Marine Genetic Resources: Experiences in Commercialization

Marc Slattery
University of Mississippi, and
National Institute for Undersea Science & Technology
Ocean Biotechnology Center & Repository

Background

Marine Genetic Resources: “genetic material of actual or potential value”. [Convention on Biological Diversity]
Ocean Habitat Diversity

- polar
- deep sea
- caves
- coral reef

- temperature
- pressure
- light
- nutrients
- predation
- competition
- pathogenesis

Marine Biotech Products

<table>
<thead>
<tr>
<th>Product</th>
<th>Application</th>
<th>Original Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluorescent Probes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Green Fluorescent Protein (GFP)</td>
<td>Reporter gene assays</td>
<td>Jellyfish: Aequora victoria</td>
</tr>
<tr>
<td>Novel Enzymes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deep Vent DNA Polymerase</td>
<td>Polymerase chain reaction (PCR)</td>
<td>Bacterium: Thermococcus litoralis</td>
</tr>
<tr>
<td>Nutritional Supplements</td>
<td>63 Fatty acids in infant formula</td>
<td>Marine microalga: Cryptecodinium cohnii</td>
</tr>
<tr>
<td>Formulaid®</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cosmetic Additives</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resilience® (Pseudopterosin)</td>
<td>Antiinflammatory</td>
<td>Gorgonian: Pseudopterogorgia elisabethae</td>
</tr>
</tbody>
</table>

Other active research areas:
- biomaterials (artificial bone from corals; stents from sea urchins; silica chips from diatoms; fiberoptic cables from sponges)
- agrochemicals (insecticides and weed killers from sponges)
- antifoulants (ship paints from soft corals)
Marine Pharmaceuticals

<table>
<thead>
<tr>
<th>Product</th>
<th>Application</th>
<th>Original Source</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pharmaceuticals</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acyclovir® (Ara-A)</td>
<td>Antiviral drug</td>
<td>Sponge: <em>Cryptotheca crypta</em></td>
</tr>
<tr>
<td>Cytosar-U® (Ara-C)</td>
<td>Anticancer drug</td>
<td></td>
</tr>
<tr>
<td><strong>Pharmaceuticals</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prialt® (conotoxin)</td>
<td>Analgesic</td>
<td>Cone snail: <em>Conus magnus</em></td>
</tr>
</tbody>
</table>

New Drug Sources over Last 25 Years*

- Natural Product: 6%
- Modified Natural Product: 28%
- Synthetic Product: 49%
- Synthetic Product based on NP Pharmacophore: 17%

*after Newman & Cragg 2007: JNP 70:461

Drug Discovery Timeline

- Discovery
- Early Development
- Preclinical Development: 3.8 yrs
- Human Clinical Trials
  - I
  - II
  - III: Post-Clinical Trials 1.5 yrs
- Launch

Academics
(funding: NIH, WHO, NOAA, etc.)

Pharmaceutical Industry

Numbers
- 100,000+ 1 clinical trials
- costly: 0.5-1B $$$/drug

I = what dosage is safe/how treatment should be given
II = evaluate effectiveness/look for side effects
III = compare new treatment to current/standard treatment

Extracts
- Bioassays
  - Active extracts
  - Lead compounds
  - Lead candidates
Laboratory Approaches

Bioassay-guided fractionation

High Through-put Screening

Chemistry-driven (slow & costly)  Biology-driven (fast, but sample-limited!!!)

Supply Concerns

1600 kg sea hare ⇒ 10 mg Dolastatin 10

Dolabella auricularia
diet-derived bioaccumulation

Symploca sp.

Current Supply Options:
- total synthesis
- harvest Symploca
- culture Symploca
- heterologous gene expression

Lesson: increased biological knowledge results in environmental protection (rare species & habitat)
Sourcing Microbial Diversity

Marine microbial diversity

Sw contains 10^6 to 10^9 microbe cells/ml; sponges can have 50% cells by weight

E.coli heterologous expression system

Molecular techniques

Microbial fermentation

Research Partnerships

Direct Benefit Sharing: IP Compensation

Public Sector

Private Sector

Utility

Diffuse Benefit Sharing: Societal Opportunities

Our Partnership Model:

Baker et al 1995; J Nat Prod 58:1325
Rosenthal 1999; Pharm Biol 37:6

- capacity enhancement [scientists & infrastructure]
- research collaborations and shared results/IP
- technology transfer and education opportunities
- access to information relevant to biodiversity
- priority research and economic contributions
Conclusions

• Marine genetic resources have tremendous potential for a variety of biotechnology applications:
  - public health
  - food security
  - environmental remediation

• There are direct [= shared IP] and diffuse [= use] benefits of marine genetic resources for society

• Commercialization of these resources requires significant Research & Development [= $$$], and even then marketable products are rare

• In all countries there needs to be increased support for fundamental research and partnerships that move information from the laboratories into products that help people live better, healthier and more productive lives

Recommendations

• Increase research on the biosynthetic capabilities of marine organisms using innovative techniques, and apply this fundamental knowledge to help detect important Marine Natural Products

• Development of technologies that foster sustainable resources rather than overharvesting

• Better tools for marine biotechnology used in solving environmental problems

• Greater emphasis for research efforts that seek to commercialize marine bioproducts