

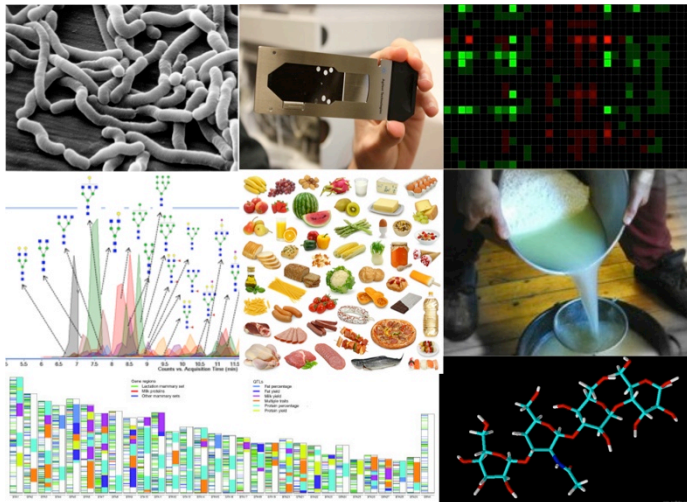


Foods for Health: Bringing Health Benefits to Genetic Traits

Foods for Health Institute



Building the Science,
Technologies and Education to
Personalize Diet and Health



FOODS
FOR HEALTH
INSTITUTE

A stylized orange eating utensil (fork or spoon) is positioned diagonally across the text. Below the word "INSTITUTE" is a red heartbeat line graphic.

Institute Goals:

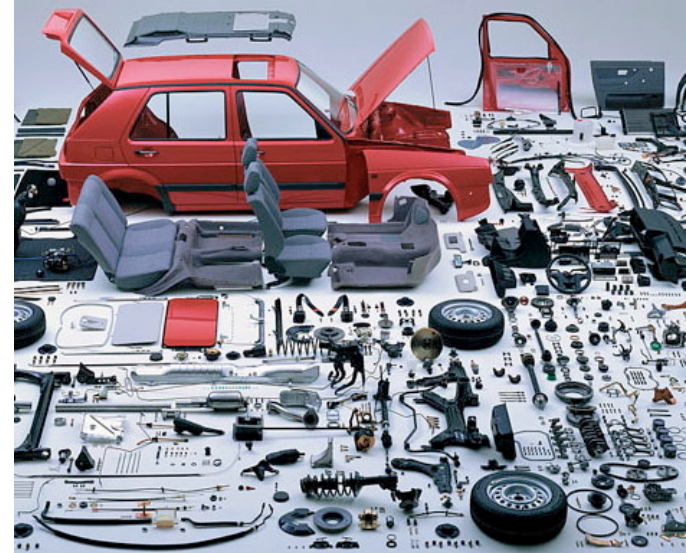
Improve Human Health

**Increase the value of
Agriculture**



The 20th Century Science

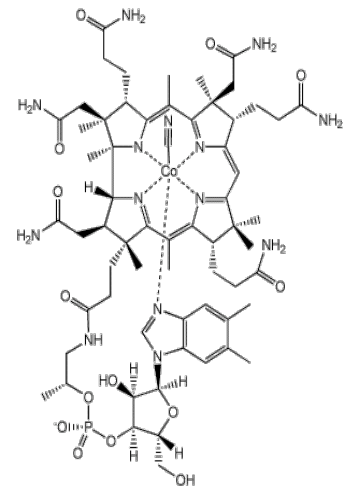
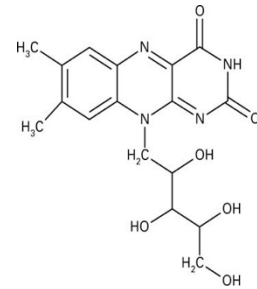
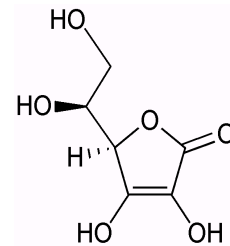
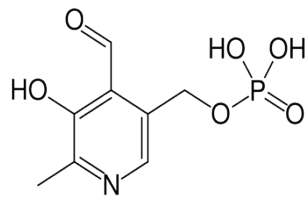
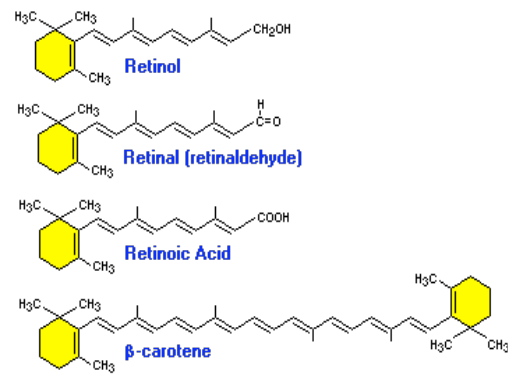
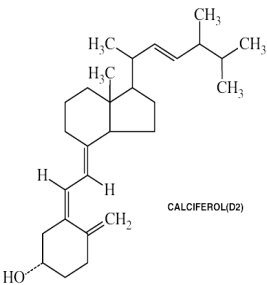
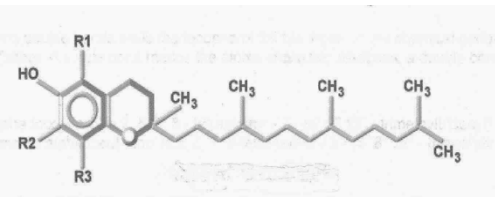
- Chemistry –Reductionist
- Industrialization of Simple Chemicals
- Key = Purify





Essential Nutrients

One of chemistry's great achievements: Identifying all of the essential nutrients for humans

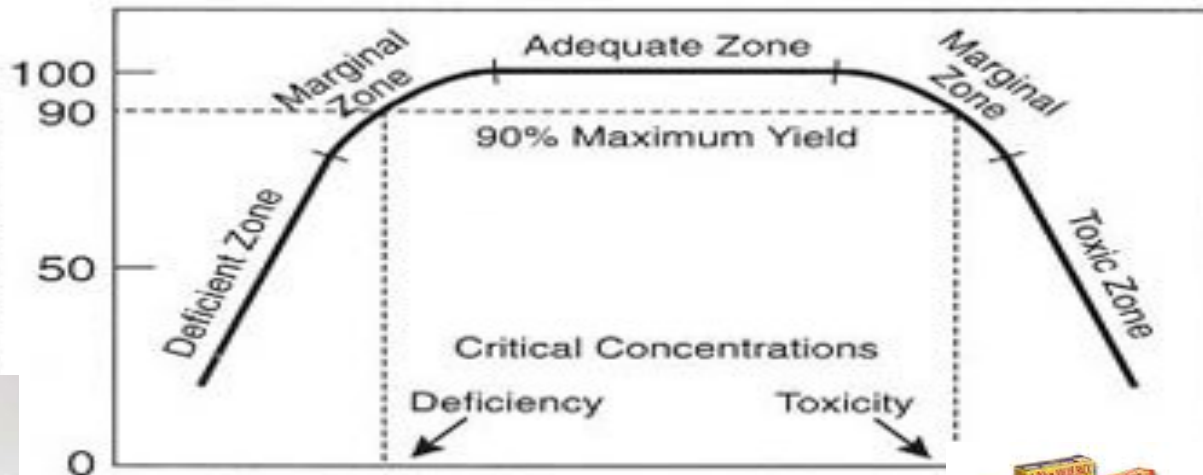


Nutrition's 1st Era



Success of the 20th Century: Essential Nutrients and their Deficiencies

- Industrial 'nutrified' foods
- Population Solutions – 'Overdose'

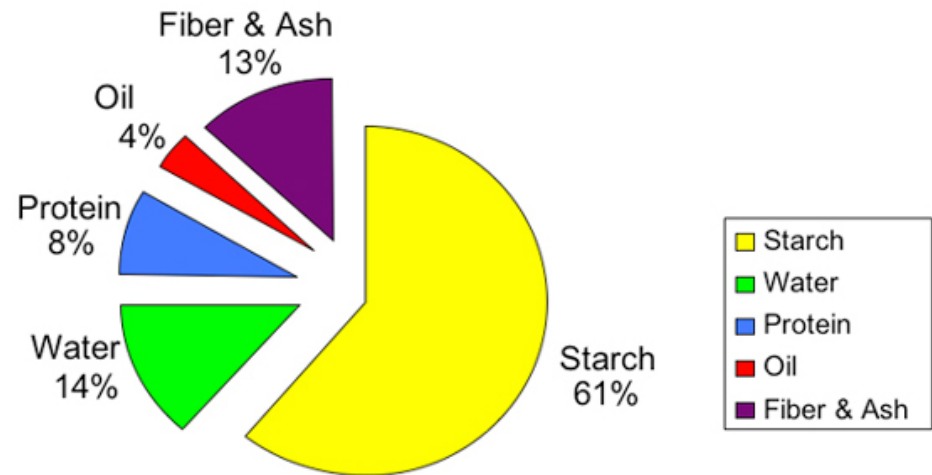


Food in the 20th century



What food is?

The simple chemical composition became the goal of food research: protein, fat, carbohydrate, vitamins, minerals, metabolites



Typical composition of #2 yellow corn



Agricultural Enterprise

Agriculture adopted a quantity model:
'just make more'

A horizontally integrated, cost driven, production engine providing inexpensive, commodity based, 'tasty', food products



Agribusiness



Farmers



Food Industry



Retailers

Agricultural Success



*Newsweek April 2012

1965 VS. 2012

| | 1965 Price* | 2012 Price |
|---|----------------|---------------|
| Gallon of milk | \$6.84 | \$3.30 |
| Issue of New York Times | .72 | 2.50 |
| Coffee | 5.41 | 5.50 |
| Share of GE | 1.58 | 20.20 |
| Tuition, room, and board at four-year university | 1,051.00 | 22,450.00 |
| NEWSWEEK cover price | 2.52 | 4.99 |
| Ounce of gold | 252.70 | 1,659.42 |
| Gas | 2.25 | 3.83 |
| Chicken (\$/lb.) | 2.81 | 1.33 |

Hostile Environment?

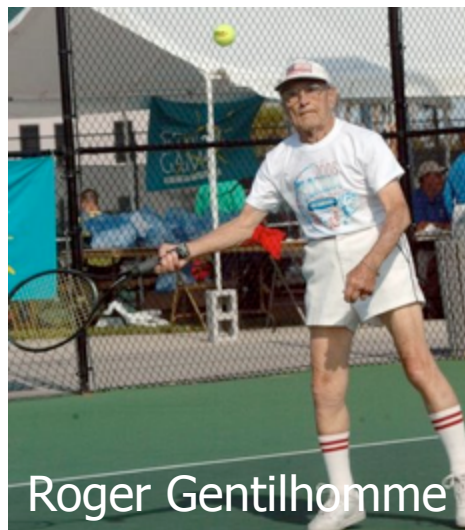




But, its not healthy
We should be enjoying the
greatest health in history
and some are,
.....but most are not



Jaring
Timmerman



Roger Gentilhomme



And, Agriculture's model is Unsustainable



- What more do you need to say?
- Food for SUV's!!!!



UC Davis's great opportunity: Health and Disease Prevention



The Challenge: How to do it!

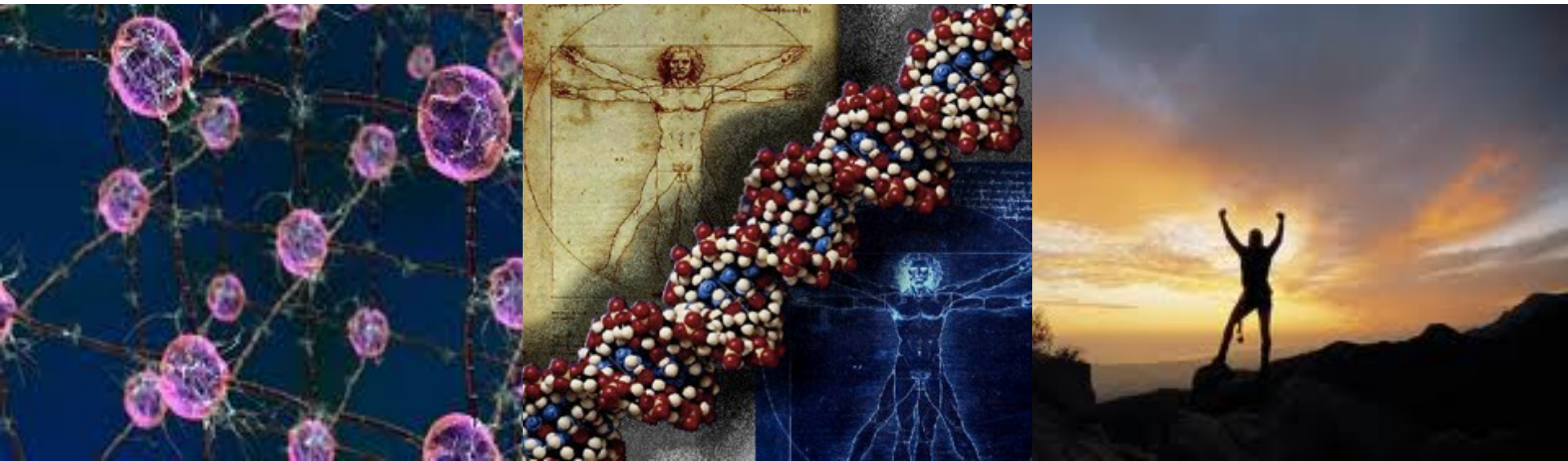
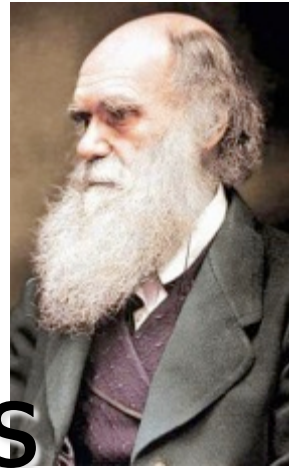
The H-AND of Food Values



The 21st Century



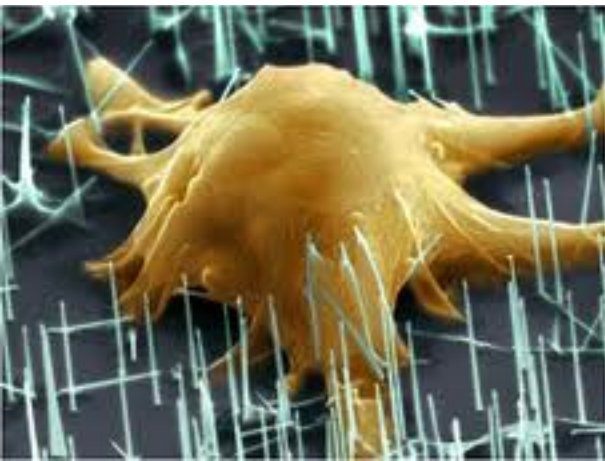
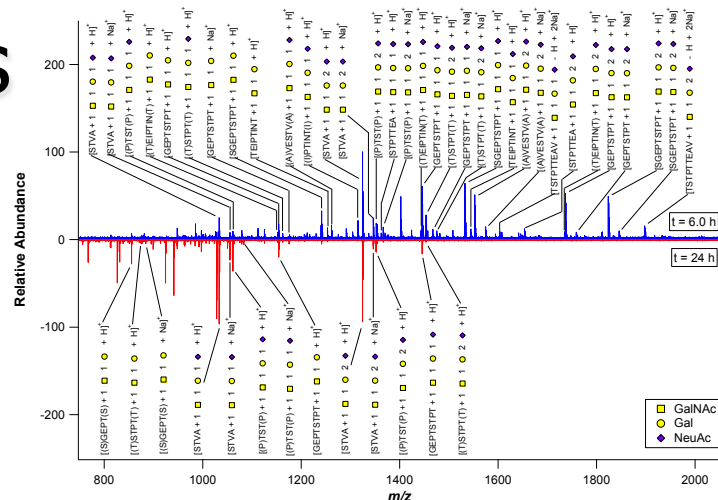
- Biology - Evolution
- Integrative
- Industrialization of Organisms and Systems for Individuals



21st Century Chemistry



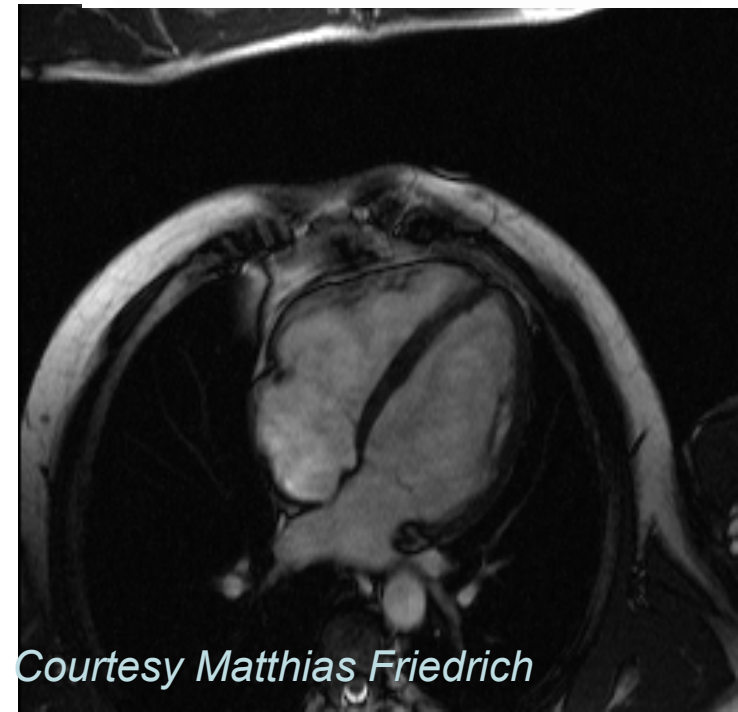
- Comprehensive
 - Entire classes of molecules
- Sensitive
 - Parts per trillion
- Accurate
 - Detailed complex structures





21st Century Mathematics

- ✓ Computational methods
- ✓ Massive Databases
 - Annotating Genomes to Neighborhood Maps
- ✓ Global networks
 - Economies to Ecosystems
- ✓ Industrialization of Research
 - Egalitarianism of Knowledge



Courtesy Matthias Friedrich

-AND- Engineering



- **Complex Systems**
measure – adjust –
measure - adjust
- **Devices**
Fast, furious, cheap
- **Smart Processing**
Networked, controlled



Food in the 21st century



What food does?

The intimate dialog between diet and our health will be annotated and guide the next generation of foods – personal, dynamic, active



Targets



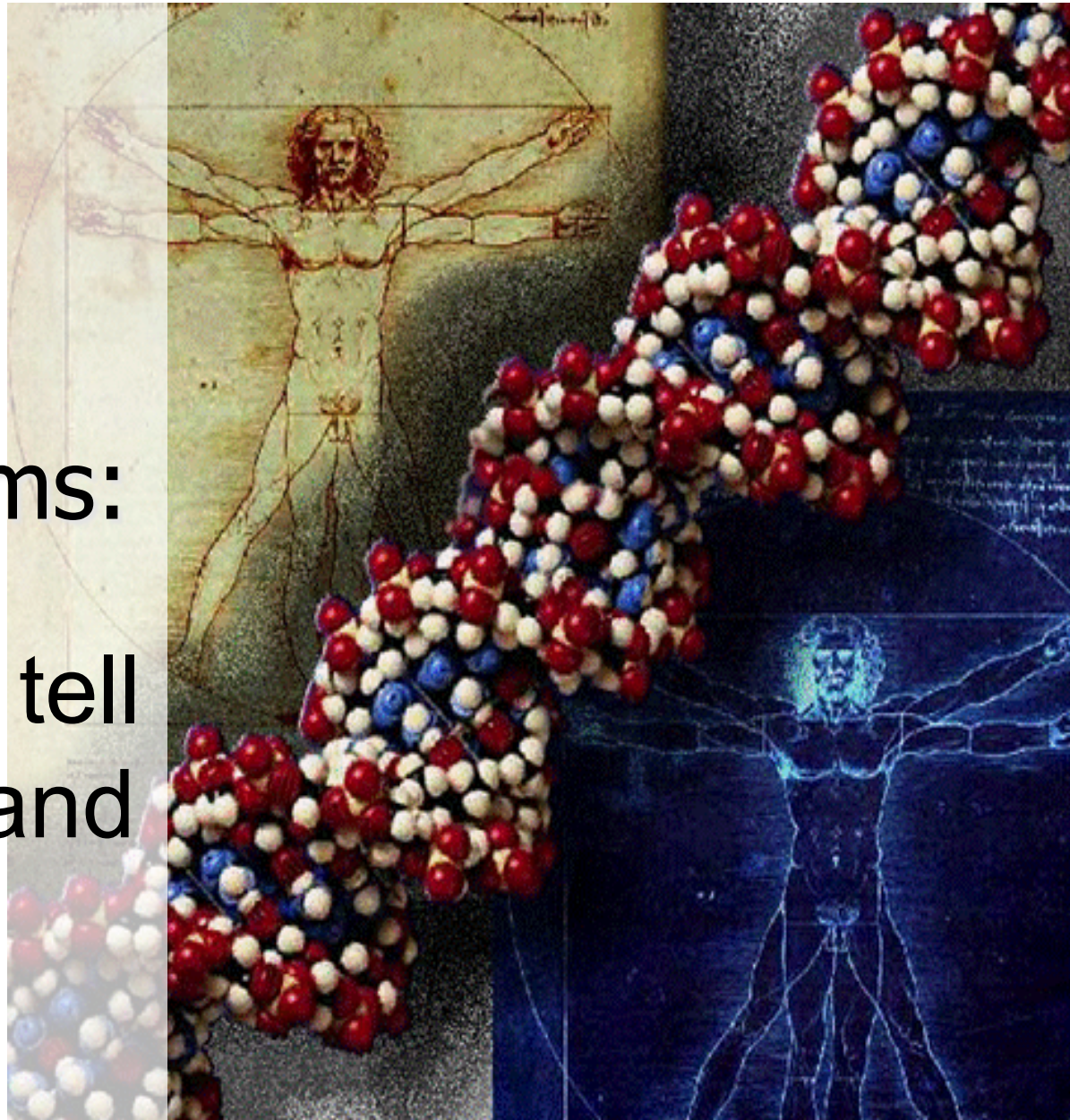
What does diet act upon that improves the health of healthy individuals?



Genomics: the Footsteps of Evolution

- Humans:
- Plants:
- Animals
- Microorganisms:

What can they tell us about Diet and Health?



Evolutionary Nutrition

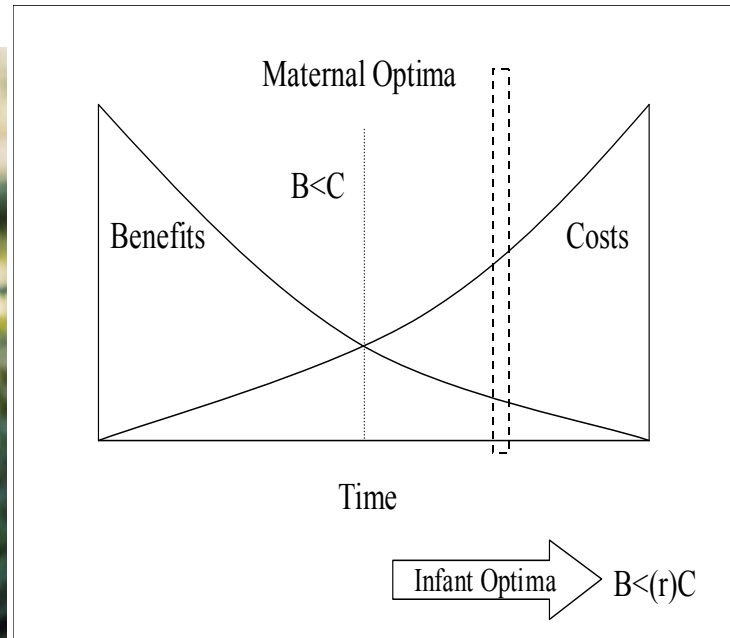


What evolved under the Darwinian Pressure to be Nourishing?

Lactation



The Darwinian Engine of Nutrition



Evolving a cost – benefit solution for Health



The Thematic principle

Concept: **“Evolutionary Nutrition”**

Example: milk, the Rosetta stone of nourishment



Mechanistic targets for health and prevention

▪



More Targets: Milk is

Personal

Active

Dynamic

Structured

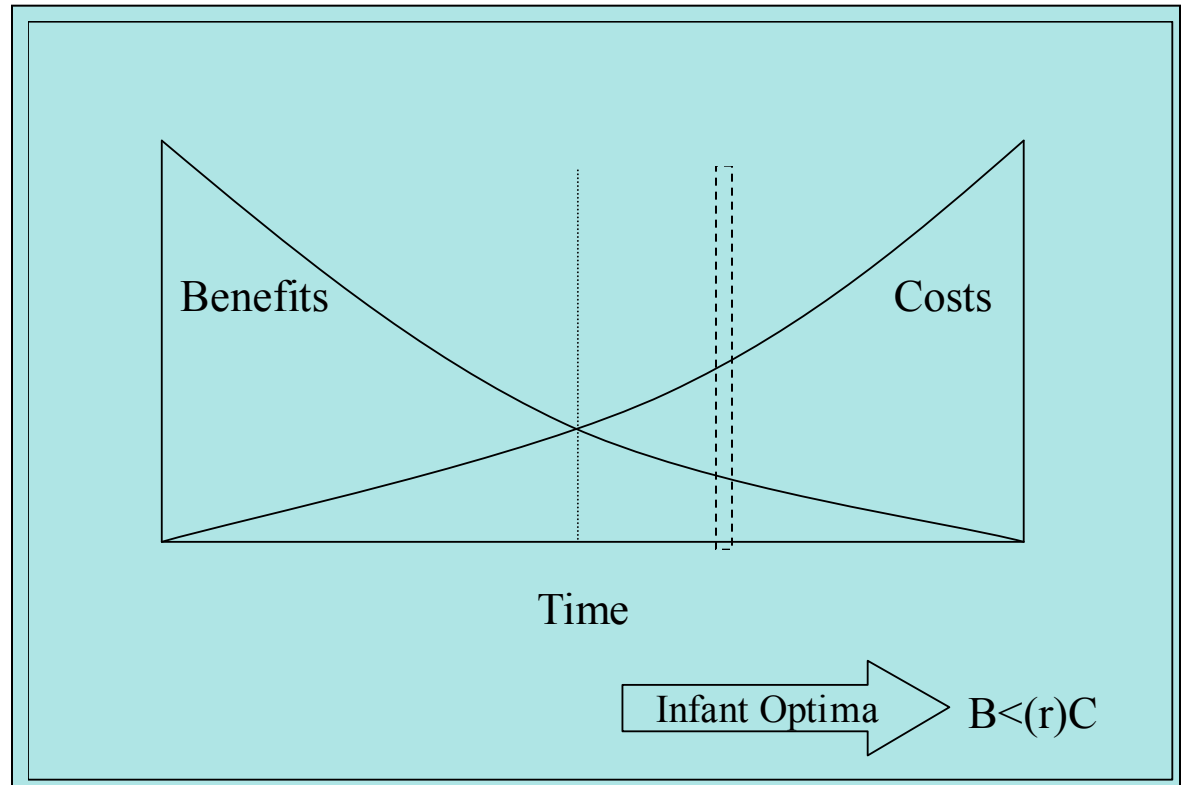


**Proof of Principle:
Biology-guided,
Integrative,
Multi-disciplinary,
Translational,
Prevention**

Lactation



The Darwinian Engine of Diet, Health & Sustainability





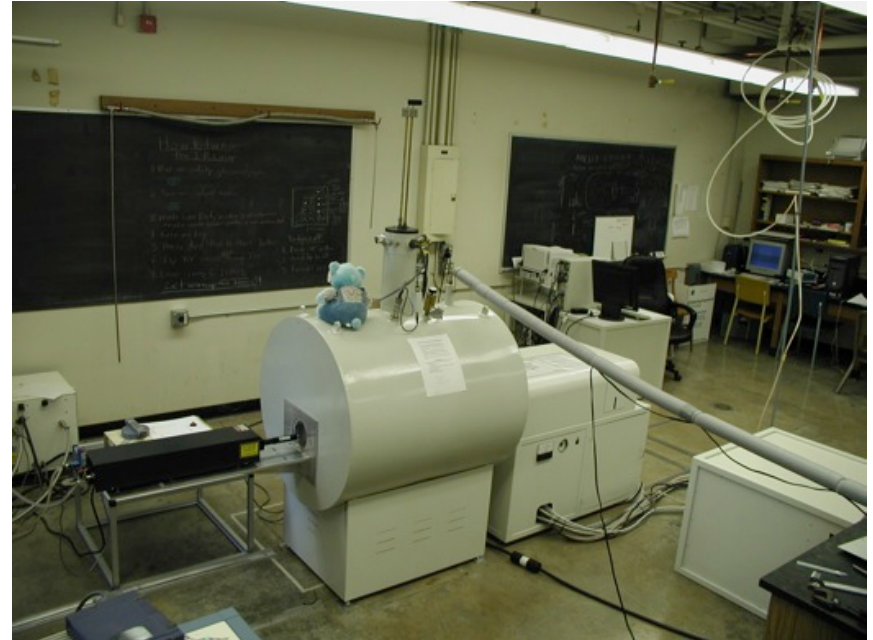
Functions of Milk?

The 3rd most abundant class of biomolecule in human breast milk is un-digestible by humans!

- What are they?



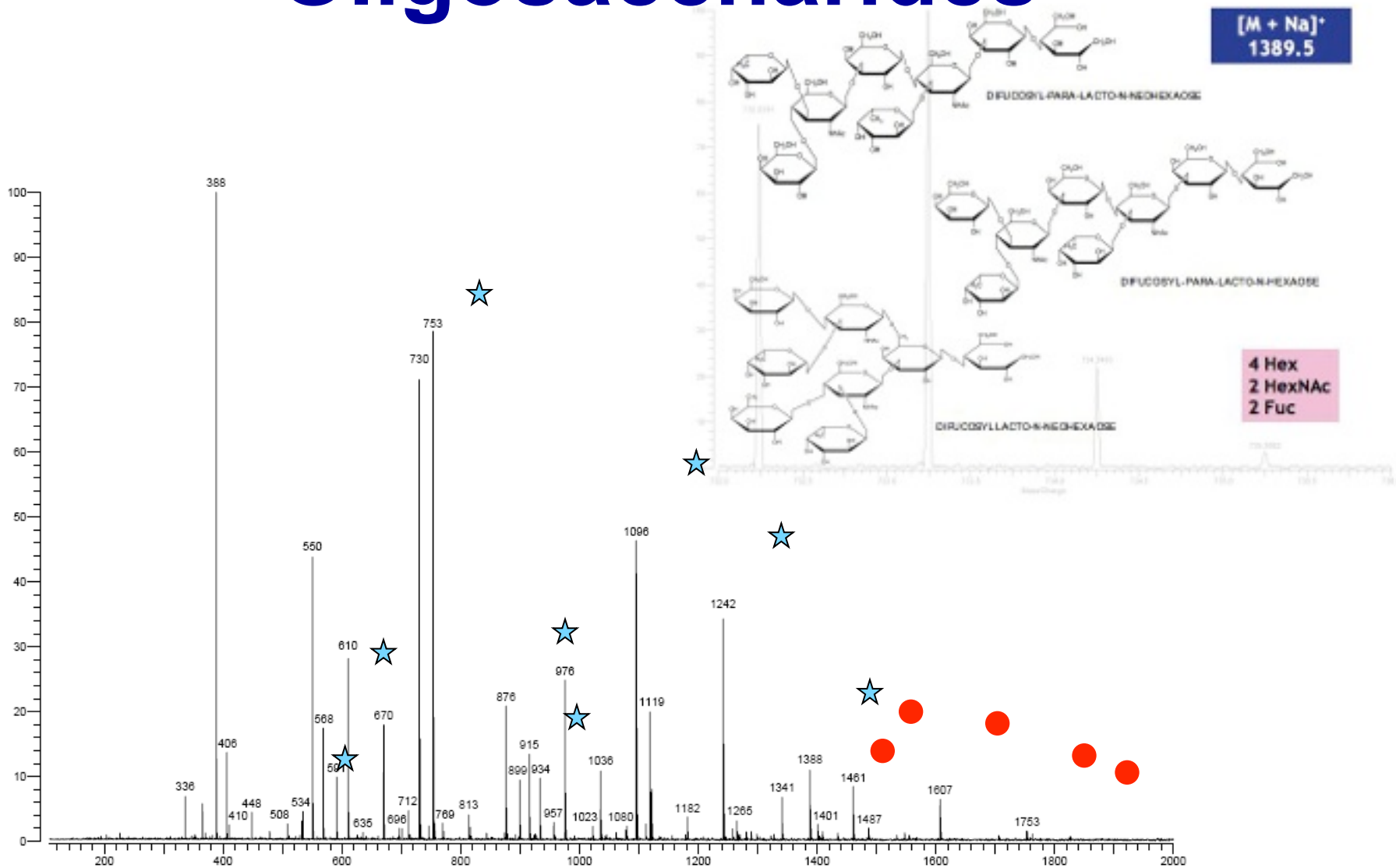
Milk Oligosaccharides



Carlito Lebrilla

- World's Leading Analytical GlycoChemist

Mass Spectra of Human Oligosaccharides





Functions of Milk?

The 3rd most abundant class of biomolecule in human breast milk is un-digestible by humans!

■ Why?

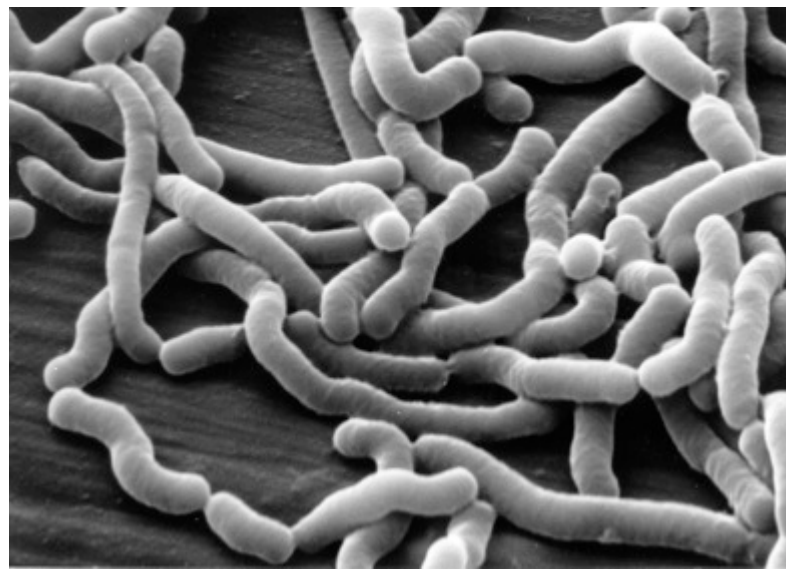
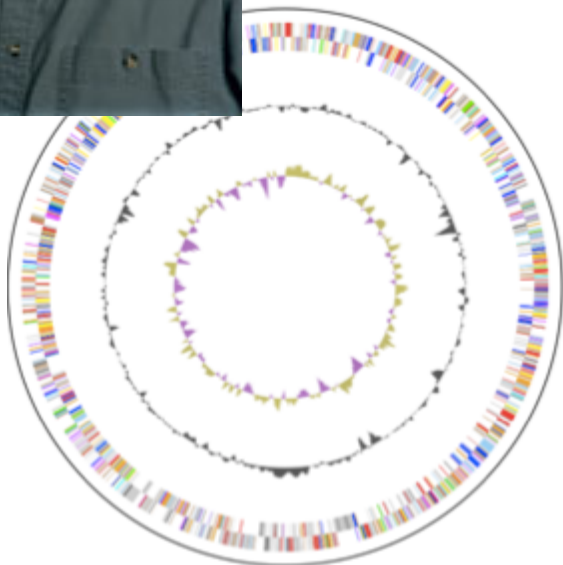




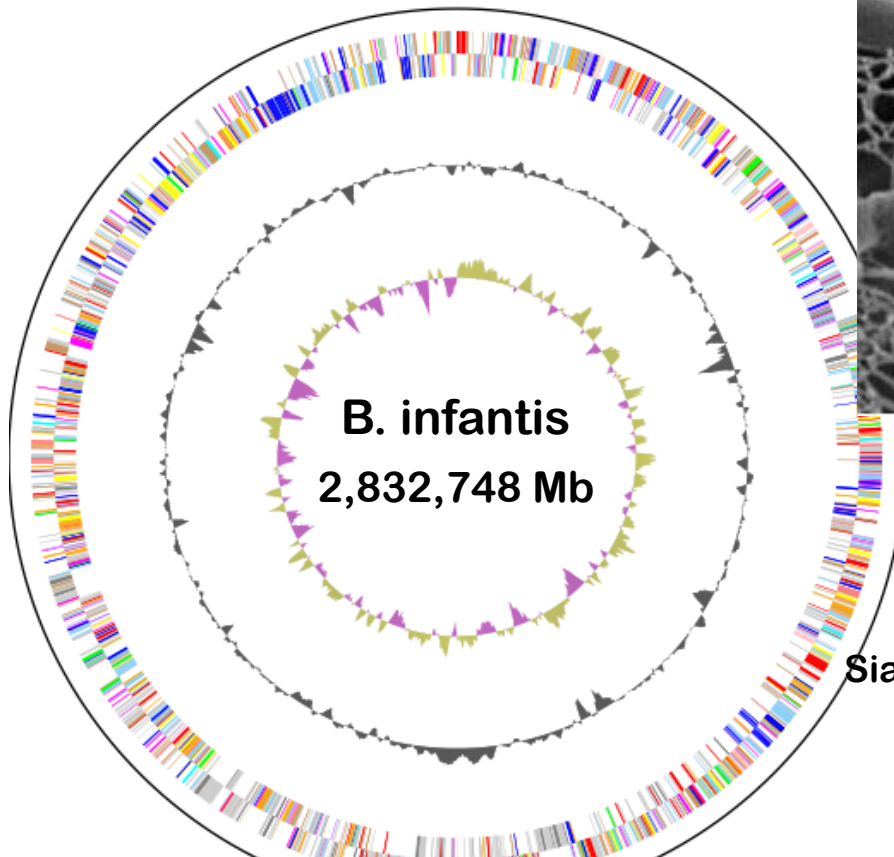
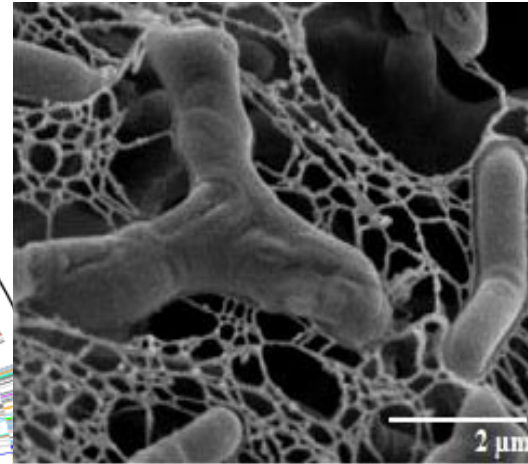
Bacteria?

David Mills

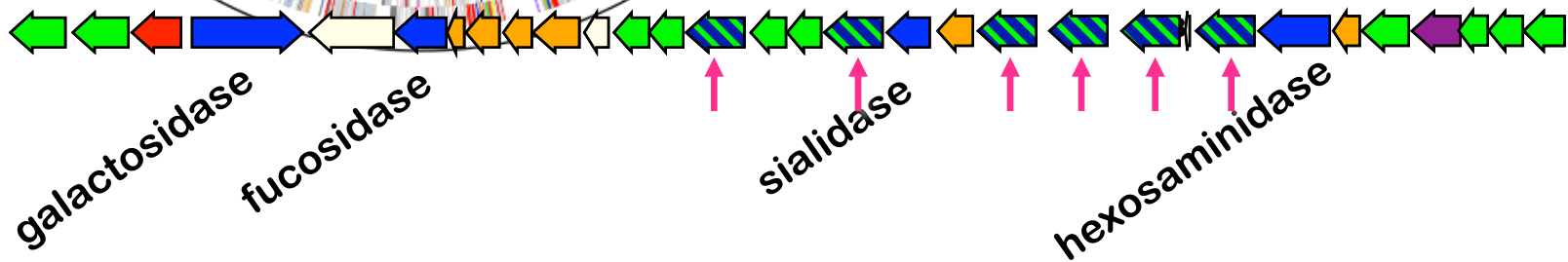
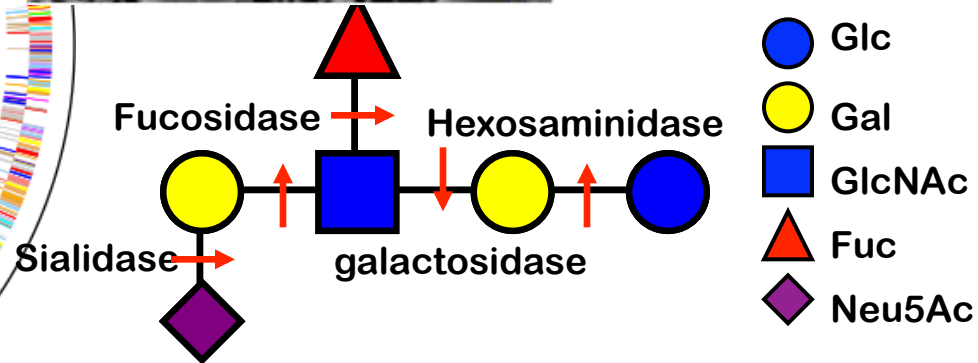
Structure, Function and Health
Benefits of Food Borne Bacteria



Bifidobacterium Infantis



B. infantis
2,832,748 Mb

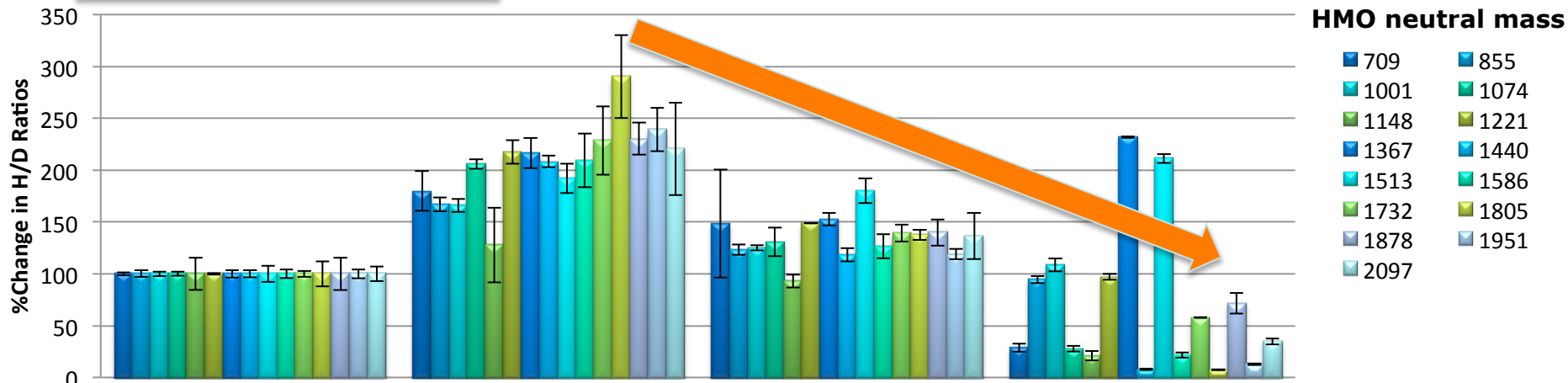


Feces Oligosaccharides of Term Infant Vary With Bacterial Population

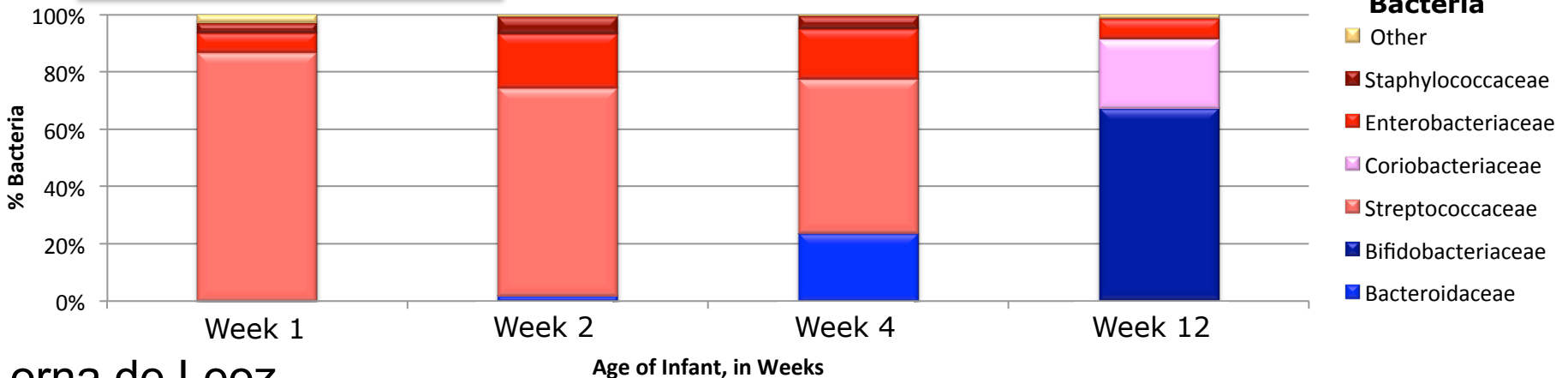


Fecal HMO Profile

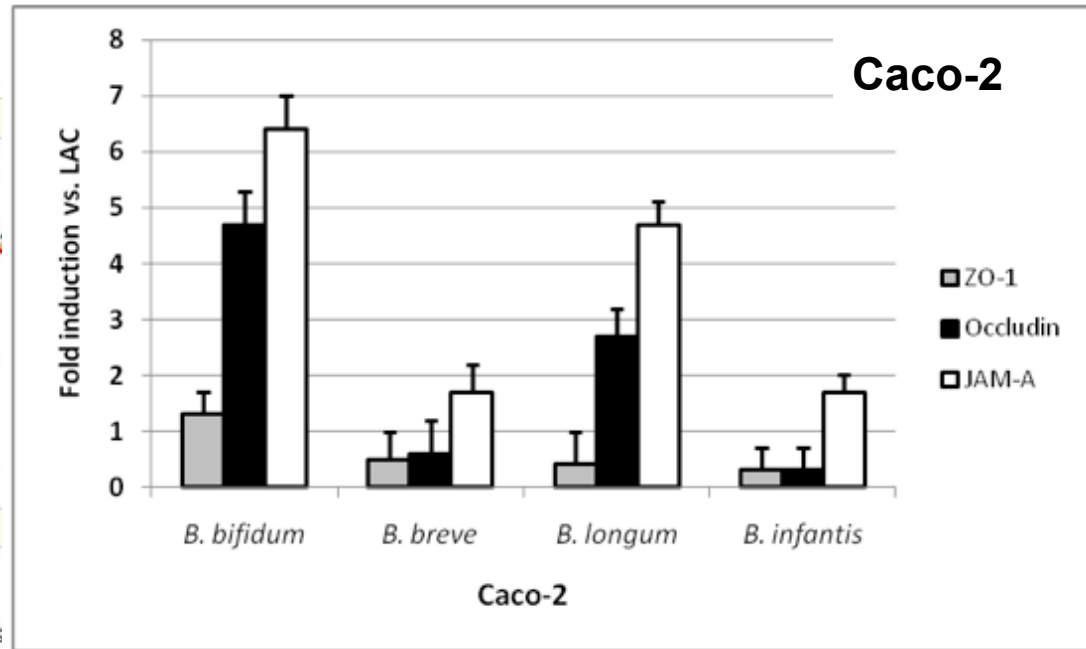
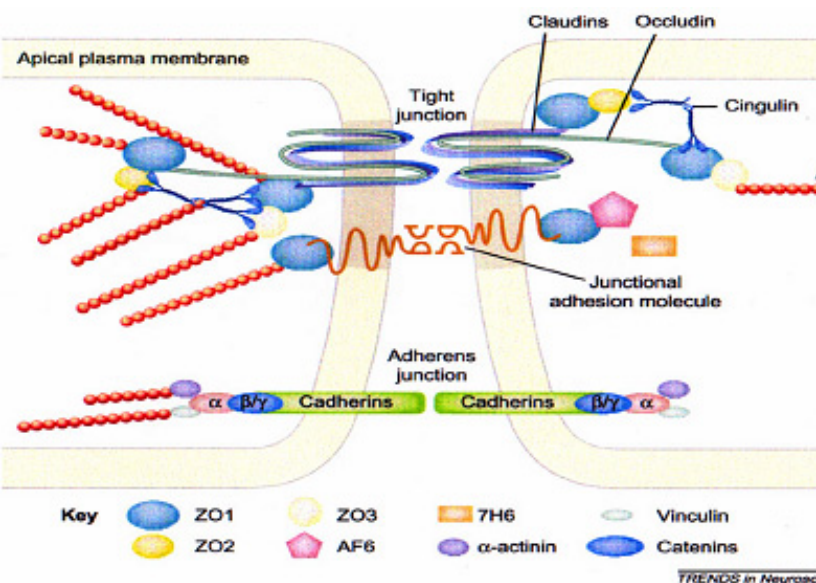
FULL TERM INFANT



Fecal Bacterial Profile



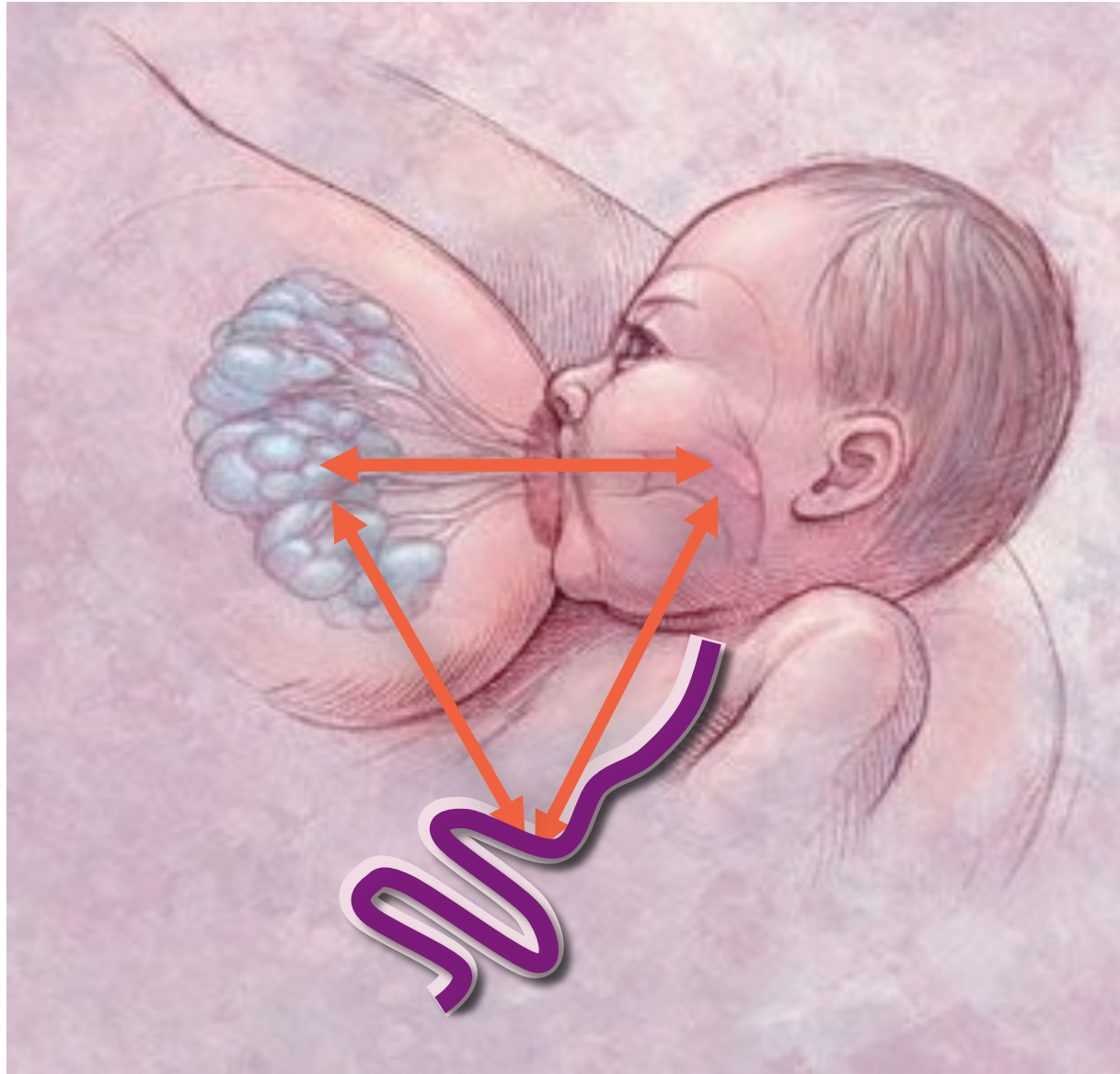
B. infantis Growth on milk oligosaccharides modulates tight junction protein expression



Chichlowski et al JPGN 2012



Tripartite Evolutionary Relationship?



Translating to Practice

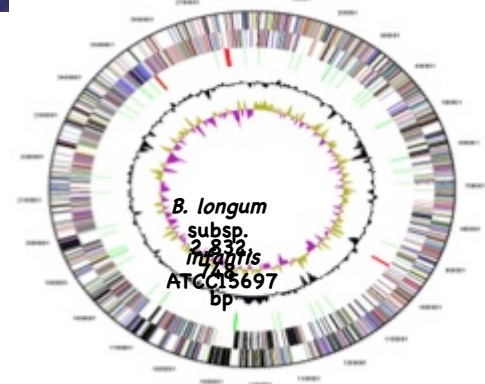


Premature Infants
at risk of sepsis
and Necrotizing
Enterocolitis

Combination of Human
milk oligosaccharides
plus *Bifidobacteria*
longum subsp. infantis
protection, growth



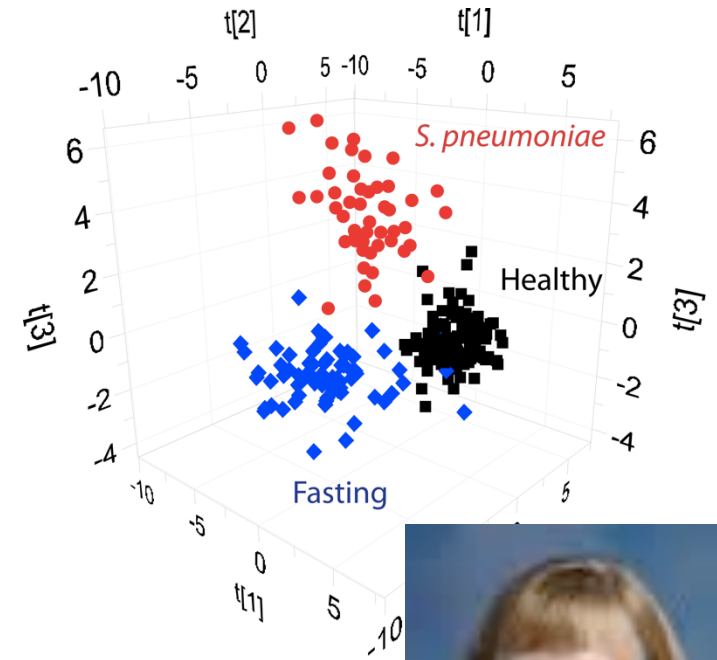
Mark Underwood
UC Davis



Urinary Metabolites as Microbiome Diagnostics



Monitor the
development of
appropriate
microflora in
infants



Carolyn Slupsky



**What have we
learned:
We're not alone!**

Opportunity: **BioProfessionals**



Our minions!



**Business
Opportunities**

Opportunity: at some point we all are fragile

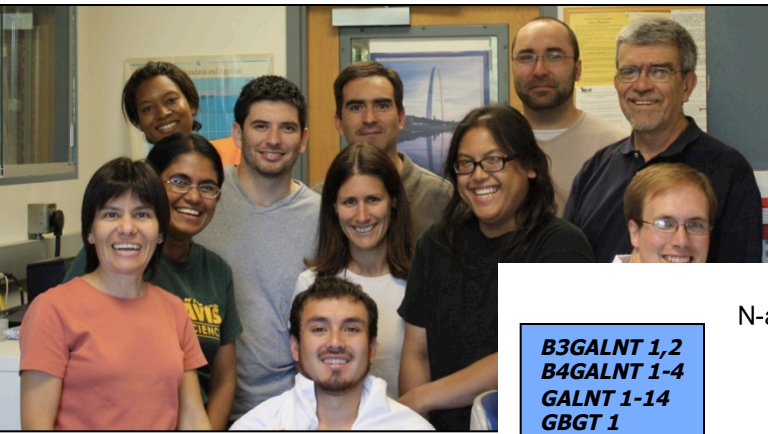


Personal microbiota management:
premature infants to weaning
from athletes to hospitals

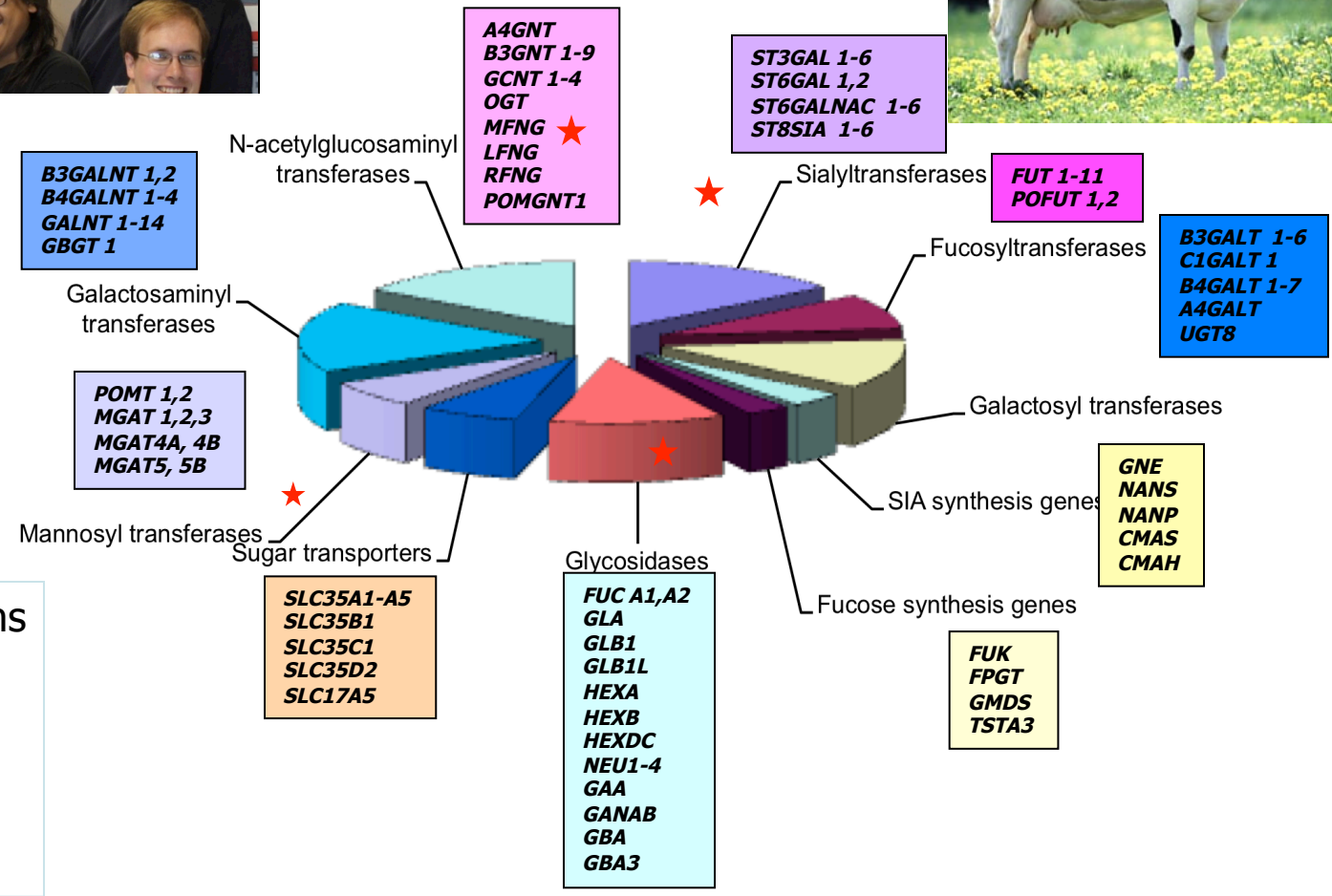




Oligosaccharide Biology in Bovine



Medrano Lab



SNP in coding regions
 ↓
 Genotyping array
 ↓
 Association study in 500 cows

UCD Milk Processing



Daniela Barile
Asst Prof FST



- Pilot-scale filtration from MMS AG Systems
- Fourier Transform Advanced IR MilkoScope
- Speed vacuum MiVac Quattro Concentrator
- Industrial freeze dryer



Conflict of Interest Statement



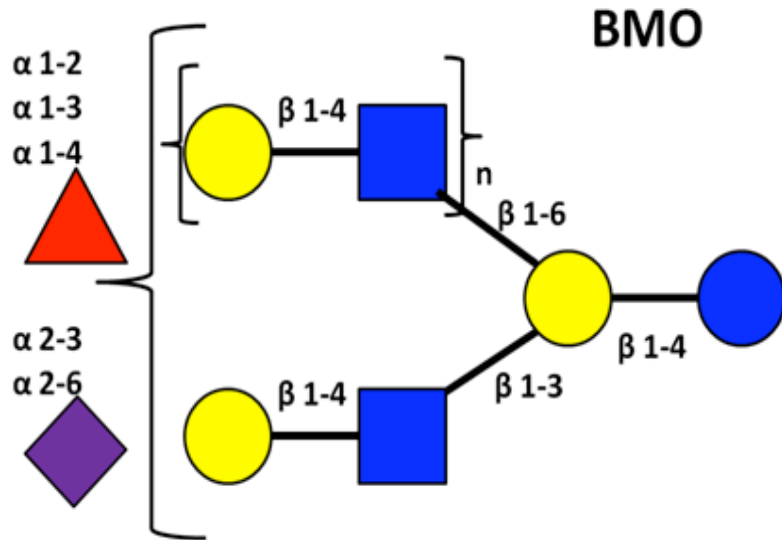
Partnering with Nature

Evolve Biosystems, Inc. is dedicated to revolutionizing patient care for distressed populations through novel dietary therapies.

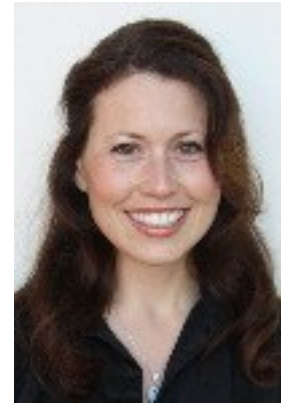
info@evolvebiosystems.com



Does consuming BMOs modulate an adult intestinal microbiota?



- Fecal microbiota Δ
- Metabolomic analyses
- “Well-being”



Jennifer Smilowitz



Carolyn Slupsky
Asst. Prof FST



Daniela Barile
Asst Prof FST



Dairy Research Institute

The Breast Milk, Gut Microbiome and Immunity (BMMI) Project

BILL & MELINDA
GATES foundation

\$8.2M/2yr
Launch in Feb

Food
(breast milk)

UC Davis Team
David Mills (PI)
Bruce German
Carlito Lebrilla

Ruslan Medzhitov
Yale



Jeff Gordon Wash U

Rob Knight
U. Colorado

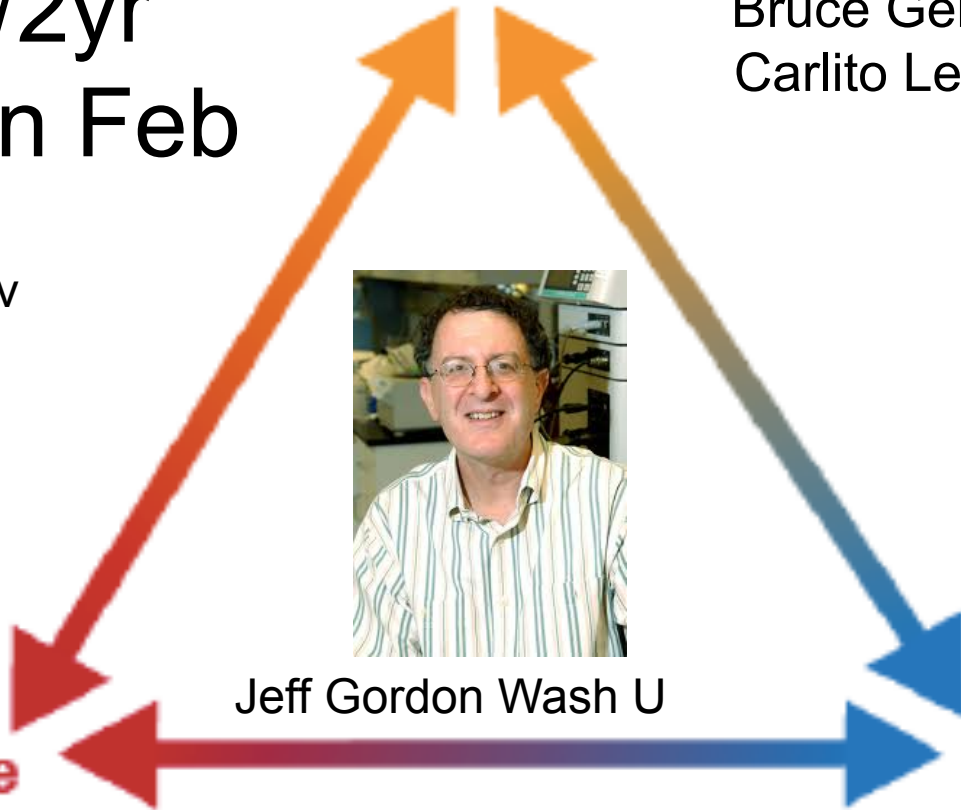


Immune
system

Gut
microbiome

Jeremy Nicholson
Imperial College London

<http://ffhi.ucdavis.edu/>



Infected Mucosa



Ho: mucosal immunity is enhanced and inflammation suppressed in chronically infected HIV patients by a *Bifidobacteria infantis* enriched microbiota

NIH, Gates Foundation, Industry



Implications to Ag 2.0



- Selective Polysaccharides will become a new component of human diets.
- Estimate of daily dose $\sim 10\%$ of calories
- Total opportunity ~ 1 trillion calories per day worldwide
- A new quality target for agriculture: structure/function designed polysaccharides



Opportunity: 'Bugs' of Delight



From chocolate to coffee, wine to beer, yogurt to cheese, bread



UC Davis has history here



California is already the world's
leading center for food
fermentation



Today



Half of agricultural production and one third of food is currently simply lost or wasted* FAO 2011*



Imagine the Future



Safe, Nourishing, Delicious
Foods that **INCREASE** in
value with time





Infant Digestomics

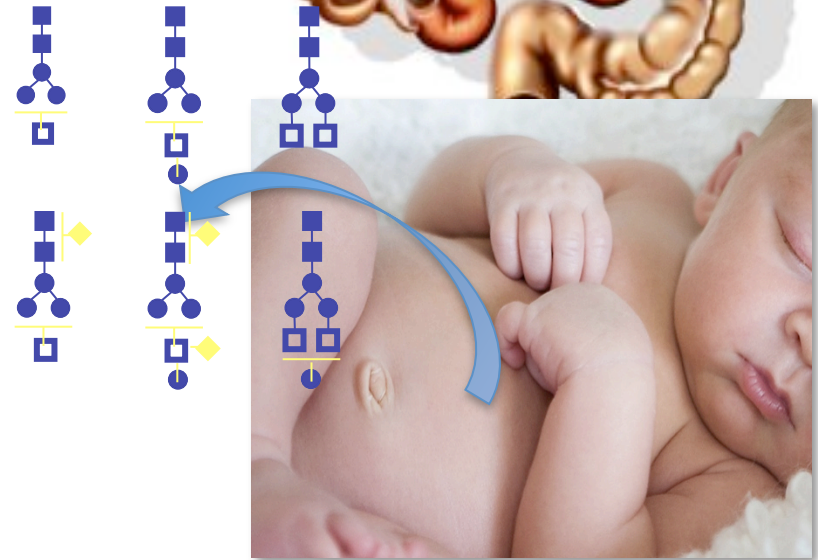
Infant Digestion as a Bioreactor

- **Digestion**

What does milk become in the baby?

- **Diversity**

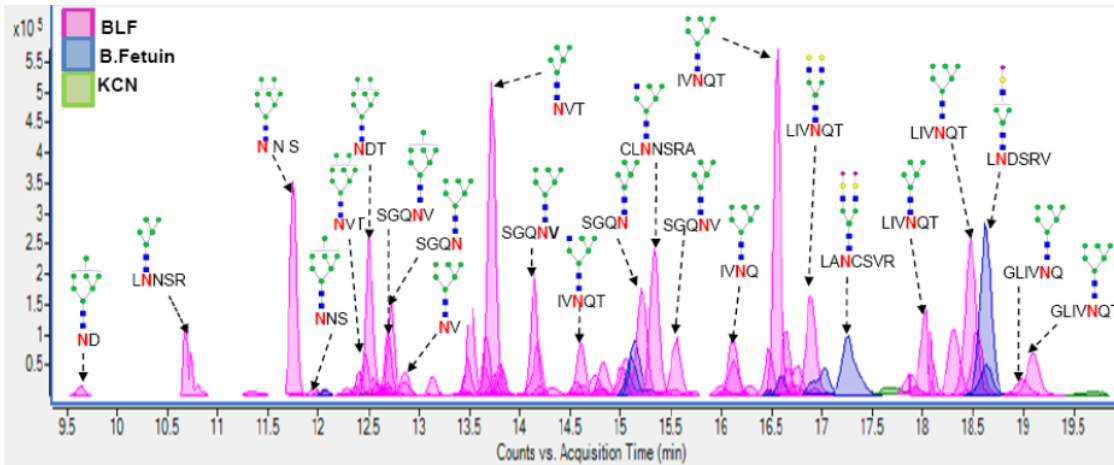
Are babies with altered health and development equally capable of digesting milk?





New View of Proteins

Milk Disassembles the Proteins into Bioactive Peptides



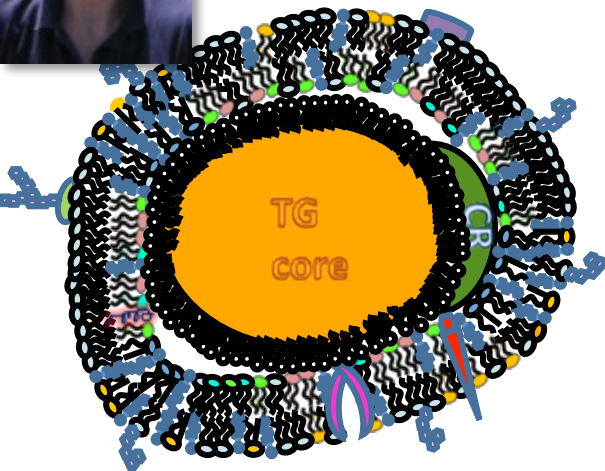
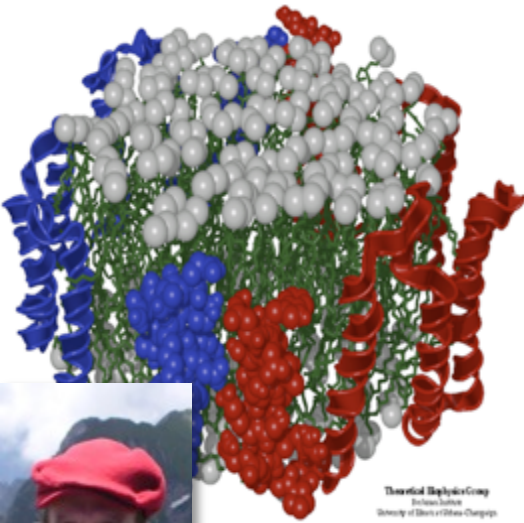
- **Sequence Specific Functions**
Intestinal Immunity
Antimicrobial actions
Optimal barrier function



Target: Lipid Nanoparticles



- Milk contains 3 distinct lipid particle classes
- Milk supports HDL a model of bioactive nanoparticles
- Self-assembly of lipid structures in the gut regulates absorption



Metrics



We are not the same

We don't all respond

Health benefits must be

DEMONSTRATED!

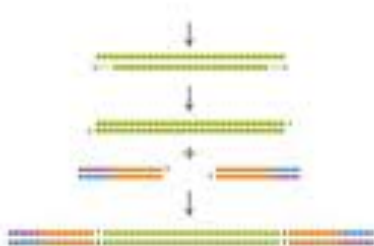


<big

t

The machine in health's future

- Genotyping is poised to become as easy as blood typing



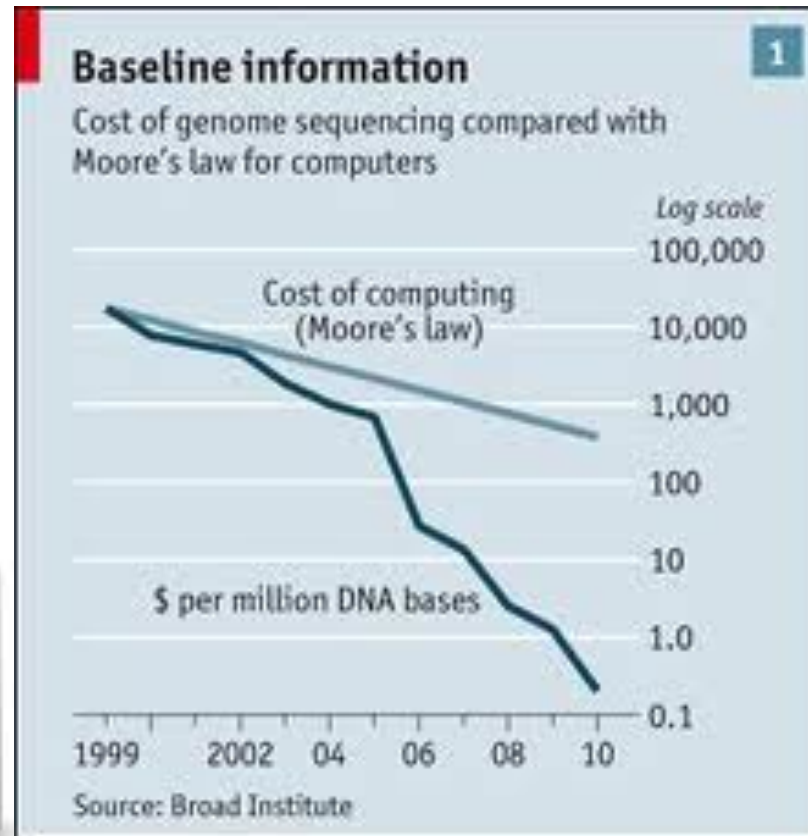
Library Preparation



Cluster Generation



Sequencing by Synthesis





Is Genotyping Enough?

- NO
- Science: multi-genic conditions, age, environment
- Economics: we will only pay for demonstrated improvements in health



Perfect Phenotypes



- Not just Genetics



20 years
10,000,000
calories



Goal: Diagnostics of Health



***You cannot manage What
You cannot measure***

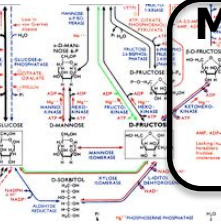
'Measure what is measurable,
and make measurable what
is not so', *Galileo Galilei.*

UCD Phenotyping People

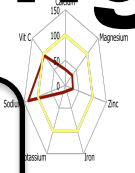


The Metrics of Human Health

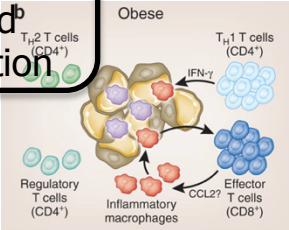
Metabolism
Glucose
Lipids
Glycans



Nutrition
Vitamins
Minerals
Amino acids



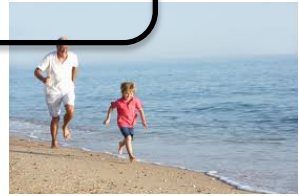
Immunity
Innate
Acquired^b
Inflammation



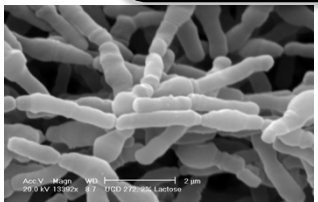
Sensation
Taste
Olfaction
Trigeminal



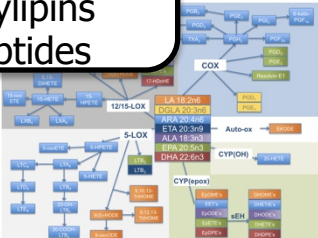
Activity
Sleep
Calories



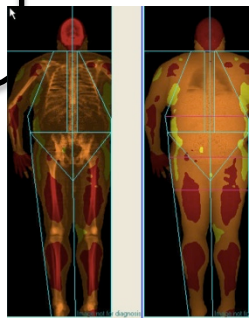
Microbiome
Genetics
Metabolites
Conjugates



Signaling
Endocrine
Oxylipins
Peptides



Anthropometry
Bone
Muscle
Adipose

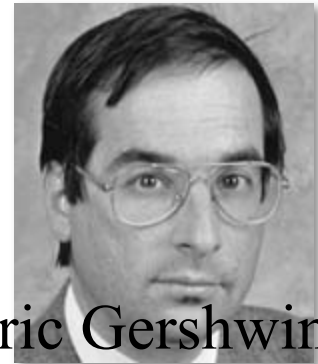


Immunology Diagnostics



Immune Senescence in Aging

Vaccination response



Eric Gershwin

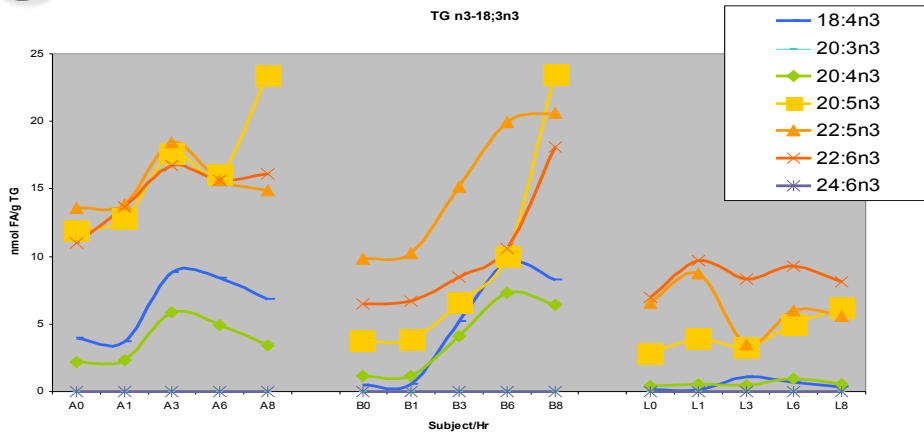


Nutritional Phenotype

Omega Status

**Its not about the fish
you ate**

**Its about the omega 3
you accumulate**



Opportunity: Metrics of Health



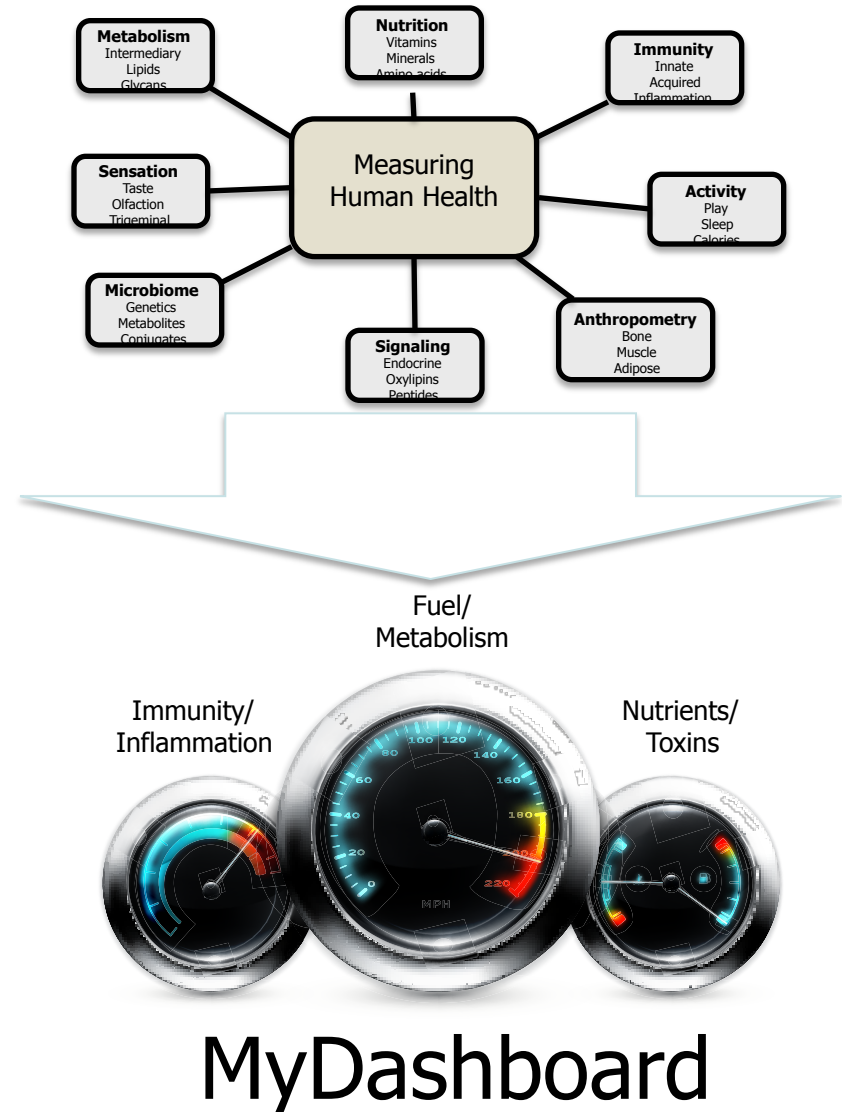
Validating Food Efficacy needs
measurement:
fast, cheap, often, accurate!



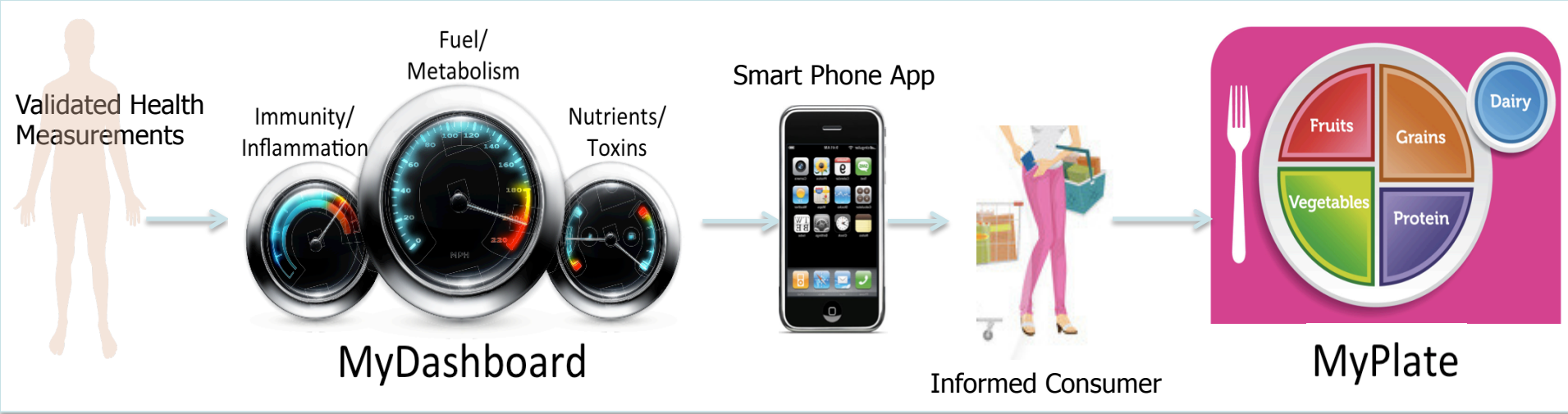
Make the Science Usable



- Convert scientific assays to simple health measures
- Deliver actionable guidance



In Practice



Different Decision Makers



■ Disease Care

Professional Clinician



■ Health and Prevention

Consumer





In Practice

Personalizing Health and Diet Education

A California Solution for Children's Health



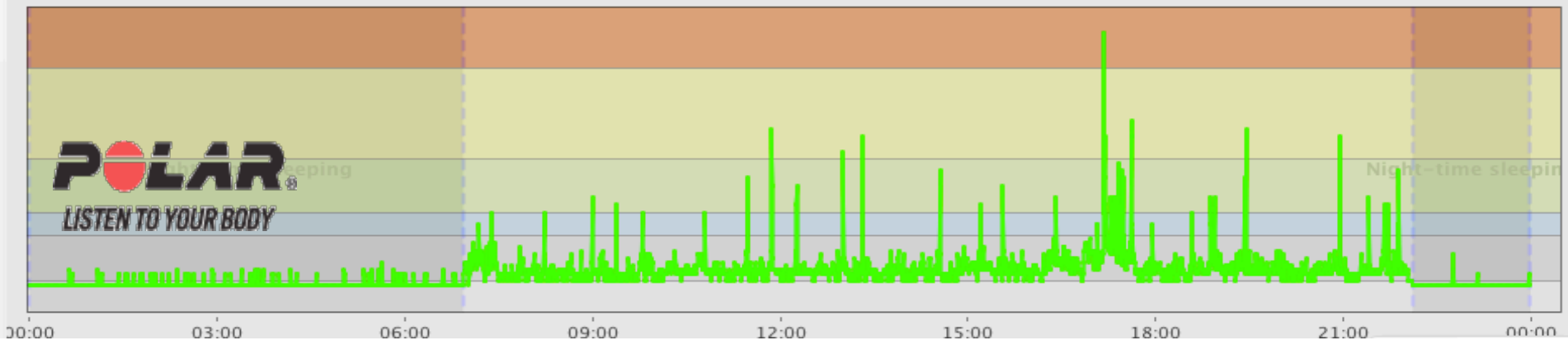
seschaefer@ucdavis.edu



Health Assessment



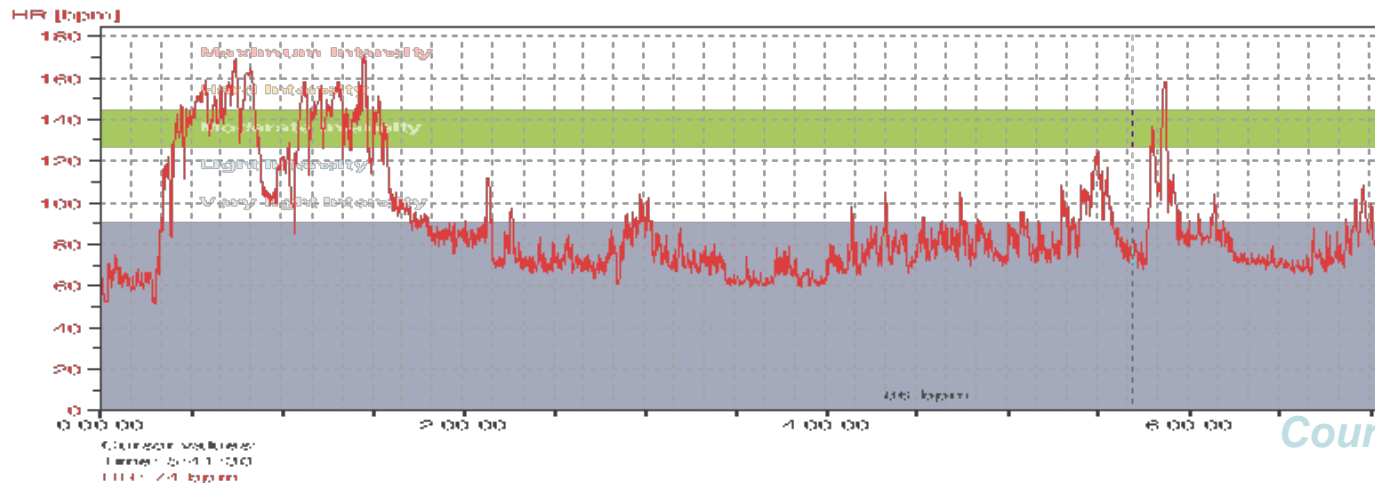
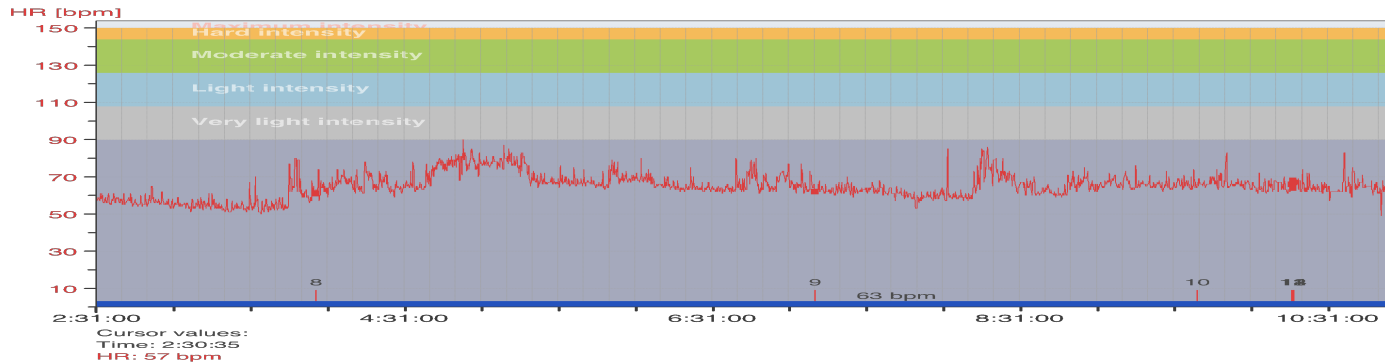
Activity and play in children



Physiology Assessment



Heart rate monitors can track performance



Diet



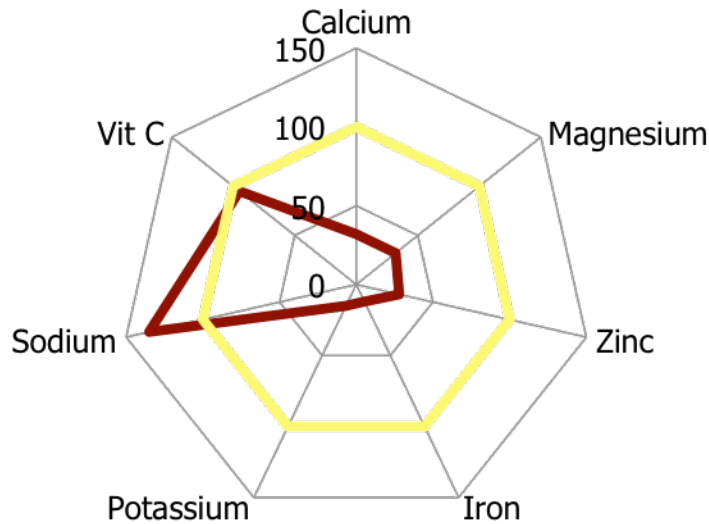
Children have no idea of the quality of the diets that they choose to eat!



Diet Assessment



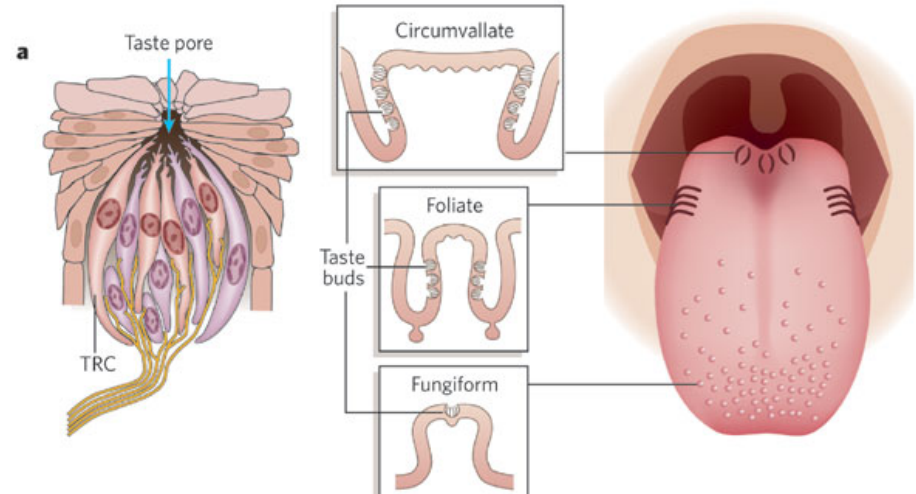
Provide: Nutrients, calories and safety of personal diets



Preference Assessment



Personalize the ability of kids to taste foods



Give children knowledge about themselves and their senses

FFHI Education Program



Getting Personal: The New Health Education

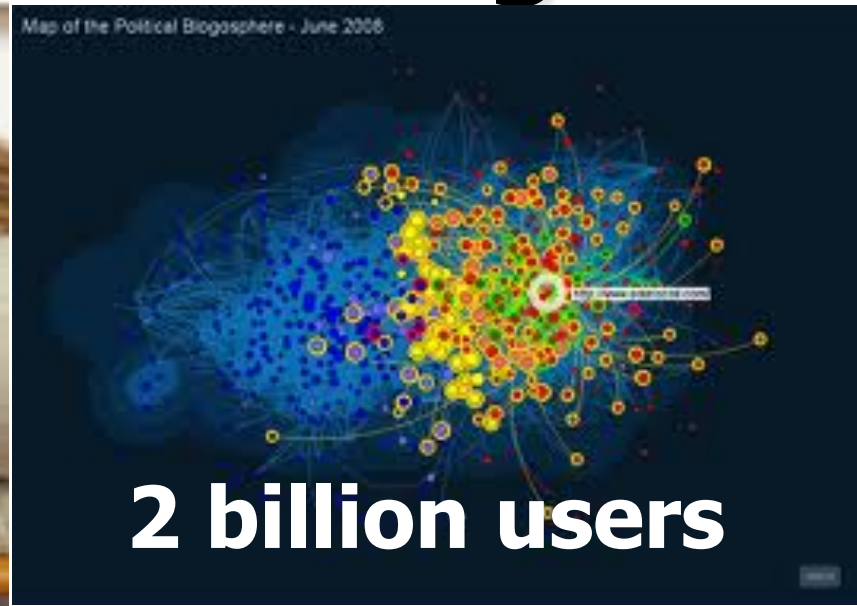
1. Getting health assessment tools into schools
2. Training teachers in personal health
3. Experiential K-12 learning
 1. Hands-on health measurement and learning
 2. Personal health gaming





Opportunity: Education of Health

Personal health education
from schools to blogs



\$500 billion budget



Personalizing Diet and Health



- will solve the major health problems of the USA
- will decrease managed health care costs dramatically
- will create unprecedented value for the Agriculture sector



Industries and Innovations

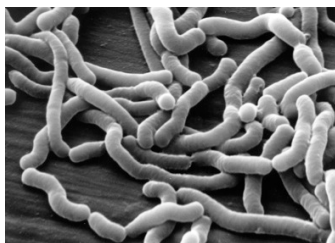


Companies offering New Varieties & Organisms:

Innovations in genetics lead to new varieties of plant, animal and microbial commodities. Microorganisms bioengineer next generation of food quality and safety.



New Device Companies: Innovations in principles, targets, unit operations and automation, become the guiding technologies for health monitoring, safety surveillance, environmental protection and diversity.



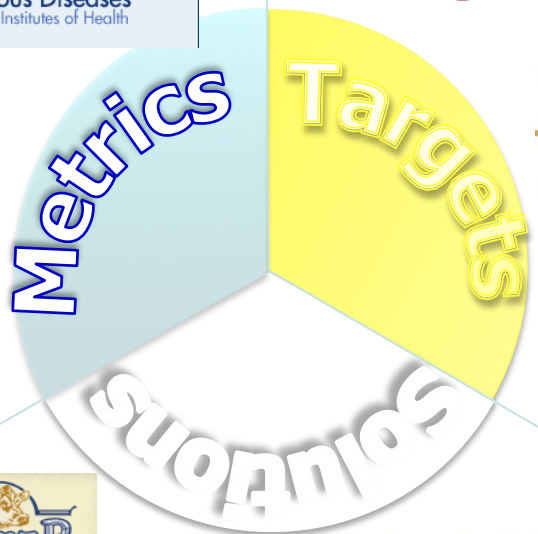
New Products & Companies: Marketing the Innovations from understanding human health diversity into personalized products, packages, devices, foods and food ingredients.



Service Companies: Innovations in information technologies assemble global datasets and individual monitoring to market: education tools, food choice and preparation, lifestyle guidance and health performance.



Support and Partners





Project Support and Collaborations

- UC Discovery CDRF – support
- DMI – support
- Nestle – Oligosaccharides & Support
- DSM – support and oligosaccharides
- Prolacta Inc. – human milk supplier
- Abbott - support
- Smithsonian – milk samples Evolution of Primates
- Agilent Technologies – Analytics – LC/MS of oligos
- Supelco – Analytics of oligosaccharide separation
- Lipomics Technologies – Analyses
- Joint Genomics Institute – Genomic Sequencing
- Cambridge University – samples
- WHNRC – Clinical trials
- NIH – Support
- NIEHS – Support
- USDA – Support
- NSF - support
- Hilmar, Sterling, Luprino – Oligosaccharides
- Teagasc Ireland Dairy – Oligosaccharides Support
- Gates Foundation - Support



Thank You