New Trends in Microbiology

Zhihong Hu
Wuhan Institute of Virology
Chinese Academy of Sciences
Outline

I. Microbes and Microbiology
II. Environmental Microbiology
III. Microbial Genomics
IV. Emerging Infectious Disease
V. Integrative Microbiology
I. Microbes and Microbiology
Microbes are the Basis of Life

- Microbes were the first life form on earth
- The root of the tree of life
- Microbes have the greatest genetic and metabolic diversity
- Define the boards of the biosphere

3.5 billion years old prokaryotic fossil
Microbes are the Majority of the Planet and Critical for Sustaining Ecosystem

- Microbes represent the single largest mass of life on earth: 50-60% of biomass
- Microbes create, maintain, and restore balance in virtually all ecosystems
- Bottom of the food chains
Biofuels Will Depend on Microbes

Bio-Ethanol

Total Ethanol

From cellulose

From corn

Graph showing the increase in total ethanol production from 2000 to 2020, with separate lines for ethanol from cellulose and corn.
Microbes are Vital to Human Health

- More than 90% of the cells in our bodies are microorganisms
- Necessary for digestion and absorption of nutrients
- Critical for the development of vascular and immune systems
- Pathogens of infectious diseases
Microbiology is Fundamental to Biology

- Microbes are ideal model for studying life science
- Microbiology plays important roles in biochemistry, genetics, evolution, molecular biology, etc.
Five Kingdoms of Life

- **Animalia**: Elephants
- **Plantae**: Trees and flowers
- **Fungi**: Mushrooms
- **Protista**: Algae
- **Monera**: Bacteria

The Tree of Life *Before* Molecular Microbiology

*FIVE KINGDOMS*
An Illustrated Guide to the Phyla of Life on Earth
THIRD EDITION

LYNN MARGULIS and KARLENE V. SCHWARTZ
Foreword by STEPHEN JAY GOULD

[Book cover image]
The Tree of Life After Molecular Microbiology

Three Domains of Life

Bacteria

Archaea

Eukarya

Carl Woese
University of Illinois

Phylogenetic structure of the prokaryotic domain: The primary kingdoms


CARL R. WOESE AND GEORGE E. FOX*
II. Environmental Microbiology
~99% of the Microbes on Earth are Uncultured

<table>
<thead>
<tr>
<th>Habitat</th>
<th>Culturability (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seawater</td>
<td>0.001–0.1</td>
</tr>
<tr>
<td>Freshwater</td>
<td>0.25</td>
</tr>
<tr>
<td>Mesotrophic lake</td>
<td>0.1–1</td>
</tr>
<tr>
<td>Unpolluted estuarine waters</td>
<td>0.1–3</td>
</tr>
<tr>
<td>Activated sludge</td>
<td>1–15</td>
</tr>
<tr>
<td>Sediments</td>
<td>0.25</td>
</tr>
<tr>
<td>Soil</td>
<td>0.3</td>
</tr>
</tbody>
</table>

Amann, Ludwig and Schleifer, Microbiol. Rev. 59, 1995
Metagenomics: *In situ* Microbial Community Analysis

“To Understand the Whole, One Must Study the Whole”

Newman & Banfield, Science 296, 2002
Extreme Environments and Extremophiles

- Black smoker
- Permafrost regions
- Solar salterns
- Hot springs

Recodes for Extremophiles

- Hottest: 121 °F
- Deepest: 2 miles underground in caves
- Most salty: 5.2 M NaCl (saturation)
- Most acidic: pH 0.8
- Most radiation: 1.5 million rads
Genome of *Thermoanaerobacter tengcongensis*

**Hot Spring in Tengchong, Yunnan, China (75 °C)**

Bao et al., Genome Research 12, 2002
Proteomics of *T. tengcongensis*

Wang *et al.*, Proteomics, 2004
The Significance of Extremophiles Researches

- Origin of life and evolution
- Adaptation of life to extreme environments
- Life on other planets
- Potential applications in industry, agriculture, medicine, and environmental remediation
Some Ongoing Research Activities in Environmental Microbiology in China

- Metagenomic projects: Continental subsurface deep drilling, deep sea, hot springs, human intestinal tract, etc.
- Genetic bases and survival strategies of extremophiles
III. Microbial Genomics
Genome Sequences of Microbes

Completed genomes:

- Archaea: 31
- Bacteria: 421
- Virus: 2118

As of Nov. 25, 2006, NCBI

Haemophilus influenzae Rd
Fleischmann et al., Science 269, 1995
Can we Define a Minimal set of Genes Essential for Life?

Protein-coding genes in the hypothetical minimal cell:

- DNA metabolism: 16
- RNA metabolism: 106
- Protein processing, folding, secretion: 15
- Cellular processing: 5
- Energetic and intermediary metabolism: 56
- Poorly characterized: 8
  Total: 206 genes

*Mycoplasma genitalium*: 382 protein-coding genes are essential.


Gil *et al*., Microbiol Mol Biol Rev. 68, 2004
Completed Sequence of *Yersinia pestis*

Achtma *et al.* PNAS 96, 1999

- 1. Justirian plague (5th-7th century)
- 2. Black Death (13th-15th century)
- 3. Modern plague (1870s onwards)

1. Justirian plague (5th-7th century)
2. Black Death (13th-15th century)
3. Modern plague (1870s onwards)

Subtypes: Antiqua, Medievalis, and Orientalis

- 2001 Parkhill *et al.* CO92 (Orientalis)
- 2002 Deng *et al.* KIM (Medievalis)
- 2004 Song *et al.* 91001 (rodent)
- 2006 Chain *et al.* Antiqua and Nepal516
Transmission and Expansion of *Y. pestis* in China

Zhou *et al*., J. Bacteriol 186, 2004
Global Gene Transcription Profile of *Y. pestis*

**Cluster I** - Synthesis and transport of ribosome proteins

**Cluster II** - Uptake and utilization of iron

**Cluster III** - Sulfur metabolism

**Cluster IV** - Energy metabolism
Metabolic Pathways in *Leptospira interrogans*  Lai

Metabolic Engineering: Antibiotic Biosynthesis

IV. Emerging Infectious Diseases
Mechanisms of Viral Emergence

Virus → Animal reservoir → Intermediate host → Vector → Transmission to humans → Inter-human transmission and further spread
The 2003 SARS Epidemic

He et al., Science 303, 2004
The full-length genome sequences had 99.8% identity to the human SARS-CoV.

Guan et al., Science 302, 2003
Phylogenetic Analysis Linked Early Cases to Civets

Molecular Evolution of the SARS Coronavirus During the Course of the SARS Epidemic in China

The Chinese SARS Molecular Epidemiology Consortium

He et al., Science 303, 2004
Re-emerging of SARS in 2003/2004 were found Directly Linked to Civets

- Very mild symptoms
- No human-to-human transmission
- Direct/indirect civet contact history

Song et al., PNAS 102, 2005
Mechanisms for Cross Species Transmission

Li et al., Science, 2005

Qu et al., J Biol Chem, 2005
Viral Adaptation to Human Receptors is Critical for Human to Human Transmission

Qu et al., J Biol Chem, 2005

Li et al., Science, 2005
Civets were viral positive in markets but negative in farms

Kan et al., J. Virol., 2005
Bats?

- One of the largest and the most diverse groups of mammals which originated 50 million years ago.
- More than 80 bat viruses belonging to 10 virus families were reported.
- Bats are natural reservoirs of a numbers of viruses such as Hendra, Nipah, Ebola and rabies.
Bats Are Natural Reservoirs of SARS-Like Coronaviruses


<table>
<thead>
<tr>
<th>Bat species</th>
<th>Antibody test: positive/total (%)</th>
<th>PCR analysis: positive/total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Fecal swabs</td>
</tr>
<tr>
<td>Rousettus leschenaulti</td>
<td>1/84 (1.2%)</td>
<td>0/110</td>
</tr>
<tr>
<td>Rousettus leschenaulti</td>
<td>0/42</td>
<td>0/45</td>
</tr>
<tr>
<td>Cynopterus sphinx</td>
<td>0/17</td>
<td>0/27</td>
</tr>
<tr>
<td>Rousettus leschenaulti</td>
<td>ND</td>
<td>0/55</td>
</tr>
<tr>
<td>Myotis ricketti</td>
<td>ND</td>
<td>0/21</td>
</tr>
<tr>
<td>Rhinolophus pusillus</td>
<td>ND</td>
<td>0/15</td>
</tr>
<tr>
<td>Rhinolophus ferrumequinum</td>
<td>0/4</td>
<td>1/8 (12.5%)*</td>
</tr>
<tr>
<td>Rhinolophus ranei</td>
<td>5/7 (71%)</td>
<td>1/8 (12.5%)†</td>
</tr>
<tr>
<td>Nyctalus plancty</td>
<td>0/1</td>
<td>0/1</td>
</tr>
<tr>
<td>Miniopterus schreibersi</td>
<td>0/1</td>
<td>0/1</td>
</tr>
<tr>
<td>Myotis altani</td>
<td>0/1</td>
<td>0/1</td>
</tr>
<tr>
<td>Rousettus leschenaulti</td>
<td>1/58 (1.8)</td>
<td>ND</td>
</tr>
<tr>
<td>Rhinolophus pearsoni</td>
<td>13/46 (28.3%)</td>
<td>3/30 (10%)‡</td>
</tr>
<tr>
<td>Rhinolophus pusillus</td>
<td>2/6 (33.3%)</td>
<td>0/6</td>
</tr>
</tbody>
</table>

Li et al., Science 310, 2005
Bat SARS-like Virus may not Infectious to Human

Spike protein

S1 domain  RBD  S2 domain

Signal  TM Cyto

RP3: VLAWNTAKQDQG----CYYRSHTKTLKPFERDELSSDENGVRTLSTYDEYPSVVEVAYOAT
HKU3-1: VLAWNTAKHDCG----NYYRSHTKTLKPFERDELSSDDCNGVYTSTYDEYDNPVVAOAT
Rm1: VLAWNTAQDQG----CYYRSYRKEKLKPFERDELSSDENGYTTSTYDEYPSIEVBYOAT
Rf1: VLAWNTAKQDVC----SYYRSKRSKIKPFERDELSSENSECVRSTSTYDENDNVGLBYOAT
GD01: VLAWNTRNIDATSTGNYNKRYLHGBKTRPERDELNVFFSPDGKCPTPALNCYWPNDYGETYTTTGGICYOPY
Tor2: VLAWNTRNIDATSTGNYNKRYLHGBKTRPERDELNVFFSPDGKCPTPALNCYWPNDYGETYTTTGGICYOPY
SZ3: VLAWNTRNIDATSTGNYNKRYLHGBKTRPERDELNVFFSPDGKCPTPALNCYWPKDYGTYTTSGGICYOPY

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RBD  S1 domain  RBD  S2 domain

Signal  TM Cyto

RP3: VLAWNTAKQDQG----CYYRSHTKTLKPFERDELSSDENGVRTLSTYDEYPSVVEVAYOAT
HKU3-1: VLAWNTAKHDCG----NYYRSHTKTLKPFERDELSSDDCNGVYTSTYDEYDNPVVAOAT
Rm1: VLAWNTAQDQG----CYYRSYRKEKLKPFERDELSSDENGYTTSTYDEYPSIEVBYOAT
Rf1: VLAWNTAKQDVC----SYYRSKRSKIKPFERDELSSENSECVRSTSTYDENDNVGLBYOAT
GD01: VLAWNTRNIDATSTGNYNKRYLHGBKTRPERDELNVFFSPDGKCPTPALNCYWPNDYGETYTTTGGICYOPY
Tor2: VLAWNTRNIDATSTGNYNKRYLHGBKTRPERDELNVFFSPDGKCPTPALNCYWPNDYGETYTTTGGICYOPY
SZ3: VLAWNTRNIDATSTGNYNKRYLHGBKTRPERDELNVFFSPDGKCPTPALNCYWPKDYGTYTTSGGICYOPY

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RBD  S1 domain  RBD  S2 domain

Signal  TM Cyto

RP3: VLAWNTAKQDQG----CYYRSHTKTLKPFERDELSSDENGVRTLSTYDEYPSVVEVAYOAT
HKU3-1: VLAWNTAKHDCG----NYYRSHTKTLKPFERDELSSDDCNGVYTSTYDEYDNPVVAOAT
Rm1: VLAWNTAQDQG----CYYRSYRKEKLKPFERDELSSDENGYTTSTYDEYPSIEVBYOAT
Rf1: VLAWNTAKQDVC----SYYRSKRSKIKPFERDELSSENSECVRSTSTYDENDNVGLBYOAT
GD01: VLAWNTRNIDATSTGNYNKRYLHGBKTRPERDELNVFFSPDGKCPTPALNCYWPNDYGETYTTTGGICYOPY
Tor2: VLAWNTRNIDATSTGNYNKRYLHGBKTRPERDELNVFFSPDGKCPTPALNCYWPNDYGETYTTTGGICYOPY
SZ3: VLAWNTRNIDATSTGNYNKRYLHGBKTRPERDELNVFFSPDGKCPTPALNCYWPKDYGTYTTSGGICYOPY
Transmission Chain of SARS-CoV?

Other animals
Wild civet
Farm civet

Bat
Market civet
Human

?
VI. Integrative Microbiology
True-color image of a *Trichodesmium* bloom (A), the *Trichodesmium* derived chlorophyll (B), and modeled N2 fixation (C).

Capone & Subramaniam, ASM News 71, 2005
Nanotechnology and Microbiology

- Using nanotechnology to study microbiology:
  - Imaging single molecules
  - Poking and pulling nanoscale objects (laser traps, optical tweezer)
  - Determining spatial organization in living microbes (AFM, near/far field microscope)

- Contribution of microbiology to nanotechnology

Merz et al., Nature 407, 2000
New Trends in Microbiology

- Environmental microbiology
- Microbial genomics
- Emerging infectious disease
- Biocomplexity
- The origins and history of life
- Engineering of microbes to improve the quality of life
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