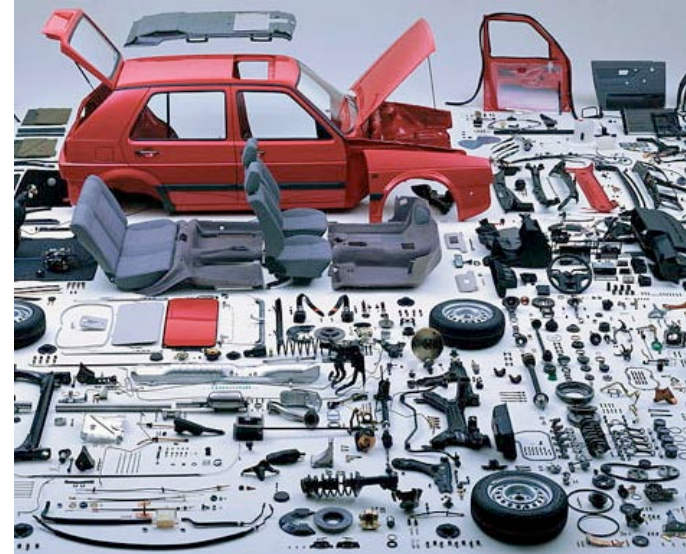


Diet, Health and Sustainability for the 21st Century: The need for Engineering



The 20th Century Science

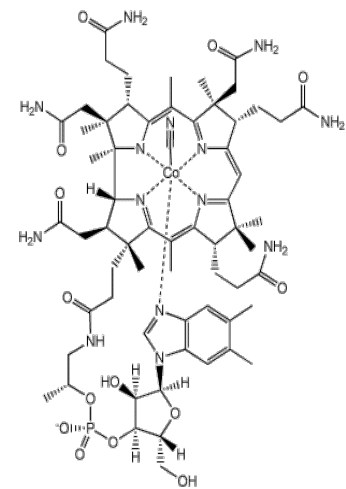
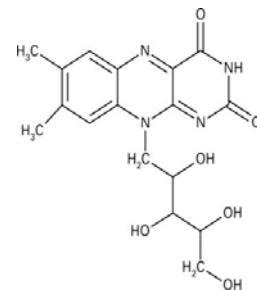
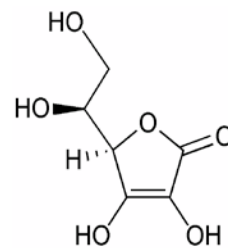
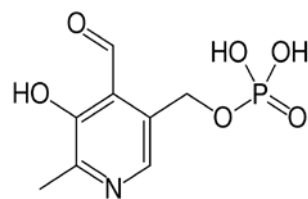
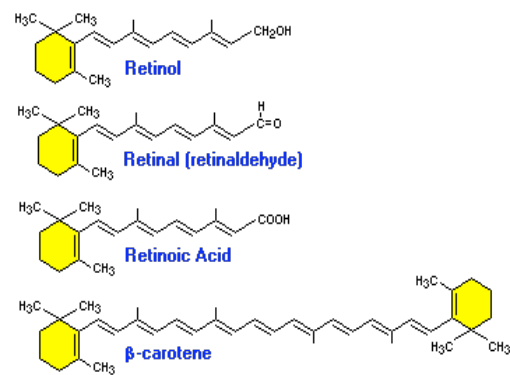
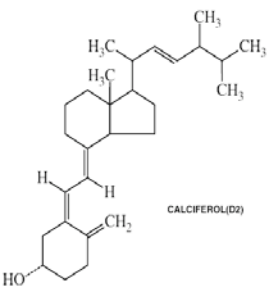
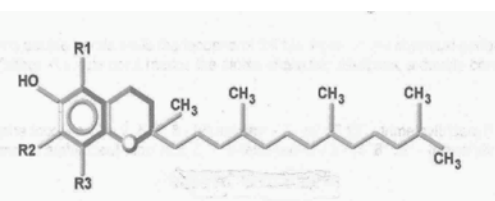
- Chemistry –Reductionist
- Industrialization of Simple Chemicals
- Key = Purify





Essential Nutrients

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

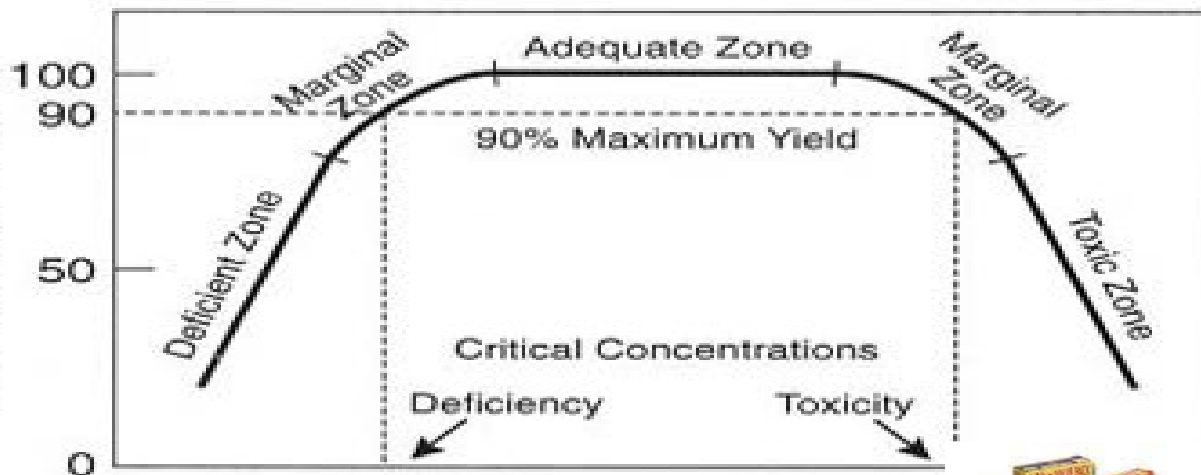


Nutrition's 1st Era



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

- Industrialized 'smart' foods
- Population Solutions – 'Overdose'





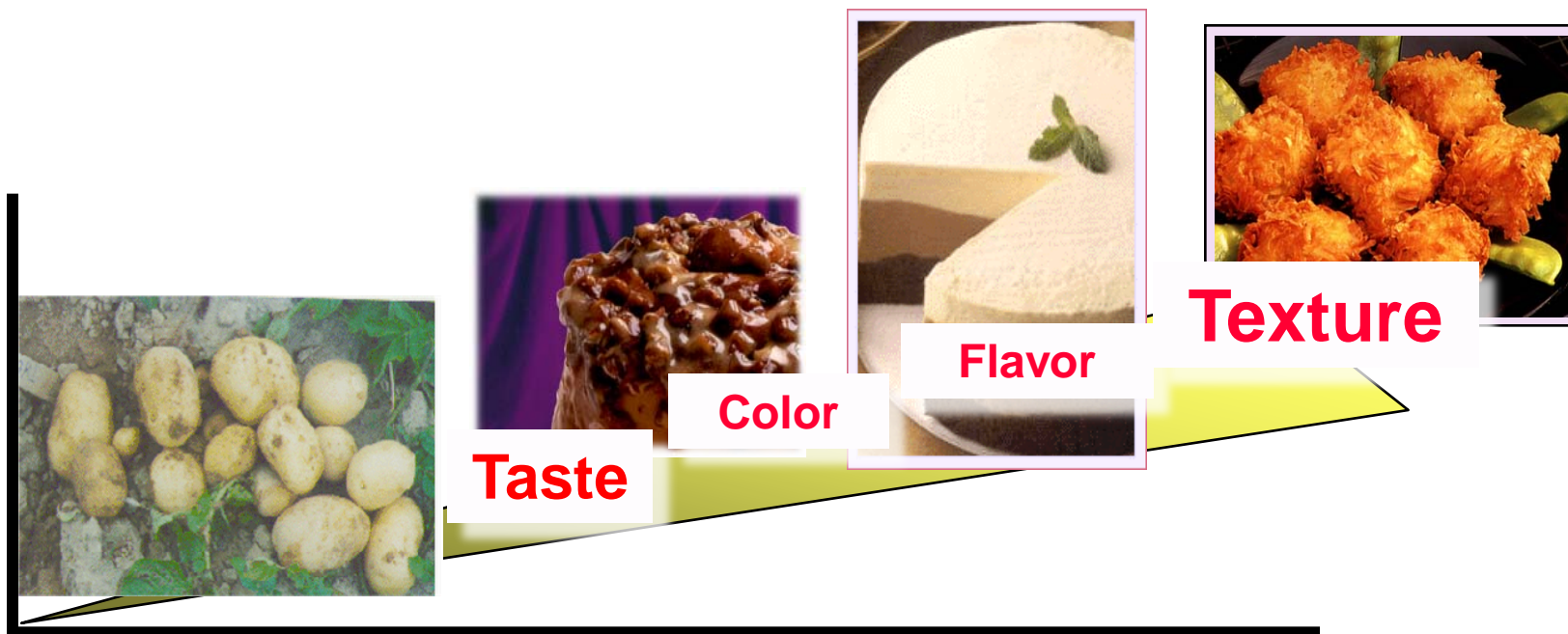
Key Reductionist Assumptions

- **Diet = Isolated Nutrients**
- **We are all the same**



Eliminating Nutritional Deficiencies Had Consequences

The food supply competes along an almost purely hedonistic (delicious) functionality axis.

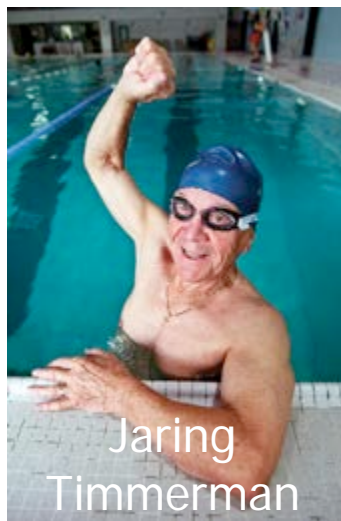


Hostile Environment?

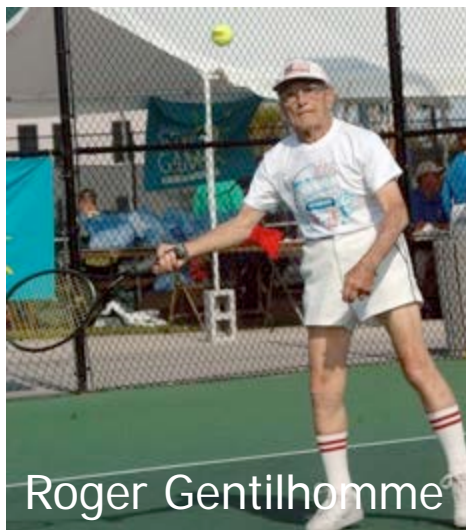




AND its not healthy
We should be enjoying the
greatest health in history
and some are,
.....but most are not



Jaring
Timmerman



Roger Gentilhomme



Institute Strategy:

A grant writing machine for:

Multi-disciplinary,

Multi-Investigator,

Collaborative,

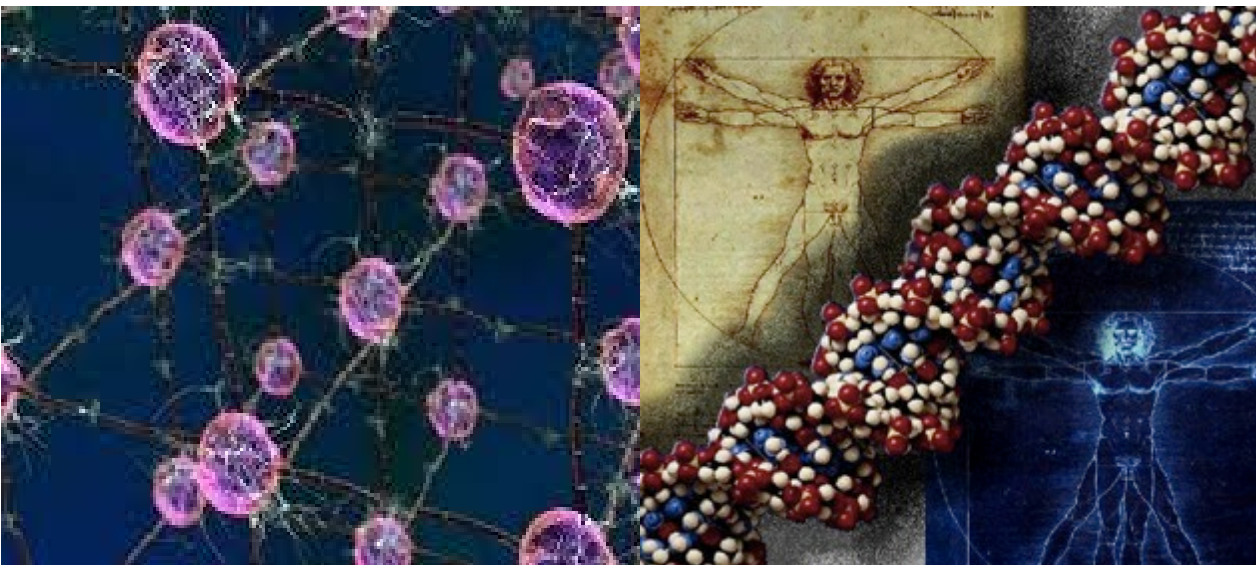
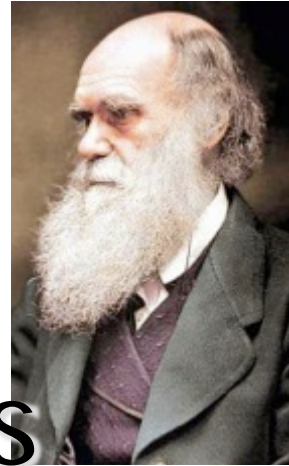
Program Projects

**UC Davis's
Comprehensive Cancer
Center opportunity:
Diet and Health for
Cancer patient
Management**

The 21st Century



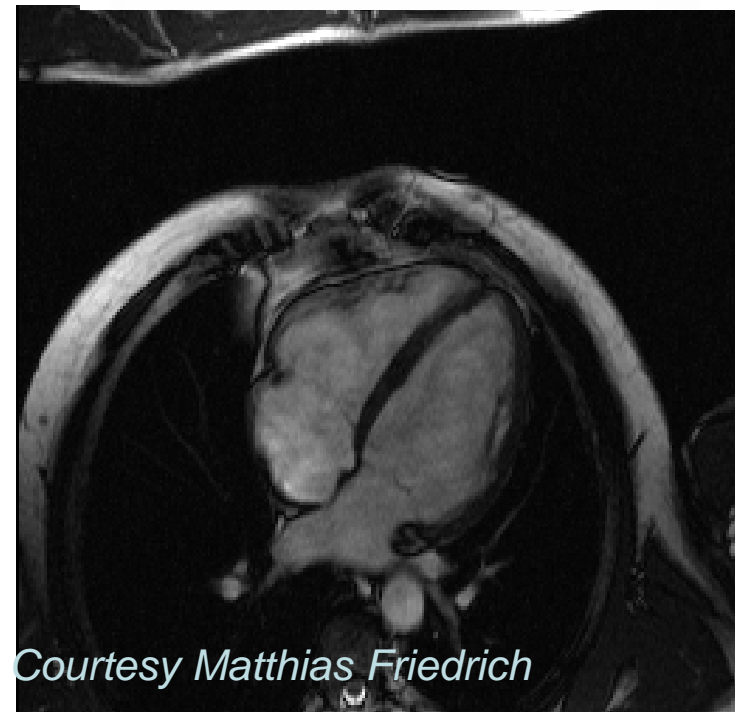
- Biology - Evolution
- Integrative
- Industrialization of Organisms and Systems for Individuals



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



Challenges



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

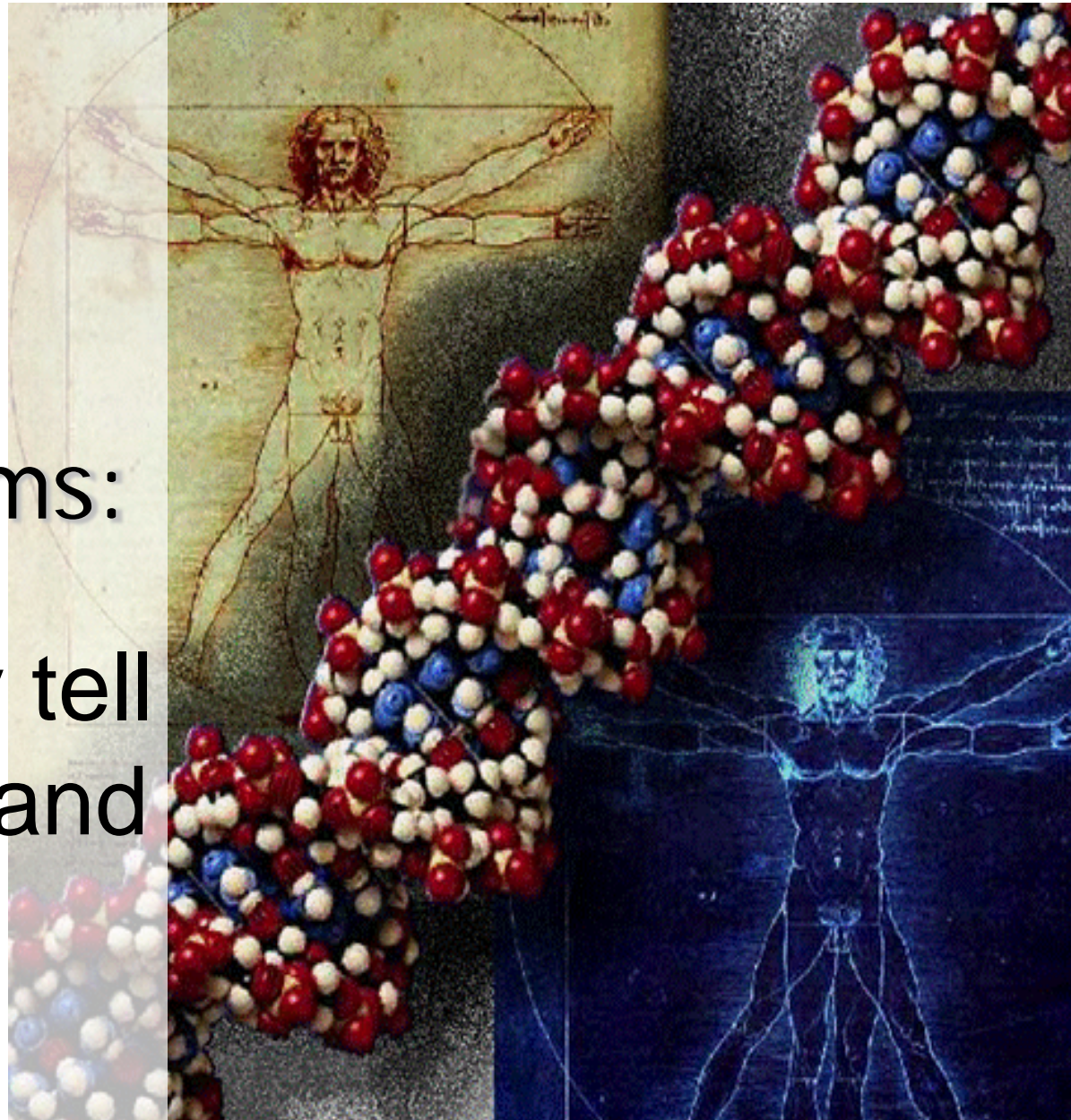




Genomics: the Footsteps of Evolution

- Humans:
- Plants:
- Animals
- Microorganisms:

What can they tell us about Diet and Health?



Evolutionary Nutrition

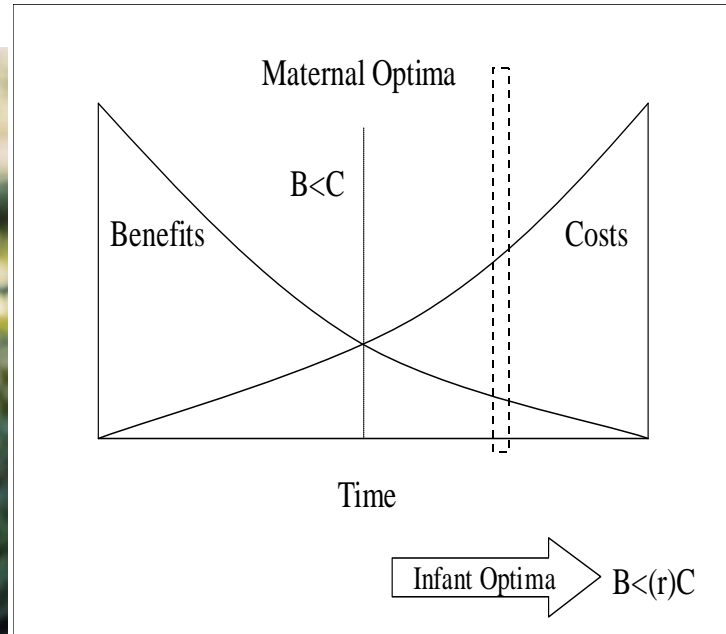


What evolved under the Darwinian Pressure to be Nourishing?

Lactation



The Darwinian Engine of Nutrition



Evolution of 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

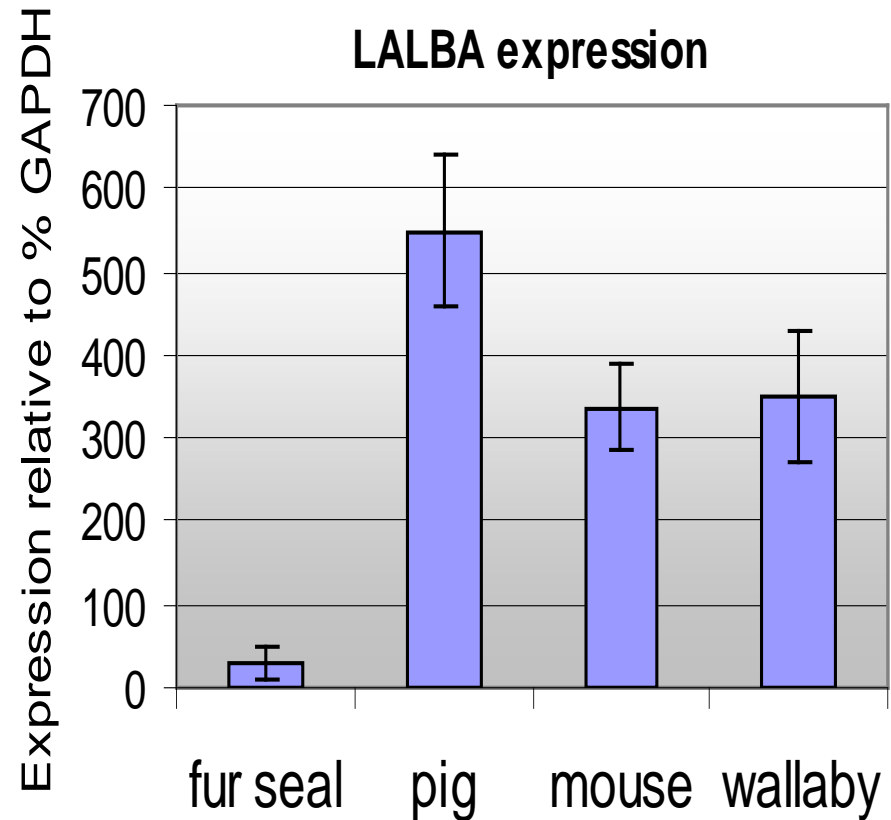
Milk's Genius



**Biodiversity of structure &
function brought to new
targets of health
e.g. α lactalbumin**

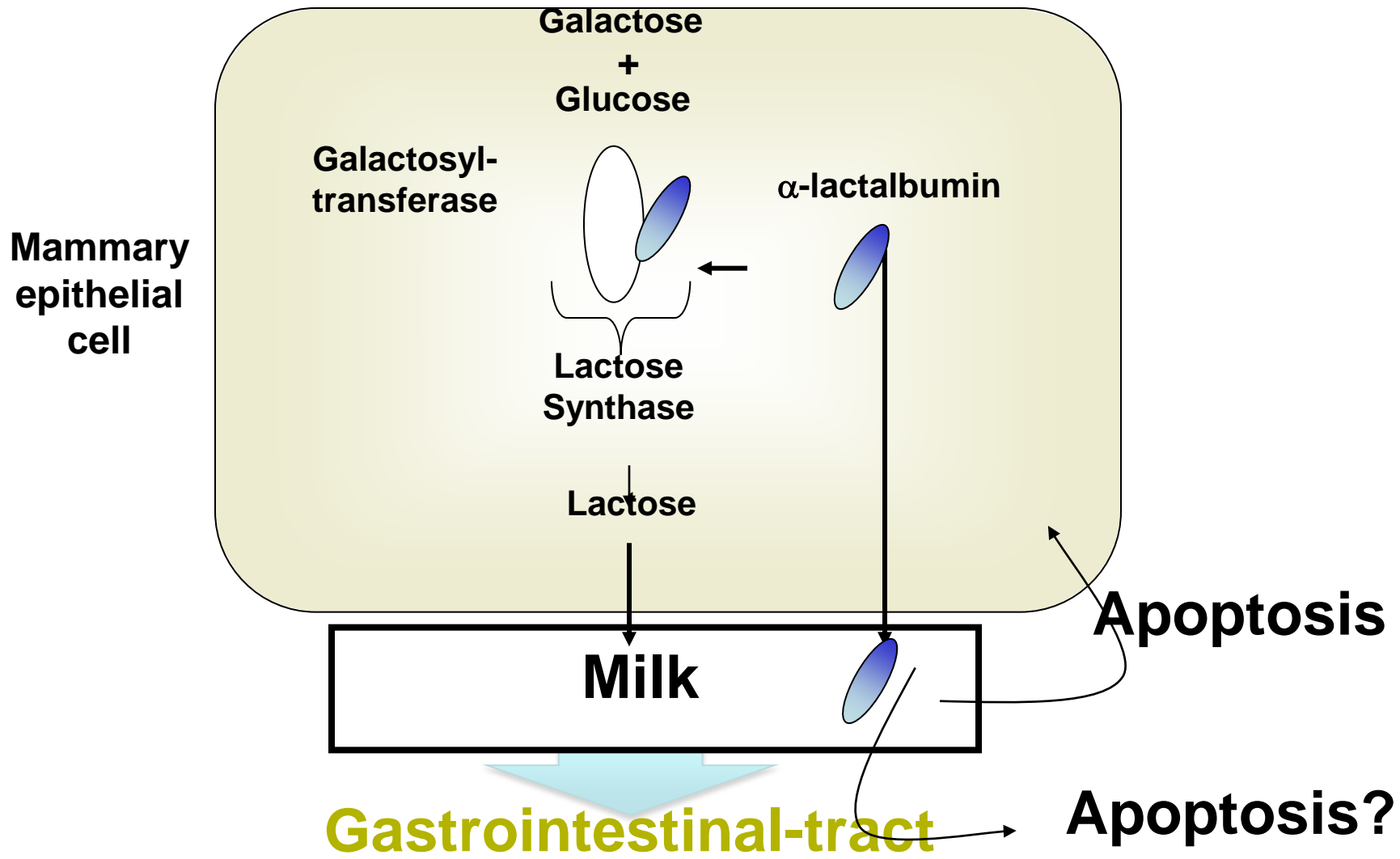
A Lactalbumin -

- The absence of α Lactalbumin is a unique trait of the Foraging Fur seal
- Is α Lactalbumin the switch for involution





Alpha lactalbumin

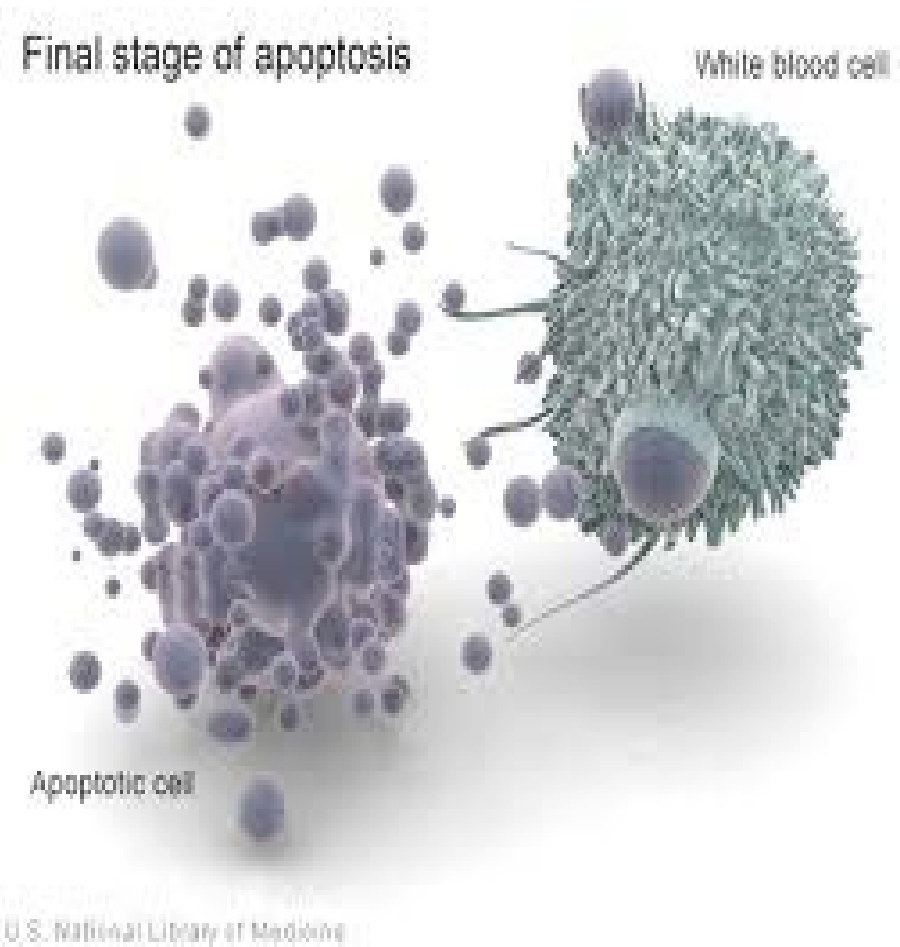


Why apoptosis?



Apoptosis is
controlled cell
suicide
Critical for:

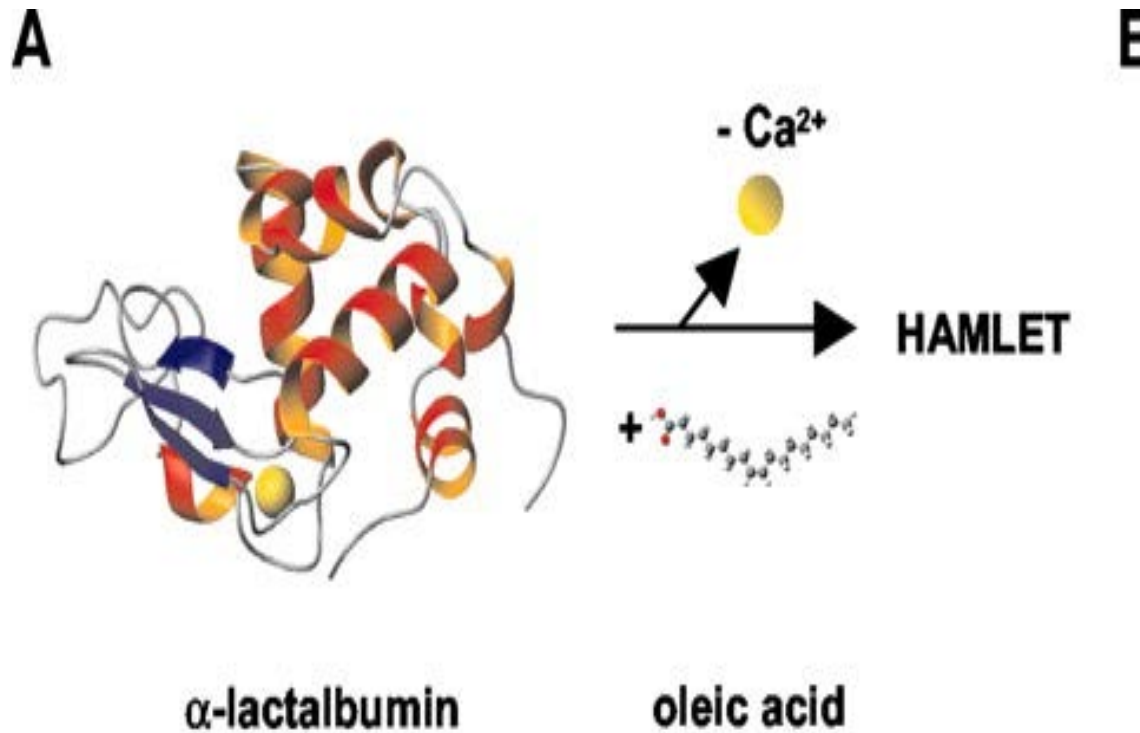
- tissue remodeling
- pathogen elimination



Nanotechnology from Evolution



HAMLET: A Novel result of Molecular Evolution in Milk Bioguided by Digestion

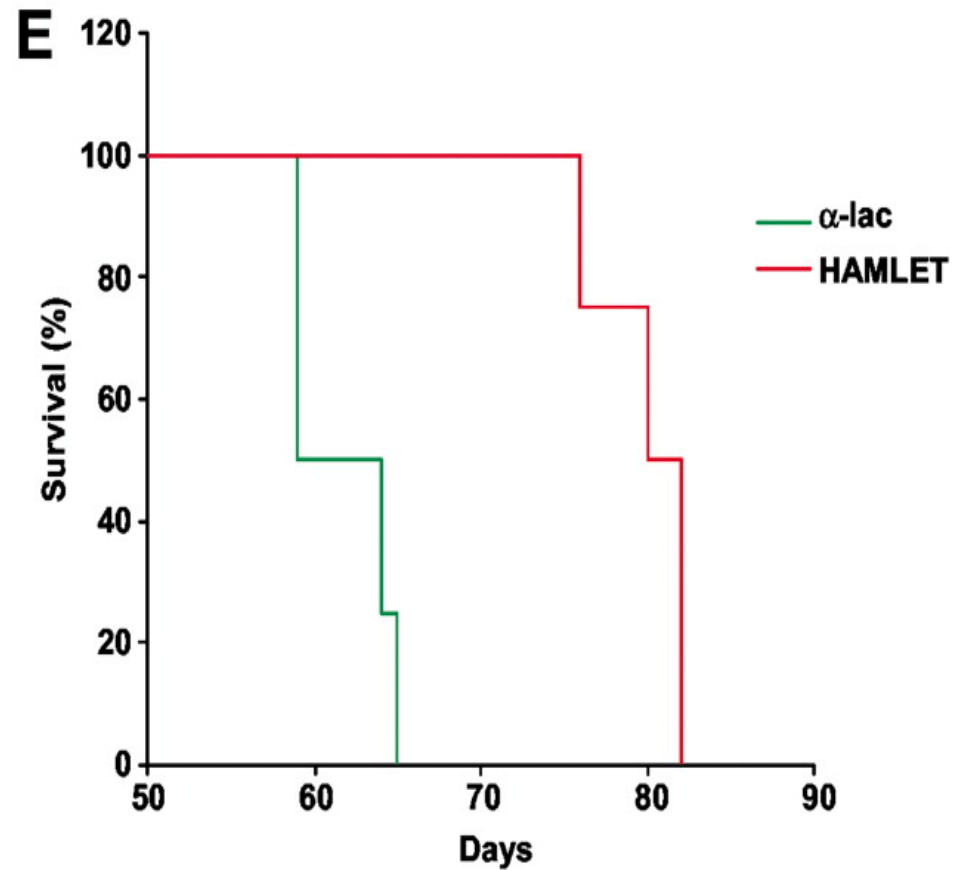
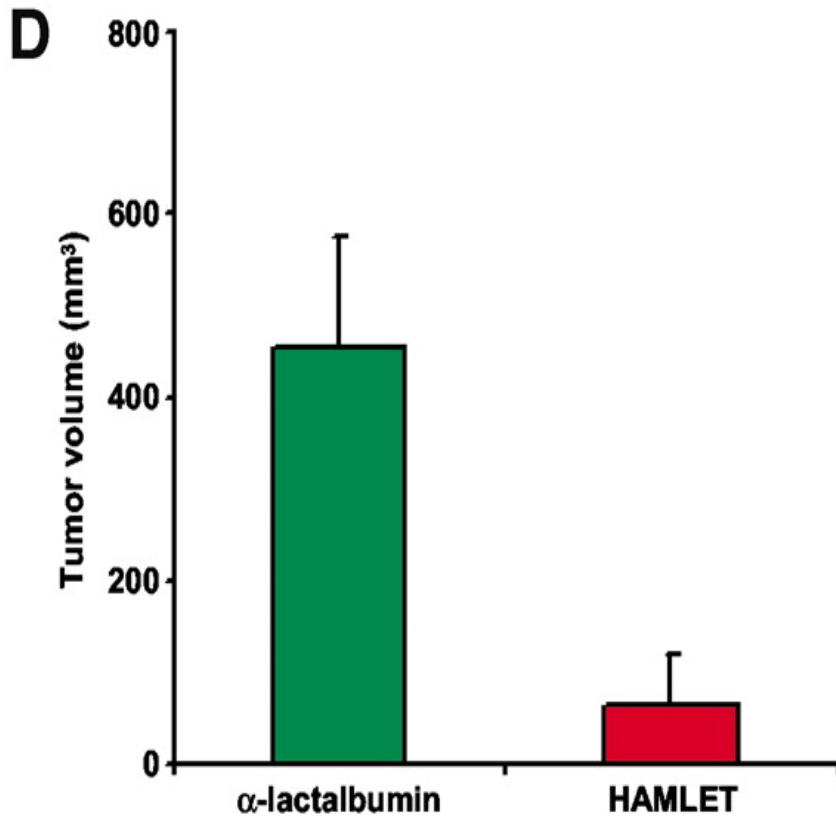


12

12



HAMLET: Eliminating Cancer cells *in vivo*



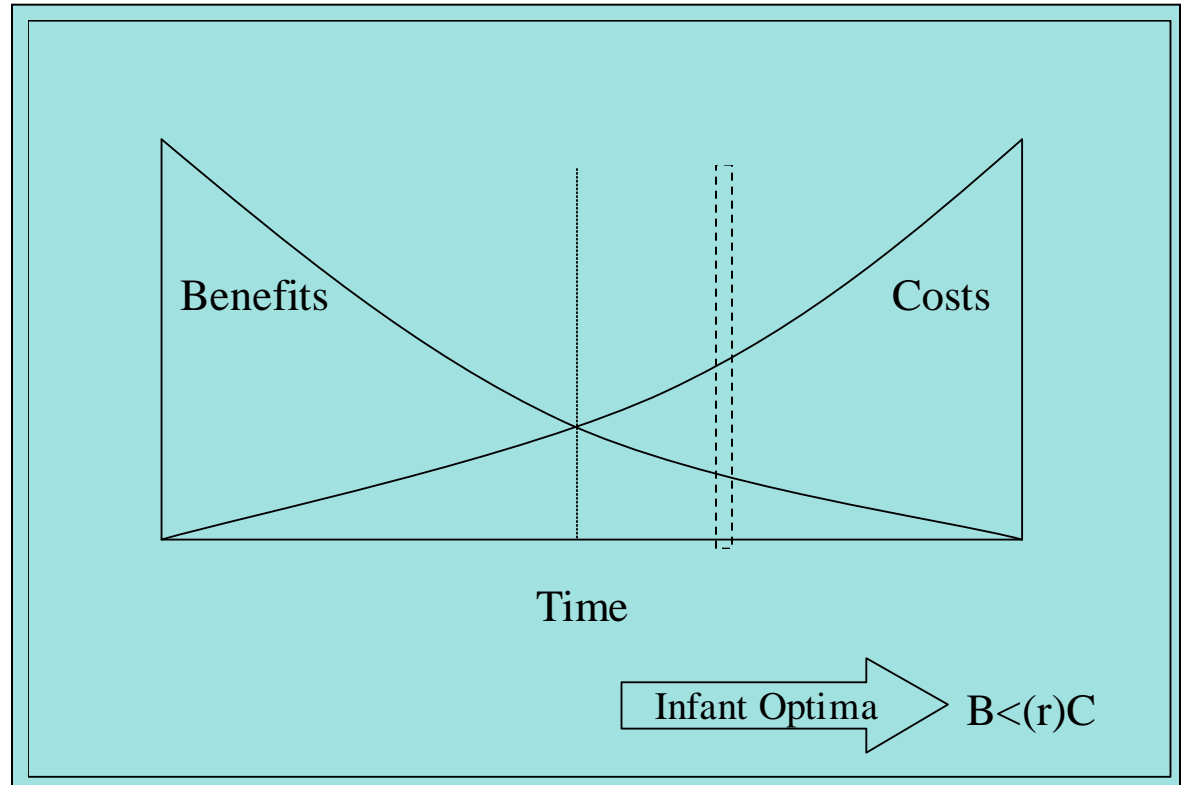


Proof of Principle: milk in action

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!

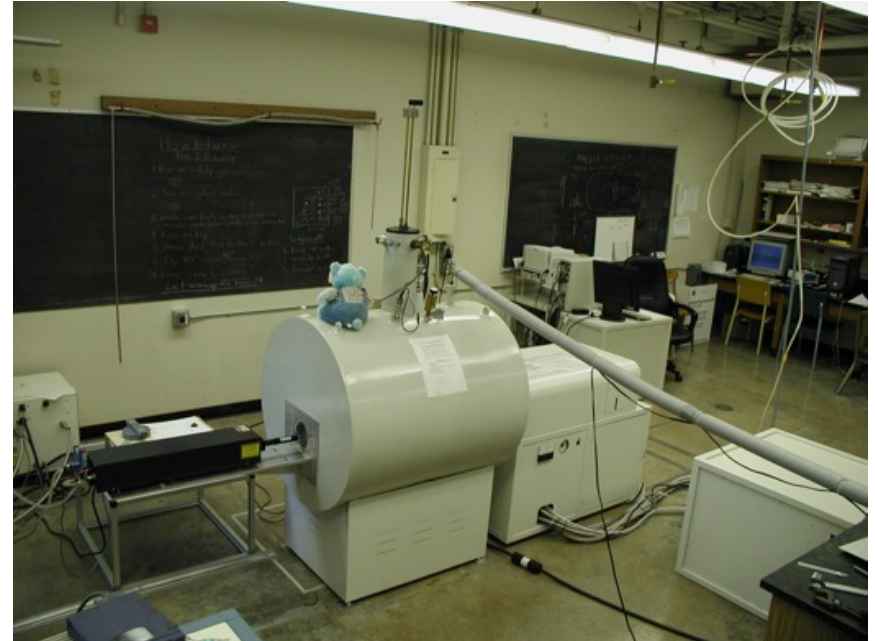
- What are they?



Glycobiology



Milk Oligosaccharides

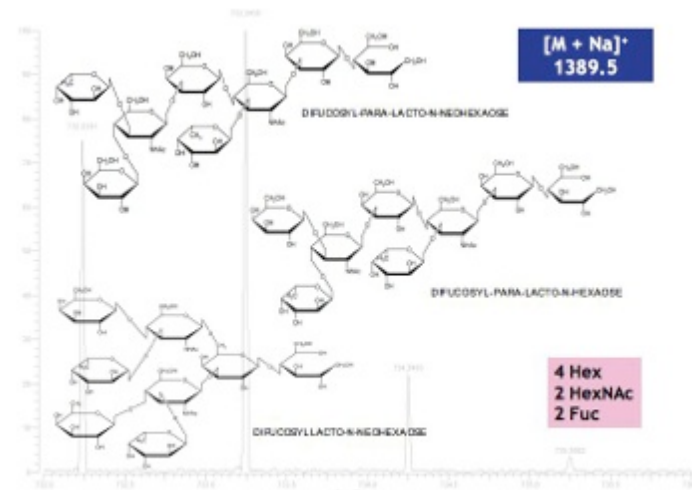
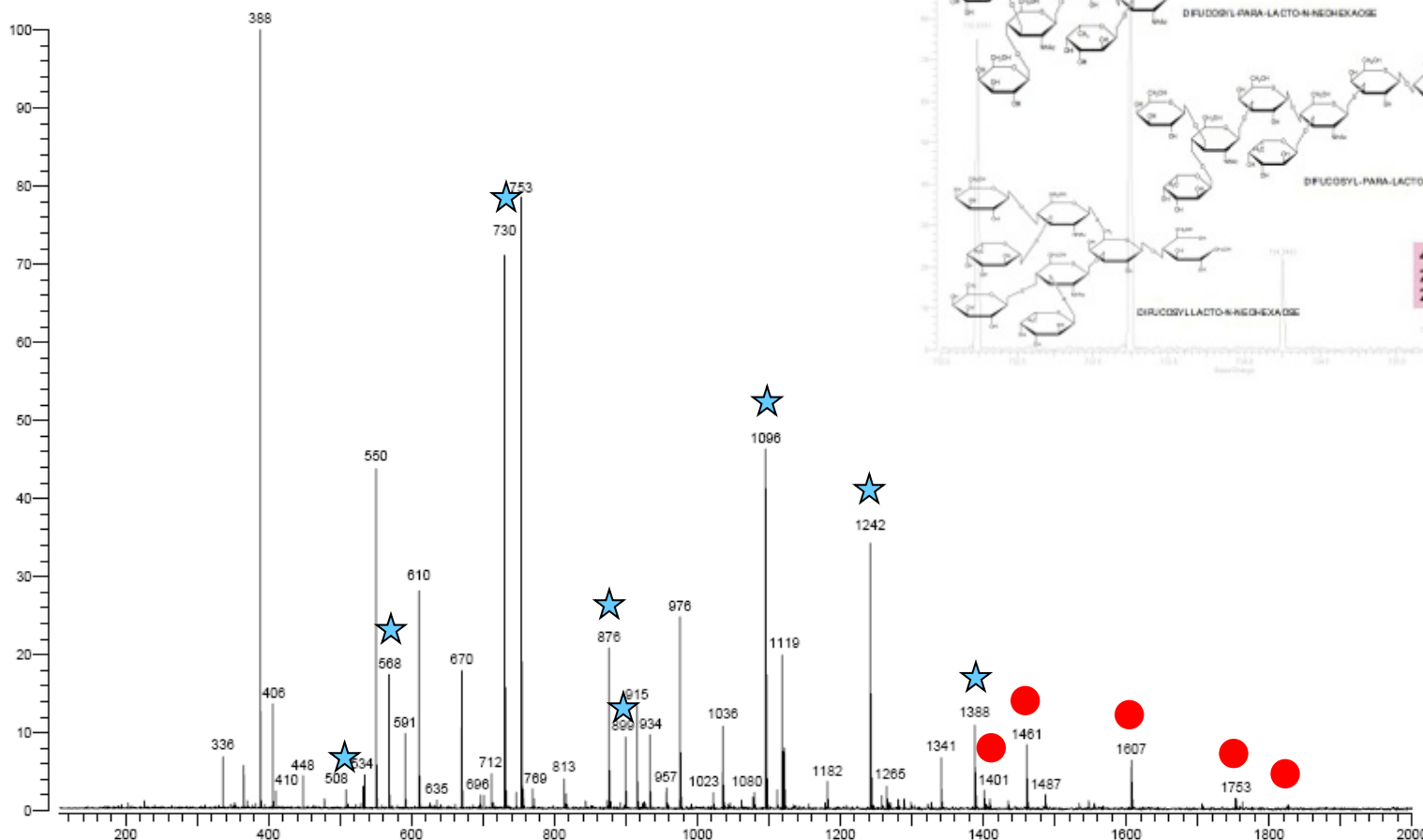


Carlito Lebrilla

- World's Leading Analytical GlycoChemist



Mass Spectra of Human Oligosaccharides





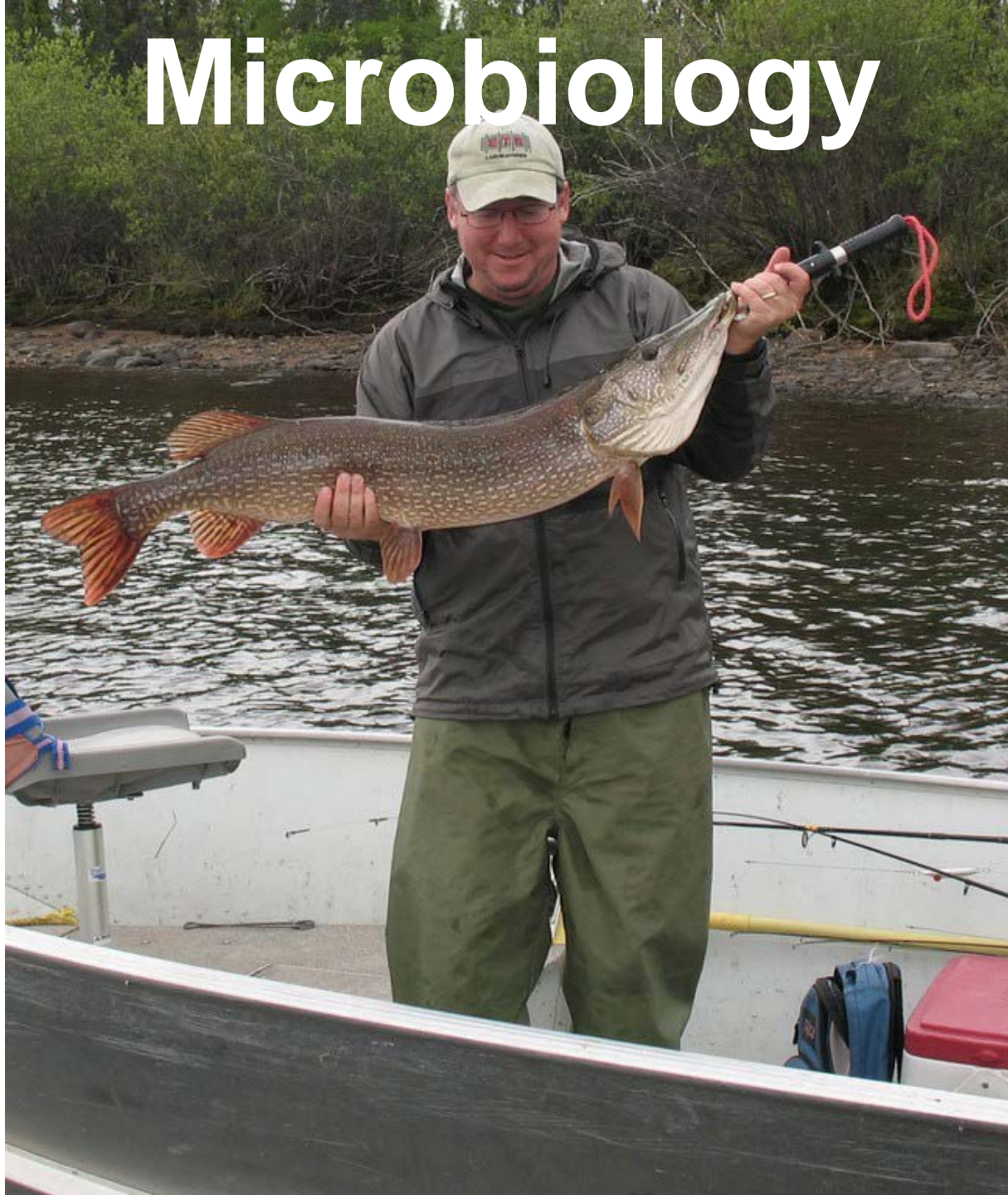
Functions of Milk?

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

■ Why?



Microbiology

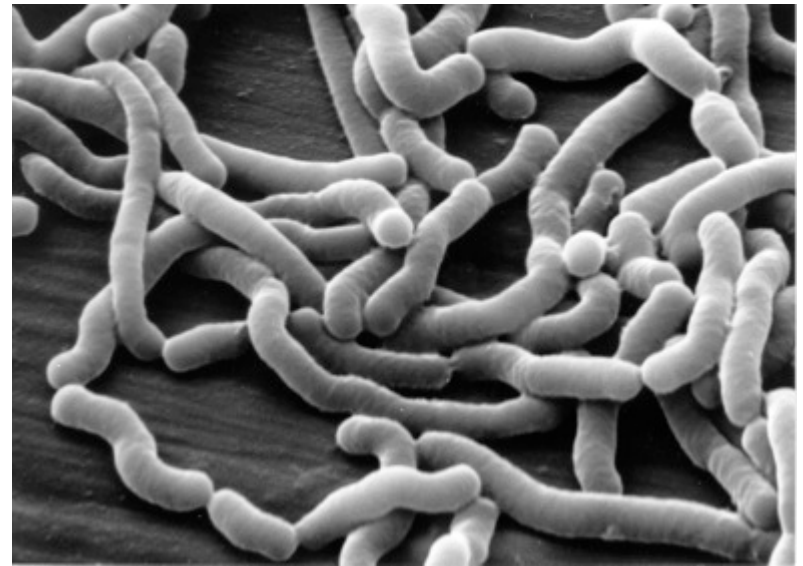
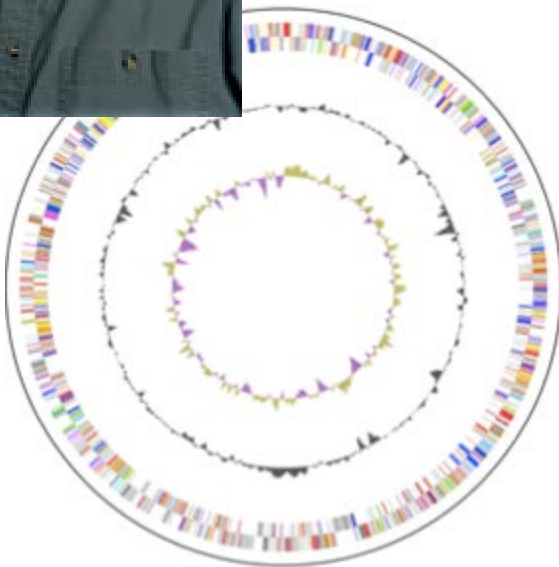


Bacteria?

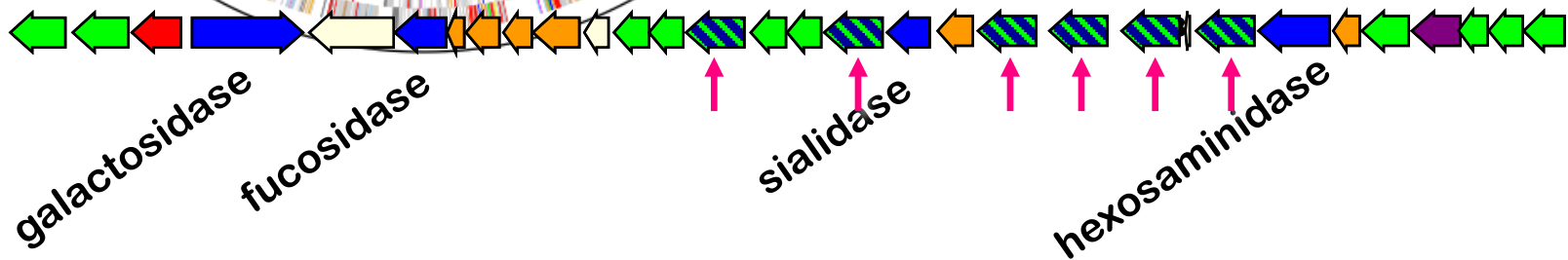
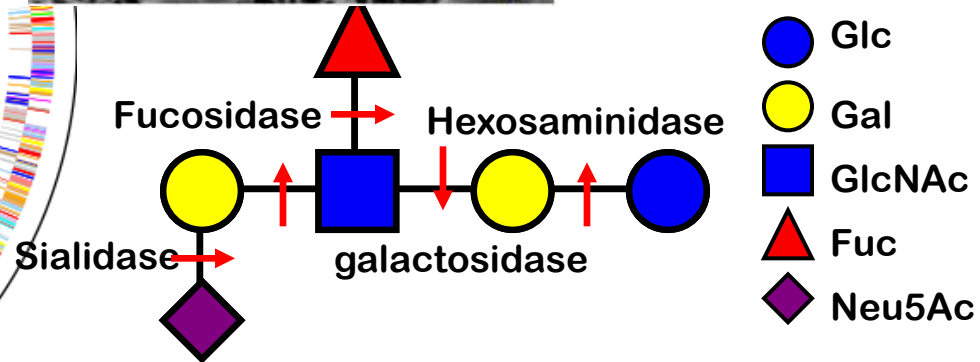
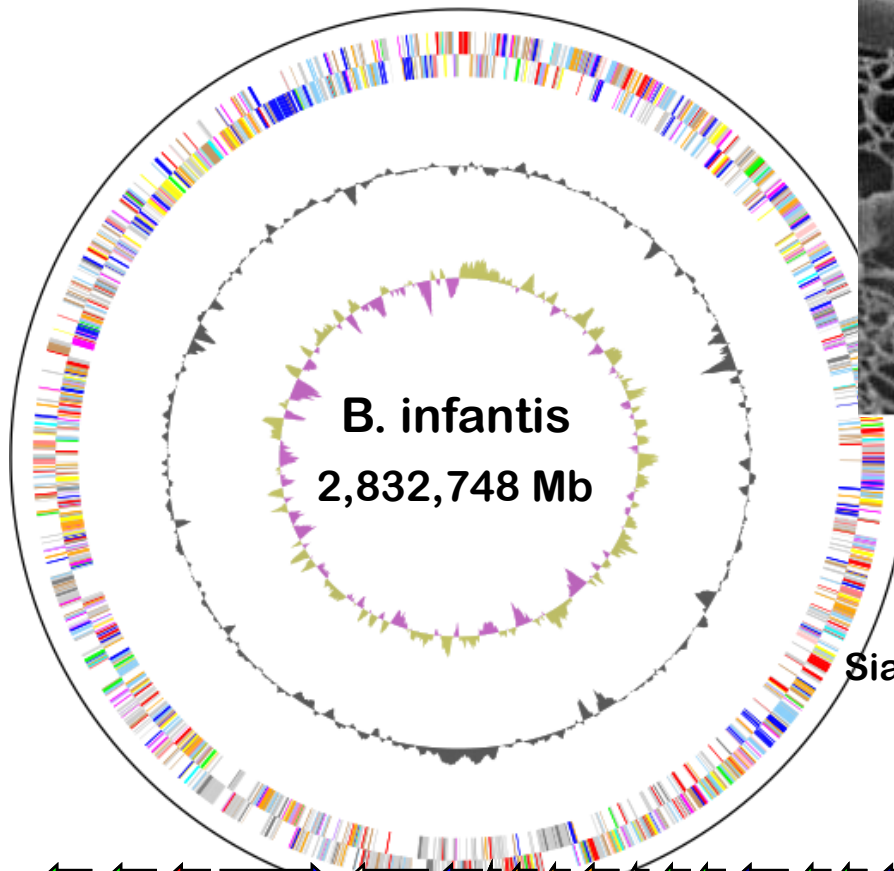
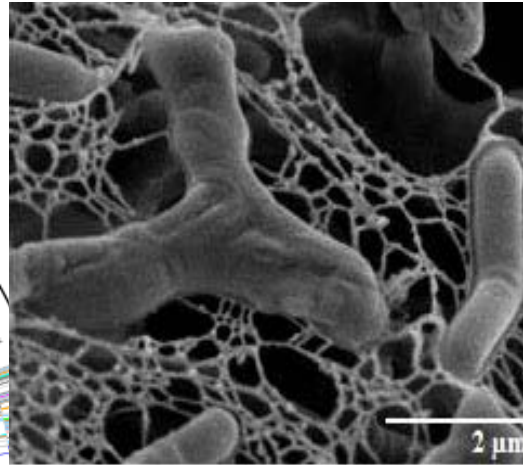


David Mills

Structure, Function and Health
Benefits of Food Borne Bacteria



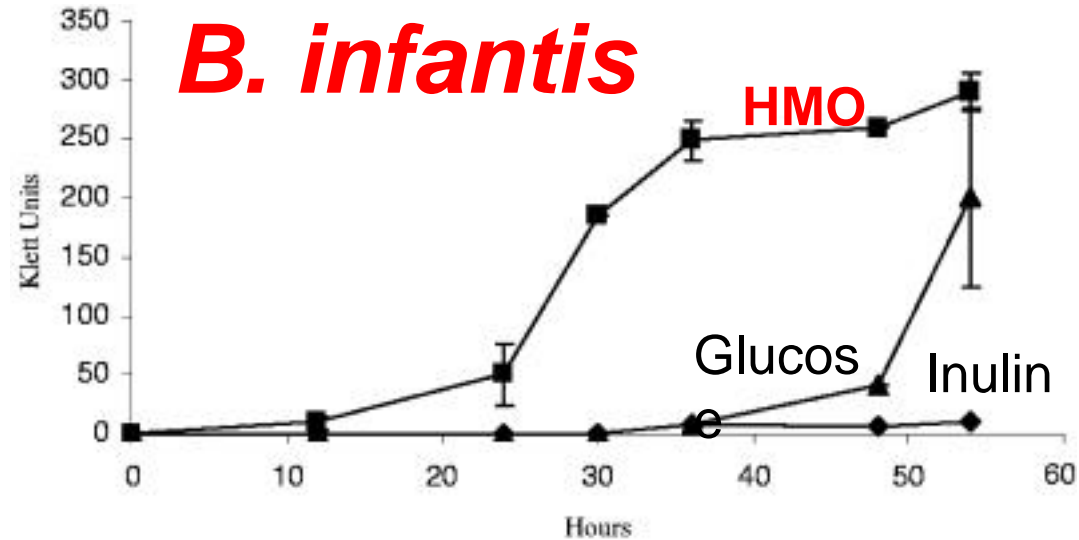
Bifidobacterium Infantis



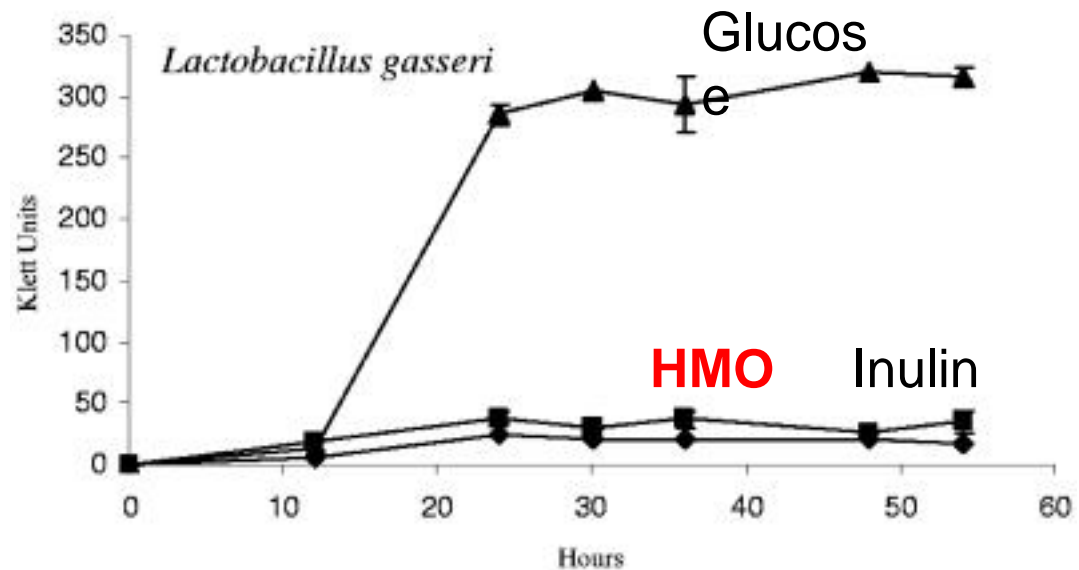
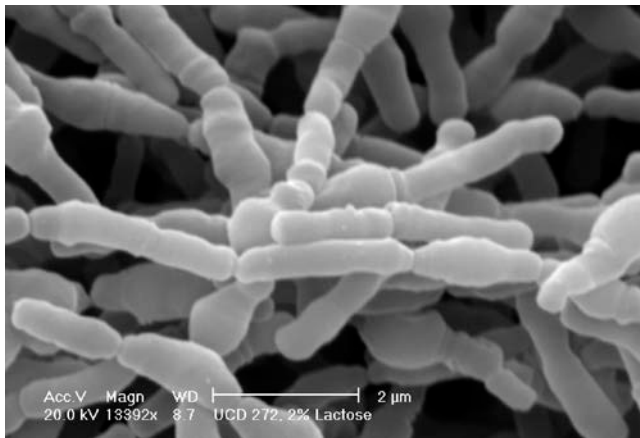
HMO are Food for Select GI Microbes



- Ward RE et al, Appl Environ Microbiol. 2006 Jun;72(6):4497-9.
- B. infantis* grows on HMO whereas *L. gasseri* only on glucose

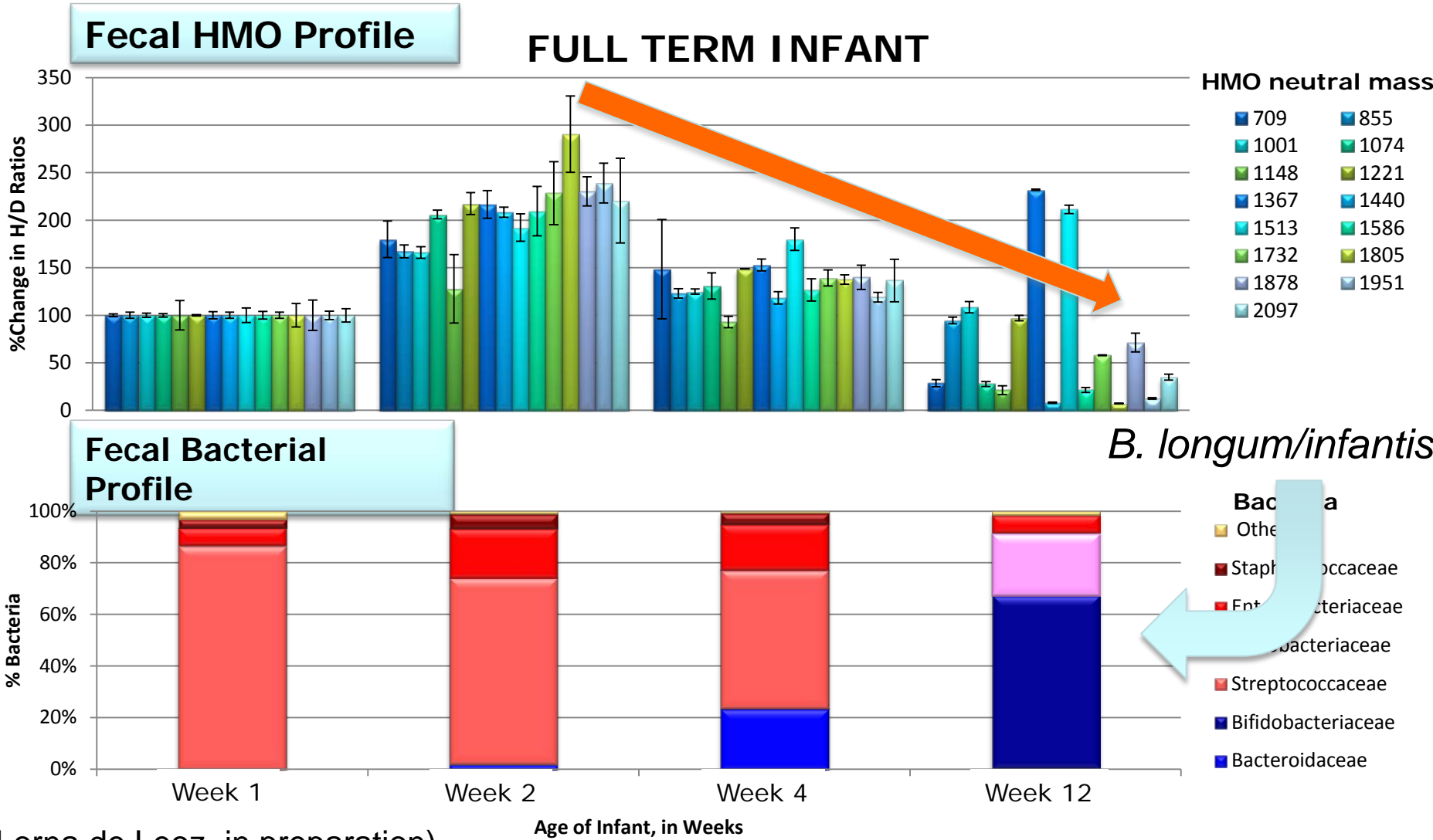


Bifidobacterium longum ssp. *infantis*



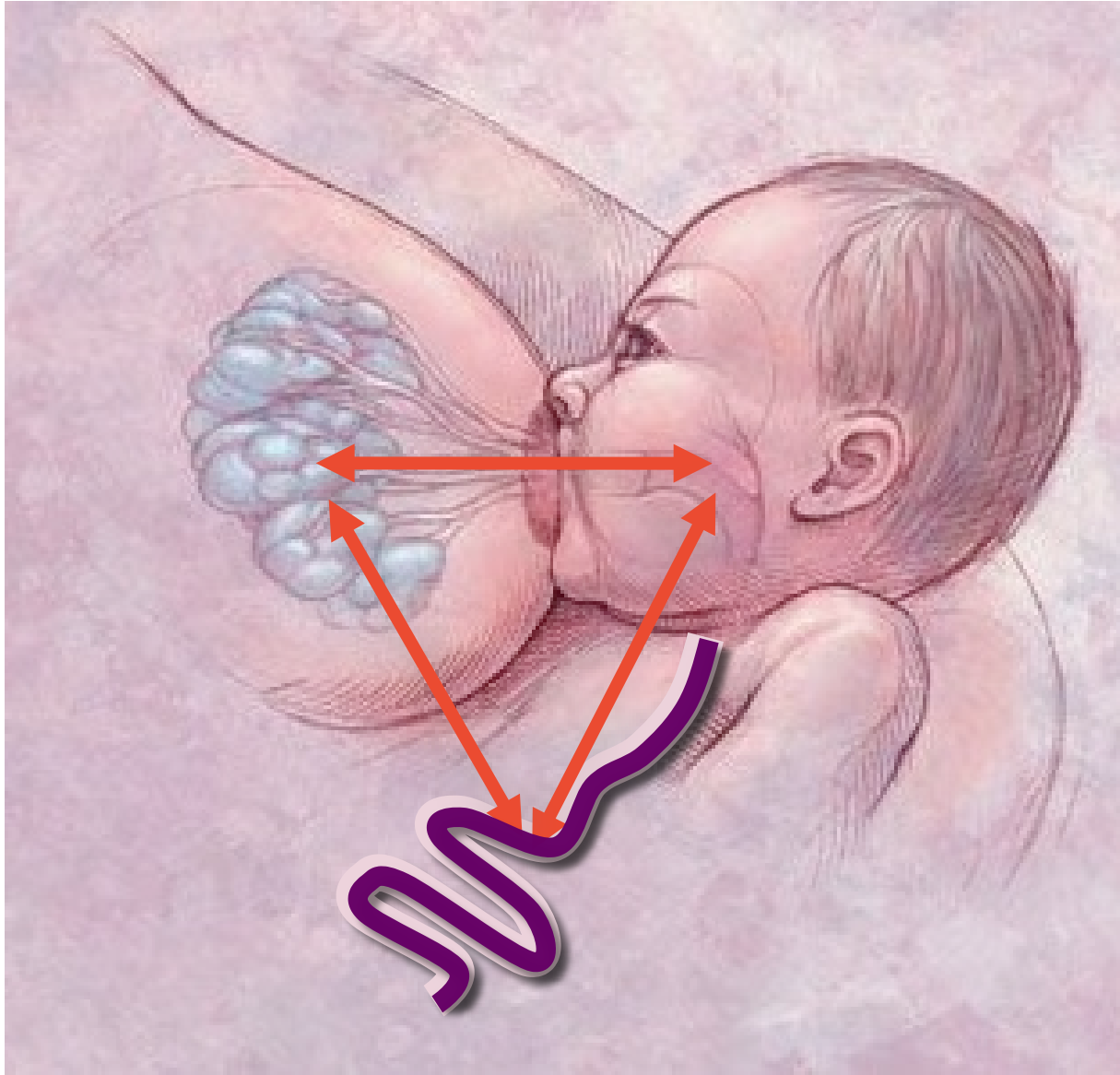


As bifidobacteria increase HMO decrease: *vivo* monitoring of consumption



(Lorna de Leoz, in preparation)

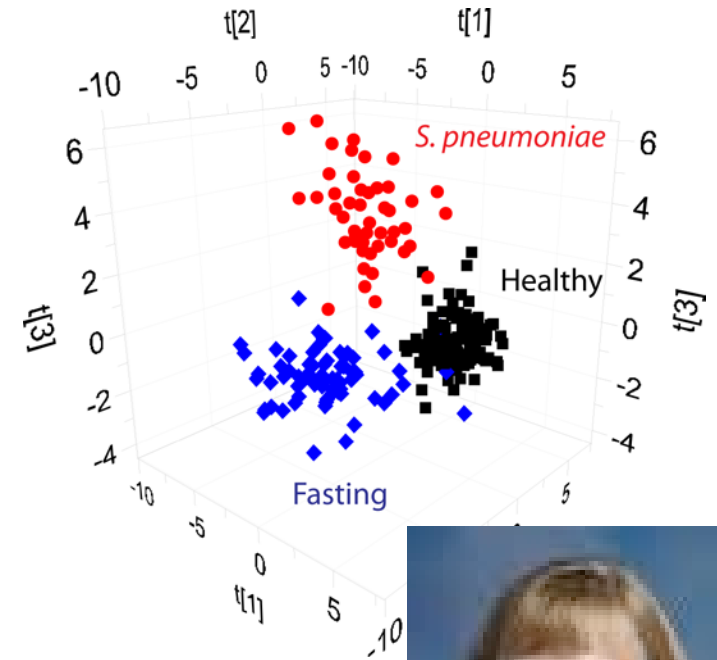
Tripartite Evolutionary Relationship



Urinary Metabolites as Microbiome Diagnostics



Monitor the development of appropriate microflora in infants



Carolyn Slupsky

Translating to Practice



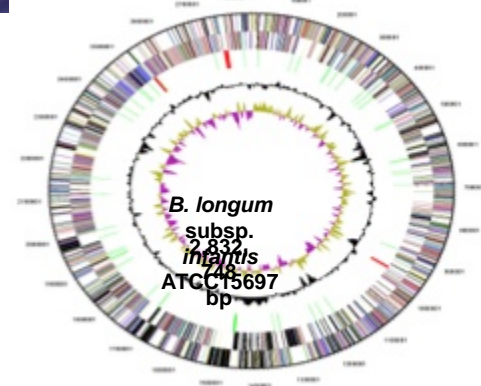
Premature Infants
at risk of sepsis
and Necrotizing
Enterocolitis



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



Mark Underwood
UC Davis





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



The bacteria in us

- Jeffrey Gordon
U. Washington
- The microflora
of lean differs
from obese
humans



More...



- **Gut Microbiota in Human Adults with Type 2 Diabetes Differs from Non-Diabetic Adults**

Nadja Larsen, et al, 2009

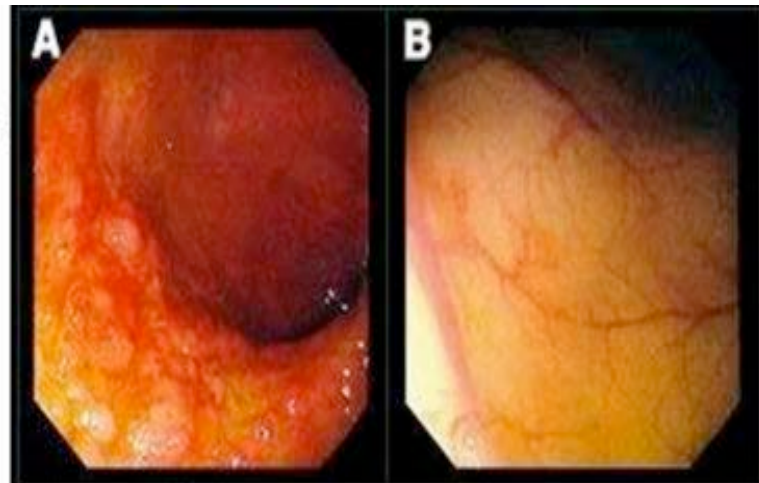
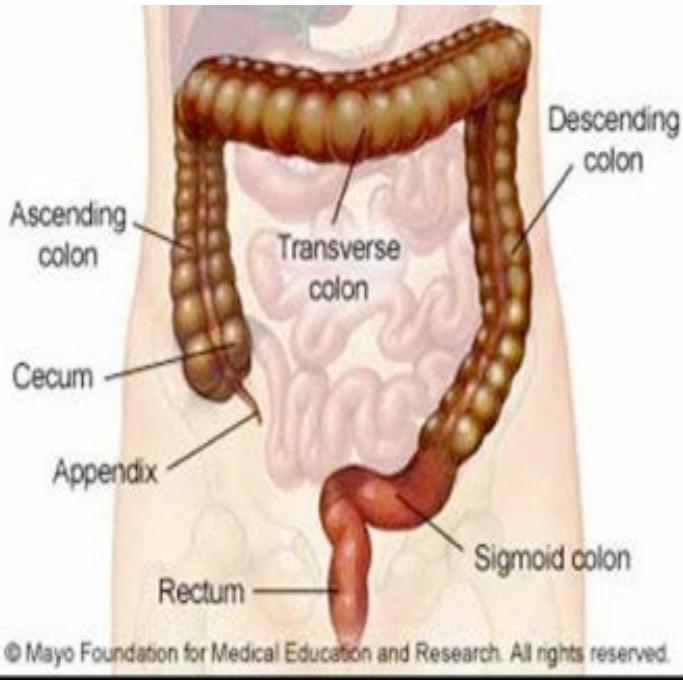


And more...



- *Gut-associated bacterial microbiota in paediatric patients with inflammatory bowel disease*

Conte et al., Gut 2006;55:1760-1767



Medscape®

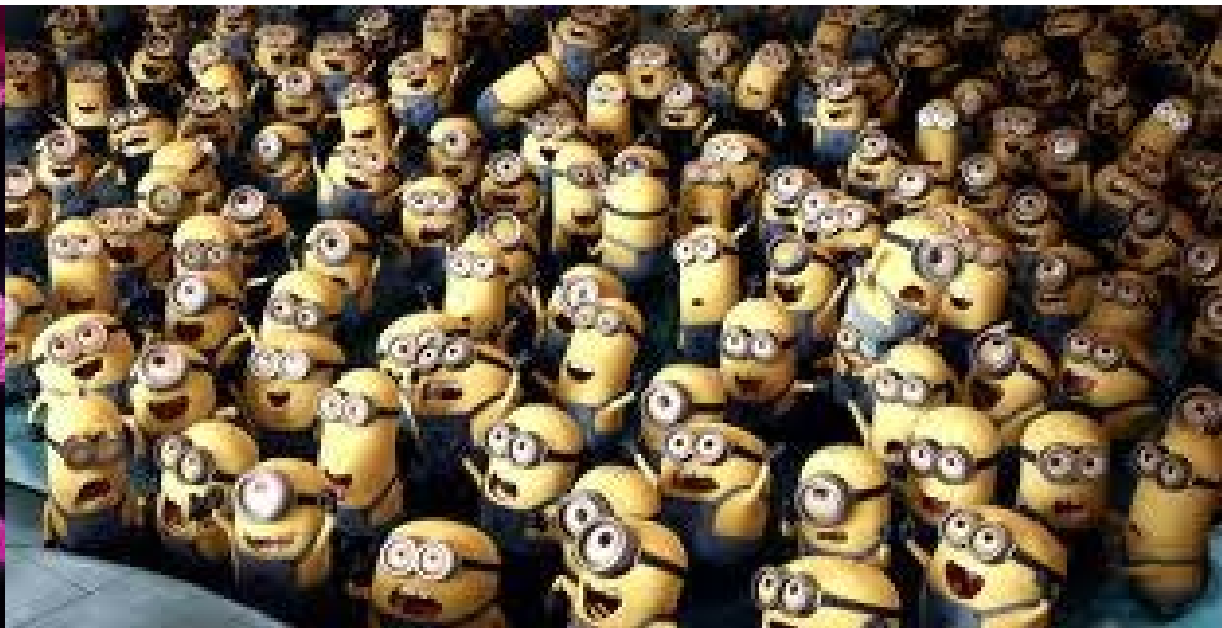
A, Ulcerative Colitis colon.

B, Healthy colon.

Opportunity: BioProfessionals



Our minions!



**Business
Opportunities**

Opportunity: 'Bugs' of Health

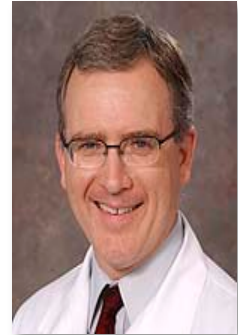
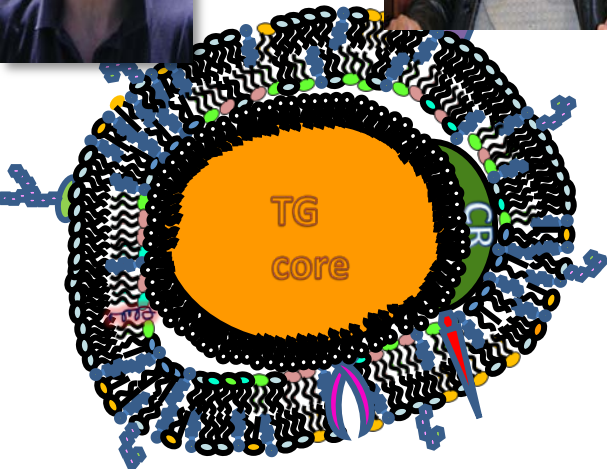
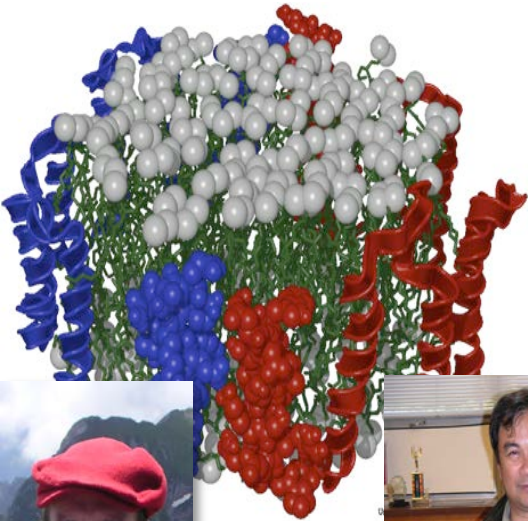
Personal microbiome management:
premature infants to weaning
from athletes to hospitals



Program: 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
- Lipid particles bind endotoxin

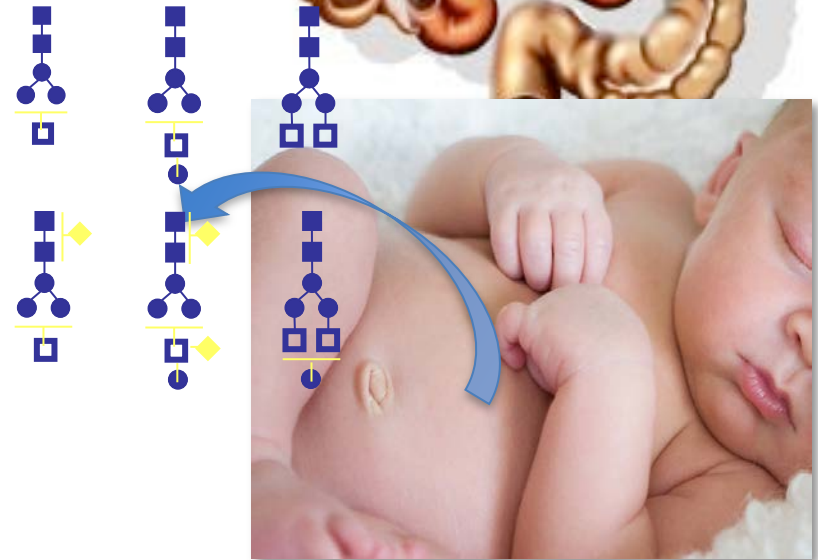




Infant Digestomics

Infant Digestion as a Bioreactor

- Digestion success
 - Release of bioactive peptides
 - Optimal kinetics of release for metabolism
- Cell Signaling
 - Intestinal Immunity
 - Neurological development – in the gut
 - Optimal barrier function



Goal: Diagnostics of Health



*You cannot manage What
You cannot measure*

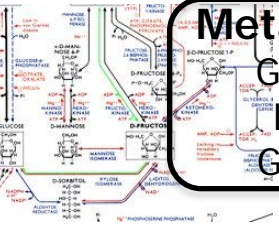
'Measure what is measurable,
and make measurable what
is not so', *Galileo Galilei.*

UCD Phenotyping People

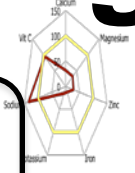


The Metrics of Human Health

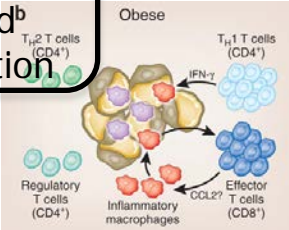
Metabolism
Glucose
Lipids
Glycans



Nutrition
Vitamins
Minerals
Amino acids



Immunity
Innate
Acquired^b
Inflammation



Sensation
Taste
Olfaction
Trigeminal



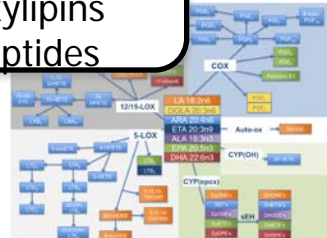
Activity
Sleep
Calories



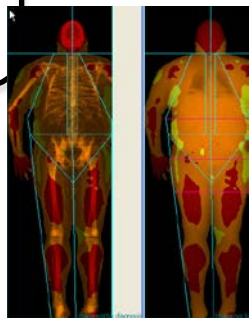
Microbiome
Genetics
Metabolites
Conjugates



Signaling
Endocrine
Oxylipins
Peptides



Anthropometry
Bone
Muscle
Adipose

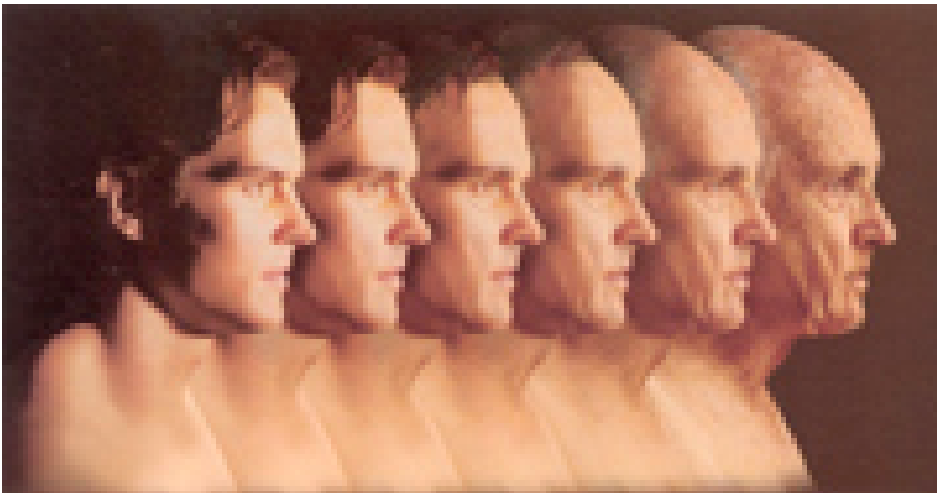


Immunology Diagnostics



Immune Senescence in Aging

Vaccination response diagnostics



Eric Gershwin

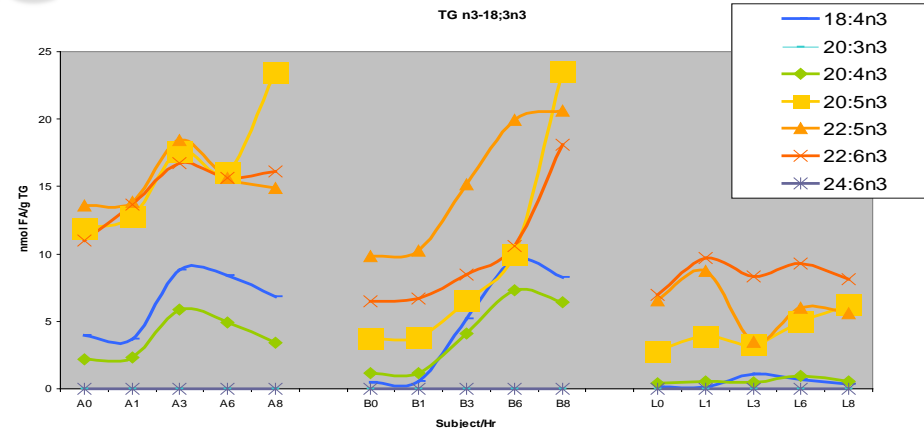
Nutritional Phenotype



Omega Status

Its not about the fish
you ate

Its about the omega 3
you accumulate

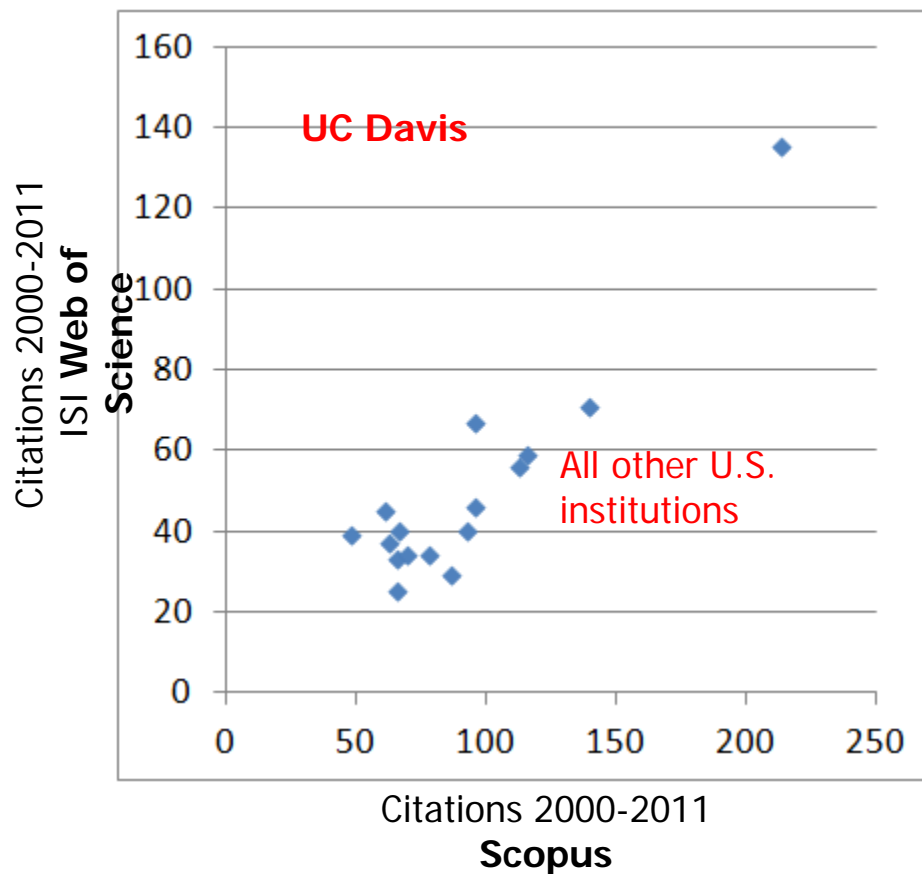




West Coast Metabolomics Center



Oliver Fiehn, Director



Opportunity: Metrics of Health



Personal Health management
needs measurement:
fast, cheap, often, accurate!





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