



Mare Geneticum – The Science

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With thanks to Thomas Vanagt, Arianna Brogiato, Dominic Muyldermans, Laura Lallier, Geoff Burton, Harriet Harden-Davies & Hiroko Muraki Gottlieb



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 vs Biodiscovery

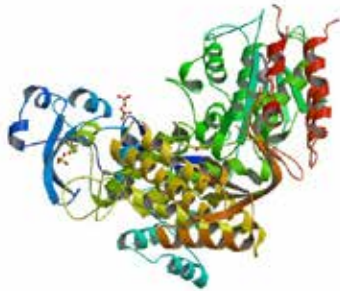
Bioprospecting (Oxford English Dictionary): “the search for plant and animal species from which medicinal drugs and other commercially valuable compounds can be obtained.”

Unlike seabed mining, marine genetic resources are not mined.

The MGR are used as **inspiration** to generate a product which is made by other means.

For this reason the words “**marine biodiscovery**” are used which suggest that it is the inspiration that is important and that the resource is not mined.

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)

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)



Anti biofilm agents

Origin: Red seaweed

Production: Chemical Synthesis

Owner: XXXXX

MGR Derived Pharmaceuticals



Yondelis for cancer

Origin: Caribbean seasquirt

Production: Semi-synthesis



Prialt for pain

Origin: Phillippino cone snail

Production: Recombinant



w-3 polyunsaturated fatty acids
for heart disease Origin: Fish

Production: Fish



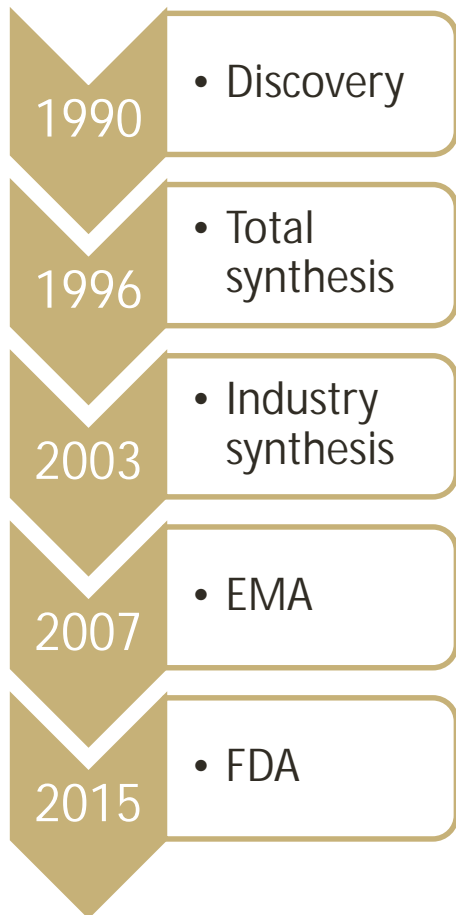
Halaven for cancer

Origin: Japanese deep water sponge

Production: Chemical synthesis

Discovery Timeline

Yondelis™



Ecteinascidia turbinata.

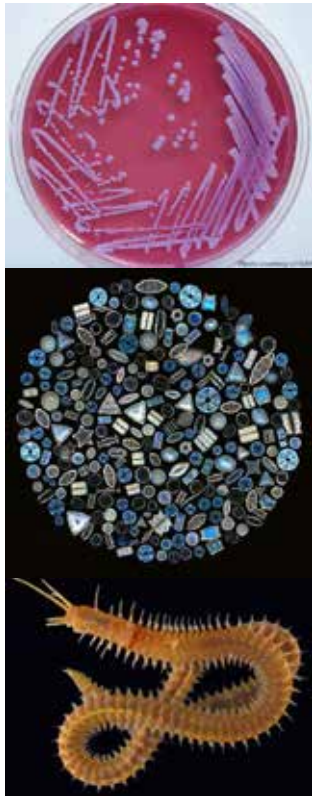


Baseline

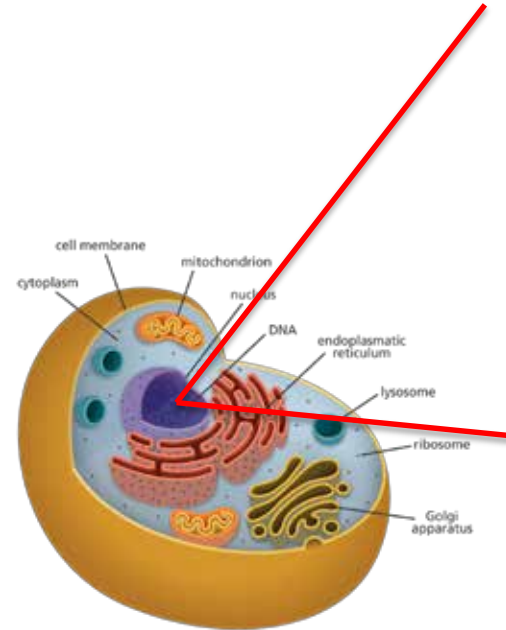


>18 Cycles

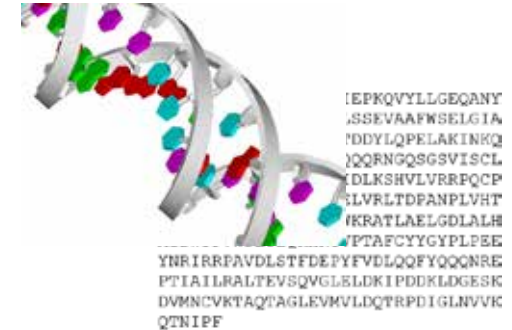
Biological Resources



Marine biological resource

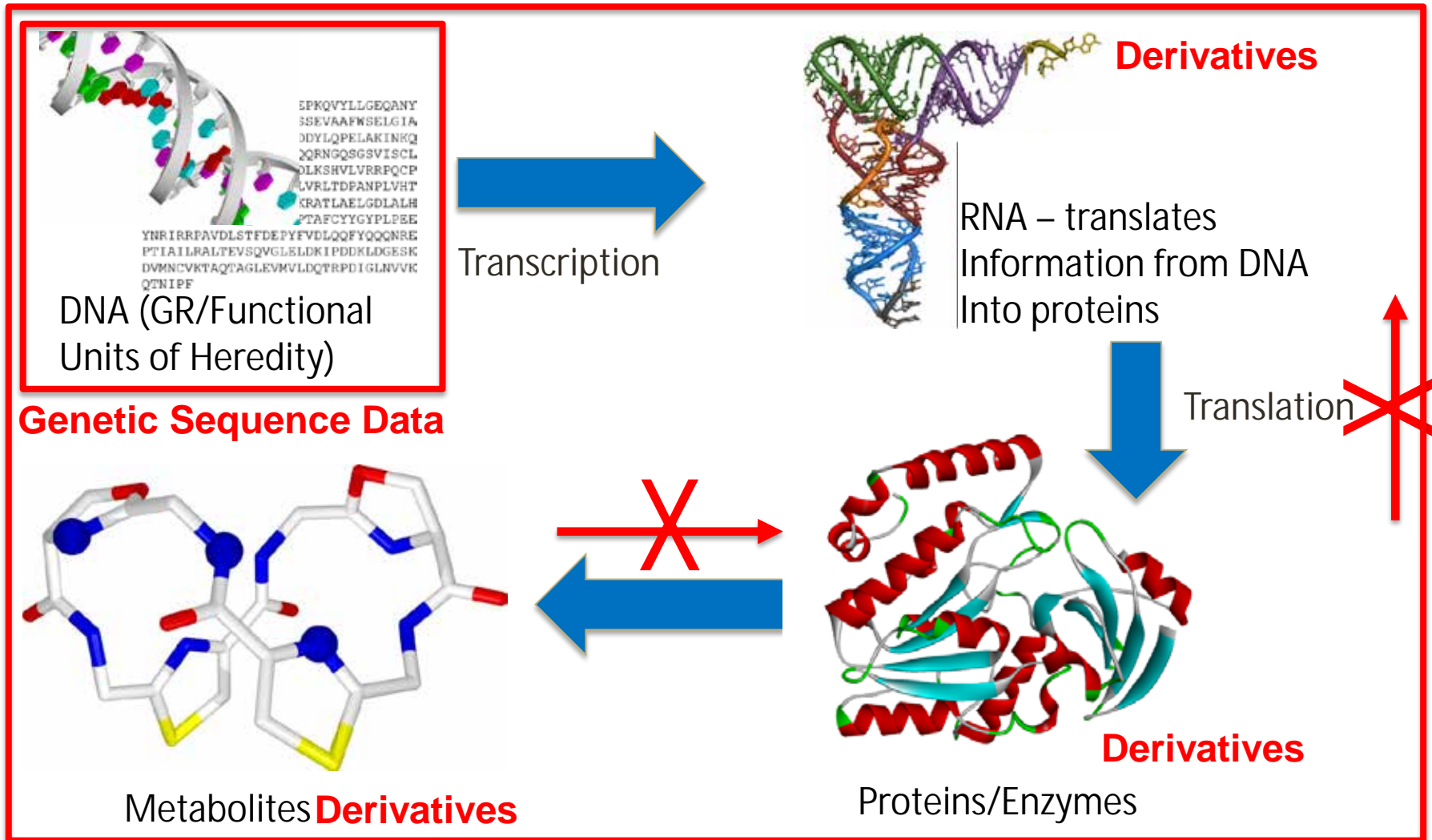


Cells (one or more)

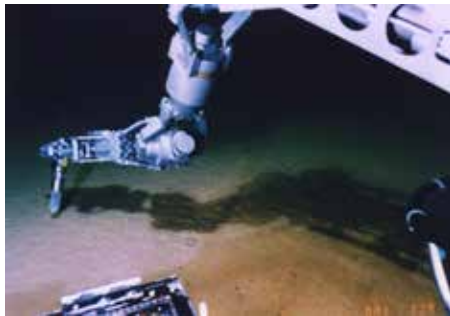


DNA (GR/Functional Units of Heredity)

The Central Dogma of Molecular Biology



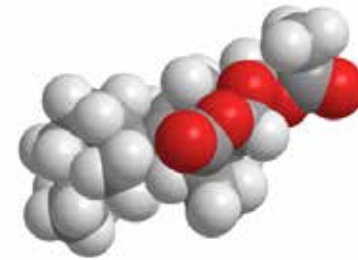
Marine Scientific Research/Bioprospecting



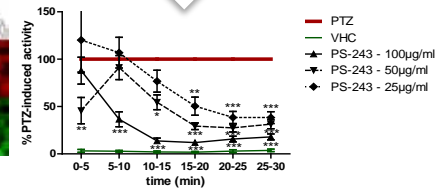
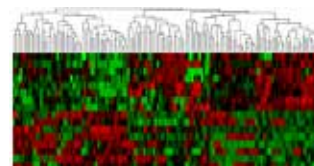
Sampling in ABNJ
Research



MGR
Research



Chemistry
Research



Bioassay
Research



Commercialisation

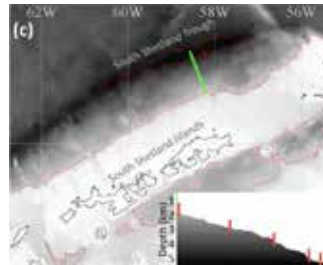


Product

MSR vs Bioprospecting

Application

- Cruise plan



Award

- Feasibility
- Checks



After Cruise

- Cruise report

| MSR ID | DATE | STARTING LAT | STARTING LONG | ENDING LAT | ENDING LONG | DEPTH | STATUS | REMARKS |
|--------|------------|--------------|---------------|------------|-------------|-------|-----------|---------|
| MSR001 | 2010/01/01 | 30S | 120E | 30S | 120E | 1000 | Completed | |
| MSR002 | 2010/01/01 | 30S | 120E | 30S | 120E | 1000 | Completed | |
| MSR003 | 2010/01/01 | 30S | 120E | 30S | 120E | 1000 | Completed | |
| MSR004 | 2010/01/01 | 30S | 120E | 30S | 120E | 1000 | Completed | |
| MSR005 | 2010/01/01 | 30S | 120E | 30S | 120E | 1000 | Completed | |
| MSR006 | 2010/01/01 | 30S | 120E | 30S | 120E | 1000 | Completed | |
| MSR007 | 2010/01/01 | 30S | 120E | 30S | 120E | 1000 | Completed | |
| MSR008 | 2010/01/01 | 30S | 120E | 30S | 120E | 1000 | Completed | |
| MSR009 | 2010/01/01 | 30S | 120E | 30S | 120E | 1000 | Completed | |
| MSR010 | 2010/01/01 | 30S | 120E | 30S | 120E | 1000 | Completed | |

MSR

- Most cruises are for basic research
- Freedom of MSR
- File cruise report to funder

How Might Bioprospecting be Accommodated?

- Require updates on cruise report to alert to change of use
- Notify when commercialisation occurs

Mare Geneticum Provides Building Blocks Based on Scientific Good Practice

Obligatory Prior
Electronic Notification (**OPEN**)



Update **OPEN**

Access

Mare Geneticum Obligatory Prior Electronic Notification

Data on OPEN could include:

Information on collector and contact point

Geographical area of sampling

Period of sampling

Research project description (cruise plan)

Expected nature of what will be collected (grab, core, sediment, invertebrate, plankton etc)

Description of targeted MGR when possible

Commitment to release samples and data in open access biorepository (but conditional on intended use)

Commitment to update OPEN at certain milestones.

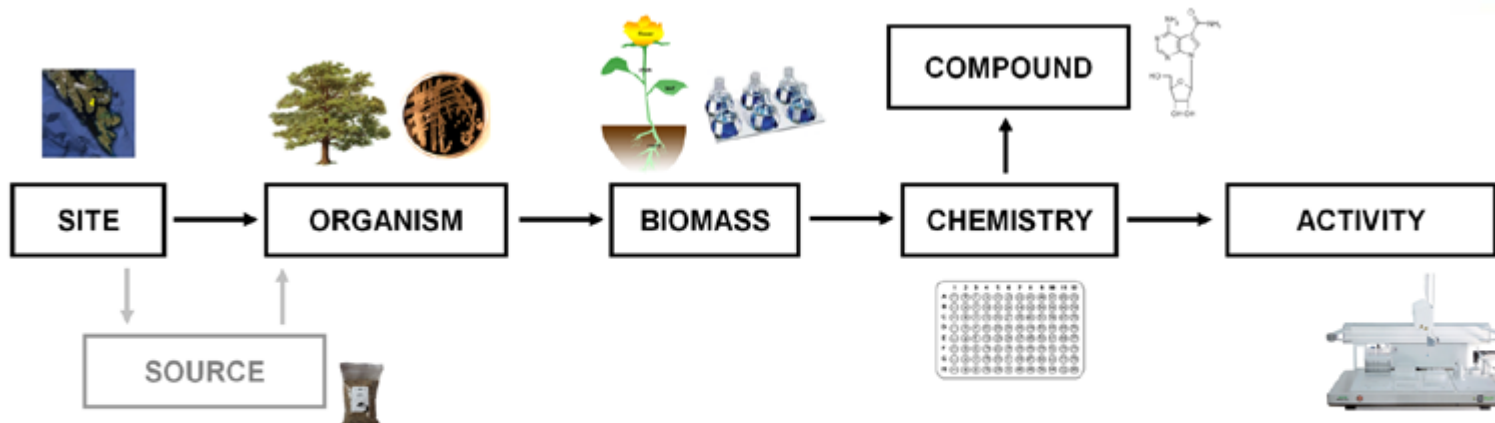
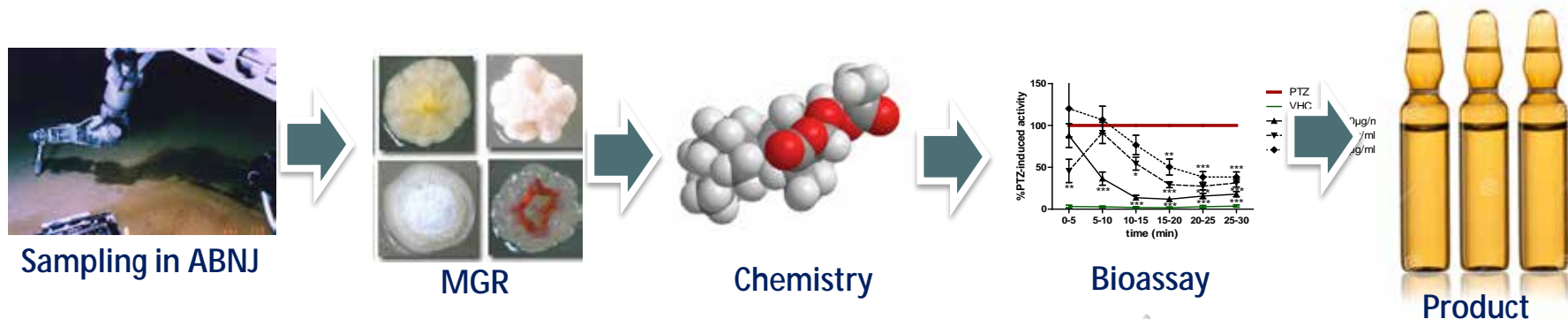
Benefits to Scientists of the OPEN System

Global data sharing platform and clearing house mechanism for marine biodiversity data in all ocean basins including ABNJ

A mechanism for international cooperation in MSR, coordination in global ocean observation and development of standards, manual and guidelines and codes of conduct in MSR and data sharing protocols

A global network of regional centres to enhance capacity, by training the next generation of scientists and area managers in applying international standards and best practices

Monitoring Sample and Data Flows



OpenNAPIS™

Functional Design

Possible to track sample from origin to exploitation
Needs improved data infrastructure

White Point Systems, Inc.
20100626

Tracking Samples can be Tricky



Vent Polymerase For DNA amplification

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: [v](#)

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]



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

PMCID: [PMC3347054](#)

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

Andrew F. Gardner¹, Sanjay Kumar, and Francine B. Perler

[Author information](#) | [Article notes](#) | [Copyright and License information](#)

This article has been cited by other articles in PMC.

ABSTRACT

[Go to:](#) [v](#)

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:](#) [v](#)

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).

England Biolabs, Inc.
Complete Genome
Type: Cocci
Minimum Temperature: 85C, Temperature Range: Hyperthermophilic
Life Relationship: Free Living, Trophic Level: Heterotroph
Accession: [NC_000246.985.3](#) ASM24698v3 scaffolds: 1 contigs: 1 N50: 2,215,172 L50: 1 NA81925
Genome 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



Benefit Sharing

- Must be multilateral compared to bilateral for Nagoya Protocol
- Benefits may include:
 - Scientific exchanges/training
 - Technology transfer
 - Capacity building (infrastructure)
 - Enhanced reputation
 - Increased number/quality of scientific publications
 - Biodiversity conservation
 - Valuable regional resources developed (knowledge, samples, data)
 - Upfront/milestone payments & royalties

Is an Open Access Approach Possible?

- Open Access approach may be used when:
 - There is no desire/need to control access
 - There is more than enough of a resource for all to utilise
- Precedents in biology/software/semiconductors
- Low cost – commensurate with size of problem

Mare Geneticum Provides Building Blocks Based on Scientific Good Practice

Obligatory Prior
Electronic Notification (**OPEN**)



Update **OPEN**
Exclusivity Period



Share Samples and Raw Data

Many Precedents in Science
'Open Innovation'

Open Access Publication/Data

Open Access in Horizon 2020

Peer-reviewed scientific publications

All projects receiving Horizon 2020 funding are **required** to make sure that any peer-reviewed journal article they publish is openly accessible, free of charge (article 29.2. Model Grant Agreement).

Research data

The Commission is running a **pilot on open access** to research data in Horizon 2020: the Open Research Data (ORD) pilot. This pilot takes into account the need to balance openness with the protection of scientific information, commercialisation and Intellectual Property Rights (IPR), privacy concerns, and security, as well as questions of data management and preservation.

Reporting Research Outcomes

The screenshot shows the Researchfish Personal Portfolio page for Prof Marcel Jaspars. The page is titled "Personal Portfolio" and features a navigation menu with "My Awards", "Personal Portfolio", "Our Members", and "My Account". The "Personal Portfolio" section is active, showing a "COMMON OUTCOMES" table and a "PROFILE" section.

COMMON OUTCOMES

| | |
|---|-----|
| Publications | 155 |
| Collaborations & Partnerships | 0 |
| Further Funding | 12 |
| Next Destination & Skills | 0 |
| Engagement Activities | 1 |
| Influence on Policy, Practice, Patients & the | 0 |

PROFILE

| | |
|------------|-----------------|
| Title | Prof |
| First name | Marcel |
| Last Name | Jaspars |
| ORCID ID | ⚠ Not connected |

You have **172** total outcomes added to your personal portfolio. You also have **146** outcomes not attributed to an award.

[Download Personal Portfolio](#)

[Add delegate or research team member](#)

[Help using this page](#)

[Help and Support](#)

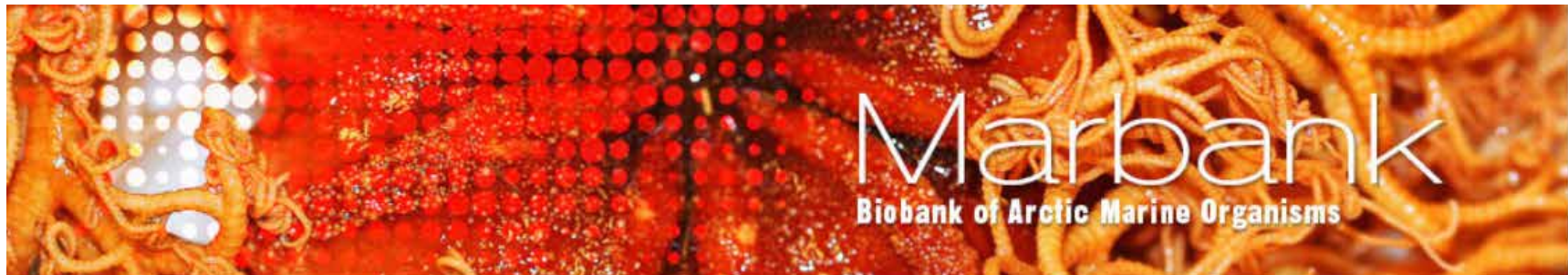
nature

Availability of data, material and methods

An inherent principle of publication is that others should be able to replicate and build upon the authors' published claims. A condition of publication in a Nature journal is that **authors are required to make materials, data, code, and associated protocols promptly available to readers without undue qualifications**. Any restrictions on the availability of materials or information must be disclosed to the editors at the time of submission. Any restrictions must **also** be disclosed in the submitted manuscript.

After publication, readers who encounter refusal by the authors to comply with these policies should contact the chief editor of the journal. In cases where editors are unable to resolve a complaint, the journal may refer the matter to the authors' funding institution and/or publish a formal statement of correction, attached online to the publication, stating that readers have been unable to obtain necessary materials to replicate the findings.

Case Study: MarBank as an MGR Repository



Home

Cold waters

Marine Products

Services

Norwegian Network

About us

Search

Contact and visiting address:

Kjersti Lie Gabrielsen,
Manager
Phone: +47 91563533
E-mail:
kjersti.gabrielsen@imr.no

Marbank
Forskningsparken i
Tromsø/Tromsø Science
Park,
Sykehusvegen 21, N-9019
Tromsø, Norway.

Postal address:
Marbank,
Havforskningsinstituttet/



<http://www.imr.no/marbank/en>

MarBank Objectives

MarBank offers *Ex situ* access to Marine Genetic Resources for research and exploitation purposes

Marine organisms are collected from their natural habitat and kept alive or processed and conserved in the biobank

Safe and easy access to quality assured marine samples

Opportunity for researchers that do not have the ability to collect MGRs *In situ*

The NCI Open Repository



DTP Developmental Therapeutics Program



Extracts from:
80,000 plants
20,000 marine organisms

Collected via contractors
'Letter of collection'
covers ABS issues

Extracts prepared using
standardised protocols

Samples made available
without cost to anyone
working on cancer
Requires signing MTA

Limited exclusivity

<https://dtp.cancer.gov/organization/npb/introduction.htm>



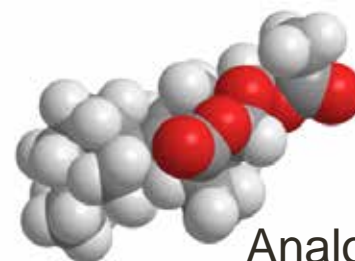
PharmaSea Case Study Using NCI Open Repository



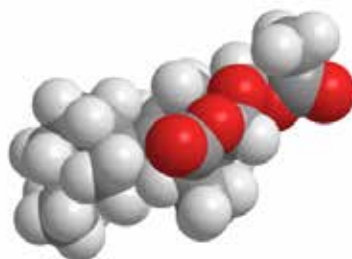
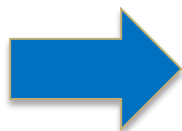
Spongionella sp
OCDN 8588-T
Collected by CRF



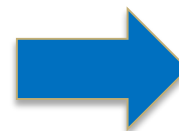
Benefit sharing obligation
(from NCI 'Letter of
Collection' & MTA) to be
agreed with relevant
Philippine authorities at point
of commercialisation



Analogues
made and
tested
IP/Publication
soon

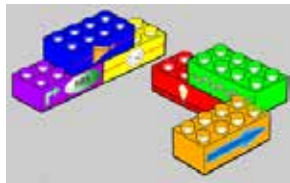


Discovery of new
Molecule with
anti-Alzheimer
properties



Effective in
animal models

Open Access Approach



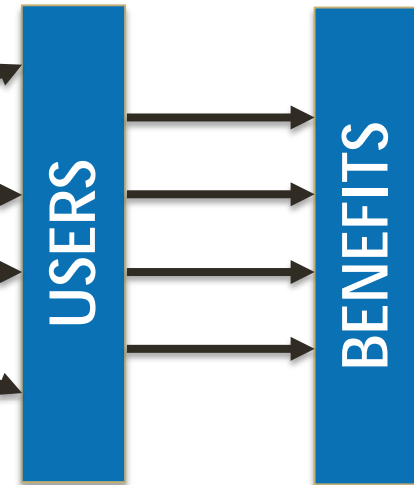
Biobricks



open source



& Raw Data



- All should be able to benefit from discoveries
- This approach will lead to greater innovation, transparency and openness
- Access for landlocked & developing countries
- **Make sure all can benefit and can exploit - requires capacity building to ensure fairness**

Mare Geneticum Provides Building Blocks Based on Scientific Good Practice

Obligatory Prior Electronic Notification (**OPEN**)

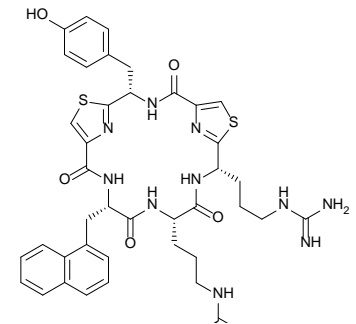


If IA requires monetary BS: royalties to be paid on commercialisation at % fixed by sector



Extend Exclusivity Period For a fee

Update **OPEN**



Update **OPEN** Exclusivity Period



Update **OPEN**



LGEQANY
KSELGIA
LAKINRQ
SSVISCL
VRRPQCP
ANPLVHT
LCEAIERYSGIFQGDPEWKRATLAEGLDLALH
AIDWTFVNSLTEQKHKYVPTAFCCYYGYPLPBE
YNRIRRPVAVDLSTFDEPFYFVDLQQFYQQNRE
PTIAILRALTEVSVQVGLDLKIPDDKLDGESK
DVMNCVKTAQTAGLEVMLDQTRPDI GLNVVK
QTNIPF

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
13 September 2007 (13.09.2007)

PCT

(10) International Publication Number
WO 2007/103739 A2

Share Samples and Raw Data



Access

Benefit Sharing

Exclusivity Periods in Scientific Practice

Protein Data Bank entries are placed on hold for one year from the date of deposition. They may be released earlier on a date specified by the Contact Author. When the corresponding electronic or paper publication occurs, the entry must be released if the journal policy requires release upon publication.

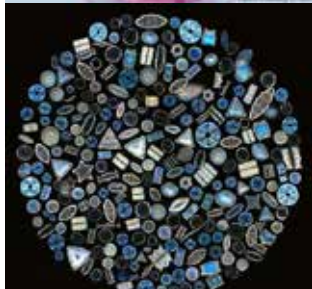


<http://www.rcsb.org/pdb/home/home.do>

Types of Data the *Mare Geneticum* Proposal Could Cover:

| Categories of information | Explanation | Types of data |
|-----------------------------------|--|--|
| Data only | Raw data (e.g. genetic sequence data) | <ul style="list-style-type: none"> • Metadata associated with the samples • Initial taxonomic analysis of the samples • Genetic sequence data (DNA) • Transcriptome data (RNA of the genes that are functional at that time) • Automatic gene/transcriptome function annotations • Protein sequence data (DNA/RNA data automatically translated to give amino acid sequence) |
| Data and analysis | Genetic sequence data which has been annotated with putative gene functions using an algorithm | <ul style="list-style-type: none"> • Initial taxonomic analysis of the samples (DNA methods?) • Automatic gene/transcriptome automatic function annotations • Protein sequence data (DNA/RNA data automatically translated to give amino acid sequence) • <i>Protein structure data (Embargo)</i> • <i>Metabolite data (mainly commercial databases)</i> |
| Data, analysis and interpretation | Critical evaluation of the data and its analysis conducted by an expert | <ul style="list-style-type: none"> • Full taxonomic analysis of the samples • Manual gene/transcriptome function annotations • <i>Protein structure data (Embargo)</i> • <i>Metabolite data (mainly commercial databases)</i> |

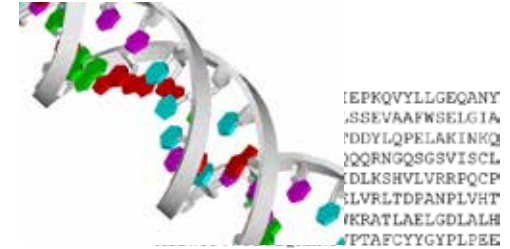
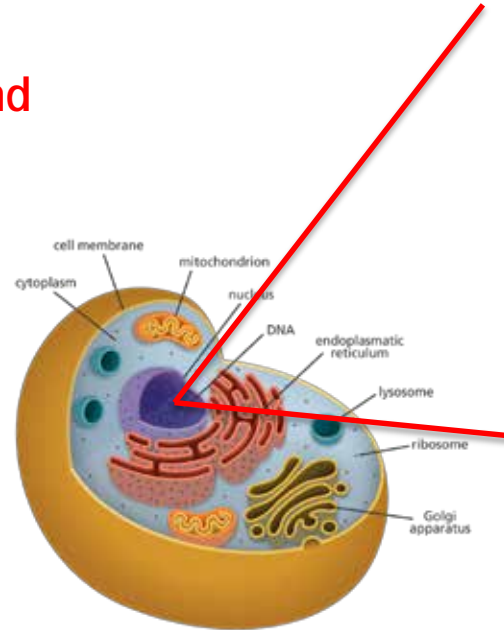
Mare Geneticum proposes open access to samples and raw data with exclusivity period



Possibility to extend exclusivity period for a fee.



Samples and Associated metadata



```

IEPKQVYLLGEGANY
LSSEVAAFWSELGIA
DDYLLQPELAKINKQ
QQQRNGQSGSVISCL
DLKSHVLVRRPQCP
SLVRLTDFANPLVHT
IKRATLAEGLDLALH
PTAFICYGYPLPEE
YNRIRRPVLDLSTFDEPFVLDLQQFYQQQNRRE
PTIAILRALTEVSVQVGLDLKIPDDKLDGSEK
DVMNCVKTAQTAGLEVHVLDQTRPDI GLNVVK
QTNIPF
    
```

DNA (GR/Functional Units of Heredity)

Raw Genetic Sequence Data

| VESSEL | CRUISE | DATE | SAMPLING GEAR | DIVE # | SAMPLE NUMBER | LATITUDE | LONGITUDE | DEPTH | SAMPLE TYPE | DESTINATION |
|--------|--------|------------|---------------|--------|----------------|------------|------------|--------|---------------|-------------|
| Scotia | 09155 | 18/07/2015 | Van Veen Grab | 3 | 09155_VV_3A | 57.968247N | 15.548597W | 1196.4 | SED SubSamp | JASPARS |
| Scotia | 09155 | 18/07/2015 | Van Veen Grab | 3 | 09155_VV_3B | 57.968247N | 15.548597W | 1196.4 | SED SubSamp | JASPARS |
| Scotia | 09155 | 18/07/2015 | Van Veen Grab | 5 | 09155_VV_5A | 57.95626N | 15.536247W | 1203.8 | SED SubSamp | JASPARS |
| Scotia | 09155 | 18/07/2015 | Van Veen Grab | 5 | 09155_VV_5B | 57.95626N | 15.536247W | 1203.8 | SED SubSamp | JASPARS |
| Scotia | 09155 | 19/07/2015 | Baited Lander | 1 | 09155_BIL_1_E1 | 57.953318N | 15.550793W | | Amphipods | PIERTNEY |
| Scotia | 09155 | 19/07/2015 | Baited Lander | 1 | 09155_BIL_1_R1 | 57.953318N | 15.550793W | | Amphipods | PIERTNEY |
| Scotia | 09155 | 19/07/2015 | Megacore | 1 | 09155_MC_1_1A | 57.95567N | 15.550255W | | SED SubSamp | JASPARS |
| Scotia | 09155 | 19/07/2015 | Megacore | 1 | 09155_MC_1_1B | 57.95567N | 15.550255W | | SED SubSamp | JASPARS |
| Scotia | 09155 | 19/07/2015 | Megacore | 2 | 09155_MC_2_6A | 57.955577N | 15.550243W | | Bacterial Mat | JASPARS |
| Scotia | 09155 | 19/07/2015 | Megacore | 2 | 09155_MC_2_6B | 57.955577N | 15.550243W | | Bacterial Mat | JASPARS |
| Scotia | 09155 | 19/07/2015 | Megacore | 2 | 09155_MC_2_6C | 57.955577N | 15.550243W | | Bacterial Mat | JASPARS |
| Scotia | 09155 | 19/07/2015 | Megacore | 2 | 09155_MC_2_6D | 57.955577N | 15.550243W | | Bacterial Mat | JASPARS |
| Scotia | 09155 | 19/07/2015 | Megacore | 2 | 09155_MC_2_6E | 57.955577N | 15.550243W | | Bacterial Mat | JASPARS |

Summary

Open access to raw data and samples

Benefits to scientists by standardising data and providing central resource (OPEN)

OPEN standardises data management, taxonomy and species identification

OPEN enhances international research coordination and cooperation

Requires capacity building/technology transfer to ensure fairness

Targeted training and sharing of expertise, methodology, guidelines and best practices

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 ° 312184)”