Bioprospecting from Marine Genetic Resources from Areas Beyond National Jurisdiction

Marcel Jaspars
Director, Marine Biodiscovery Centre; Leader PharmaSea Consortium
University of Aberdeen
Scotland, UK
m.jaspars@abdn.ac.uk

With thanks to Oonagh McMeel and Thomas Vanagt
Marcel Jaspars

Professor of Organic Chemistry, University of Aberdeen, UK

Director of Marine Biodiscovery Centre, University of Aberdeen, UK

Co-founder and Chief Scientific Officer of Ripptide Pharma


Scientific Leader, PharmaSea EU FP7 Consortium

Chair of the Advisory Panel of Policy and Legal Experts – aiming to provide clear recommendations and ready-to-use solutions to address critical policy and legal barriers which impede the access and sustainable use of MGR for European biotechnological research, development and commercialisation
Term has no meaning to biologists and is not defined in UNCLOS but is taken to mean the Nagoya Equivalent:

“Marine genetic material” means any material of plant, animal, microbial or other origin, found in the marine environment, containing functional units of heredity; “Marine genetic resources” means marine genetic material of actual or potential value

Diversity of habitat is assumed to translate to biological diversity

3 Jørgensen Nat Rev Microbiology, 2007, 5, 770
Marine Species Diversity

Animal Diversity

Species estimate (Log)

Phylum

Marine
Terrestrial

Of the major divisions of animal life ~20 have no representatives on land.

Microbial Diversity

There is no clear estimate of marine microbial diversity or its economic value.
Can we determine which legal regime an organism came from?

NO!
Biological Diversity = Chemical Diversity
Bioprospecting is the discovery of compounds and associated ideas from genetic resources to develop novel biomedicines, biomedical research tools, antifoulants, catalysts, nutraceuticals, cosmeceuticals, etc. Unlike seabed mining, marine genetic resources are not mined.

Why use marine genetic resources?
Offers advantage over comparable terrestrial resource:
  Superior performance
  Better economics
Unprecedented activity in particular application:
  Enzymes: new reactivity/new biotransformation
  Small molecules: novel chemical structures & new mechanism of action
  Materials: new properties
Elements of good practice already exist at all stages of the marine biodiscovery pipeline.
In Situ versus Ex Situ Considerations

Sampling Metadata
- Location
- Depth
- Temperature
- Salinity
- pH
- Oxygen content
- Seafloor conditions

Sample storage – specific depending on end use
- Ambient temperature
- Cooler (4°C)
- Freezer (-20°C)
- -80°C Freezer
- Liquid nitrogen (-196°C)
- Formaldehyde
- Ethanol
- DNA/RNA preservation liquids

Needs standardisation
Different Markets

From the European Commissions ‘Blue Growth’ missive

**NOW:** niche market focused on high-value products for the health, cosmetic and industrial bio-materials sectors. (high value/high risk/low volume)

**THEN:** medium-sized market, e.g. lipids, sugars, polymers, proteins as inputs for the food, feed and chemical industries (medium cost/medium risk/medium volume)

**LATER:** mass-market products, together with a range of high added value specialised products (low/medium cost/low risk/high volume)
Non-Pharma MGR Derived Products on the Market

Vent Polymerase – for DNA amplification  
Origin: Vent bacterium (Naples, Italy)  
Production: Recombinant  
Owner: New England Biolabs

Fuelzyme™-LF
THE NEXT-GENERATION, HIGH-PERFORMANCE  
ALPHA-AMYLASE FOR MASH LIQUEFACTION

Fuelzyme – Enzyme used in biodiesel production  
Origin: Deep sea bacterium (location unknown)  
Production: Recombinant  
Owner: Verenium (BASF)

Cosmetic screening infra-red rays  
Origin: Vent bacterium (location unknown)  
Production: Bacterial culture  
Owner: Sederma (Croda)

Anti biofilm agents  
Origin: Red seaweed  
Production: Chemical Synthesis  
Owner: XXXXXX
MGR Derived Pharmaceutical Products on the Market

All from EEZ apart from 1 (high seas) – All prior to CBD coming into force
None rely on harvesting natural source except fish oils
None from ABNJ – mainly reef derived

7 successful compounds came from 28,000 known marine compounds

Mainly anti-cancer with a few analgesics and antivirals

Mainly start-ups at early stage with large pharma at late stage
Before Getting to Preclinical Trials:

>110,000 screening events
>700 active dereplicated extracts

Active, non toxic, novel chemistry

At 30 Months:
13,689 Strains
>14,000 Active Extracts
>80 Active Compounds

1 Drug Lead
2 Drug Leads

45% From existing partner collections
55% New samples from cold/hot/deep habitats

Screening
Microbial Library
Extracts
Molecular Leads
Scale Up
Microorganisms
Extract Library
Molecular Families

Up to ~6,000 metres
**Real Benefit Scenario**

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990</td>
<td>Discovery</td>
<td></td>
</tr>
<tr>
<td>1996</td>
<td>Total synthesis</td>
<td></td>
</tr>
<tr>
<td>2003</td>
<td>Industry synthesis</td>
<td></td>
</tr>
<tr>
<td>2007</td>
<td>EMA</td>
<td></td>
</tr>
<tr>
<td>2015</td>
<td>FDA</td>
<td></td>
</tr>
</tbody>
</table>

- **Cost in 2014 to bring drug to market US$2,558 M* - >70% Clinical trials**
- **Typical industry royalties on natural products developed into drugs is 1-3%**
- **Halaven (Eisai), derived from a Japanese sponge makes US$200 M per year – in principle yielding US$ 2-6 M pa.**
- **Currently 7 approved marine drugs – total royalties would be US$ 10-50 M.**
- **Blockbuster drug (> US$ 1 Bn pa income) would yield US$10-30 M pa**
- **Currently 7 approved marine drugs come from ~28,000 discovered marine compounds (1 in 4000 chance) – none are ‘blockbusters’**
- **All examples were discovered pre-CBD – not clear if actual royalties are being paid**
- **Other markets – nutraceuticals/cosmeceuticals, lower risk, quicker to market, lower investment and lower returns.**

Monitoring Sample and Data Flows

Possible to track sample from origin to exploitation (needs better databases)

Modifications to DNA or compound may make it hard to trace MGR origin
Tracking Samples can be Tricky

Vent Polymerase
For DNA amplification
An UNCLOS implementing agreement developed over the next few years would need to be flexible enough to deal with rapid scientific progress.
Nightmare (But Realistic) Scenario

Vector and host may have associated IP rights

Gene 1

Gene 2

Gene 3

Gene 4 (ABNJ)

Host

Known bioactive compound

Originally found in Australian EEZ Marine organism

Marine organism

Vector

© 2009 www.outline-world-map.com
Questions for Discussion

• How can we make sure MSR on MGR is not impeded?
• How will the process be monitored/policed and by whom?
• Traceability becomes an issue as benefits may take a long time to be realised. Who will trace this?
• How can we manage expectations for financial returns?
• Can we make an IA flexible enough to cope with scientific progress?
“The research leading to these results has received funding from the European Union's Seventh Framework Programme (FP7/2007-2013 under grant agreement n° 312184)”