# Recent Trends of Research in Life Sciences

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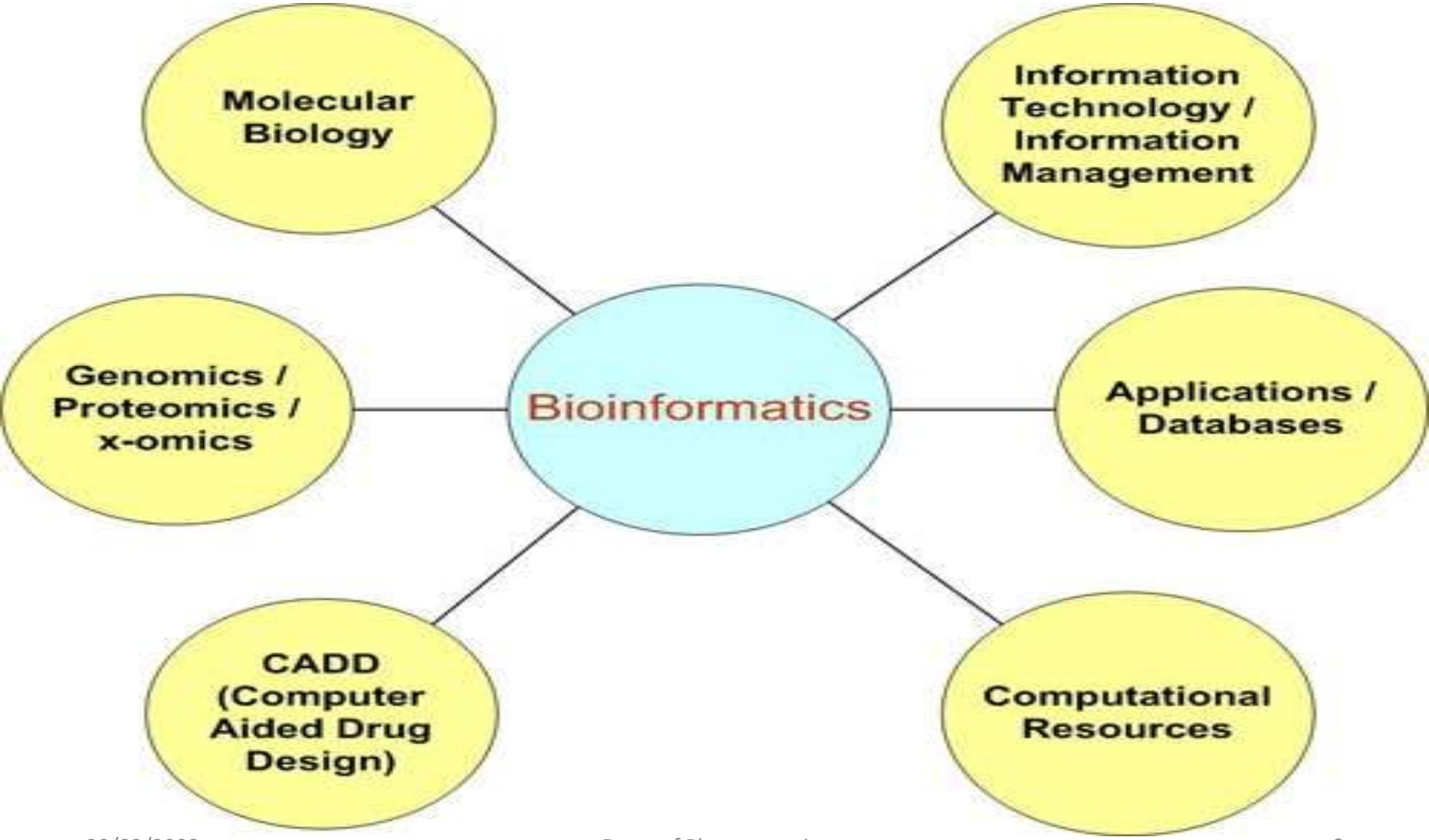
# BASIC PRINCIPLE OF RESEARCH

- ***It is not enough to identify a problem***
- ***Not enough to solve a problem***
- ***Need to identify and fix the root cause-otherwise problem is likely recur***

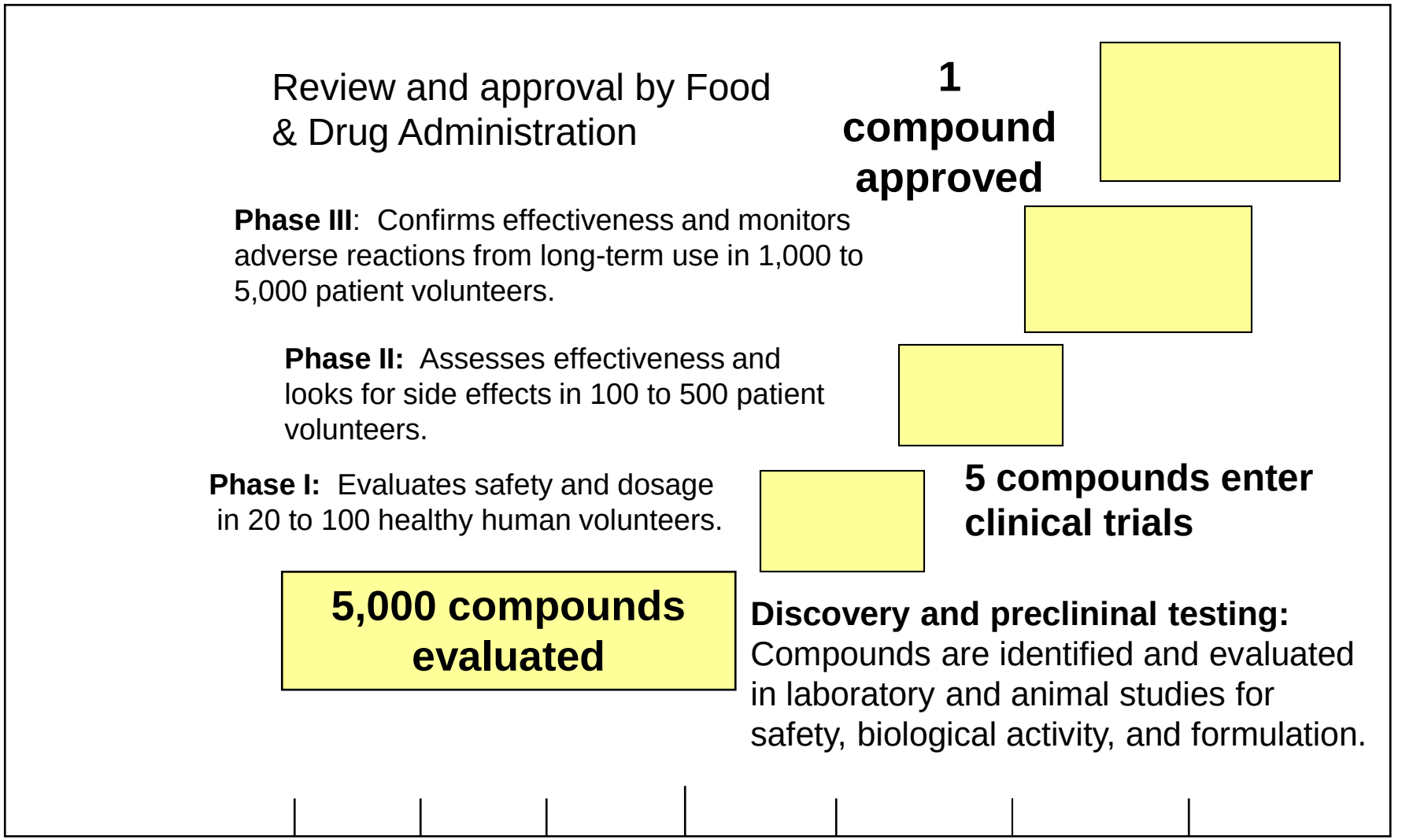
***IDENTIFICATION OF***

***ROOT CAUSE IS NECESSARY***

# Bioinformatics



# Bringing a New Drug to Market




Source: Tufts Center for the Study of Drug Development

# Focus on Biological Research in 21st Century

*" The new paradigm, now emerging is that all the 'genes' will be known (in the sense of being resident in databases available electronically), and that the starting "point of a biological investigation will be theoretical."*

*- Walter Gilbert*

# Rational Approach to Drug Discovery

Identify target

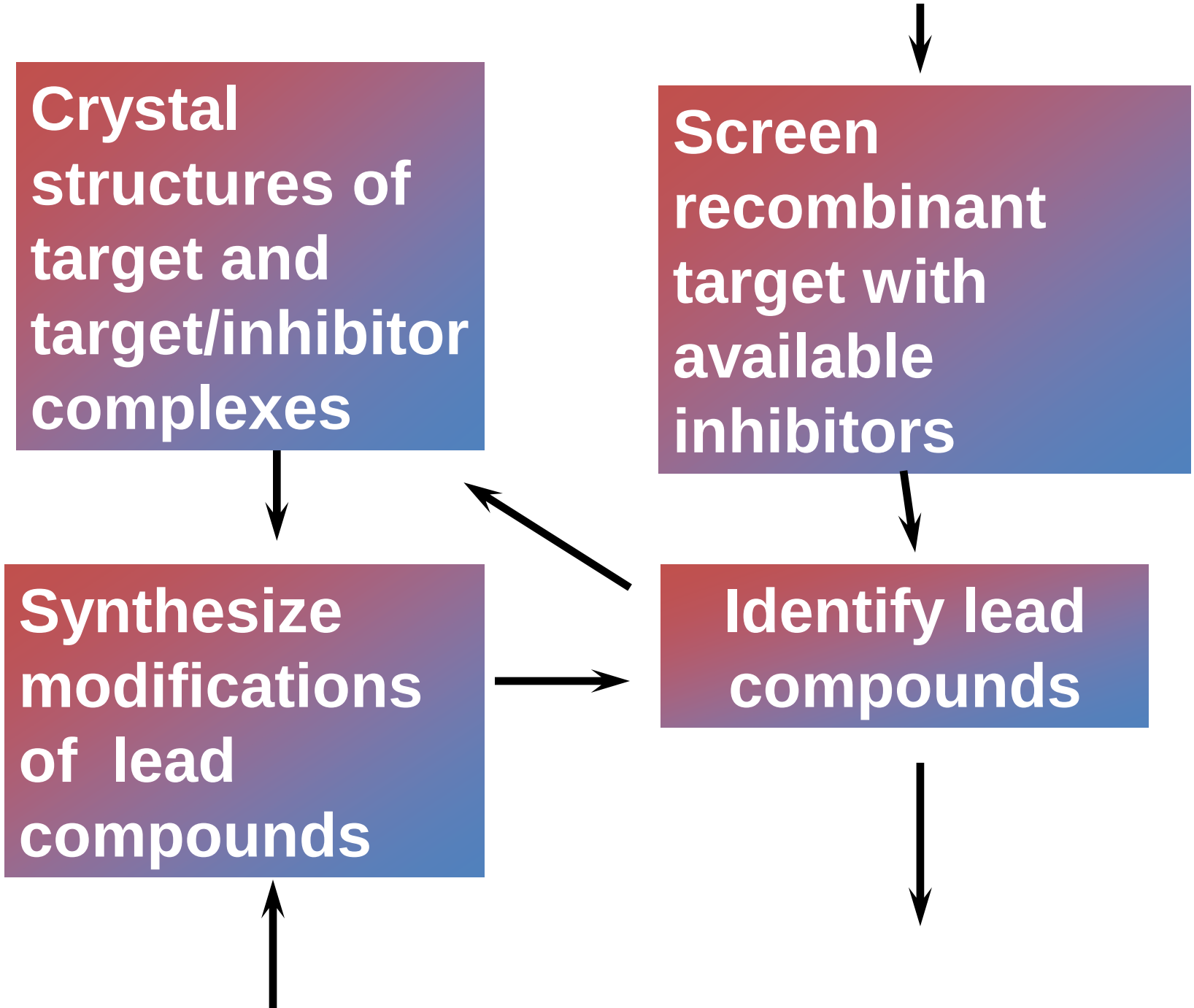
↓

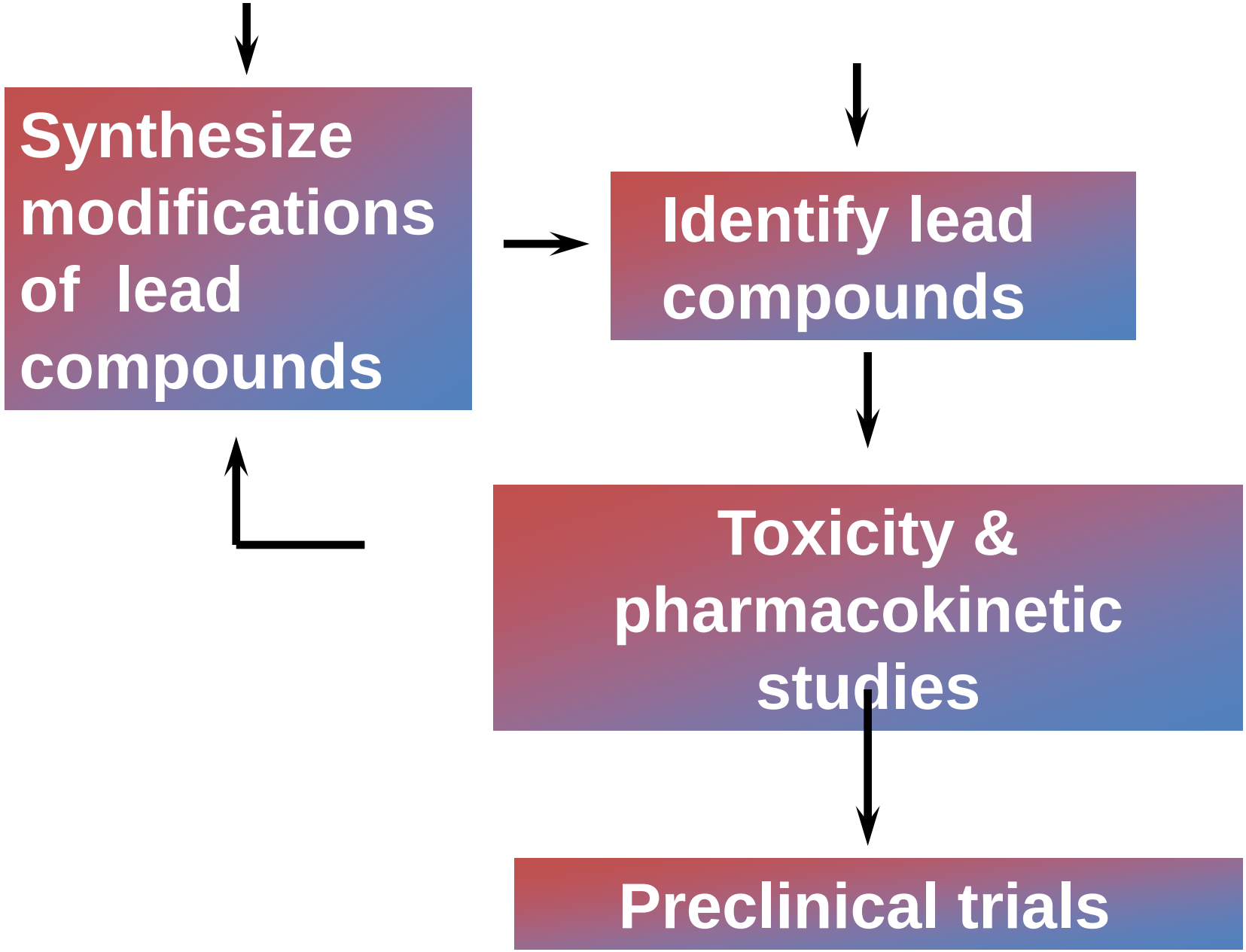
Clone gene encoding target

↓

Express target in recombinant form

↓


Crystal structures of target and target/inhibitor complexes
Screen recombinant target with available inhibitors
Synthesize modifications of lead compounds
Identify lead compounds


Synthesize modifications of lead compounds
Identify lead compounds
Toxicity & pharmacokinetic studies
Preclinical trials

# Case study: Malaria

- ***P. falciparum presents a fascinating model system. The life-cycle complexity is both a challenge and an opportunity.***
- ***Unfortunately at the molecular level much remains unknown.***
- ***Its genome, currently being sequenced, is already yielding valuable data.***

# Malarial Drugs

- Up until now, nearly all prophylaxis and therapeutic intervention has been based on traditional medicines or their derivatives eg quinine, paraquine, chloroquine etc.
- Effective also have been type I antifolates eg sulphones and sulphonamides which mimic PABA, and the type II antifolates eg pyrimethamine, trimethoprim and proguanil which mimic dihydrofolate.

# List of Drugs

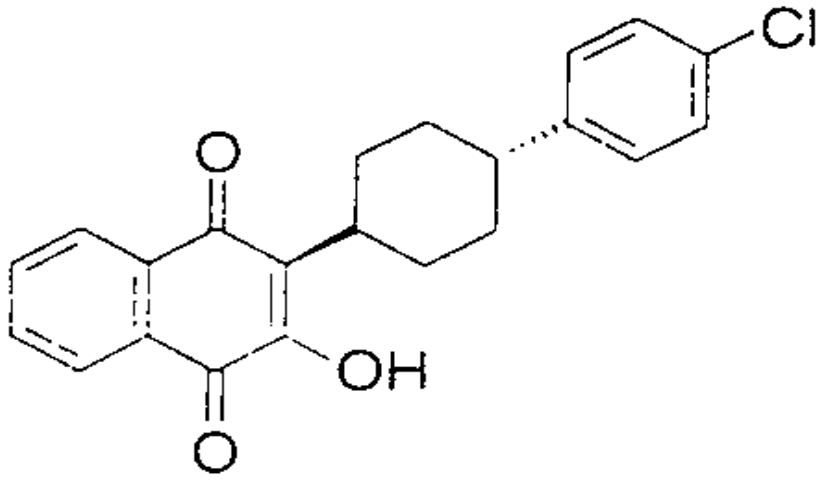
- Chloroquine
  - Avloclor ®; Nivaquine®
- Antifolate
  - Pyrimethamine (Daraprim®)
  - Proguanil (Paludrine®)
- Combination drugs
  - Pyrimethamine & Sulfadoxine combination eg.: Fansidar ®

**Resistance to these drugs poses a threat to control morbidity and mortality of malaria.**

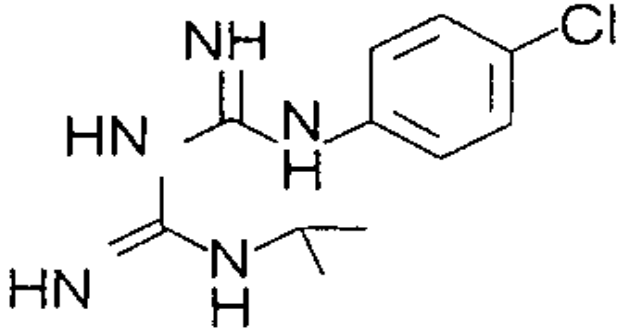
# Drug Resistance (DR)

- **Mechanisms of drug resistance**
  - Formation of altered target
    - Target has decreased affinity for substrate/analogue
  - Decreased access to target
    - Mutations decrease membrane permeability
    - Specific transport systems altered/deleted
  - Increased level of enzymes which cleave substrates
    - e.g. Increased expression of β-lactamase
    - Gene amplification
  - Decreased activation of drug
    - Drugs require activation by enzymes near site
    - Activation pathway suppressed/deleted

# Malaria: Novel drug combinations
# Structural formula: Atovaquone & Proguanil




Atovaquone

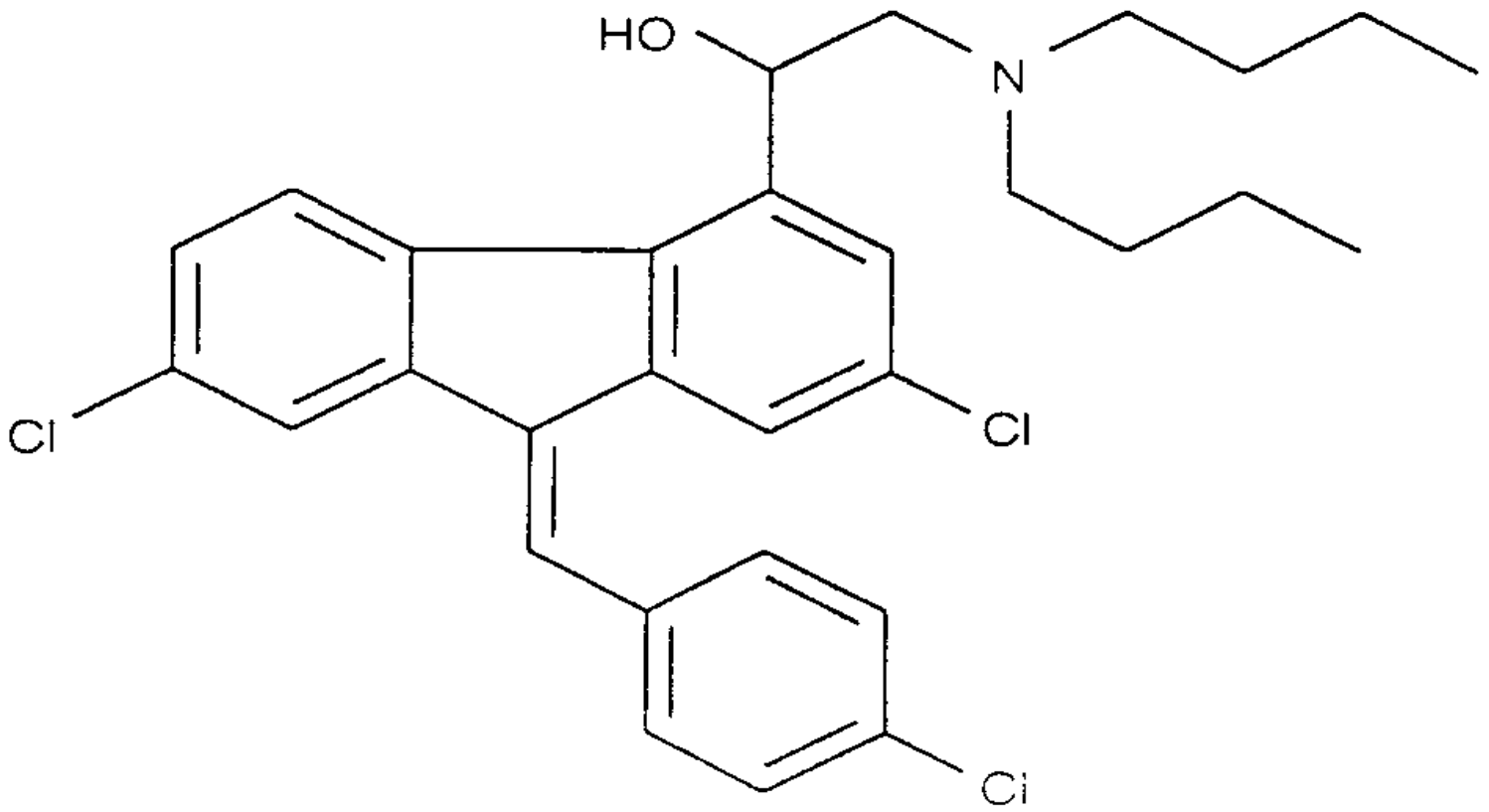



Proguanil

Co–artemether (CGP 56697)

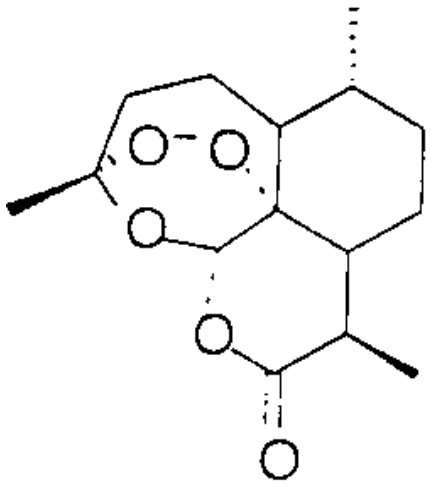
# Drugs targeting Dihydrofolate reductase and Dihydroopteroate synthethase

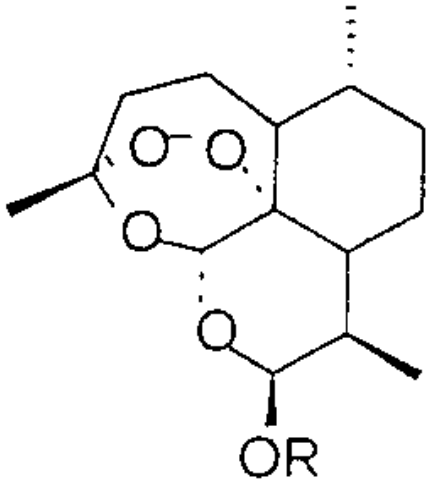
## Structural formula of Lumefantrine (Benflumethol)




Chlorproguanil–dapsone

# Artemisinin derivatives as drugs
# Structural formula of Arteminsinins

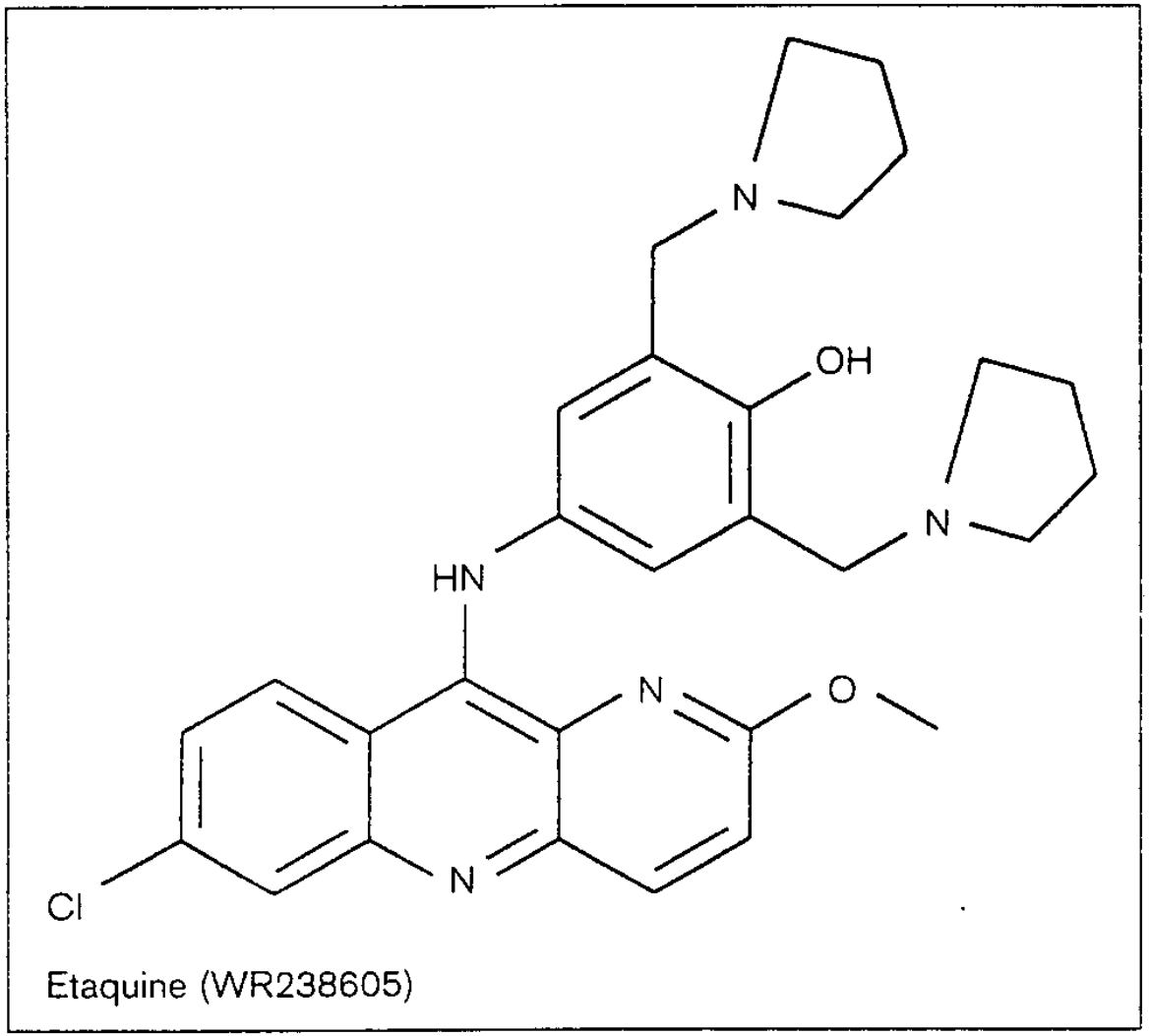





Artemisinin

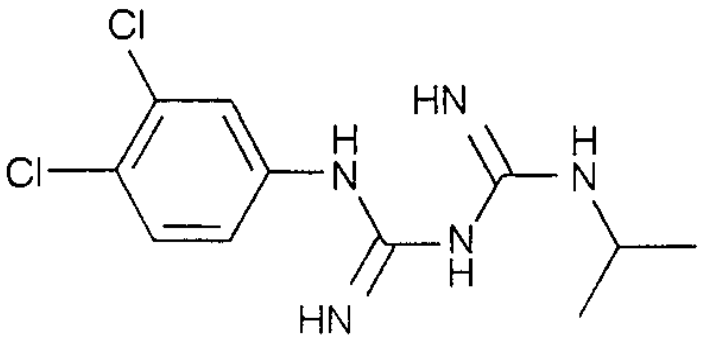
| | |
|---|---|
| Dihydroartemisin | R = H |
| Arteether | R = Et |
| Artemether | R = Me |
| Artesunic acid | R = $(OC)CH_2CH_2COOH$ |
| Artelinic acid | R = $CH_2Ph(cooh)$-p |

# Quinolines
# Structural formula of Pyronaridine

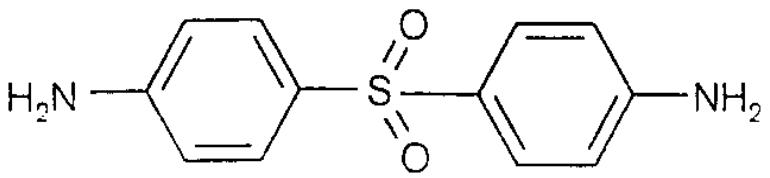



Etaquine (WR238605)

# Novel drug combinations
# Structural formula of Chlorproguanil and Dapsone

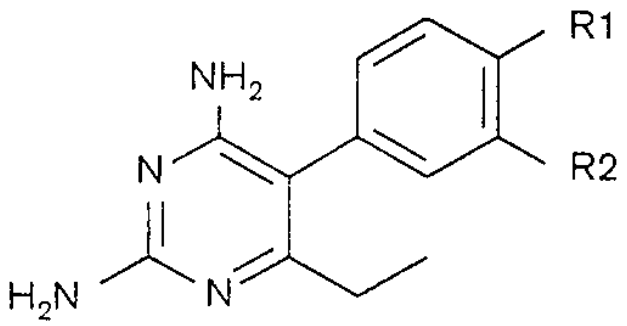



Chlorproguanil



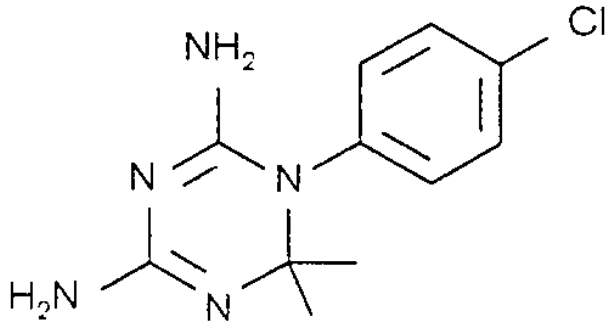

Dapsone

# Dihydrofolate reductase inhibitors
# Structural formula of Pyrimethamine & Cycloguanil



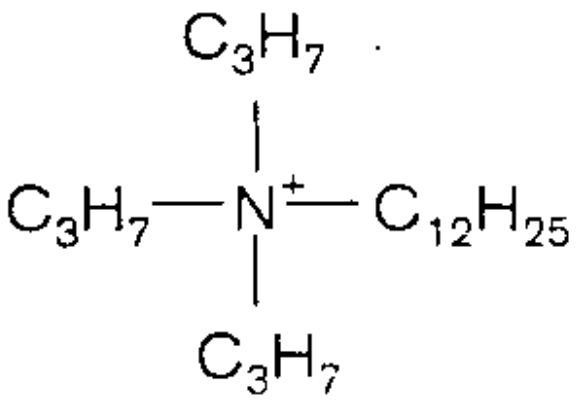

Pyrimethamine R1 = Cl, R2 = H

SCC R1 = H, R2 = Cl

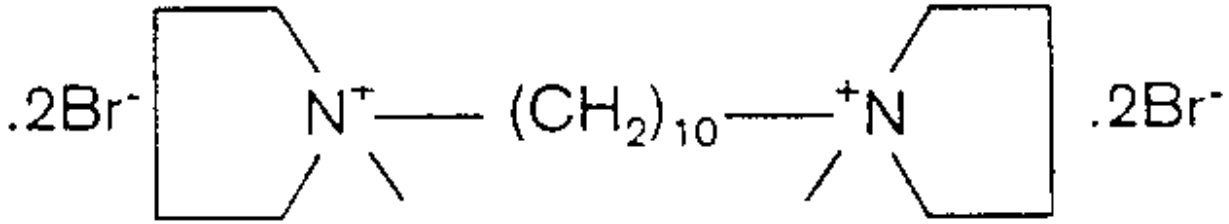



Cycloguanil

# Inhibitors of phospholipid metabolism
# Structural formula of E13 and G23




E13



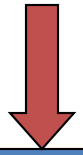

G23

# An Ideal Target

- Is generally an enzyme/receptor in a pathway and its inhibition leads to either killing a pathogenic organism (Malarial Parasite) or to modify some aspects of metabolism of body that is functioning dormally.
- An ideal target…
  - Is essential for the survival of the organism.
  - Located at a critical step in the metabolic pathway.
  - Makes the organism vulnerable.
  - Concentration of target gene product is low.
  - The enzyme amenable for simple HTS assays

# How Bioinformatics can help in Target Identification?

- Homologous & Orthologous genes
- Gene Order
- Gene Clusters
- Molecular Pathways & Wire diagrams
- Gene Ontology

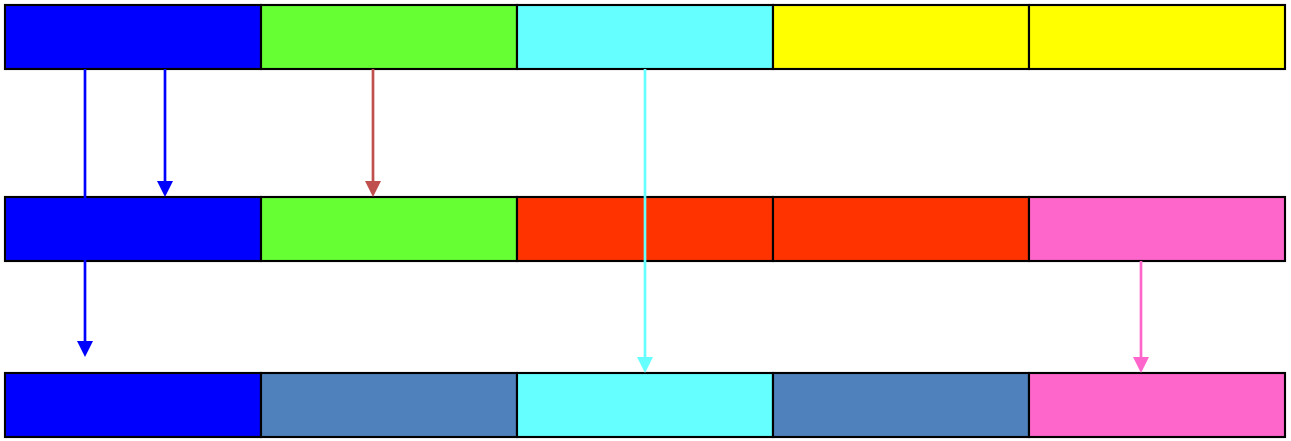


Identification of Unique Genes of Parasite as potential drug target.

# Comparative Genomics of Malarial Parasites: Source for identification of new target molecules.

- Genome comparisons of malarial parasites of human.
- Genome comparisons of malarial parasites of human and rodent.
- Comparison of genomes of –
  - Human
  - Malarial parasite
  - Mosquito

# What one should look for?




**Proteins that are shared by –**

- All genomes
- Exclusively by Human & P.f.
- Exclusively by Human & Mosquito
- Exclusively by P.f. & Mosquito

**Unique proteins in –**

**Human**

**P.f.** **Targets for anti-malarial drugs**

**Mosquito**

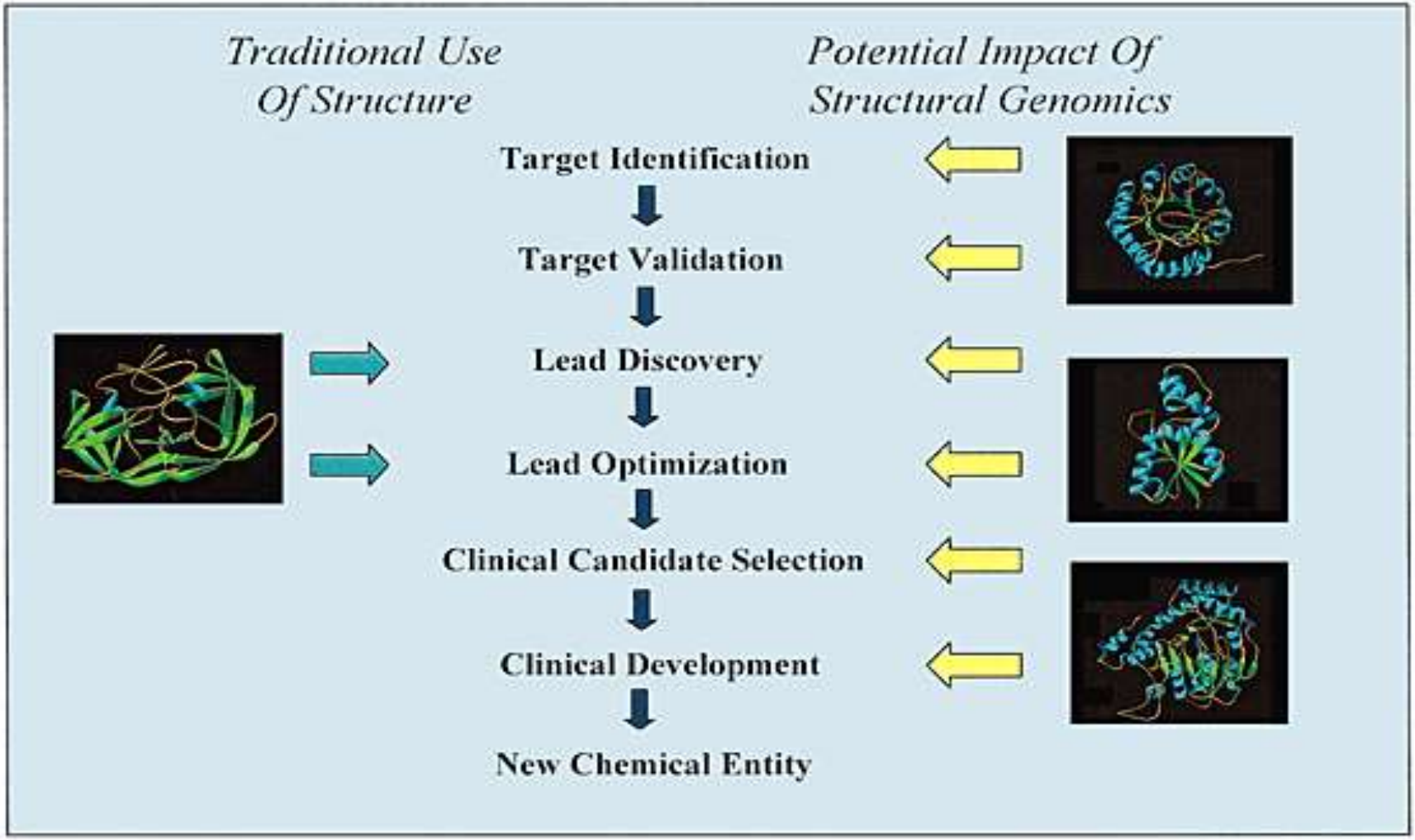
# Structural Genomics

- ***Organise all known proteins into families.***
- ***Determine structures of at least one member of every family.***
- ***Solve structures of more than 10,000 protein in next 10 years.***
- ***Generate knowledge and rules from known protein structures.***
- ***Apply this knowledge to predict the structure of each and every protein of known organisms.***

# *Objectives of Structural Genomics*

- ***Selection of Targets for structure determination to obtain maximum information return on total efforts***
- ***Develop mechanism that facilitates cooperation and prevent work duplication***

# Impact of Structural Genomics on Drug Discovery




Dry, S. et. al. (2000) Nat. Struc.Biol. 7:976-949.

# *Drug Development Flowchart*

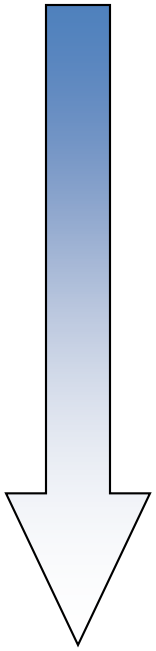
- ***Check if structure is known***
- ***If unknown, model it using KNOWLEDGE-BASED HOMOLOGY MODELING APPROACH.***
- ***Search for small molecules/ inhibitors***
- ***Structure-based Drug Design***
- ***Drug-Protein Interactions***
- ***Docking***

# Why Modeling?

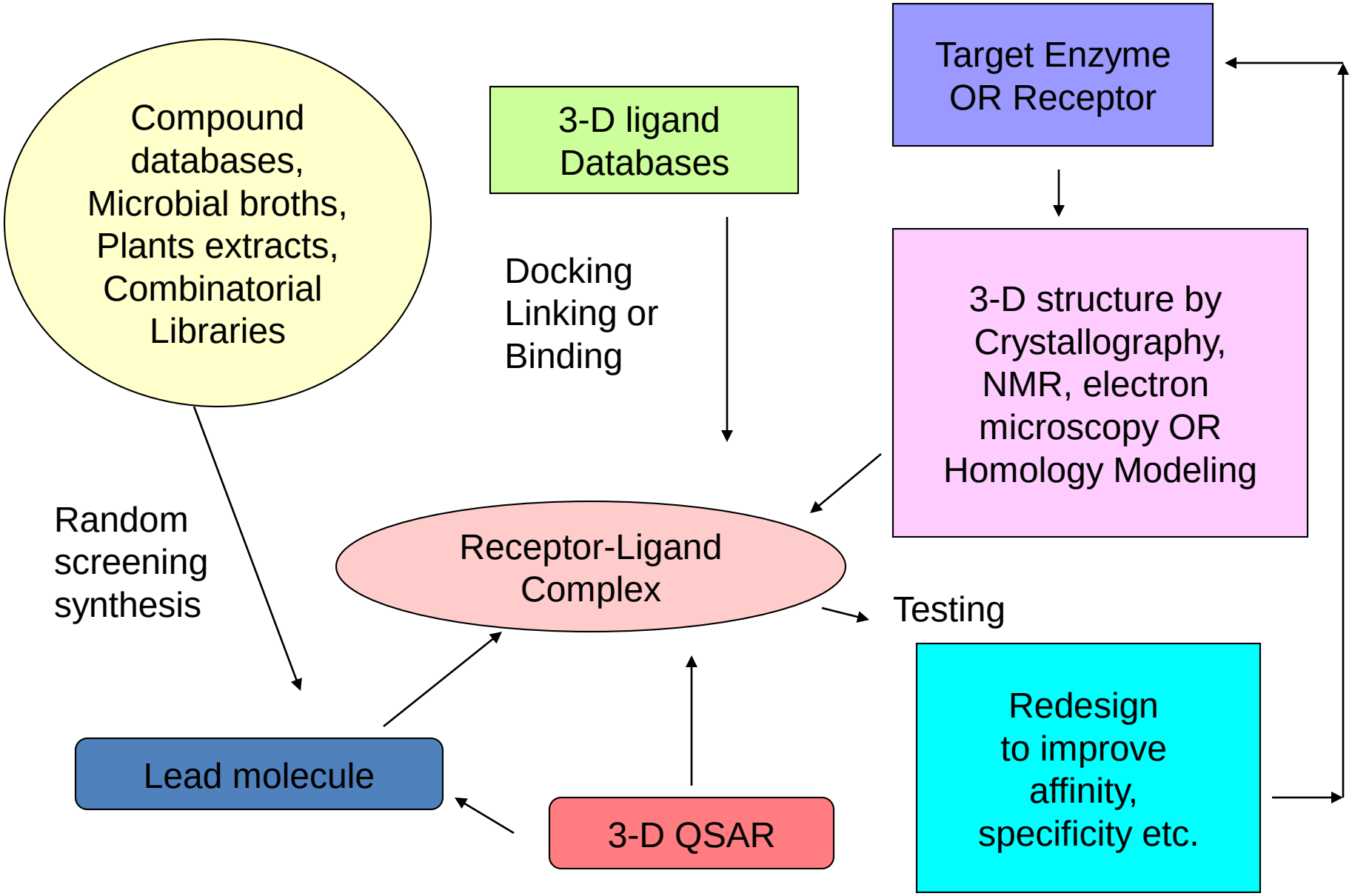
- ***Experimental determination of structure is still a time consuming and expensive process.***
- ***Number of known sequences are more than number of known structures.***
- ***Structure information is essential in understanding function.***

# Sequence identities & Molecular Modeling methods

| Methods | Sequence Identity with known structures |
| --- | --- |
| • *ab initio* | 0-20% |
| • Fold recognition | 20-35% |
| • Homology Modeling | >35% |



# STRUCTURE-BASED DRUG DESIGN



# Docking Methods

- Docking of ligands to proteins is a formidable problem since it entails optimization of the 6 positional degrees of freedom.
- Rigid vs Flexible
- Speed vs Reliability
- Manual Interactive Docking

# GRID Based Docking Methods

- Grid Based methods
  - GRID (Goodford, 1985, J. Med. Chem. 28:849)
  - GREEN (Tomioka & Itai, 1994, J. Comp. Aided. Mol. Des. 8:347)
  - MCSS (Mirankar & Karplus, 1991, Proteins, 11:29).
- Functional groups are placed at regularly spaced (0.3-0.5A) lattice points in the active site and their interaction energies are evaluated.

# Automated Docking Methods

- Basic Idea is to fill the active site of the Target protein with a set of spheres.
- Match the centre of these spheres as good as possible with the atoms in the database of small molecules with known 3-D structures.
- Examples:
  - DOCK, CAVEAT, AUTODOCK, LEGEND, ADAM, LINKOR, LUDI.

# Prediction & Design of New Drugs

- Prediction of 3-D PfDHFR using bacterial DHFR and homology modeling approach.
- Search for the compounds using bifunctional basic groups that could form stable H-bonds in a plane with carboxyl group.
- Optimize the structure of small molecules and then dock them on PfDHFR model.
- Toyoda et. al. (1997). BBRC 235:515-519 could identify two compounds.

# How molecular modeling could be used in identifying new leads

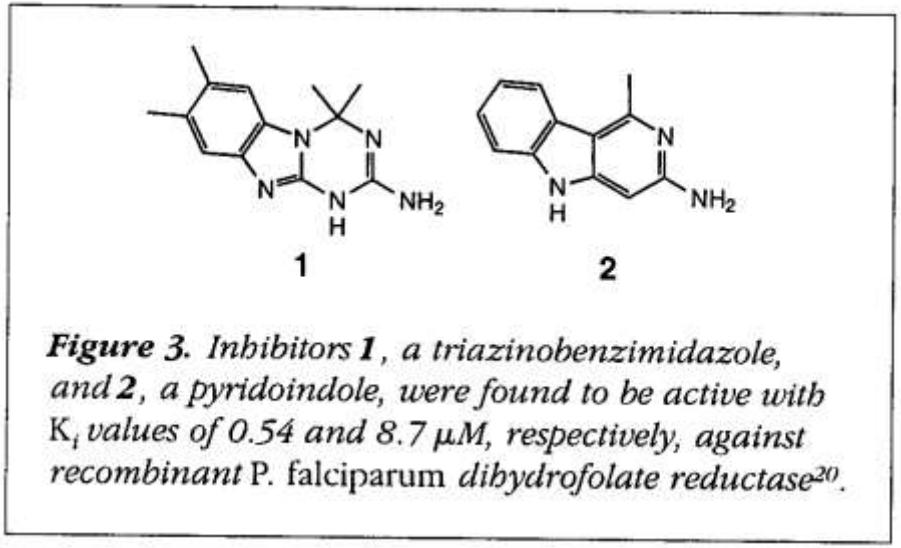



***Figure 3.*** *Inhibitors* ***1****, a triazinobenzimidazole, and* ***2****, a pyridoindole, were found to be active with* $K_i$ *values of 0.54 and 8.7 μM, respectively, against recombinant* P. falciparum *dihydrofolate reductase*[20].

- These two compounds
  a triazinobenzimidazole &
  a pyridoindole were found to be active with high $K_i$ against recombinant wild type DHFR.

- Thus demonstrate use of molecular modeling in malarial drug design.

# Genome Update: Public domain

- ***Published Complete Genomes:*** ***59***
  - ***Archaeal*** ***9***
  - ***Bacterial*** ***36***
  - ***Eukaryal*** ***14***

- ***Ongoing Genomes:*** ***335***
  - ***Prokaryotic*** ***203***
  - ***Eukaryotic*** ***132***

**Private sector holds data of more than 100 finished & unfinished genomes.**

# Challenges in Post-Genomic era: Unlocking Secretes of quantitative variation

- For even after genomes have been sequenced and the functions of most genes revealed, we will have no better understanding of the naturally occurring variation that determines why one person is more disease prone than another, or why one variety of tomato yields more fruit than the next.
- Identifying genes like *fw2.2* is a critical first step toward attaining this understanding.

# Value of Genome Sequence Data

- Genome sequence data provides, in a rapid and cost effective manner, the primary information used by each organism to carry on all of its life functions.
- This data set constitutes a stable, primary resource for both basic and applied research.
- This resource is the essential link required to efficiently utilize the vast amounts of potentially applicable data and expertise available in other

# Challenges

- **Genome databases have individual genes with relatively limited functional annotation (enzymatic reaction, structural role)**

- **Molecular reactions need to be placed in the context of higher level cellular functions**

# The "*omics*" Series

- Genomics
  - Gene identification & charaterisation
- Transcriptomics
  - Expression profiles of mRNA
- Proteomics
  - functions & interactions of proteins
- Structural Genomics
  - Large scale structure determination
- Cellinomics
  - Metabolic Pathways
  - Cell-cell interactions
- Pharmacogenomics
  - Genome-based drug design

# Different levels of function

- **Atomic: Binds ATP**
- **Molecular reaction: adds phosphate (phosphofructokinase)**
- **Pathway: Gluconeogenesis**
- **Network: Energy metabolism**

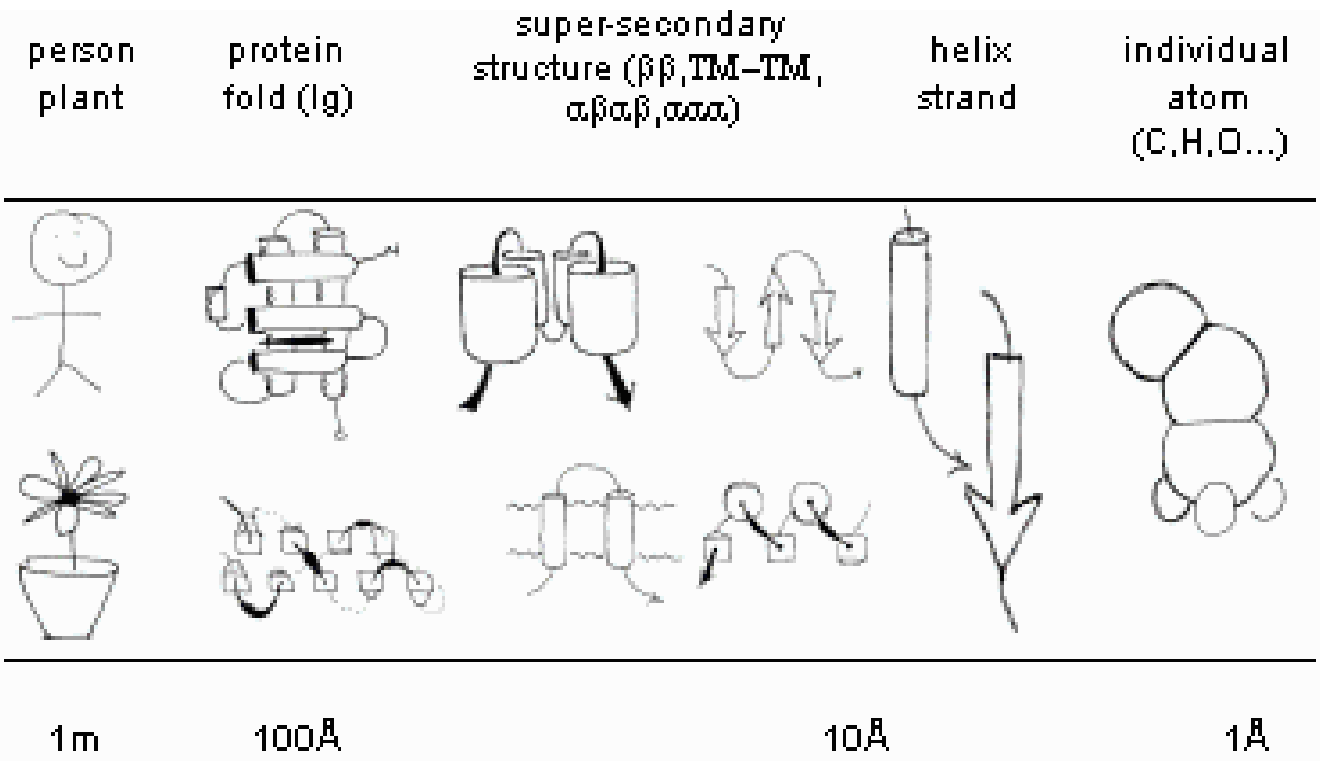
**Typically present in genome database**

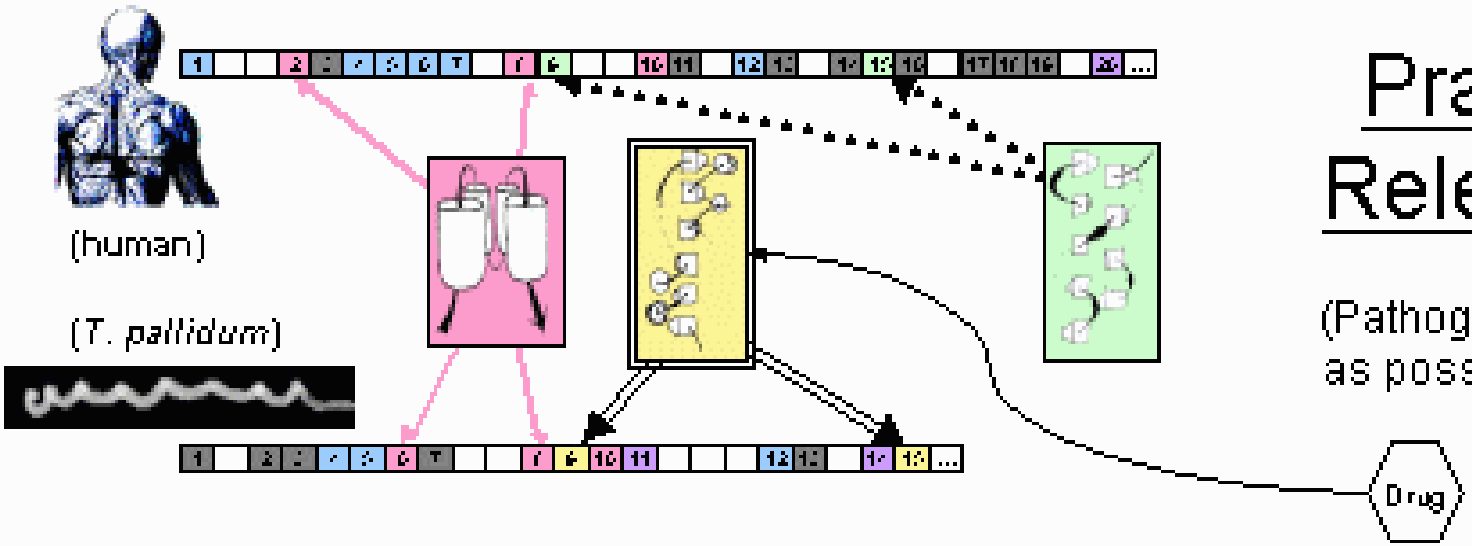
**Typically, little informatics support for making these connections**

# Data Mining: Finding the Needle in the Haystack

- Data mining refers to the new genre of BI tools used to sift through the mass of raw data.
- DM applications should be able to process -
  - **TEMPORAL** (Time studied) and
  - **SPATIAL** (Organism, organ, cell type etc) data.
  - The gained 'knowledge' to reprocess data.
  - Data using techniques beyond Bayesian (similarity search) methods.
- An extension of DM is the concept of **'KNOWLEDGE DISCOVERY'**, which open up new avenues of research with new questions and different perspectives.

# At What Structural Resolution Are Organisms Different?

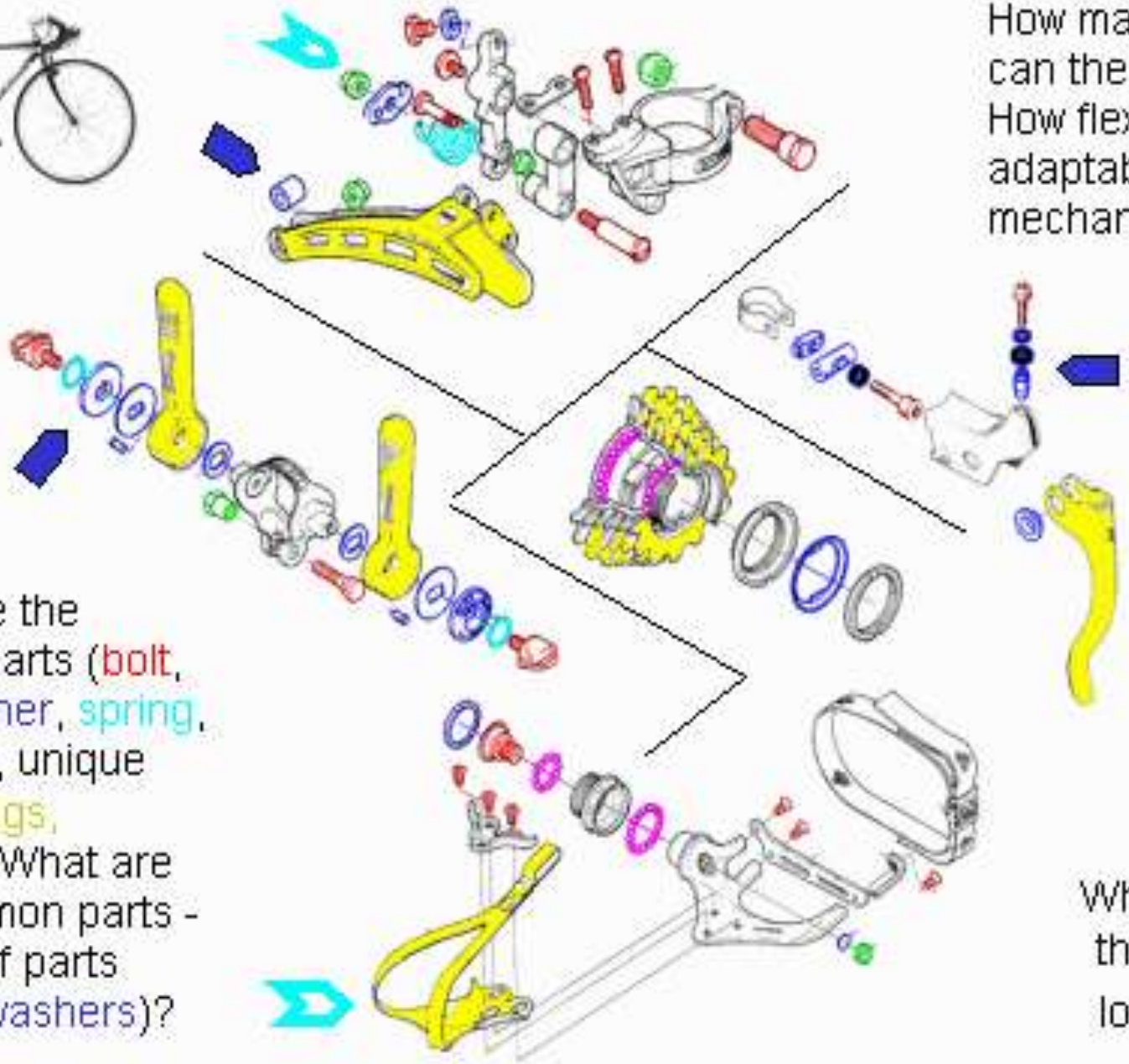



# Practical Relevance

(Pathogen only folds as possible targets)

# A Parts List Approach to Bike Maintenance



How many roles can these play? How flexible and adaptable are they mechanically?

What are the shared parts (bolt, nut, washer, spring, bearing), unique parts (cogs, levers)? What are the common parts -- types of parts (nuts & washers)?

Where are the parts located?

# Commercial Structural Genomics Initiatives

- **IBM (Blue Gene project: 2000)**
  - **Computational protein folding**
- **Geneformatics (1999)**
  - **Modeling for identifying active sites**
- **Prospect Genomics (1999)**
  - **Homology modeling**
- **Protein Pathways (1999)**
  - **Phylogenetic profiling, domain analysis, expression profiling**
- **Structural Bioinformatics Inc (1996)**
  - **Homology modeling, docking**

# *Currents Areas of Interest Research*

- ***Life Science – Biosensors, Genome Sequence and genetic disorders, Microbiome, Stem Cell and organ culture, Biotechnology, Genetically Modified Organisms, Developmental Biology, Bio-energy, Astrobiology, Neuroscience, Medical Technology***
- ***Artificial Intelligence***
- ***Machine Learning***

# *New Researches in Neuroscience*

- ***A study of the 100 most-cited neuroscience articles has revealed that 78 of these papers cover five topics -***

***1. Neurological disorders,***

***2. Prefrontal cortex,***

***3. Brain connectivity,***

***4. Brain mapping and***

***5. Methodology studies.***

# Examples of Artificial Intelligence

- An expert system is a computer program that is designed to hold the accumulated knowledge of one or more domain experts
- It reasons with knowledge of some specialist subject with a view to solving problems or giving advice
- They are tested by being placed in the same real world problem solving situation

# Applications of Artificial Intelligence

## Medical system
## for diagnosis of respiratory conditions

# Machine Learning!

Machine learning is a scientific discipline concerned with the design and development of algorithms that allow machines to mimic human intelligence.

# Human Intelligence VS Artificial Intelligence

**Pros**

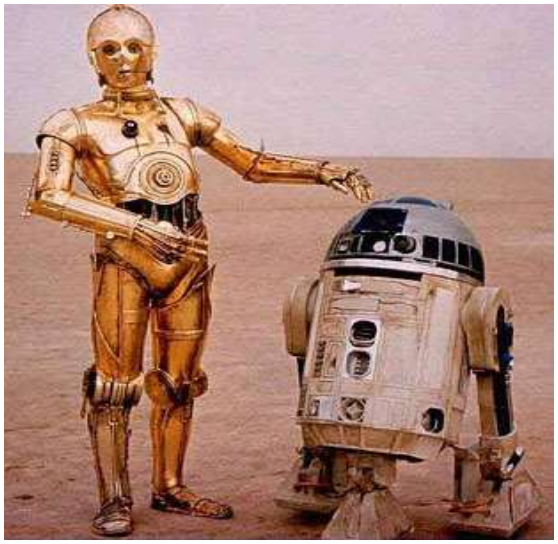
## Human Intelligence

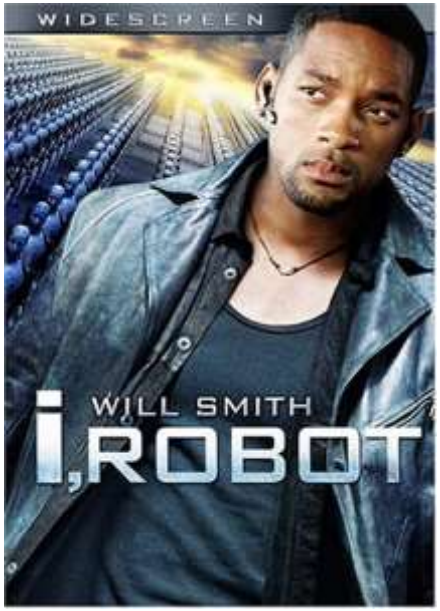
- Intuition, Common sense, Judgment, Creativity, Beliefs, Analysis, Aptitude etc
- The ability to demonstrate their intelligence by communicating effectively
- Plausible Reasoning and Critical thinking

## Artificial Intelligence

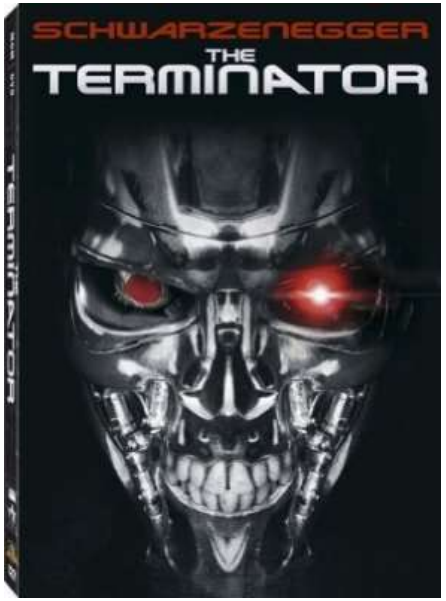
- Ability to simulate human behavior and cognitive processes
- Capture and preserve human expertise
- Fast Response. The ability to comprehend large amounts of data quickly.
- Works accurately
- Saves man power

# Artificial Intelligence in the Movies



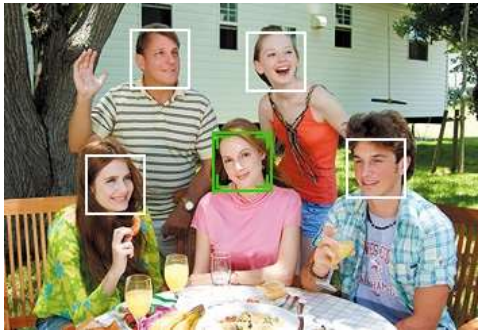




# Artificial Intelligence in Real Life

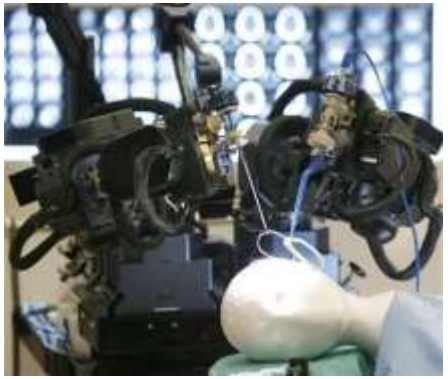
## A young science (≈ 50 years old)

- Exciting and dynamic field, lots of uncharted territory left
- Impressive success stories
- "Intelligent" in specialized domains
- Many application areas

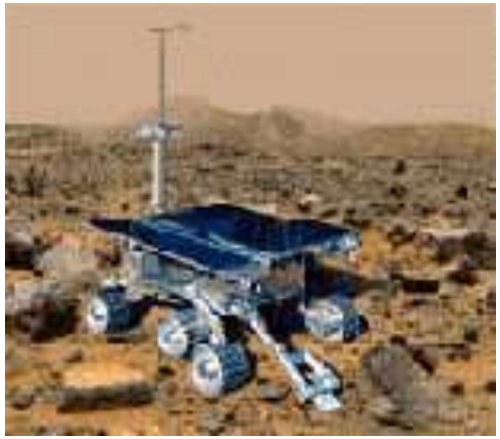
Face detection

Formal verification



# Why the interest in AI?

Labor/Professional



Science

Google

YAHOO!

Search engines

Medicine/Diagnosis

Appliances


What else?

# Genetic Disorders

- ***Millions of people suffer from devastating genetic disorders like cancer, sickle cell anemia, cystic fibrosis, muscular dystrophy, Huntington's disease and many more.***
- ***Cause huge pain and suffering that could be avoided if these diseases could simply be cured by rewriting the genetic code of patients? That is how promising the CRISPR-Cas9 gene-editing technology is!***
- ***One of the hottest developments in recent years is the CRISPR gene editing process (clustered regularly interspaced short palindromic repeats)***
- ***It's the technique to delete or insert certain genes, or even chemically repair DNA.***
- ***Its possible applications are arguably endless and there's a lot of current research happening all over the world.***
- ***Dupont filed first patent application in 2007***
- ***Berkley team filed patent in 2012 but with experiments on prokaryotes***
- ***Feng Zhang from Harvard filed patent with experiments on eukaryotes.***
- ***Who will win this legal battle of patent?***

# Astrobiology

- ***Astrobiology is the study of the origin, evolution, and distribution of life in the context of cosmic evolution.***
- ***It includes habitability in the Solar System and beyond.***
- ***It makes it trans-disciplinary document of relevance for many communities, from astronomers to planetary scientists and from atmospheric physicists to life scientists.***
- ***The first scientific Roadmap for European Astrobiology was published on 21 March 2016 as a result of European Commission-funded AstRoMap project (2013-2015).***

# Diversity of Human Cells

- ***Adult humans consist of more than 200 different kinds of cells.***
- ***Major are - nerve cells (neurons), muscle cells (myocytes), skin (epithelial) cells, blood cells (erythrocytes, monocytes, lymphocytes, etc.), bone cells (osteocytes), and cartilage cells (chondrocytes).***
- ***Cells essential for embryonic development but not incorporated into the body of the embryo, include the extra-embryonic tissues, placenta, and umbilical cord.***
- ***All of these cells are generated from a single, totipotent cell, the zygote, or fertilized egg.***

# What is a stem cell?

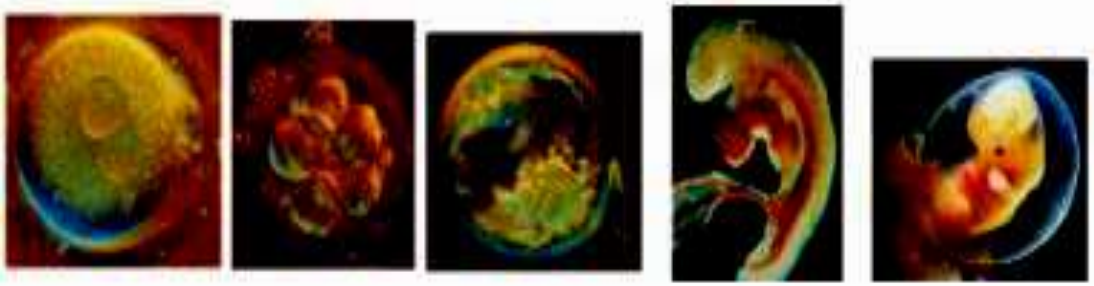
- A stem cell is a "blank" cell/ precursor cell that can give rise to multiple tissue types such as a skin, muscle, or nerve cell.
- A stem cell is essentially the building block of the human body.

# Characters of Stem Cells

1. Stem cells are very unique cells.
2. They have amazing ability to develop into several distinct cell types in the body.
3. Can be used as a repair system for the body.
4. Can theoretically divide without limit in a living organism in order to replenish various types of cells.
5. When a stem cell divides, each new cell has the potential to either remain a stem cell or become another type of cell with a more specialized function (i.e. a muscle cell, a red blood cell, a brain cell, etc.).

# Stem Cells

**Human Developmental Continuum** ⟶



Single-cell Embryo | 3-day Embryo | 5-7 day Embryo | 4-week Embryo | 6-week Embryo

**Embryonic Stem (ES) cells**
*Totipotent*

**Embryonic Germ (EG) cells**
(primordial germ cells)
*Pluripotent*

**Fetal Tissue Stem cells**
*Pluripotent or Multipotent*

Infant

Adult

**Cord Blood Stem cells**
**Placental Stem cells**
*Pluripotent or Multipotent*

**"Adult" Stem cells**
*Pluripotent or Multipotent*

Teratocarcinoma (germ cell tumor)

**Embryonal Carcinoma (EC) cells**
*Pluripotent*

## *Three unique properties of stem cells*

- ***Capable of dividing and renewing themselves for long periods;***
- ***They are "unspecialized" and can give rise to specialized cell types.***
- ***A stem cell is "uncommitted," until it receives a signal to develop into a specialized cell.***

# STEM CELL RESEARCH

- ***Pharmaceuticals: diabetes, cardiac anomalies, neuro-degeneration, and infertility***
- ***Neutraceuticals : produce heterologous nutrients***
- ***Understanding early embryonic development***
- ***Model for in vitro drug and immunity screening***
- ***Producing environment friendly animals eg. Phytase and methane***
- ***Tissue remodeling and engineering***
- ***Cell-cell communication and differentiation***
- ***Conservation***
- ***Germ stem cells challenge age old dogma of female born with fixed number of oocytes***

# Benefits of the normal flora

1. ***Synthesize and excrete vitamins Vitamin K and Vitamin B12***

2. ***Prevent colonization by pathogens competing for attachment sites or for essential nutrients***

3. ***May antagonize other bacteria the production of substances which inhibit or kill non-indigenous species(nonspecific fatty acids, peroxides, bacteriocins).***

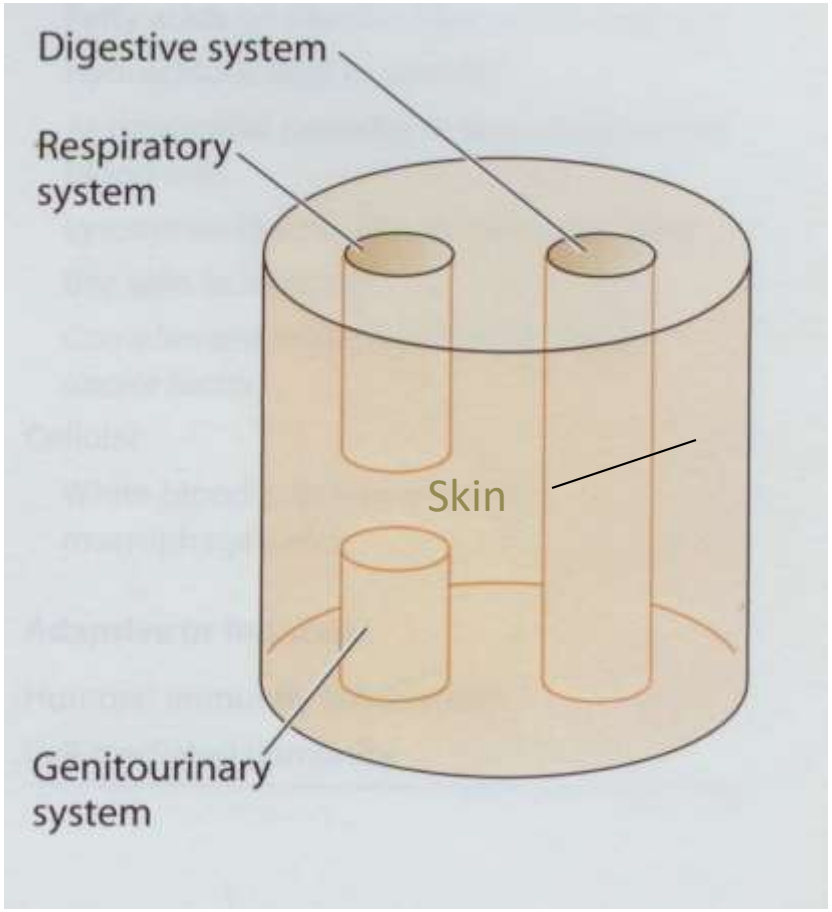
4. ***Stimulate the development of certain tissues i.e. intestines, certain lymphatic tissues, capillary density***

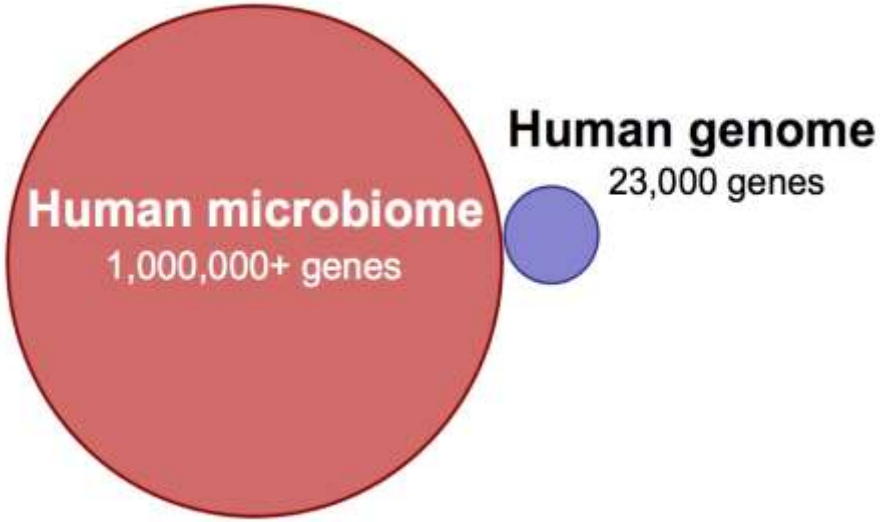
5. ***Stimulate the production of cross-reactive antibodies. Low levels of antibodies produced against components of the normal flora are known to cross react with certain related pathogens, and thereby prevent infection or invasion.***

# Gut microbiota

- ***Synthesis of vitamins and harvest of otherwise inaccessible nutrients***
- ***Metabolism of xenobiotics and other metabotypes***
- ***Renewal of gut epithelial cells***
- ***Development and activity of the immune system***
- ***Cardiac size?***
- ***Locomotion***

# A microbe's view of us

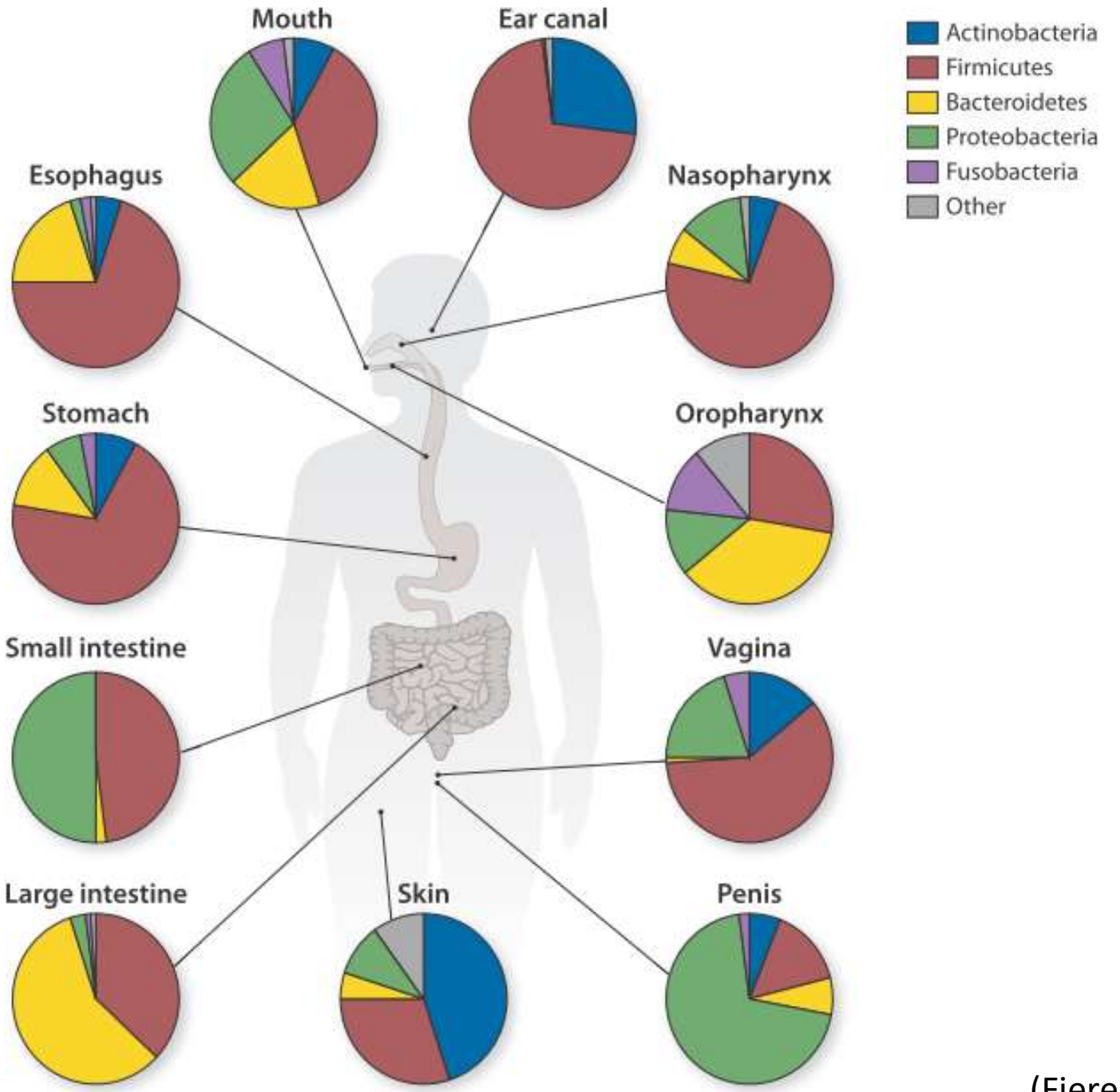



***Bacterial cells outnumber your body cells 10:1 and comprise up to 4-6 lbs of your body mass***

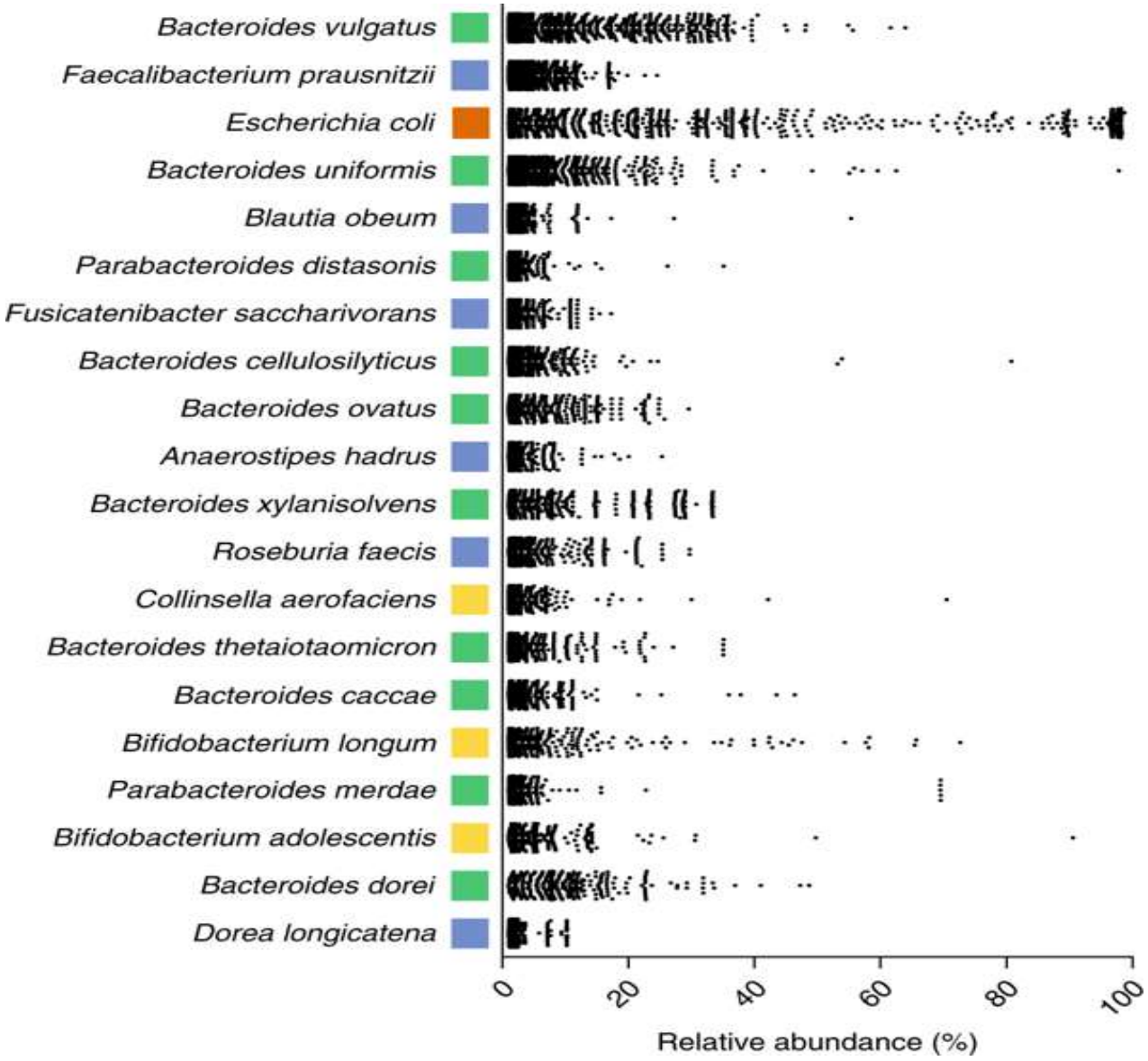
# *Sites that harbor a normal flora:*

- *–Skin and mucous membranes*
- *–Upper respiratory tract*
- *–Gastrointestinal tract*
- *–Outer opening of urethra*
- *–External genitalia*
- *–Vagina*
- *–External ear canal*
- *–External eye (lids, conjunctiva)*

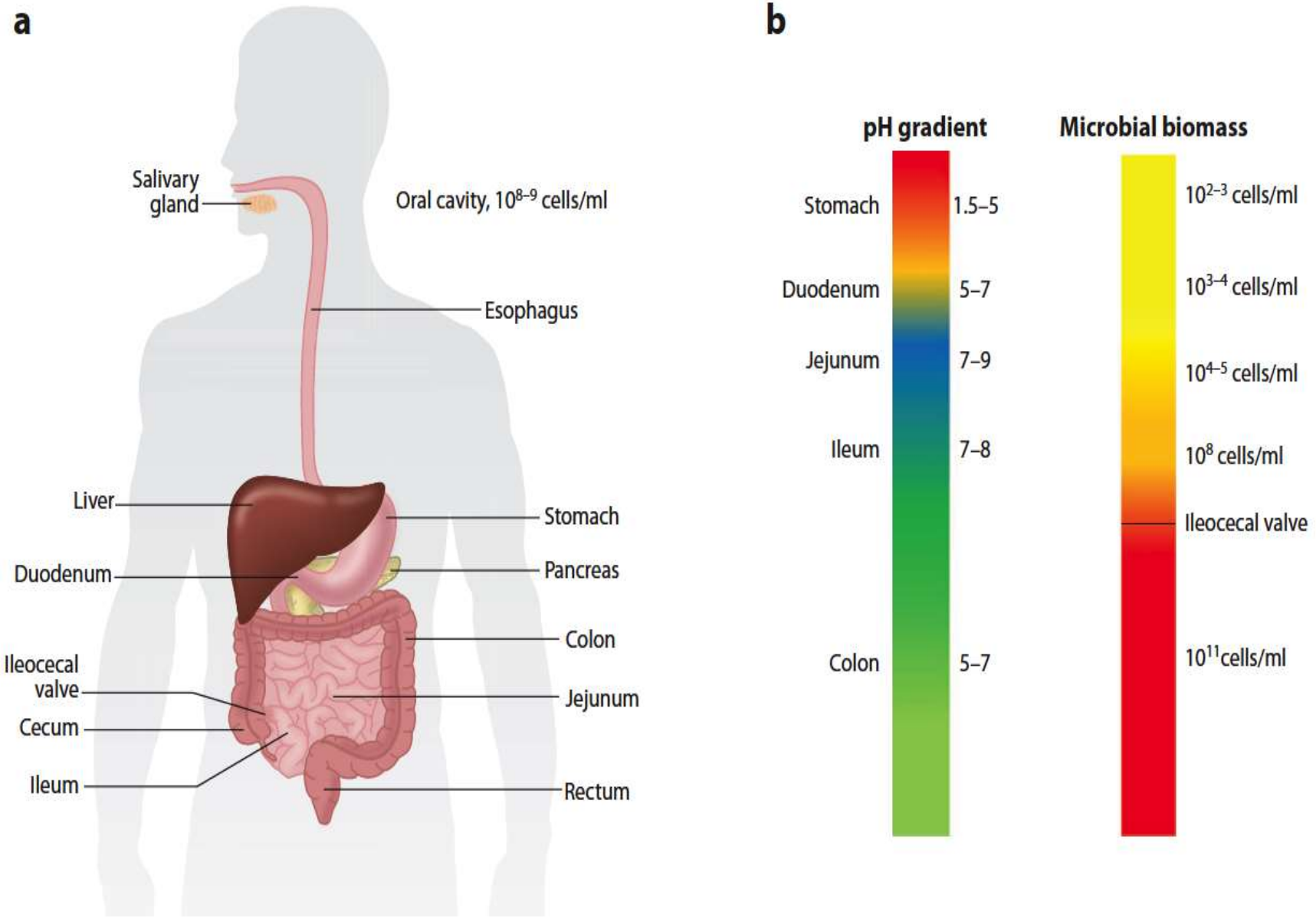



(Fierer et al 2012)

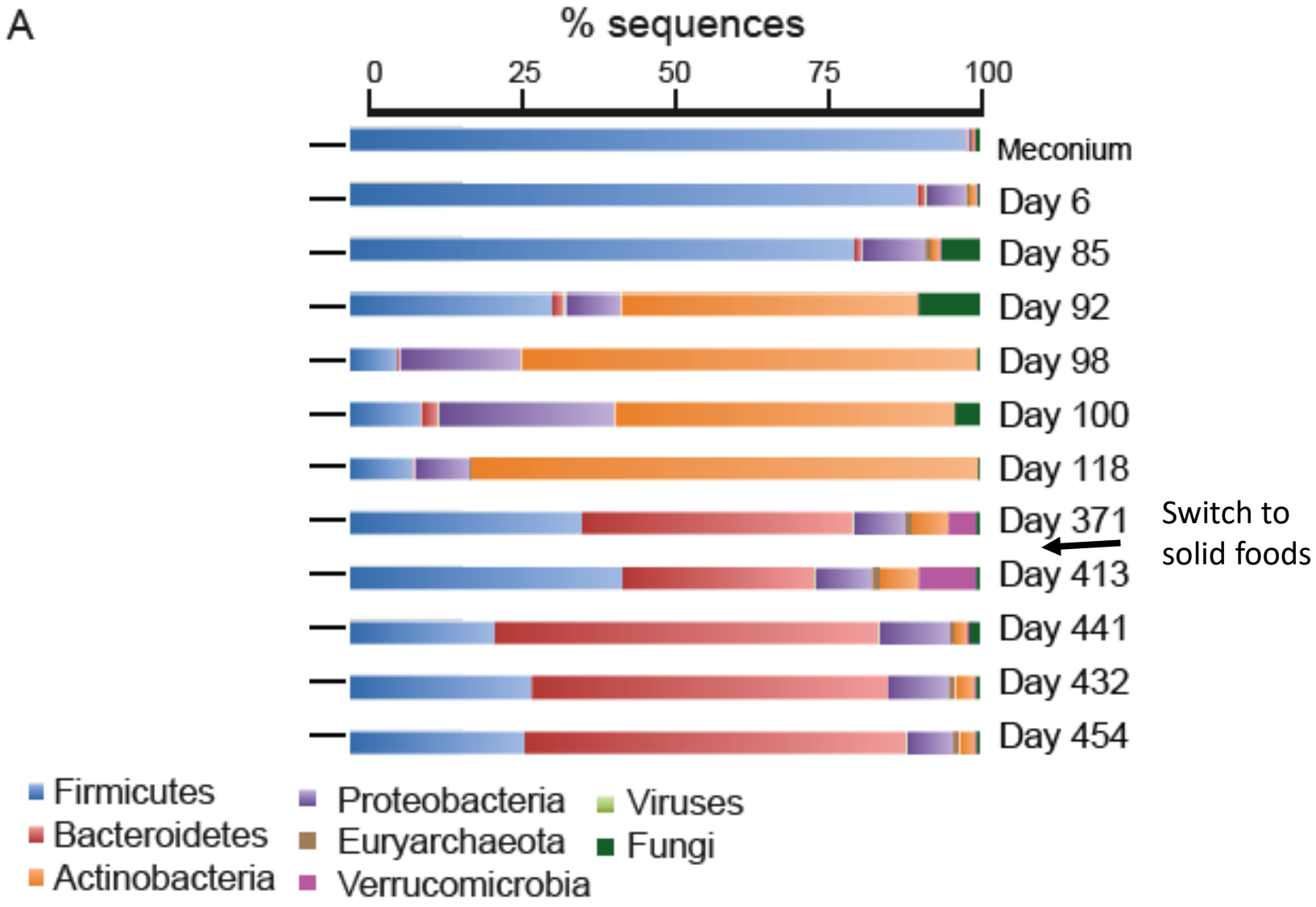
# Dominant bacterial species within the human gastrointestinal micro-biota (Nature Biotechnology, 2019)



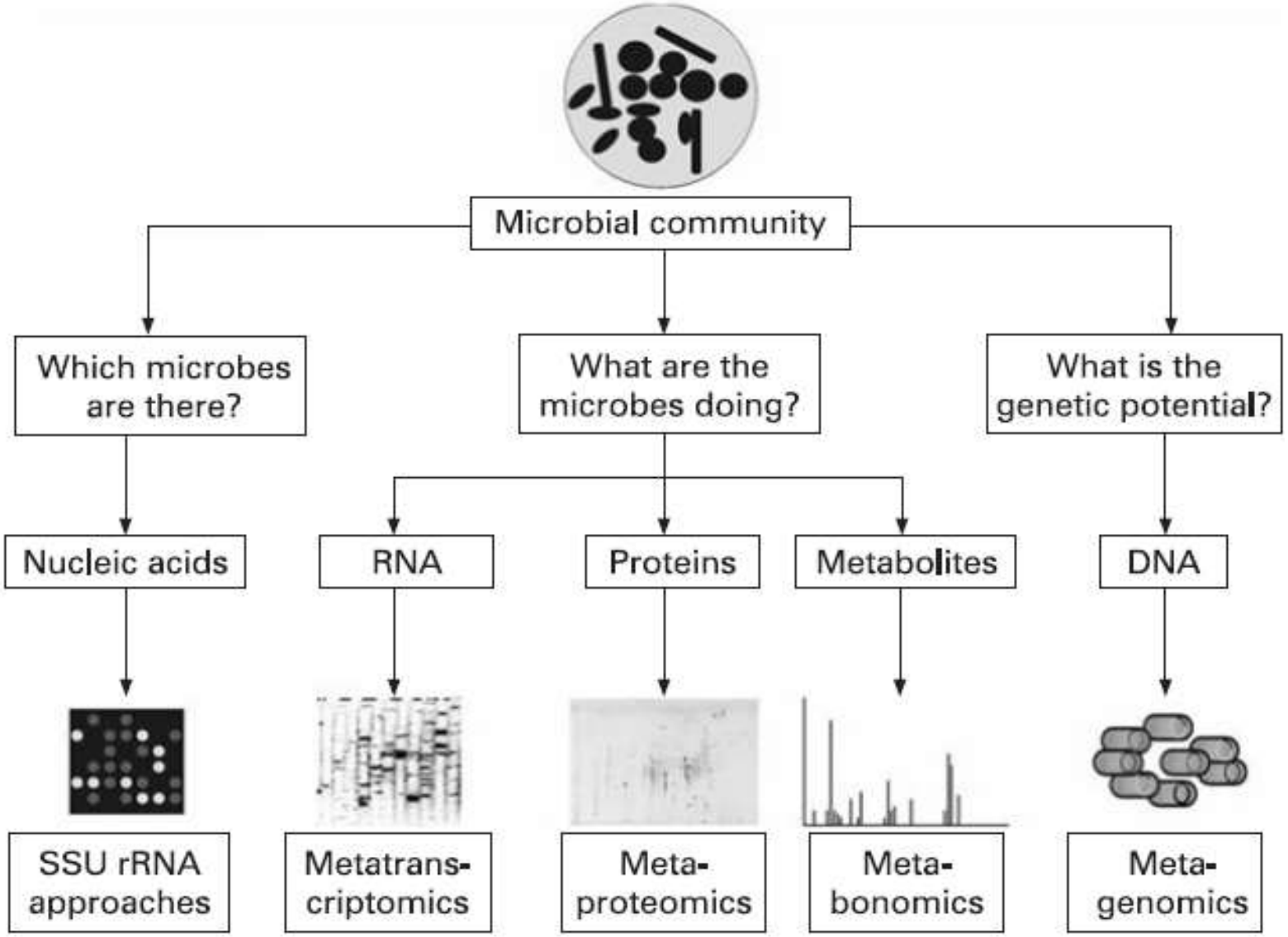
# Relationship between Microbial Biomass and pH



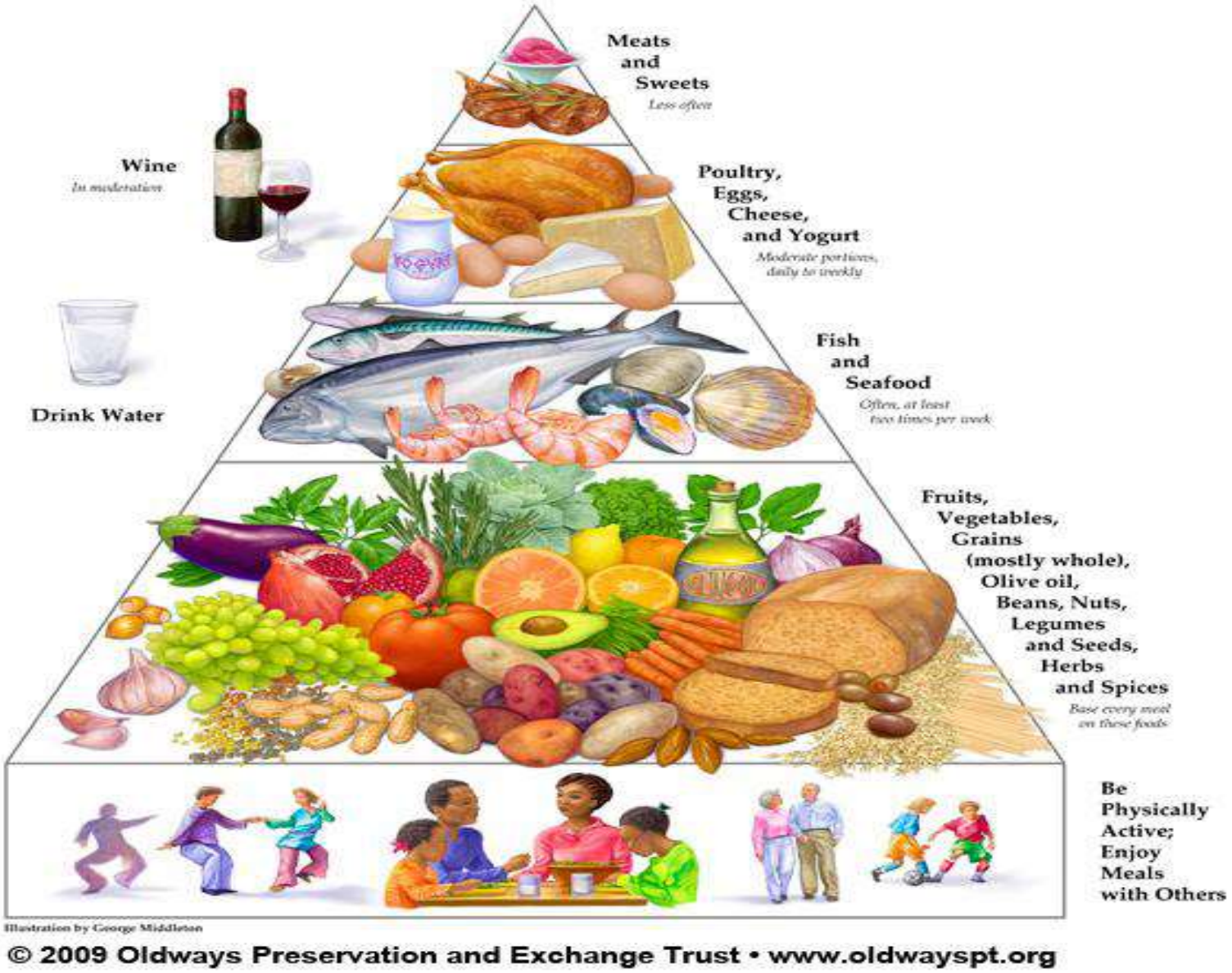
# Succession of Microbial Communities in Gut



# Characteristics of Microbial Communities

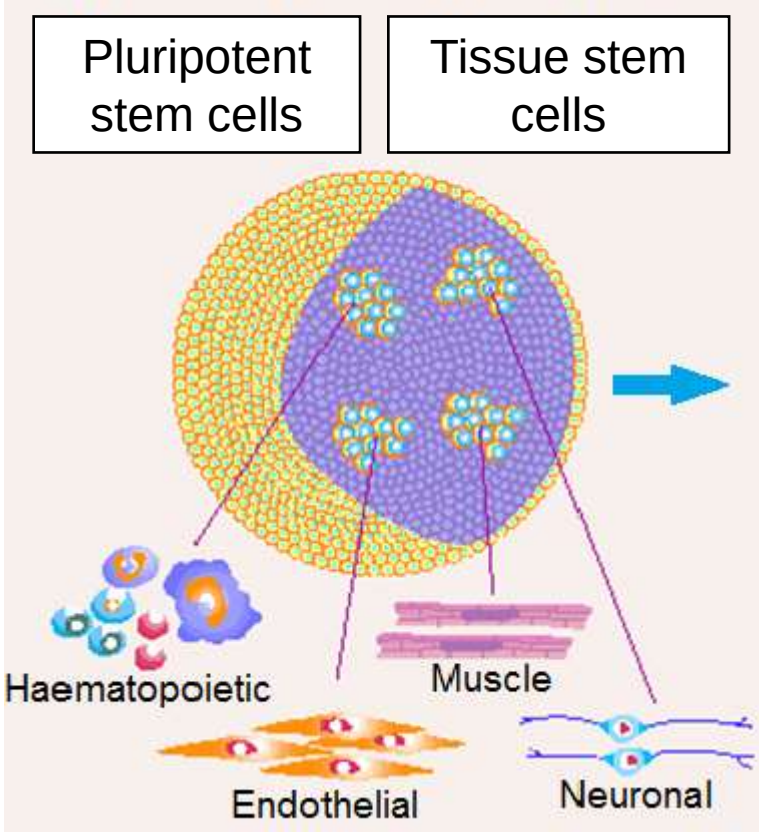


# Diet Affects Microbial Populations



# What makes stem cells so valuable?

## Biology




## Applications

### Cell therapy

Transplantation of specific cells and precursors

### Research

Genetic, molecular and biologic control of tissue growth and development; *in vitro* and *in vivo* system for understanding function of genes and proteins

### New drugs

Early efficacy and toxicity screening system for drug and chemical development

No one stem cell type fits all applications
Research must continue using all types of stem cells

Image modified from Keller & Snodgrass, *Nat Med* 1999; 5(2): 151-152.

# What Diseases Do Stem Cells Treat? Have the Potential to Treat?

- Blood Diseases (including immune system disorders)
- Genetic metabolic disorders (very limited/experimental)
- Tissue/organ replacement (very limited/experimental)

## Potential to Treat

- Heart Disease
- Neurological Diseases (Parkinson's, Alzheimers, Huntington's & others)
- Stroke
- Type 1 Diabetes
- Macular Degeneration (a common cause of blindness)
- Cancer
- HIV/AIDS
- Spinal Cord Injury
- Multiple Sclerosis
- ALS (Lou Gehrig's Disease)
- Liver

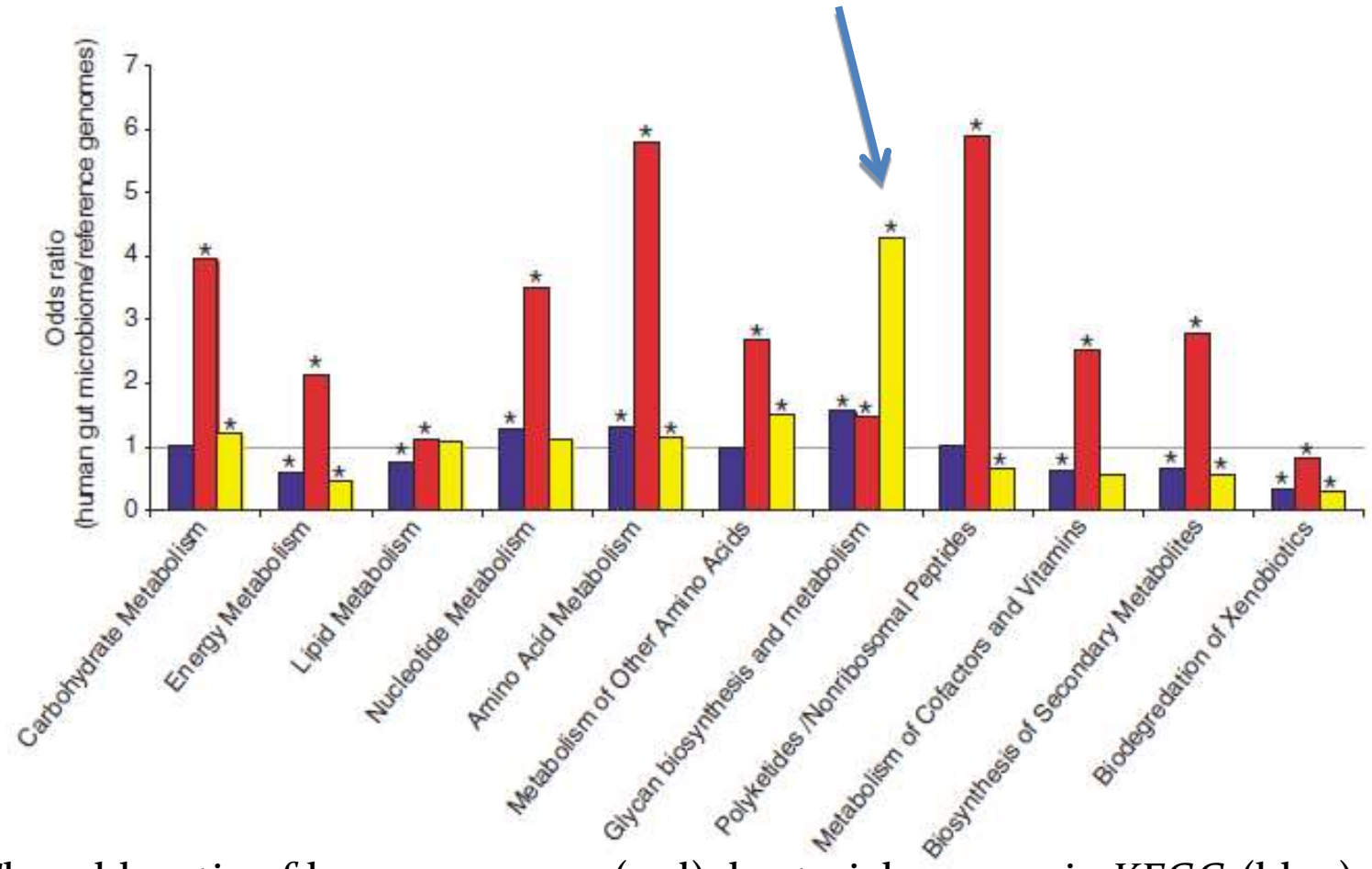
# Transgenic animals with important agricultural traits

- ***Bovine alpha lactalbumin in mammary glands of sows–improves lactation performance***
- ***Sheep carrying Kerartin – IGF-1 construct shows expression in skin for clear fleece in transgenic animals***
- ***Transgenic pig bearing an hMt-pGH construct tightly regulated by Zinc feeding - improves traits as growth rate, feed conversion, body fat muscle ratio***
- ***Phytase gene exclusively expressed in salivary gland enables the pigs to digest phytate which can be metabolized by the intestine. Release low phosphorus in manure***

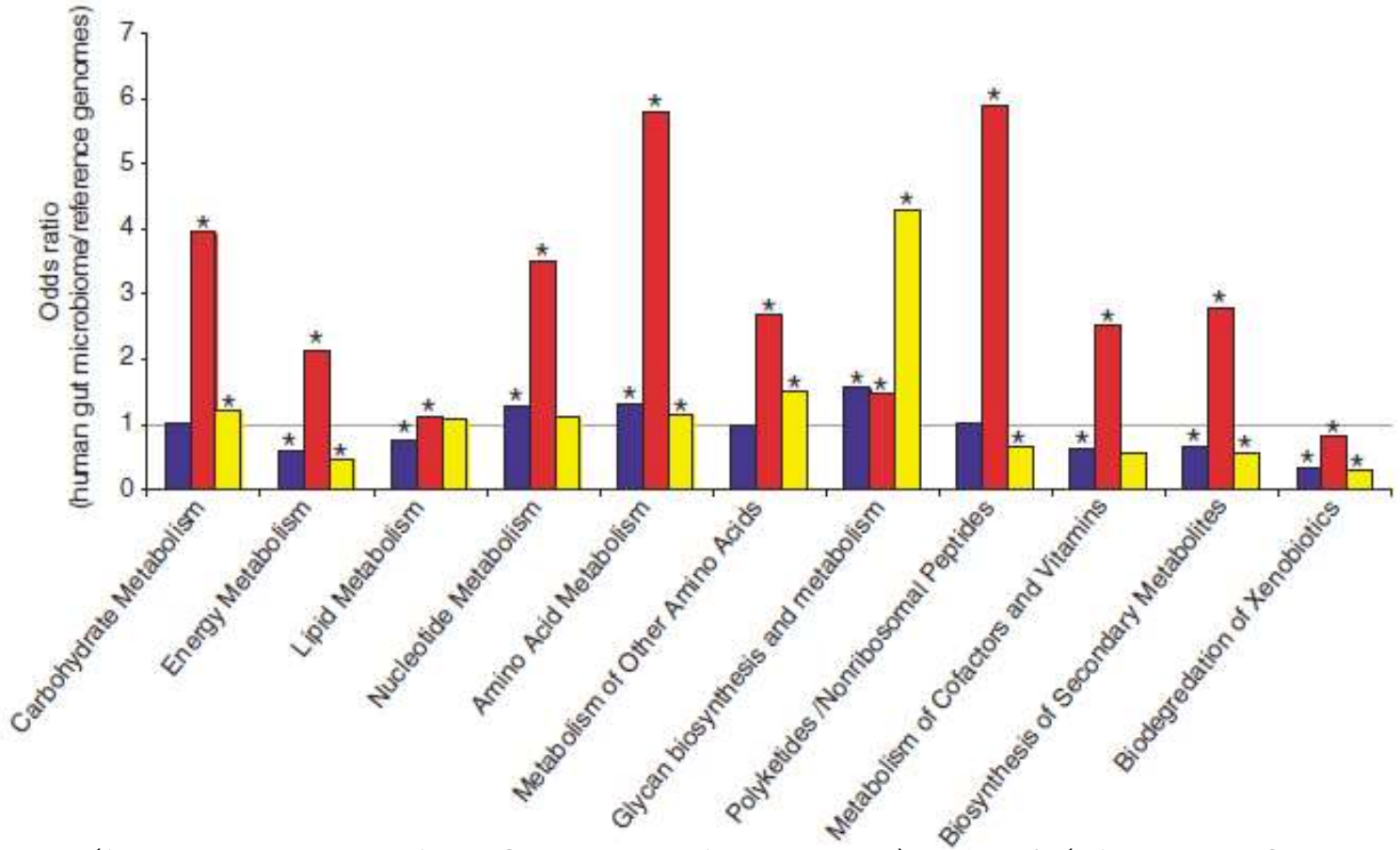
# Transgenic in Biomedicine

## Proteins synthesized in farm animals milk

| | | |
|---|---|---|
| • Bovine | - 2 | Human lactoferrin |
| • Caprine | - 5 | TPA |
| • Ovine | - 4 | Alpha AT |
| • Pigs | - 2 | AT III |
| • Rabbits | - 7 | Alpha glucosidase |

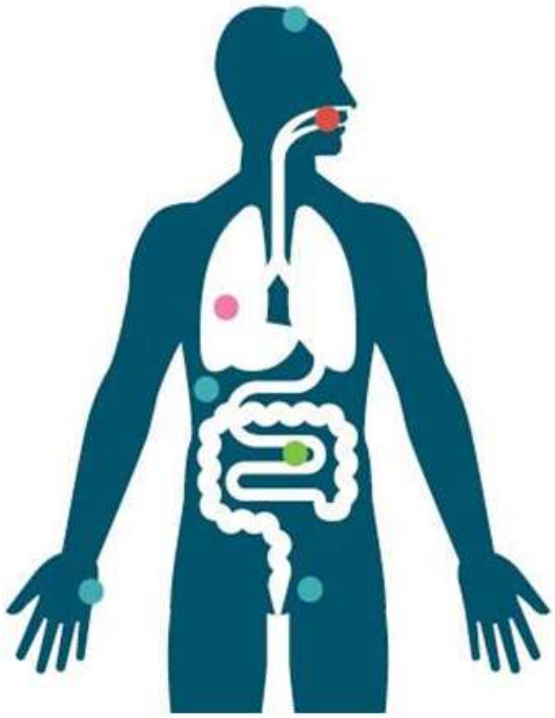



The odds ratio of human genome (red), bacterial genome in KEGG (blue), and archaeal genome (yellow). The graph shows that the human distal gut metabolic functions can regulate most metabolic processes, however, the presence of  certain bacteria and archaea do contribute to metabolic processes




KEGG(kyoto encycopedia of genes and genomes), COG's(clusters of orthologous groups). Used to compare function groups of genes against a baseline bacterial metabolism. And score for enrichment

# The Human Mycobiome



**ORAL CAVITY**

- *Alternaria*
- *Aspergillus*
- *Aureobasidium*
- *Candida*
- *Cladosporium*
- *Cryptococcus*
- *Fusarium*
- *Gibberella*
- *Glomus*
- *Pichia*
- *Saccharomyces*
- *Teratosphaeria*

**LUNGS**

- *Aspergillus*
- *Candida*
- *Cladosporium*
- *Penicillium*
- *Cryptococcus*

**GASTRO-INTESTINAL**

- *Aspergillus*
- *Candida*
- *Cladosporium*
- *Cryptococcus*
- *Fusarium*
- *Penicillium*
- *Pneumocystis*
- *Mucor*
- *Saccharomyces*

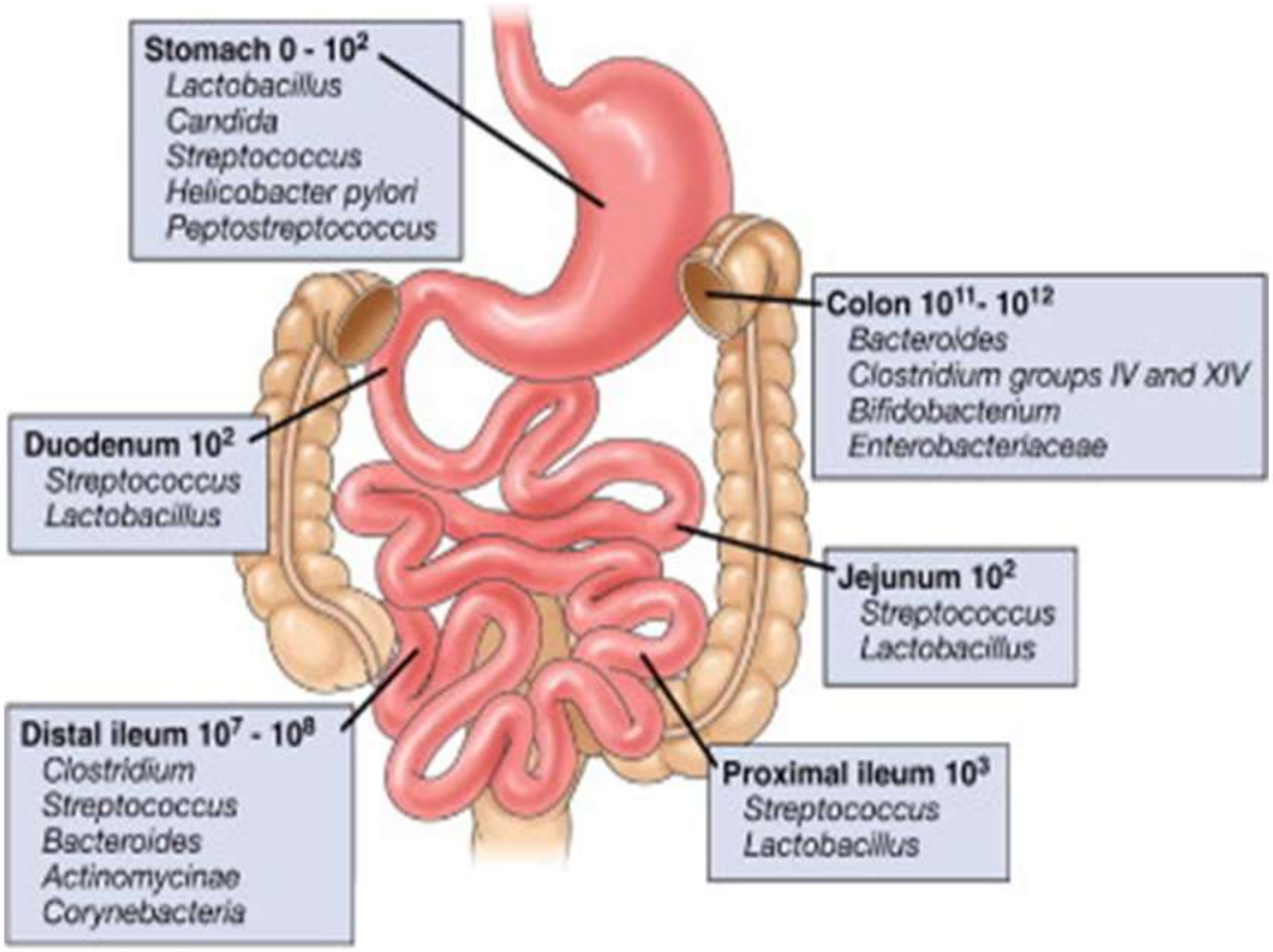
**SKIN**

- *Candida*
- *Cryptococcus*
- *Debaryomyces*
- *Epidermophyton*
- *Malassezia*
- *Microsporum*
- *Rhodotorula*
- *Trichophyton*
- *Aspergillus*
- *Chrysosporium*
- *Epicoccum*
- *Leptosphaerulina*
- *Penicillium*
- *Phoma*
- *Saccharomyces*
- *Ustilago*

*Potentially pathogenic lineages

- Early surveys have revealed several pathogenic species that may increase one's risk of disease when the healthy microbiome is disrupted.
- *Candida* and *Aspergillus* species are among the most common members of the human mycobiome.
- When the balance of a microbial community is disrupted, fungal species can flourish and cause disease

# Quantitative Analysis of Microbial Communities




Gastroenterology 2008 134(2)

# *Research questions to be answered in HMP*

- ***How stable and resilient is an individual's microbiota throughout one day and during his/her lifespan?***
- ***How similar are microbiomes between members of a family, community or across communities in different environments?***
- ***Do all humans have an identifiable "core" microbiome and how is it acquired and transmitted?***
- ***What affects the genetic diversity of the microbiome and how does this diversity affect adaptation by the microrganism and the host to markedly different lifestyles and to various physiological or pathophysiological states?***

# Chicken Microbiome

- ***The chicken microbiome is the community of microorganisms living in and on a chicken.***
- ***A healthy balance of microorganisms makes for a healthy chicken.***
- ***Microorganisms found in the guts of chickens do not usually make chickens ill, but if some of those microbes get onto the meat during processing and then into the human gut, they can cause illness in people.***

# The Soil Microbiome

- ***The soil microbiome is the community of microorganisms that live in the soil.***
- ***It is huge – scientists have found that virtually every soil sample they analyse contains around 30 000 species of microorganisms.***

# Drugs the soil

- ***Some microbes in the soil microbiome make chemicals that destroy other microorganisms; maybe they can help us too.***
- ***However, we have not found a way to culture 90% of the microorganisms that grow in soil in the laboratory, so we have a long way to go.***
- ***In 2015, scientists discovered teixobactin – a completely new type of antibiotic from soil bacteria that cured MRSA and TB in mice.***

# Finding New Antibiotics

- Antibiotic resistance in bacteria means the time may come when we can no longer cure bacterial diseases with the antibiotics we have now.
- Scientists are searching for new antibiotics in many places, such as crocodile blood, fish slime, the deep sea abyss and soil.