



Bioprospecting from Marine Genetic Resources from Areas Beyond National Jurisdiction

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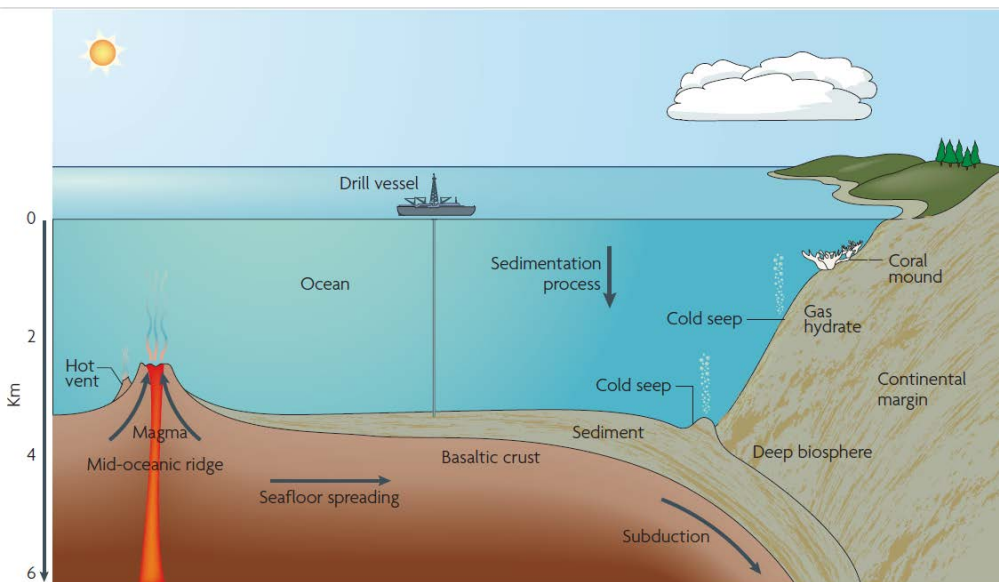
Chair of the Advisory Panel of Policy and Legal Experts – aiming to provide clear recommendations and ready-to-use solutions to address critical policy and legal barriers which impede the access and sustainable use of MGR for European biotechnological research, development and commercialisation

Marine Genetic Resources

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 ;

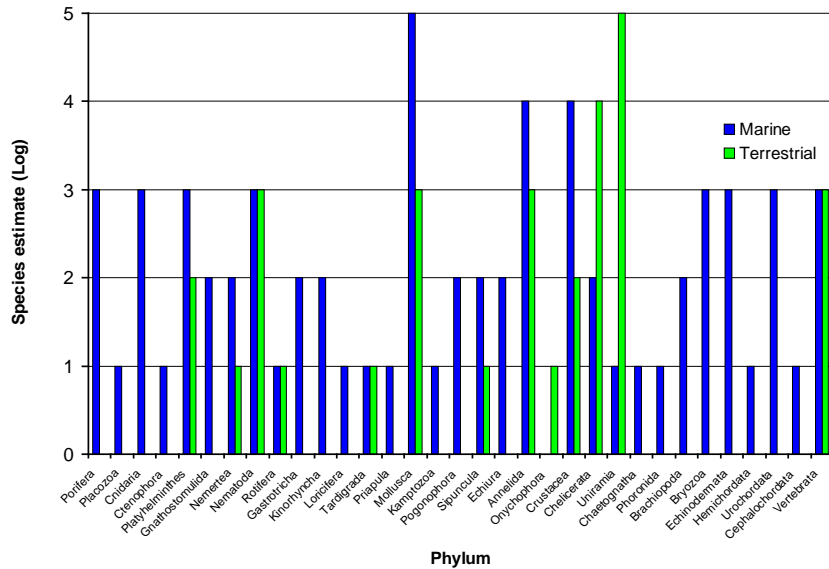
“Marine genetic resources” means **marine** genetic material of actual or potential value”



Diversity of habitat is assumed to translate to biological diversity

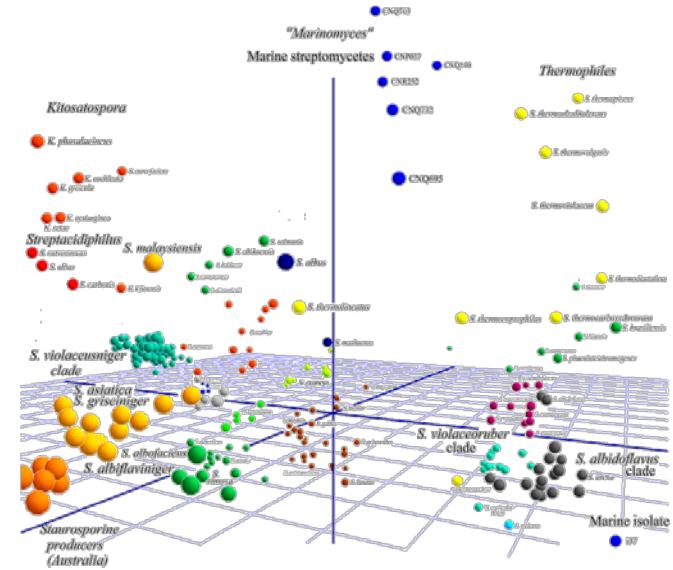
Marine Species Diversity

Animal Diversity



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

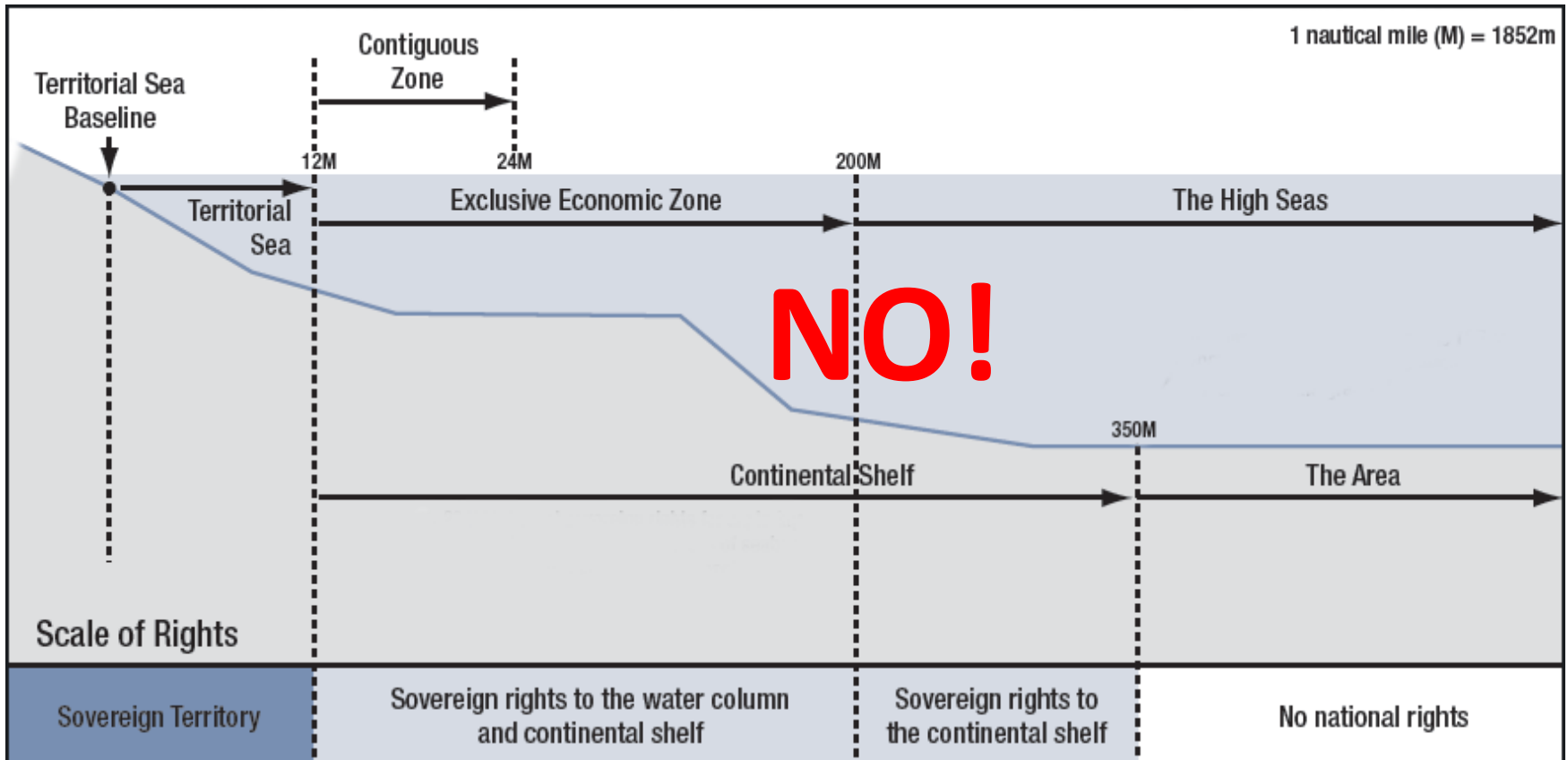
Microbial Diversity



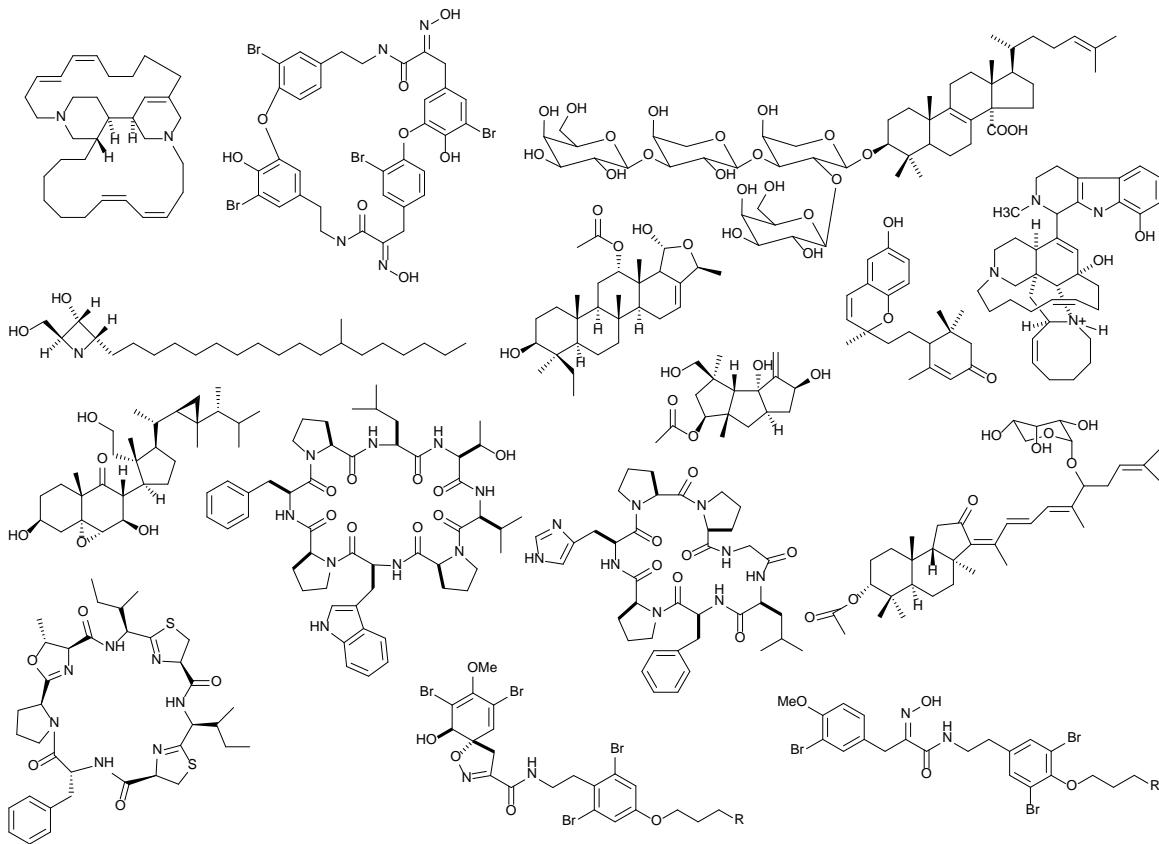
There is no clear estimate of marine microbial diversity or its economic value

MGR from EEZ or ABNJ

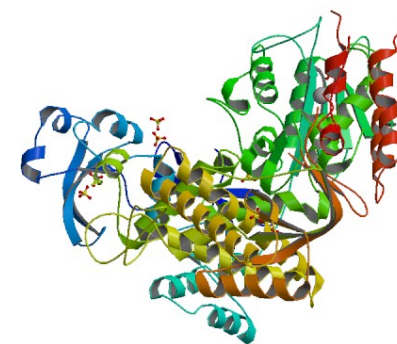
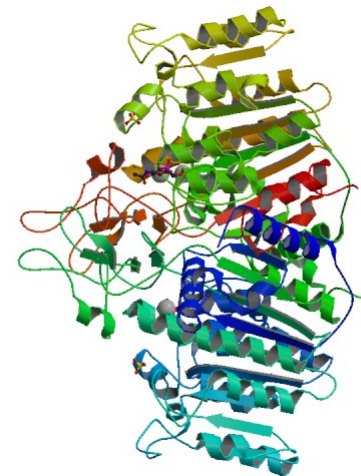
Can we determine which legal regime an organism came from?



Biological Diversity = Chemical Diversity



Small Molecules



Biomolecules

The Marine Bioprospecting Process

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

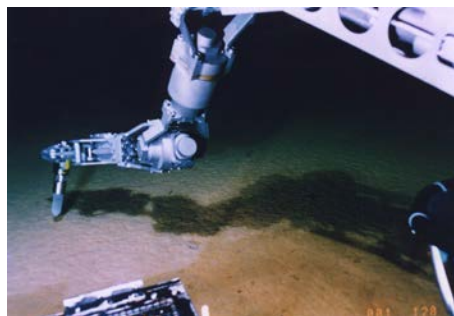
Unprecedented activity in particular application:

- Enzymes: new reactivity/new biotransformation

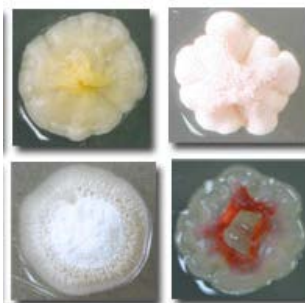
- Small molecules: novel chemical structures & new mechanism of action

- Materials: new properties

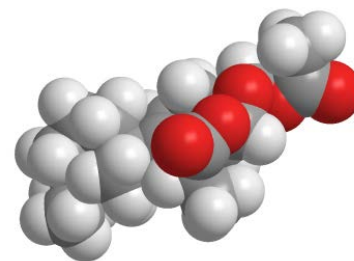
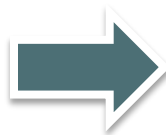
Bioprospecting Biodiversity Beyond National Jurisdiction



Sampling in ABNJ



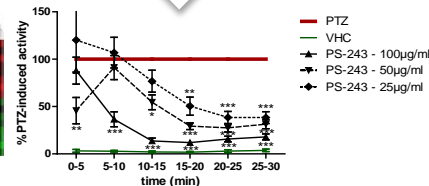
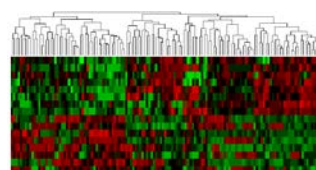
MGR



Chemistry



Product



Bioassay

Elements of good practice already exist at all stages of the marine biodiscovery pipeline

In Situ versus Ex Situ Considerations

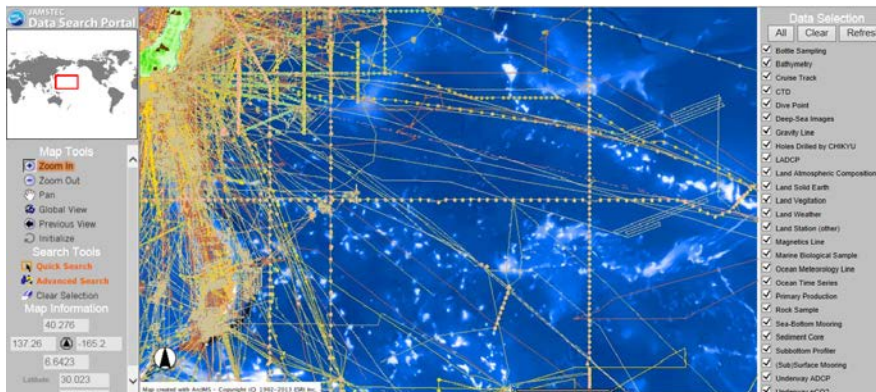
Sampling Metadata

- | 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



Cosmetic screening infra-red rays

Origin: Vent bacterium (location unknown)

Production: Bacterial culture

Owner: Sederma (Croda)



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)



Anti biofilm agents

Origin: Red seaweed

Production: Chemical Synthesis

Owner: XXXXX

MGR Derived Pharmaceutical Products on the Market



Soft tissue carcinoma



Ecteinascidia turbinata



Chronic pain (analgesic)



Conus magus



Breast cancer



Halichondria okadai



Ara-C
(cytarabine)
treatment of leukemia



Ara-A (vidarabine)
antiviral



Tethya crypta



Hodgkin's Lymphoma



Dolabella auricularia



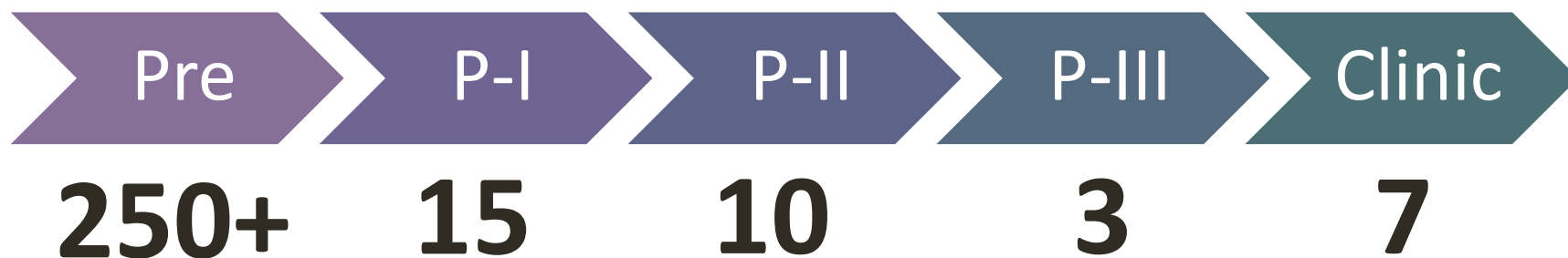
lowering very high
triglyceride levels



Purified
fish oil

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

Pharmaceutical Pipeline



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:



45%

From existing partner collections

>110,000 screening events

> 700 active dereplicated extracts

Active, non toxic, novel chemistry

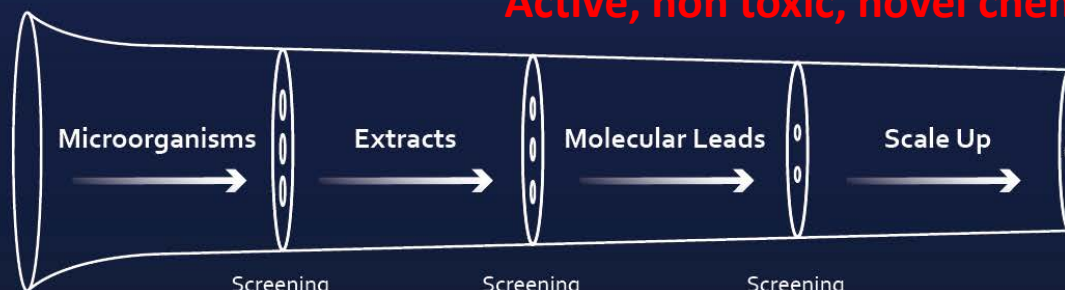


55%

New samples from cold/hot/deep habitats

At 30 Months:

Up to -6,000 metres



2
Drug Leads

Screening

Screening

Screening

Microbial Library

Extract Library

Molecular Families



13,689

Strains

>14,000

**Active
Extracts**

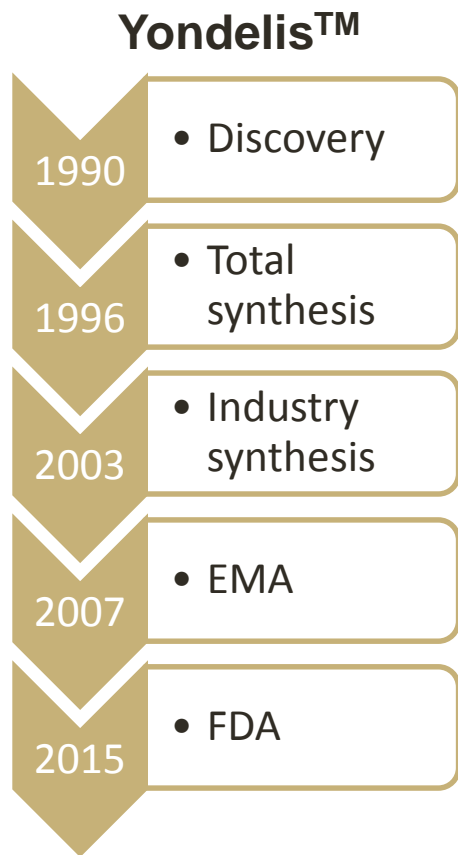
>80

**Active
Compounds**

1

**Drug
Lead**

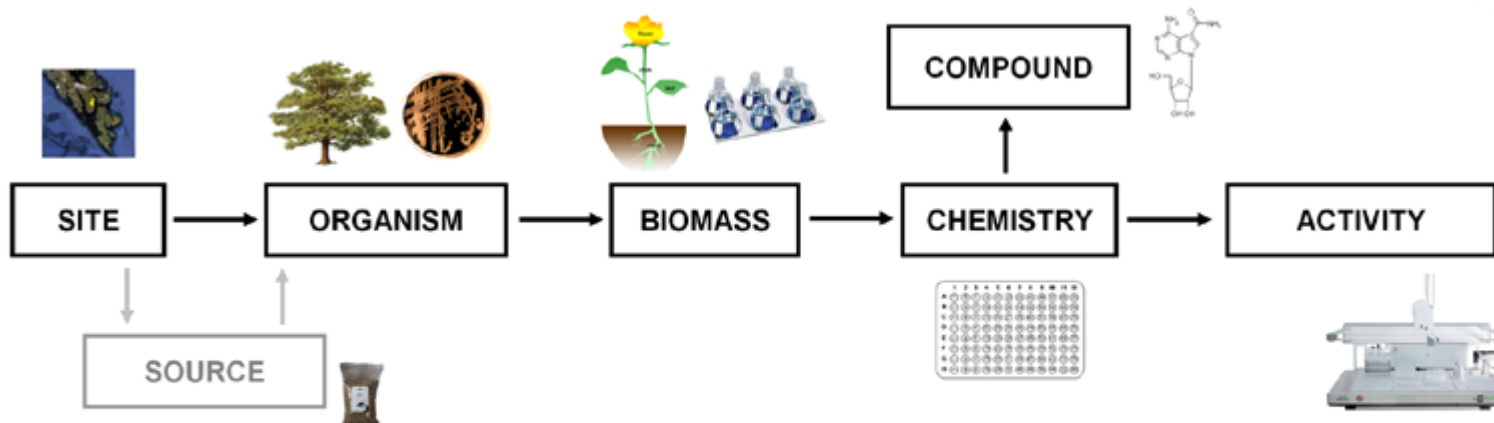
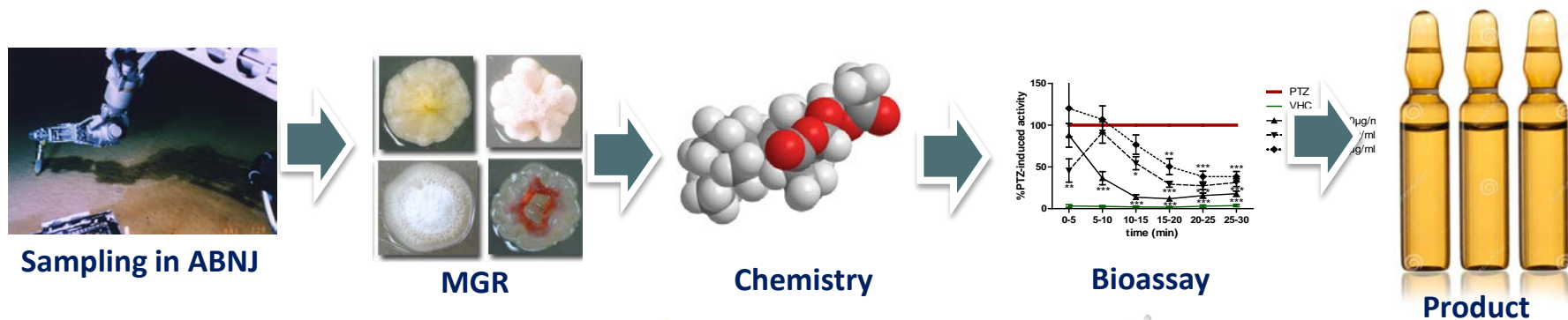
Real Benefit Scenario



- 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.

*Tufts Study http://csdd.tufts.edu/news/complete_story/cost_study_press_event_webcast

Monitoring Sample and Data Flows



OpenNAPIS™

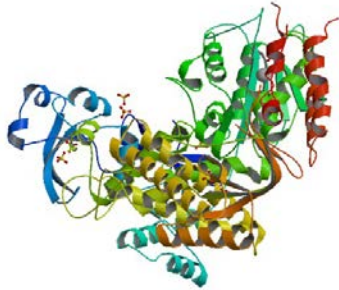
Functional Design

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

Modifications to DNA or compound may make it hard to trace MGR origin

White Point Systems, Inc.
20100626

Tracking Samples can be Tricky



Vent Polymerase For DNA amplification



Journal of
Bacteriology

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J Bacteriol. 2012 May; 194(5): 2375–2376.
doi: [10.1128/JB.00123-12](https://doi.org/10.1128/JB.00123-12)

PMCID: PMC3347054

Genome Sequence of the Model Hyperthermophilic Archaeon *Thermococcus litoralis* NS-C

Andrew F. Gardner,¹ Sanjay Kumar, and Francine B. Perler

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ABSTRACT

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The hyperthermophilic archaeon *Thermococcus litoralis* strain NS-C, first isolated in 1985, has been a foundational organism for archaeal research in biocatalysis, DNA replication, metabolism, and the discovery of inteins. Here, we present the genome sequence of *T. litoralis* with a focus on the replication machinery and inteins.

GENOME ANNOUNCEMENT

[Go to:](#)

Thermococcus litoralis strain NS-C was isolated from a shallow submarine hot spring at Lucrino Beach near Naples, Italy (1), and successfully grown in culture (14). Since then, *T. litoralis* has been the focus of studies on biocatalysis (10), archaeal metabolism (2, 3, 6, 7, 9, 11, 13, 17, 21), DNA replication (4, 5, 8, 12, 20), and protein splicing (15).

NCBI Resources How To

Genome

[Create alert](#) [Limits](#) [Advanced](#)

Thermococcus litoralis

Representative genome: **Thermococcus litoralis DSM 5473**

Download sequences in FASTA format for **genome**, **protein**
Download genome annotation in GFF, **GenBank** or **tabular** format
BLAST against *Thermococcus litoralis* **genome**, **protein**

Display Settings: Overview

Send to:

Organism Overview

ID: 12449

Thermococcus litoralis

Thermococcus litoralis overview

Lineage: Archaea[545]; Euryarchaeota[344]; Thermococci[25]; Thermococcales[25]; Thermococcaceae[24]; Thermococcus[17]; Thermococcus litoralis[1]

England Biolabs, Inc.
Complete Genome
Type: Cocci
Minimum Temperature: 85C, Temperature Range: Hyperthermophilic
Relationship: Free Living, Trophic Level: Heterotroph
Accession: GCF_000246985.3 ASM24698v3 scaffolds: 1 contigs: 1 N50: 2,215,172 L50: 1 NA81925
Length (Mb): 2.21517
GC content: 2292
GC: 43.1

of the model hyperthermophilic archaeon *Thermococcus litoralis* NS-C. Gardner AF, et al. J Bacteriol 2012 May

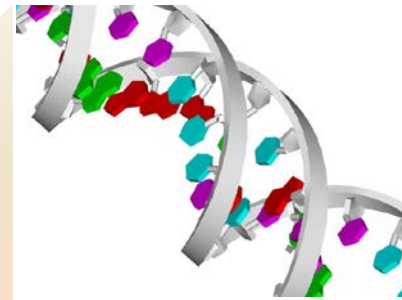


Synthetic Biology – From Genes to Products

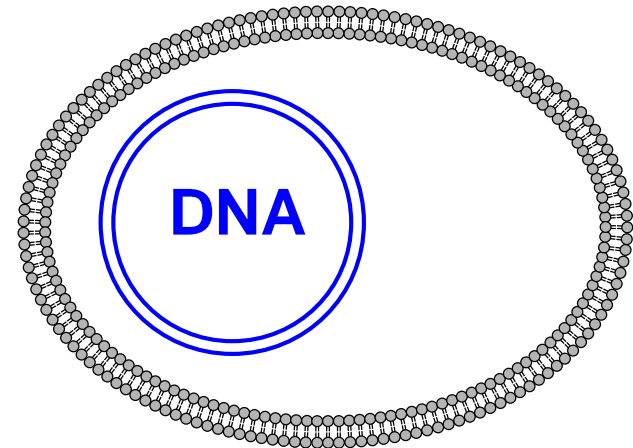
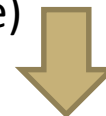
An UNCLOS implementing agreement developed over the next few years would need to be flexible enough to deal with rapid scientific progress



MGR



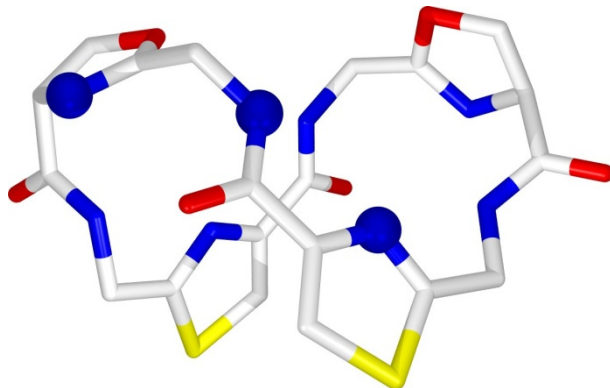
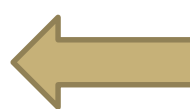
DNA (Synthetic genes
From sequence)



Cell with engineered DNA

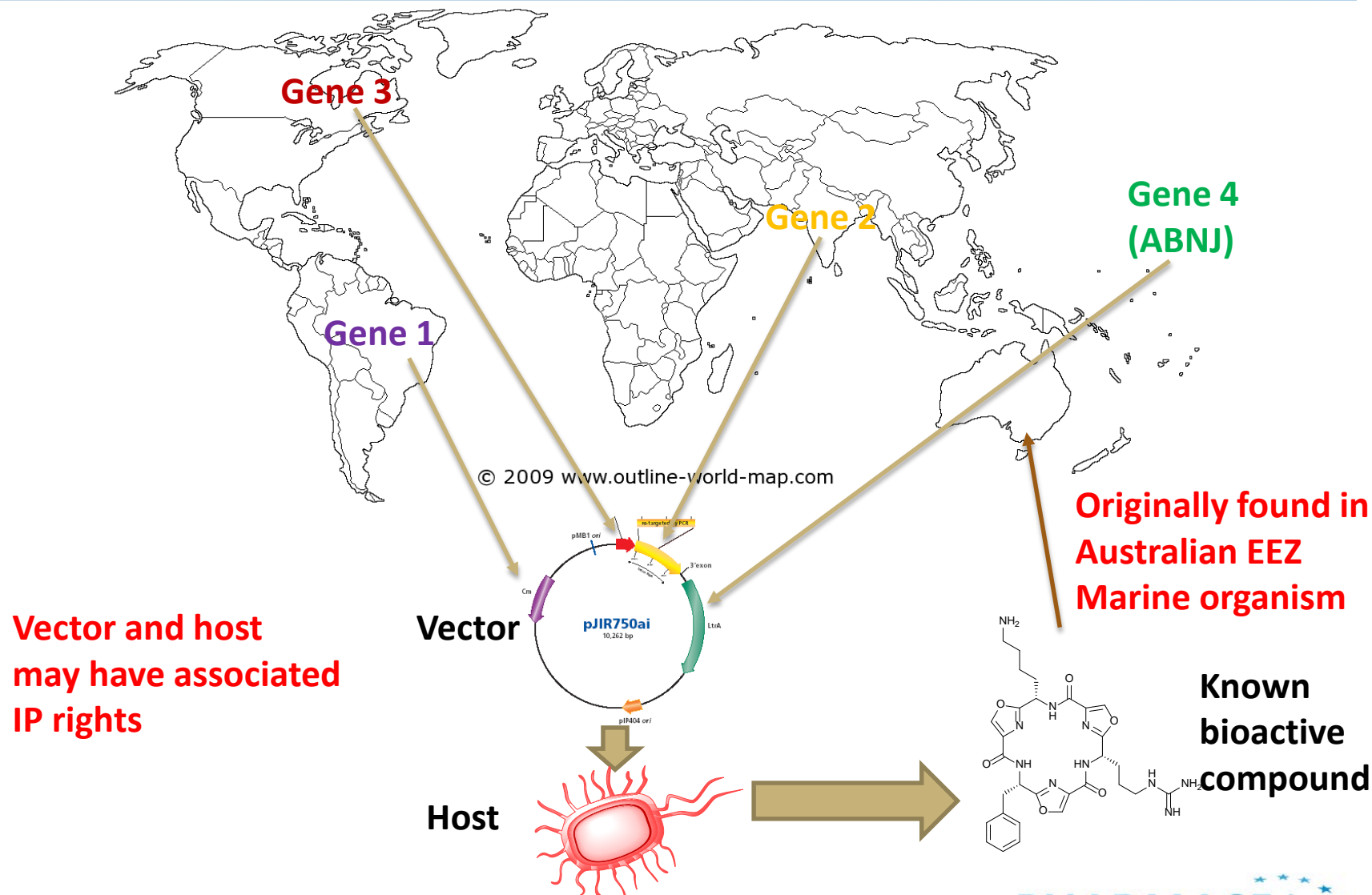


Grow cells



Product

Nightmare (But Realistic) Scenario



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?

PHARMASEA



“The research leading to these results has received funding from the European Union's Seventh Framework Programme (FP7/2007-2013 under grant agreement n^o 312184)”