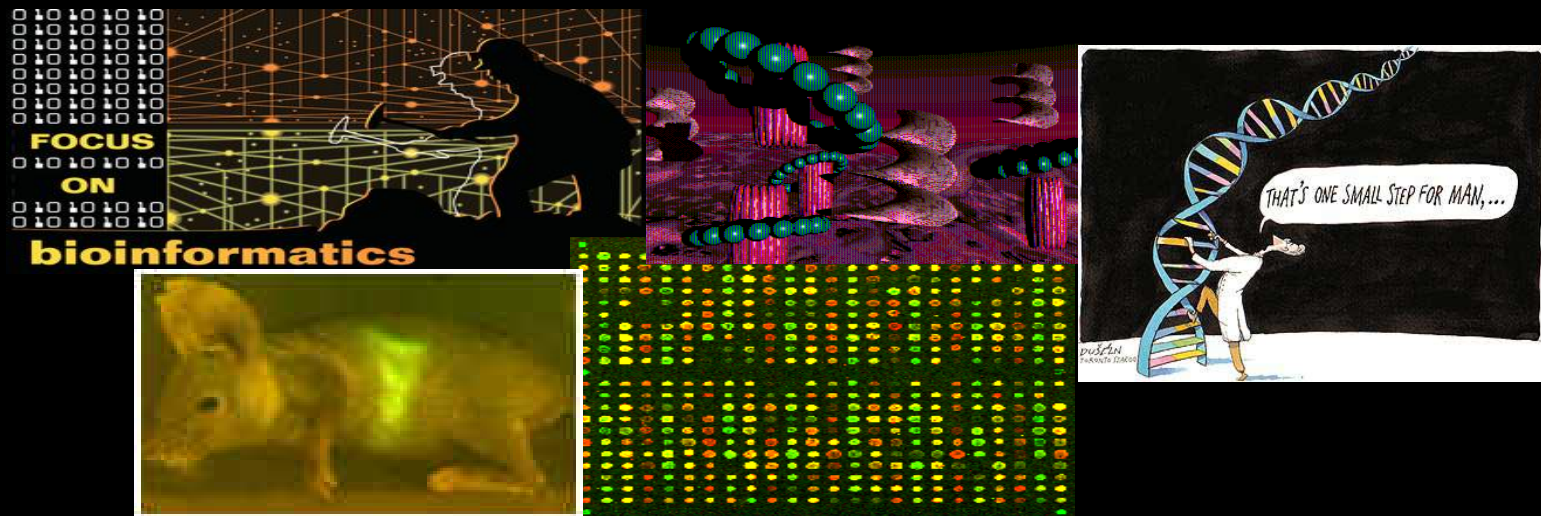


Genomics: Trends in Environmental Health Sciences



Claudia Thompson, Ph.D.
Program Administrator, SBRP

Why use Genomics?

Whole organism view

- Identify total physiological capacity
- More complete understanding
- New drugs/vaccines/remediation strategies

Comparative studies

- Differences between tissues, individuals, strains, species
- Developmental changes
- Changes in response to growth conditions
- Evolution

Produce resources of data and materials

- More efficient
- Collaborative

Genomics in Health

- Identify the genetic and environmental risk factors for all common disease
- Develop “sentinel systems” for early detection of disease and molecular taxonomy of illness
- Develop and deploy high-throughput robotic screening of small molecules for academic researchers
- Catalyze development of large human cohorts for genotype-phenotype correlations

Why Genomics in Environmental Health?

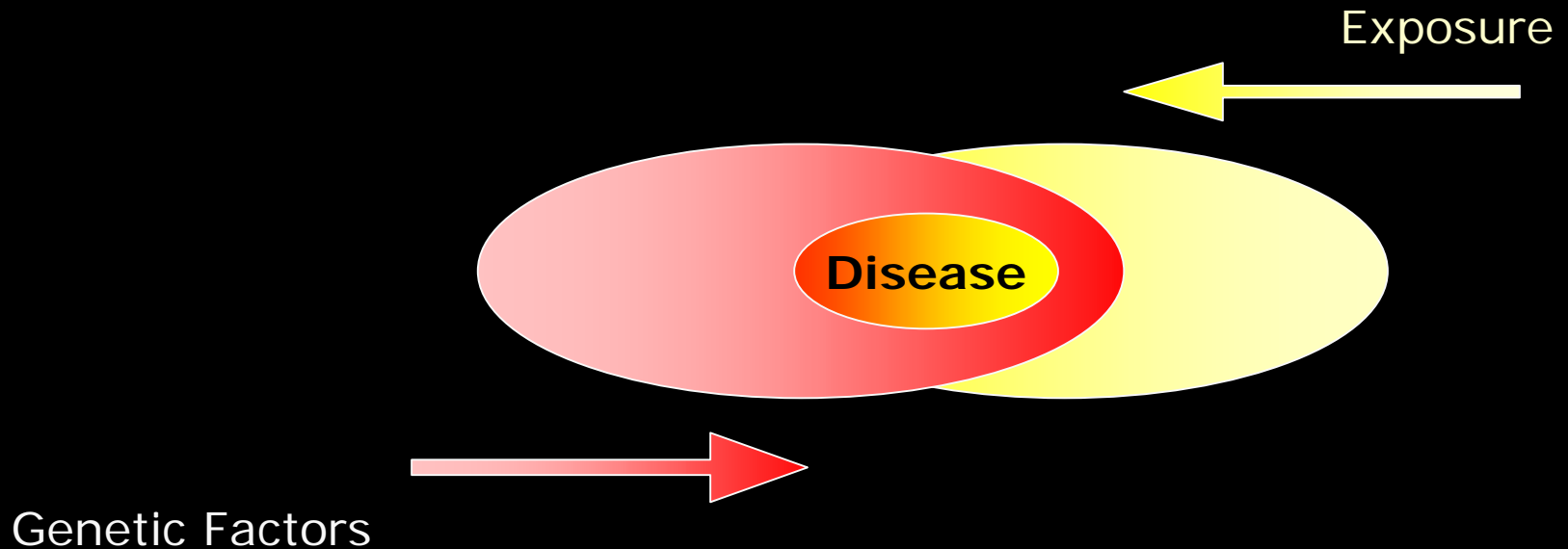
Inherently complex

- Everyone's 'environment' is different
- Toxins can affect more than one pathway
- Exposure is often at low levels for very long periods
- Most real-life exposures are to a mixture of potential toxins with non-linear interactions

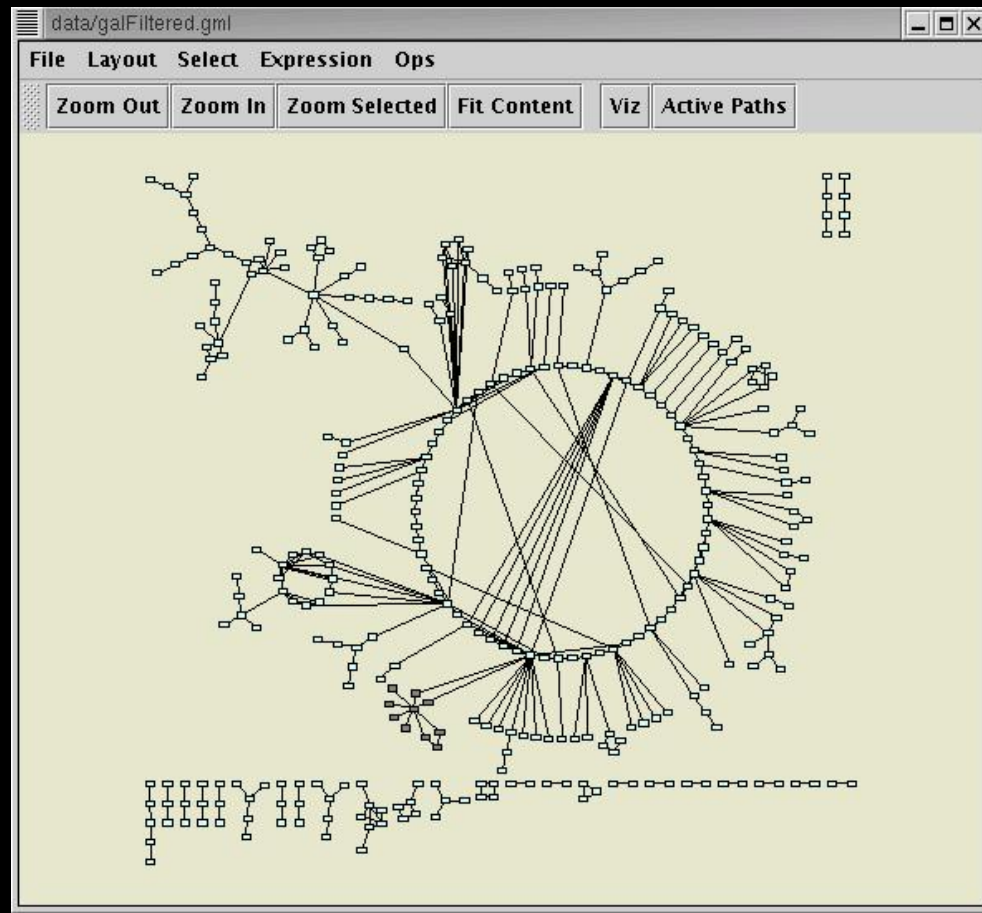
There is no other way to tackle these problems

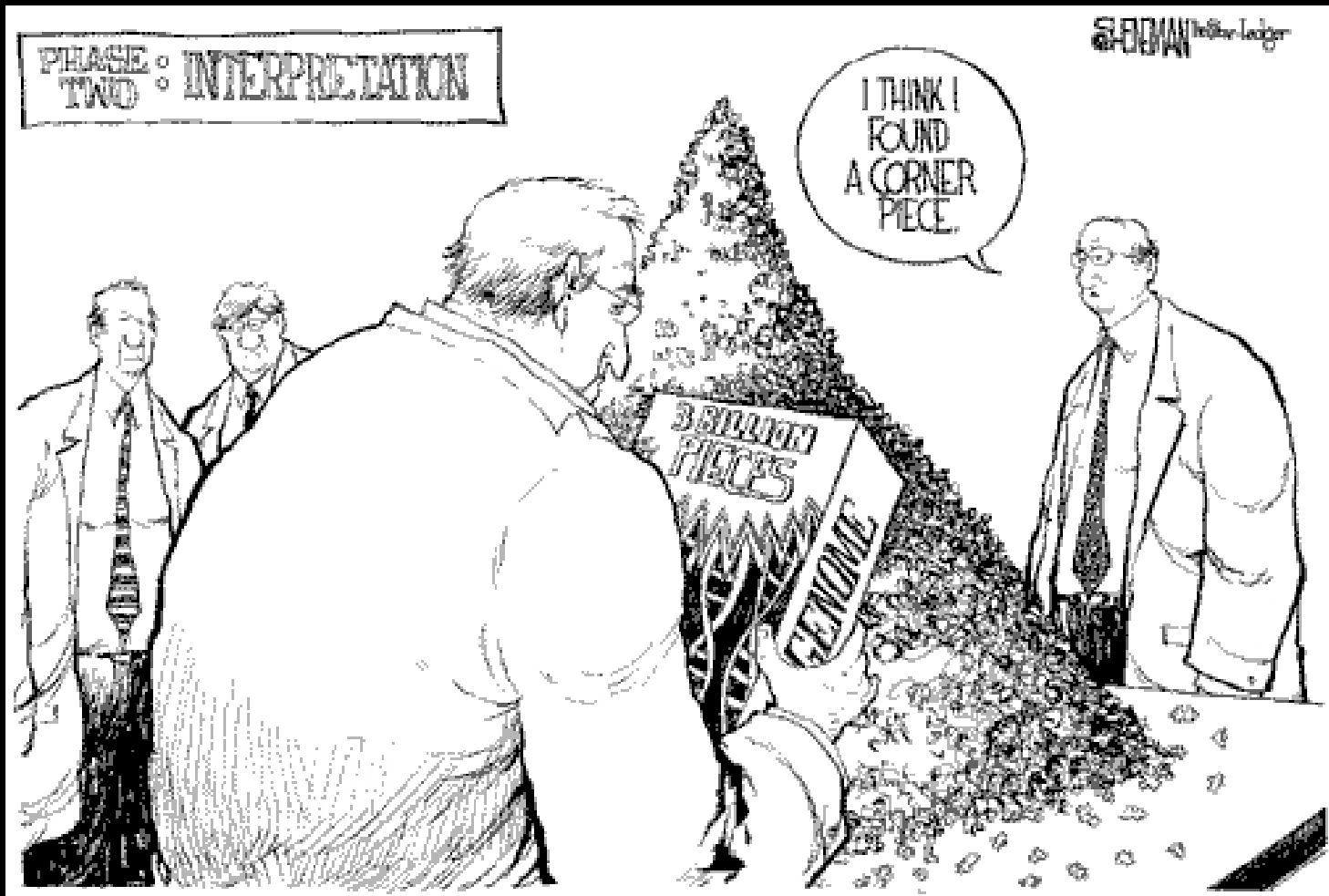
Environmental Exposure and Risk of Disease

- Environmental Factors/Age
 - Genetic Factors
 - Most likely as a "Gene-Environment Interaction"
- Life style; Infectious diseases;
Toxicants; Stress; Radiation;
Medicines; Diet; others.



A New Level of Complexity in Biomedical Research





Drew Sheneman, New Jersey -- The Newark Star Ledger, [E-mail Drew](mailto:drewsheneman@starledger.com).

*These are exciting and challenging times for biological researchers. The wealth of information and capabilities now being generated by the various genome projects and other biological endeavors will lead over the next two decades to more insights into living systems than have been amassed in the past two millennia. Biology truly is undergoing a revolution. **David A. Smith***

Genomics metaphor
Weather

We can now predict hurricanes better than we could 100 years ago.

But we still can't really control hurricanes (or earthquakes).

Improved building codes greatly reduce mortality.

But we are far from having complete control over nature.

We may never have the degree of control that some people are predicting.

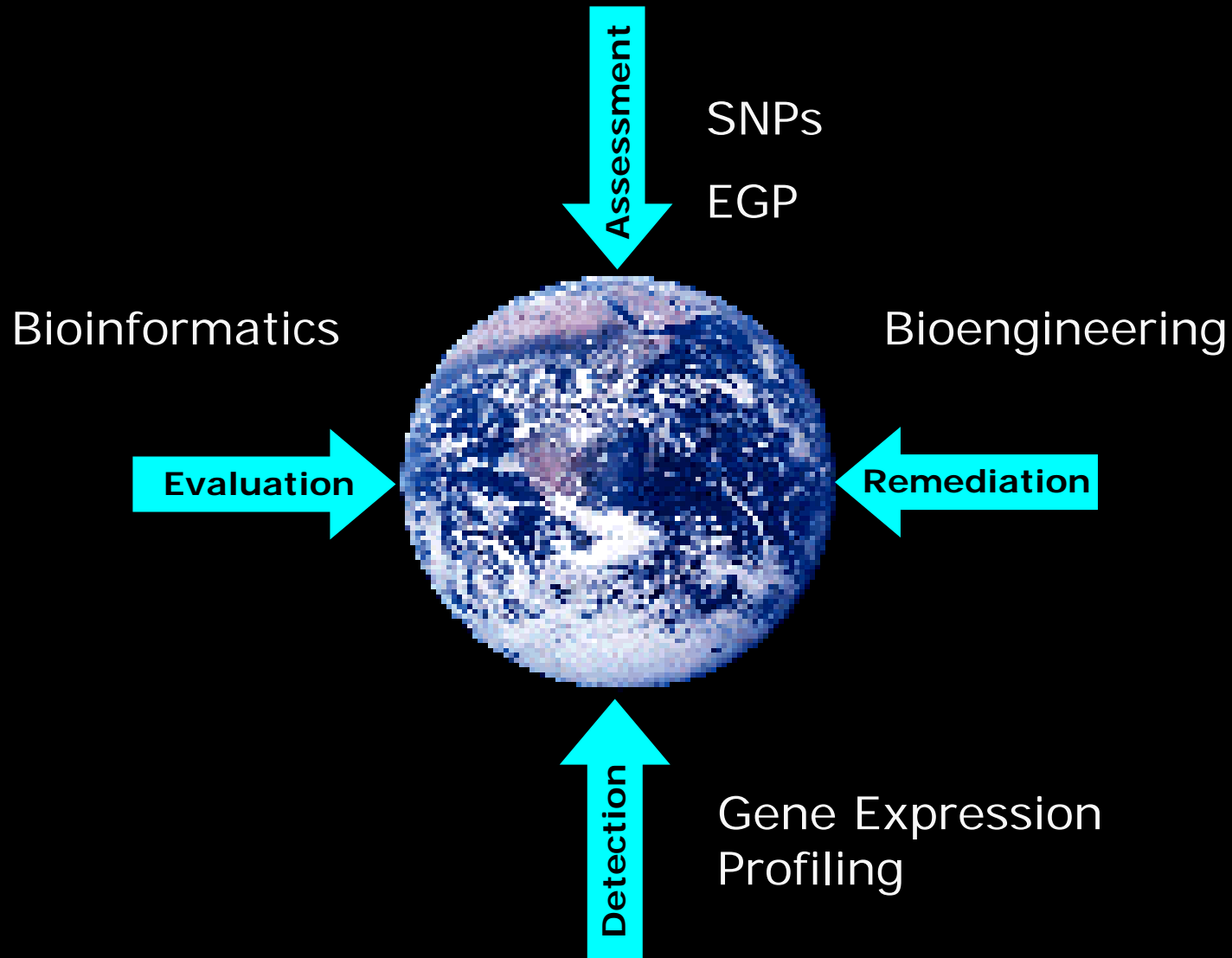
Racing to the beginning of the road, Robert Weinberg, 1998

Initiatives

GOAL: Develop research initiatives that will incorporate high-throughput, quick turn around environmental health data in a way that is relevant and can be extrapolated to the human condition.

- Environmental Genome Project
- Toxicogenomics Centers
- Environmental Health Sciences Centers
- Children's Centers
- Mouse Genomics Centers
- Superfund Basic Research Program

Genomic Strategies for Reducing Risk



Applications of Genomic Research in Risk Reduction

Exposure Assessment

- Genetic Diversity - Ecological Populations
- Gene Expression Profiling - Human Population
- Single Nucleotide Polymorphisms - Susceptibility

Remediation Technologies

- Bioengineered Plants and Microbes
- Adaptive Changes

Genomics Strategy for Developing Transgenic Plants for Remediation

Observation - Phytochelation Synthase complexes with heavy metals. *Brassica juncea* is an effective metal bioaccumulator

Strategy - Microarray analysis to identify new genes and stress-signaling pathways involved in heavy metal accumulation in plants

Outcome - Transgenic overexpression of Phytocheleton Synthase in *Brassica juncea* or other plant species with associated metal detoxification mechanisms to enhance heavy metal tolerance and accumulation

Systems Biology Approach

GENOME

What Is Possible

TRANSCRIPTOME

What Appears To Be Happening

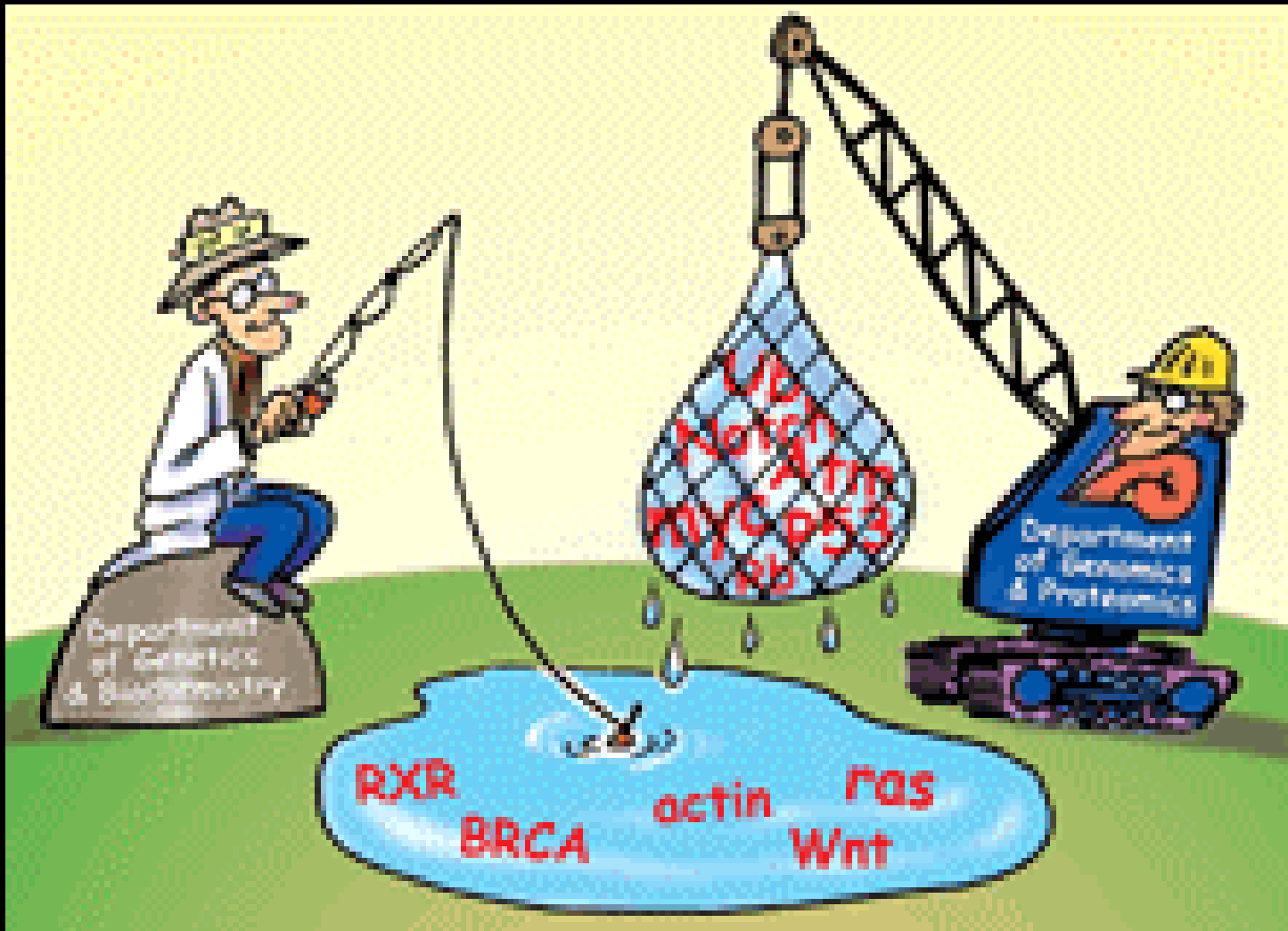
PROTEOME

What Makes It Happen

METABONOME

What Has Happened And Is Happening

**Better
Characterization
Of Disease Risk**



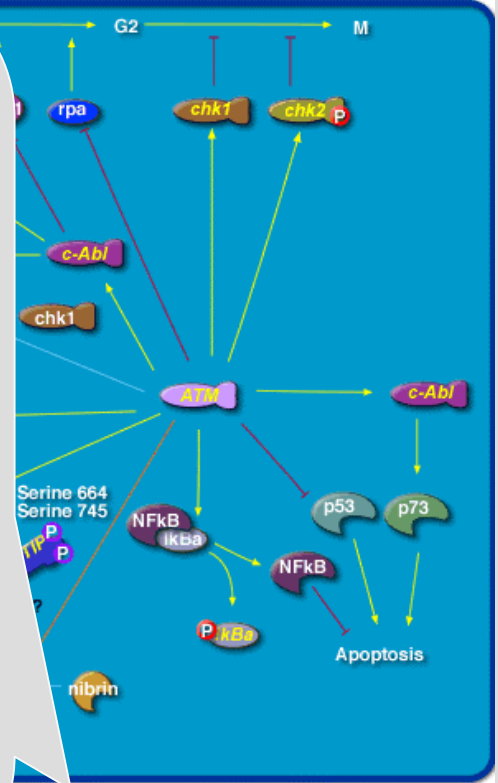
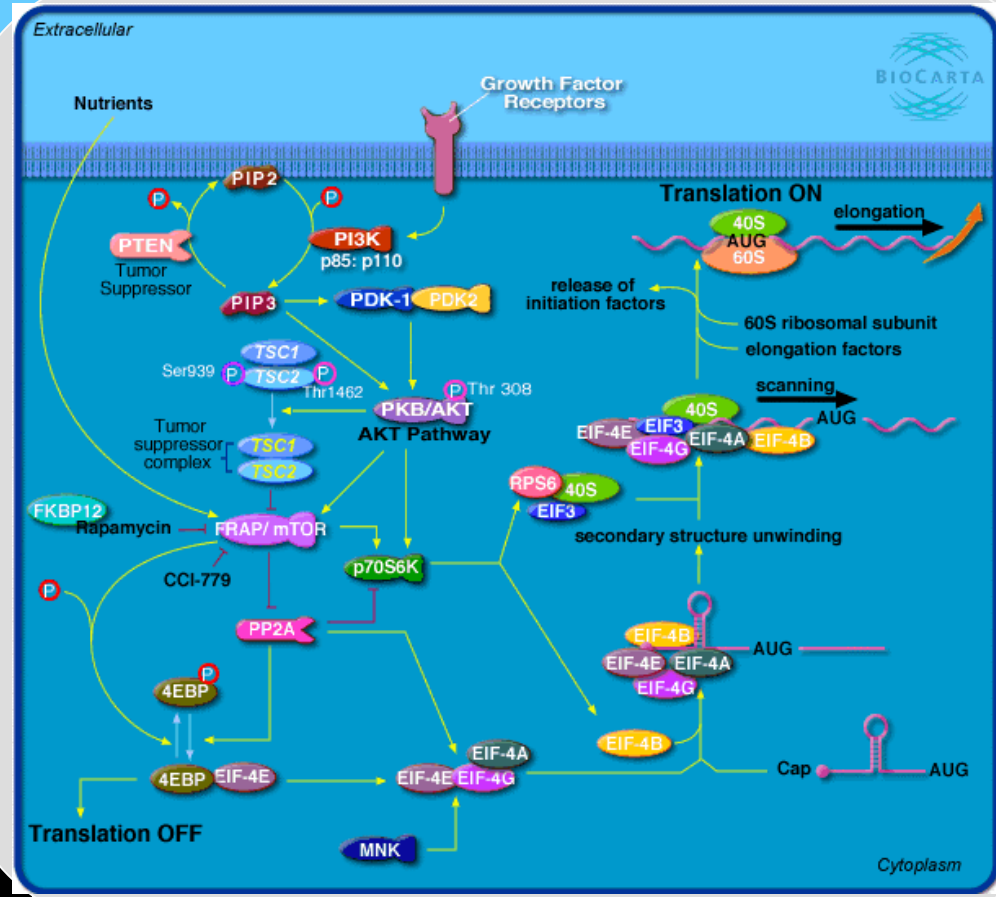


The Birth of Systems Biology

Systems Biology Today



But Why?



The Problem!

“take that multiply it by infinity;
take it to the depths of forever;
and you will still only have a glimpse
of what I am talking about.”

“Meet Joe Black”

The NIH Roadmap

- “Omics” and Systems Biology Related Solicitations
- <http://nihroadmap.nih.gov/>

Overarching Themes

- New Pathways to Discovery
- Research Teams of the Future
- Re-engineering the Clinical Research Enterprise

New Pathways to Discovery

- Building Blocks, Biological Pathways, and Networks
- Molecular Libraries and Imaging
- Structural Biology
- Bioinformatics and Computational Biology
- Nanomedicine

Research Teams of the Future

- High-Risk Research
- Interdisciplinary Research
- Public-Private Partnerships

Building Blocks, Biological Pathways & Networks

Technology Centers for Networks & Pathways (RFA-RM-04-019)

- 'Proteomics' technology development and application to improve temporal, spatial and quantitative resolution
- Ultimate goal is to enable global studies of Pathway/Network dynamics
- **Application Receipt date 2/22/05**

Solicitation (PA) for collaborations with funded centers will be announced soon

Building Blocks, Biological Pathways & Networks

Novel Preclinical Tools for Predictive ADME-Toxicology (RFA RM 04-023)

- development, standardization, and/or validation of economical, improved tools for efficient, reliable prediction and determination of ADME/TOX characteristics
- translate scientific advances in evaluating pharmacokinetics and toxicology of chemical compounds,
- Use advanced strategies in bioinformatics, computational techniques, molecular and cellular assays, nanotechnology, and imaging technologies
- **Application receipt date – 1/21/2005**

Bioinformatics and Computational Biology

National Centers for Biomedical Computing (RFA-RM-04-022)

- Development of tools and resources to support computational biology
- Basic research in computational science
- Application Receipt date 1/24/05

A solicitation (PA) for collaborations with funded centers will be announced soon

“It is our job as scientists to attempt, as best we can, to look into the future, see the changes ahead, and anticipate the side effects of these changes. But we know from past experiences that there are few important and useful discoveries that do not have some unanticipated, undesirable side effects. It is our responsibility to alert leaders in public policy and suggest to them how we might prevent or minimize any negative health consequences.”

*Dr. David Rall
(1990)*