAP1 (pp32)
PP2A catalytic
Lck
MEKK4(MAP3K4)
MEK4(MAP2K4)
c-Raf-1
AFAP
I-kB
PAK1
c-Abl
AKT(PKB)
STAT3
STAT5A
c-Cbl
PKC-alpha
Erk (MAPK1/3)
CBP
p300
NF-kB
p38beta (MAPK11)
PKC-delta
STAT5B
C/EBP
CREB1
STAT1
c-Jun
c-Myc
c-Jun/c-Jun
IRF8
SAA1
SC5b-9 membrane attack complex
RAR-alpha/RXR-alpha
C1q
SP1
ETS1
PU.1
alpha-2/beta-1 integrin
MNDA
KNG
MBL
C3aR
PLAUR (uPAR)
MIF
AGP1 (ORM1)
Miz-1
Calpain 1(mu)/2(m)
Coagulation factor XII
C1qRp
CD53
A2M receptor
IL-12
A2M
(b)
HC
PDGF-C
EGFR
VEGF-A
IFN-gamma
CD74
MHC class II
IFN type I
ILT3
IFN-alpha/beta receptor
TGF-beta 1
IL-1 beta
LPS
TREM2
DAP12
TNF-alpha
PDGF-R-beta
VEGFR-1
GRB2
IRS-1
FAK1
JAK2
Tyk2
JAK1
CD44
Syk
IKK-epsilon
CIN85
SHPS-1
c-Src
PHAP1 (pp32)
PP2A catalytic
Lck
MEKK4(MAP3K4)
MEK4(MAP2K4)
c-Raf-1
AFAP
I-kB
PAK1
c-Abl
AKT(PKB)
STAT3
STAT5A
c-Cbl
PKC-alpha
Erk (MAPK1/3)
CBP
p300
NF-kB
p38beta (MAPK11)
PKC-delta
STAT5B
C/EBP
STAT1
IRF8
c-Jun
c-Myc
c-Jun/c-Jun
CREB1
SAA1
SC5b-9 membrane attack complex
RAR-alpha/RXR-alpha
SERPINE2
CRP
CD83
C1q
SP1
ETS1
PU.1
CD84
Collagen IV
PLA2
alpha-2/beta-1 integrin
MNDA
CD68
KNG
MBL
C3aR
PLAUR (uPAR)
SAA2
Fc gamma RII alpha
IL-6
MIF
AGP1 (ORM1)
Miz-1
SAA4
NCAM1
CCR5
Calpain 1(mu)/2(m)
Thrombin
Coagulation factor XII
C1qRp
CD53
A2M receptor
IL-12
A2M
IL-2
Fibrinogen (fibrin)
Ceruloplasmin

n=1 clinical trials???





Butcher et al. Nature Biotechnology **22**, 1253 - 1259 (2004)


Systems Sciences
Modeling Concept
Analysis
Synthesis
Data bases
Systems Biology
Hypotheses
Modeling tool
Genetic Modification
Visualization
Quantitative Measurement
Information Sciences
Life Sciences

Course aims

- The aim of the course is to provide students with a broad spectrum overview of the field of systems biology and present the different technologies and methods employed in this type of research approach.
- Specific aims include the following:
- Convey the concept & rationale behind systems biology & omics-related research approaches & experimental design.
- Provide an overview of available web-based databases, including KEGG, GenBank, PDB, UniProt...
- Explain the strengths and weaknesses behind different computer programming languages and the appropriate applications, including Perl, R...
- Educate students on the current state of systems biology and potential future research directions to assist students in applying these methods to their research.

Enjoy and ask lots of questions!!