Diet, Health and Sustainability for the 21st Century: The need for Engineering
The 20th Century Science

- Chemistry – Reductionist
- Industrialization of Simple Chemicals
- Key = Purify
One of chemistry’s great achievements: Identifying all of the essential nutrients for humans

**Essential Nutrients**
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 it's not healthy
We should be enjoying the
greatest health in history
and some are,
...........but most are not
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

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
Milk’s Genius

Biodiversity of structure & function brought to new targets of health

 e.g. $\alpha$ lactalbumin
A Lactalbumin -

- The absence of $\alpha$-Lactalbumin is a unique trait of the Foraging Fur seal.
- Is $\alpha$-Lactalbumin the switch for involution?
Alpha lactalbumin

Galactose + Glucose

Galactosyl-transferase

Lactose Synthase

Lactose

Mammary epithelial cell

α-lactalbumin

Milk

Gastrointestinal-tract

Apoptosis

Apoptosis?
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

\[ \text{\textbackslash - Ca}^{2+} \rightarrow \text{HAMLET} \]

\[ + \text{oleic acid} \]

\[ \alpha\text{-lactalbumin} \]

Fischer et al., 2004
HAMLET: Eliminating Cancer cells \textit{in vivo}

D

\begin{itemize}
  \item \text{\textit{\textalpha}-lactalbumin}
  \item \text{HAMLET}
\end{itemize}

E

\begin{itemize}
  \item \text{\textit{\textalpha}-lac}
  \item \text{HAMLET}
\end{itemize}
Proof of Principle: milk in action
Lactation

The Darwinian Engine of Diet, Health & Sustainability

Katie Hinde, UCLA

The image shows a graph with 'Benefits' on the left and 'Costs' on the right, with 'Time' as the x-axis. The graph indicates a point labeled 'Infant Optima' where benefits are maximized, and another point labeled 'B<(r)C' indicating a balance or optimal condition.
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 3\textsuperscript{rd} most abundant class of biomolecule in human breast milk is un-digestible by humans!

Why?
Bifidobacterium Infantis

B. infantis
2,832,748 Mb

galactosidase
fucosidase
sialidase
hexosaminidase

Fucosidase
Hexosaminidase
galactosidase
Sialidase

Glc
Gal
GlcNAc
Fuc
Neu5Ac
HMO are Food for Select GI Microbes


- **B. infantis** grows on HMO whereas **L. gasseri** only on glucose

![Graphs showing growth of Bifidobacterium longum ssp. infantis and Lactobacillus gasseri](image-url)
As bifidobacteria increase HMO decrease: *in 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
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
Opportunity: BioProfessionals

Our minions!
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

- Sensation
  - Taste
  - Olfaction
  - Trigeminal

- Microbiome
  - Genetics
  - Metabolites
  - Conjugates

- Nutrition
  - Vitamins
  - Minerals
  - Amino acids

- Immunity
  - Innate
  - Acquired
  - Inflammation

- Activity
  - Sleep
  - Calories

- Anthropometry
  - Bone
  - Muscle
  - Adipose

- Signaling
  - Endocrine
  - Oxylipins
  - Peptides
Immune Senescence in Aging
Vaccination response diagnostics
Nutritional Phenotype

Omega Status

It's not about the fish you ate
It's 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