

Marine biotech for biomedical applications: European Marine Biology Resource Center (EMBRC)

Unlocking the potential of marine biotechnology

Marco Borra

In charge of international cooperation and strategic partnership

&

EMBRC^{IT} Liaison Officer

Stazione Zoologica Anton Dohrn

Napoli

The Earth

- 72 % of the surface is **water**
- > 90 % of the biosphere is **water**
- So Earth is really the **BLUE** planet



Healthy Oceans, Healthy Lives

Covering 72% of our planet, oceans make life on Earth possible. All life, including our own, depends on the ocean.

Marine Food is a source of protein rich in essential fatty acids. With more than 1 billion people depending on fish for their basic protein; a soaring world population (9-11 billion people by 2050); most of the world's fisheries now stressed by overfishing.

Marine natural products and **marine animal models** provide important information that leads to medical breakthroughs and powerful abilities.

Providing the largest carbon sink potential of the planet, the ocean is an essential regulator of our **climate** system;

Energy source: tides, waves, biofuels..

What is Marine Biotechnology?

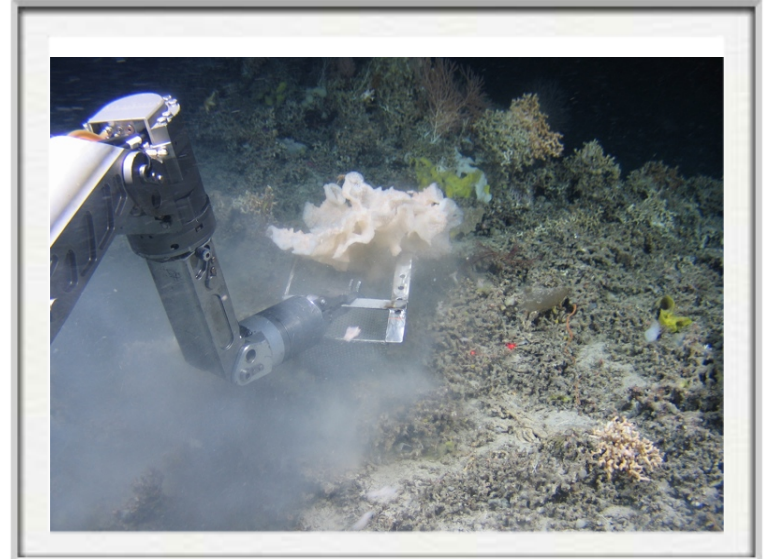
... Marine biotechnology explores and uses marine bioresources as the target for origin of biotechnological applications, which are used for the production of products and services



The Marine Biotech Opportunity

- BioTechnology is the driver of the next wave of industrial **innovation**

- Biotechnology is key to **sustainable** industrial manufacturing

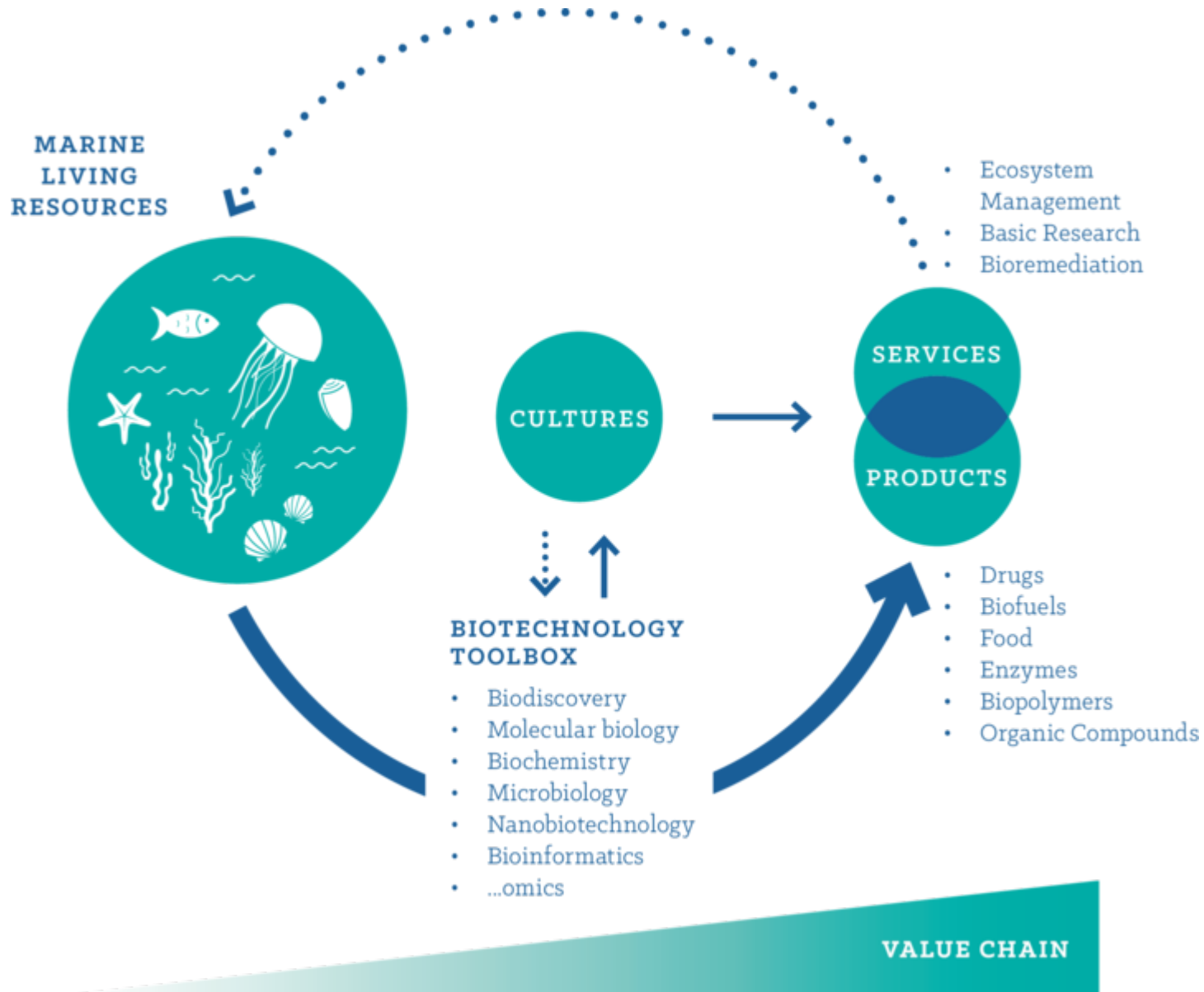


- Marine biodiversity is a rich source of medicines and natural products, potentially exploitable in the blue biotech industry

The marine environment is our ocean of opportunity for new materials, new compounds and new processes for our **society**

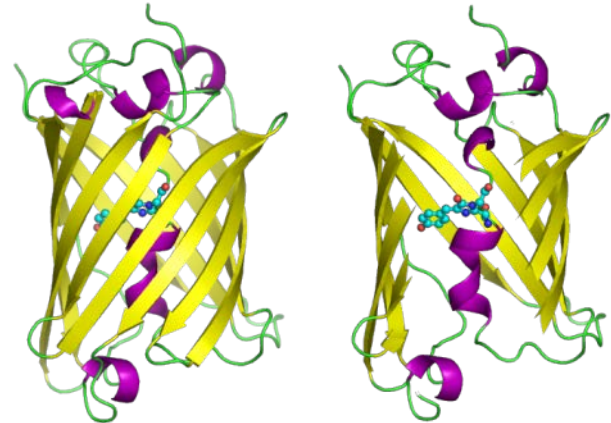
..Health, ..Food, ..Energy, ..Environment, ..Industry

The potential

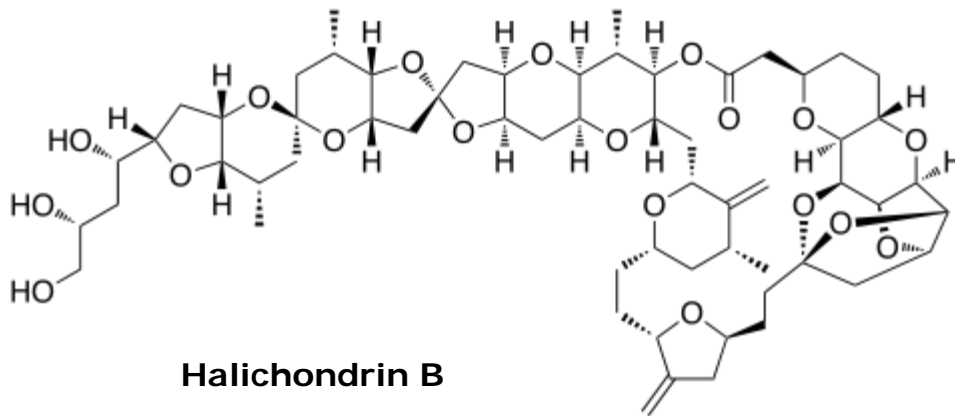


Examples of applications:

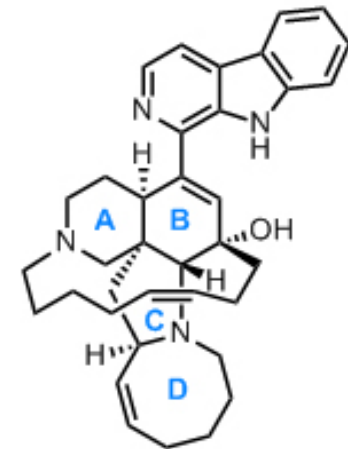
- Pigments
- Antioxidants
- Pharmaceutical use
- Nutraceutical use
- Cosmeceutical use



Green fluorescent protein



Halichondrin B



Manzamine A

Examples of Marine Biotechnology successes

Cosmeceuticals

- European market > € 27.6 billion per year (COLIPA – The European Cosmetics Association, 2006)

	% of market
• Skin care products	25.7
• Hair products	23.7
• 'Toiletries'	23.4

	% production growth
• Facial serviettes	4.9
• Whitening agents	6.0
• Anti-age/anti-wrinkle cream	0.5
• Trend towards 'natural products'	



Resilience™ by Estée Lauder contains anti-inflammatory pseudopterosin



Products contain blue-green algae extracts

Examples of Marine Biotechnology successes

Biomaterials (bone and tissue)

Source organism	Biomaterial	Health application
Macro-algae	Polysaccharides, calcareous algae	Bone and tissue scaffold
Crustacean and Molluscs	Chitin, chitosan, protein-derived peptides	Tissue repair
Finfish	Protein - collagen	Tissue repair, collagen reinforced cements – bone repair
Sponges	Uses skeletal structure	Bone and tissue scaffold, tissue repair, bone grafting

Biomaterials (adhesives)

Source organism	Bioactive compounds	Health application
Molluscs Goose barnacle Mussels	Proteins Proteoglycans	Wound closure Orthopaedics Prosthetics Collection bags
Echinoderms Starfish Urchins	Proteins	Orthopaedics

Another example:

Slime eel used for new biomaterial

Source: Vancouver Aquarium (2014)

<http://www.youtube.com/watch?v=pmaal7Hf0WA>



Bioactives for health



Cone snail
Conus magus

Ziconotide / Prialt Elan / Azur Pharma

- Neuropathic Pain
 ω - conotoxin MVIIA



Caribbean sea-squirt
Trididemnum solidum

Didemin B

- Cyclic peptide
Phase I/II clinical
trials on-hold



Caribbean sea-
squirt
*Ecteinascidia
turbinata*

Yondelis / Trabectedin PharmaMar/J&J

- Anti-tumour
Ecteinascidin-743



Sea hare
*Dolabella
auricularia*

Dolastatin 10 /TZT-1027

- Anti-tumour
Phase I/II clinical trials



Sacoglossan
Elysia rufescens

Kahalalide F - PharmaMar

- Anti-tumour
Phase II clinical trials



Bryozoan
Bugula neritina

Bryostatin 1 – GPC Biotech

- Macrocyclic lactone
Phase II clinical trials

Molinski et al., Nature Reviews Drug Discovery, January 2009, Volume 8, 69-85

Functional Foods/Food & Feed Ingredients/Nutraceuticals

Target Areas

- Ingredients and added-value products research
- Using fish processing waste, under-utilised species, algae

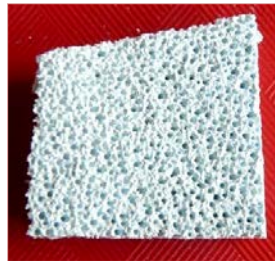


Target Areas

- Bone replacement market
- Drug delivery systems
- Adhesives



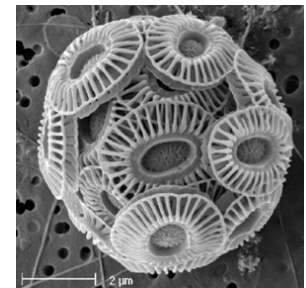
Spinal fracture repair using marine collagen reinforced cement



Bone tissue growth scaffold formed from natural sponge



Biodegradable polymer from brown seaweed for drug delivery



Drug Delivery Systems

« Functionalization of the living diatom *Thalassiosira* sp. with thiol moieties ». Y.Lang et Al., **Nature**, 2013

Time to market for new products

	Time to market for new products		
	1-5 years	5-10 years	10+ years
Industry sector	Food, Agriculture, Cosmetics	Chemicals, Advanced Materials, Medical Devices	Pharmaceutical, Medical Devices, Energy
Source organism	Macro and micro algae, fish processing waste, fish and shellfish	Macro and micro algae, marine invertebrates, fish processing waste, sponges, marine fungi	Macro and micro algae, marine invertebrates, sponges, marine bacteria and viruses
Compounds	<ul style="list-style-type: none"> • Pigments incl. carotenoids • Lipids/fatty acids • Proteins/peptides/amino acids • Minerals • Polysaccharides • Biopolymers • Enzymes • Secondary metabolites incl. phenolics 	<ul style="list-style-type: none"> • Pigments incl. carotenoids • Lipids/fatty acids • Proteins/peptides/amino acids • Minerals • Polysaccharides • Biopolymers • Enzymes • Secondary metabolites, incl. phenolics 	<ul style="list-style-type: none"> • Pigments incl. carotenoids • Lipids/fatty acids • Proteins/peptides/amino acids • Minerals • Polysaccharides • Biopolymers • Enzymes • Secondary metabolites incl. phenolics
Examples of Applications (current and future)	<ul style="list-style-type: none"> • Functional ingredients incl. antioxidants • Nutraceuticals • Food supplements • Human and animal nutrition • Cosmetics • Personal care • Cosmeceuticals • Horticulture growth stimulants • Fertilisers • Cleaning and detergents 	<ul style="list-style-type: none"> • Industrial adhesives • Medical adhesives • Animal health • Tissue and bone replacement • Wound dressings • Dental material • Anti-bacterial • Anti-obesity • Micro-encapsulation • Drug delivery • Bioremediation 	<ul style="list-style-type: none"> • Nano particles • Anti-cancer • Anti-inflammatory • Anti-infective • Anti-viral • Anaesthetics • Other medical therapeutics

Dermod Hurst, Marine Institute, Ireland

EMBRC & Marine Biotechnology

“Better R&D infrastructure and platforms will be needed to improve our understanding of marine bioresources and to improve our access to and development of these resources.”

“The outlook for marine biotechnology has changed profoundly in the last decade in large part owing to advances in science and technology in particular “omics” sciences. These advances provide new insights into marine bioresources and improve the ability to access, manipulate and develop these resources to address some of today’s grand challenges.”

OECD, 2013. Marine Biotechnology.

Ecosystems Model Organisms Experimental Aquaria & Mesocosms 'Omic Platforms Bioimaging



EUROPEAN MARINE BIOLOGICAL RESOURCE CENTRE

*Responding to the Global Societal Grand Challenges
through
Advanced Marine Biology and Ecology Research*

- *Biomedicine*
- *Sustainability of Food Production*
- *Industrial Process Innovation*
- *Environmental Adaptations to Climate and Pollution*



EMBRC is in the **ESFRI roadmap of Pan-EU RIs** *(since 2008)*

Social Sc. & Hum. (5)	Life Sciences (13)		Environmental Sciences (9)		Energy (7)	Material and Analytical Facilities (6)	Physics and Astronomy (10)		e-Infra-structures (1)
SHARE	BBMRI	ELIXIR	ICOS	EURO-ARGO	ECCSEL	EUROFEL	ELI	TIARA*	PRACE
European Social Survey	ECRIN	INFRA FRONTIER	LIFEWATCH	IAGOS	Windscanner	EMFL	SPIRAL2	CTA	
CESSDA	INSTRUCT	EATRIS	EMS	EPOS	EU-SOLARIS	European XFEL	E-ELT	SKA	
CLARIN	EU-OPENSCREEN	EMBRC	SIAEOS	EISCAT_3D	JHR	ESRF Upgrade	KM3NeT	FAIR	
DARIAH	Euro BioImaging	ERINHA BSL4 Lab		COPAL	IFMIF	NEUTRON ESS	SLHC-PP*	ILC-HIGRADE*	
	ISBE	MIRRI			HIPER	ILL20/20 Upgrade			
	ANAEE				MYRRHA				

Partners

- 9 Nodes
- 26 Stations (operators)

EMBRC nodes

Belgium

France

Greece

Israel

Italy

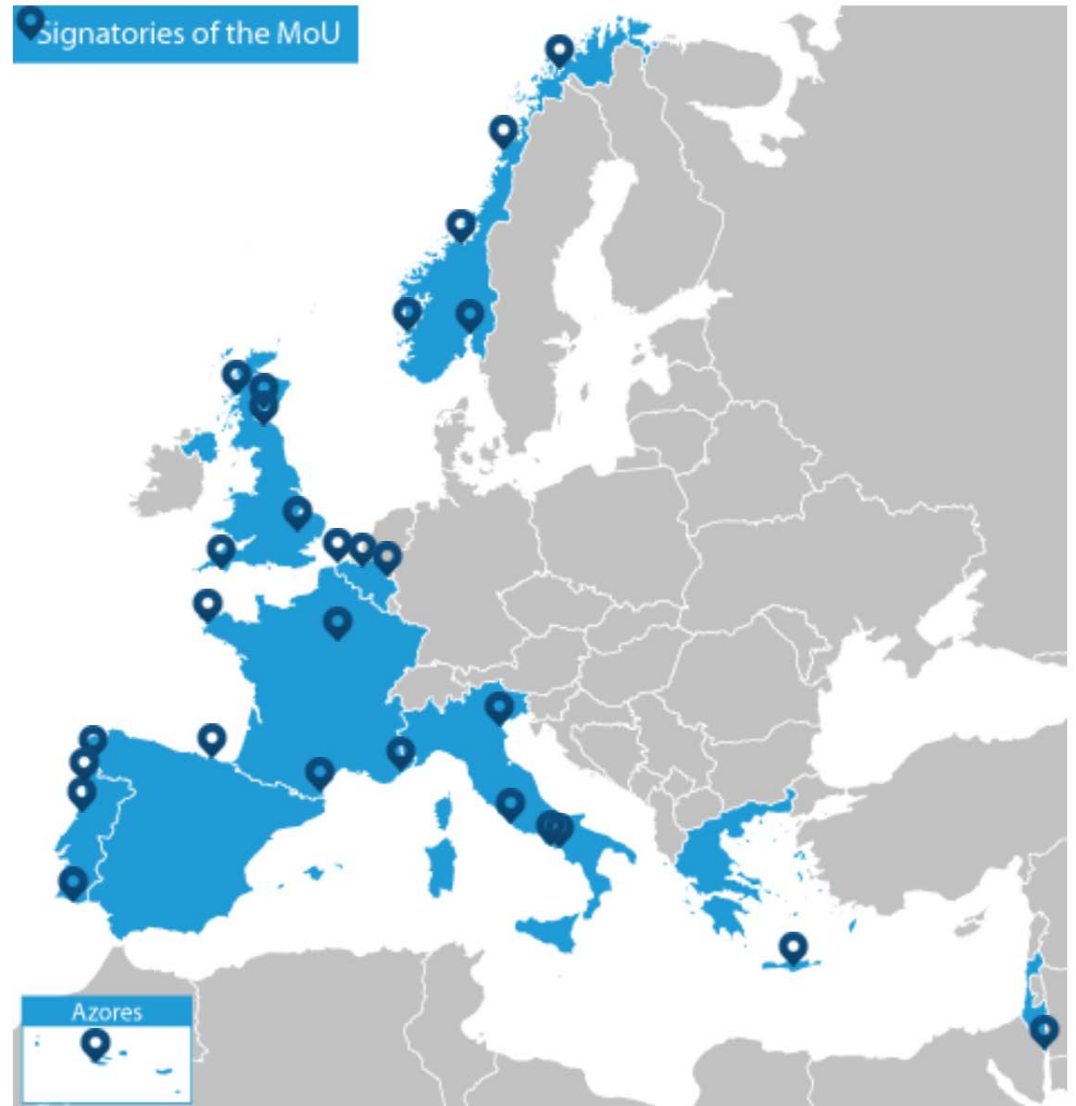
Norway

Portugal

Spain

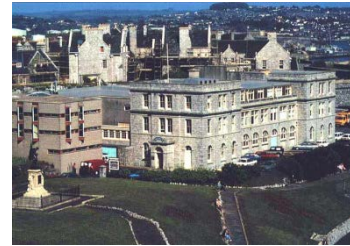
United Kingdom

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Evolving Marine Stations

- First marine stations were built in the 19th Century to access the sea
- Rationale: Cataloguing of marine life and resources, education and scientific research. Hosting visiting researchers.
- More than 20 Nobel Prizes have been awarded in medicine, chemistry and physiology using marine animals as models



Track record of Marine stations

- THEODORE BOVERI, CELL BIOLOGIST FROM Univ. Wurzburg would spend summers at SZN which contributed to establish the chromosomal basis of inheritance
- TIM HUNT (Sea Urchin eggs=> Cyclins; proteins, which controls cell cycle division; related to cancer)
- TAQ Polymerase: From hot spring source DNA replication enzyme!
- MARINE MODEL ORGANISMS HAVE ALONG HISTORY OF CONTRIBUTION to biomedical research understanding basic cell biology and physiology.
- Meyer et al 2015; trends in pharmaceutical science:
<http://marinepharmacology.midwestern.edu/clinPipeline.htm>

Evolving European Marine Stations

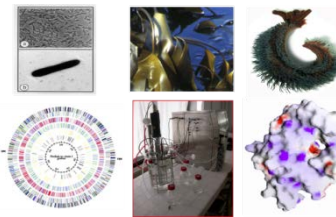
- The coastal zone supports an enormous breadth of economic activities, with a wide range of academic and industrial users needing access to marine resources



Aquaculture



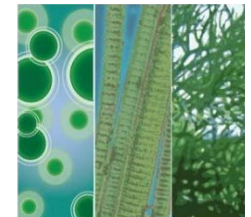
Renewable Energy



Marine Bio-tech

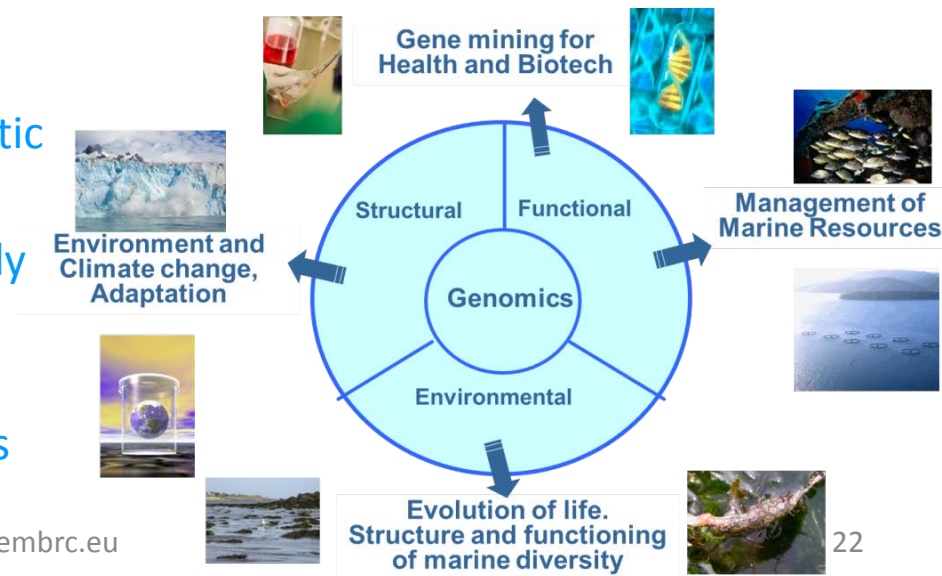


Fisheries



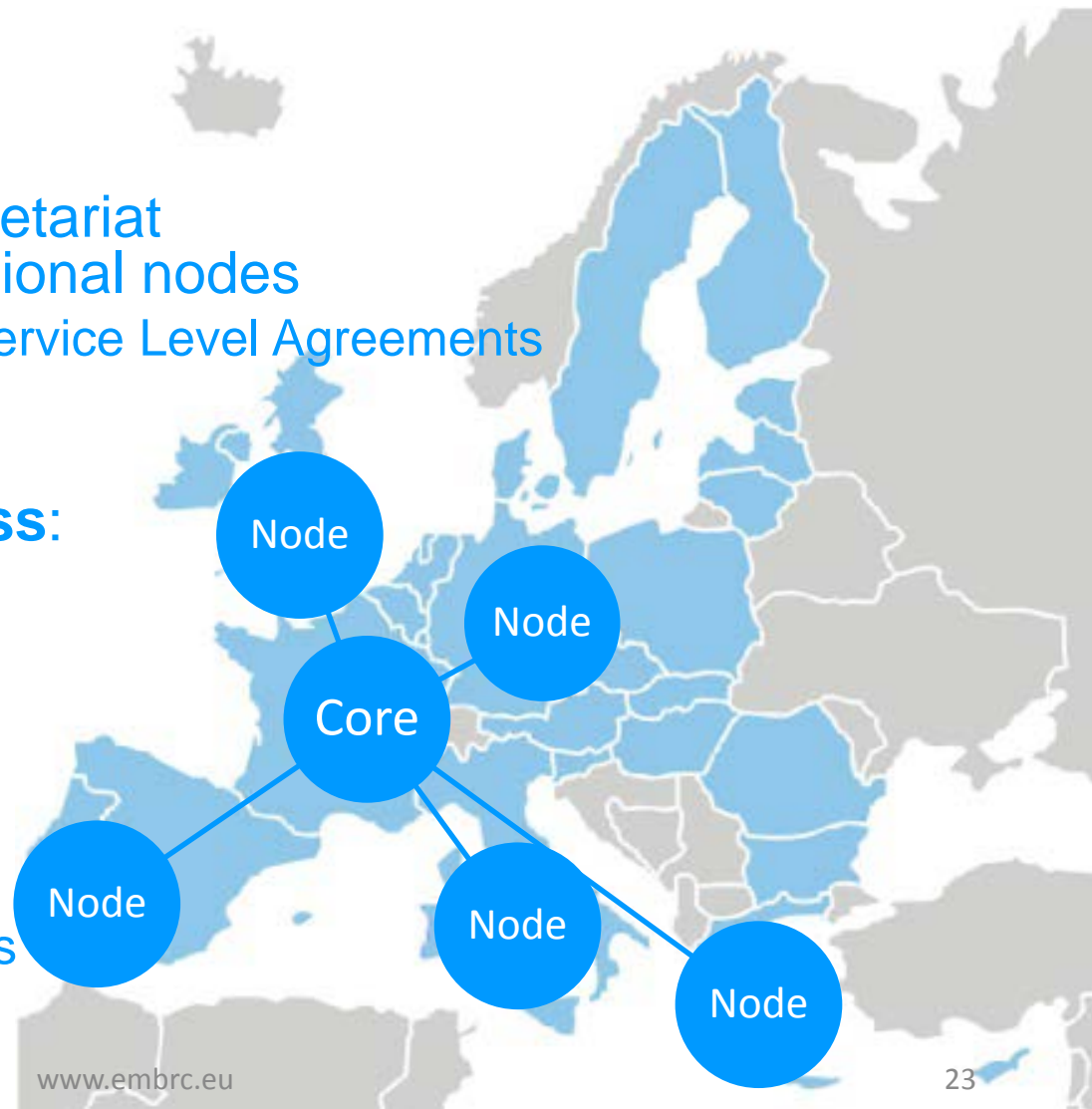
Bio-fuel

- New technologies are transforming the possibilities for marine stations: from “omics” to advances in optical and acoustic imaging techniques
- Unique marine biodiversity is a potentially rich source of medicines and natural products
- Observatories for climate change impacts



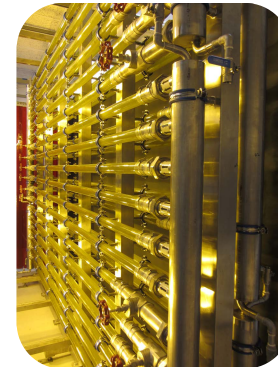
How does it work?

- **EMBRC Headquarters:**
Executive Director + Secretariat
for the coordination of national nodes
 - Service provided under Service Level Agreements
- **Use:**
Single entry-point access:
 - On-site access
 - Remote access
- **User groups:**
 - Academic users
 - Industry/Private Sector
 - Public/private partnerships
 - Facility rental



Service Areas

- Six Core Access Services:
 - Natural Ecosystems
 - Controlled Experimental Facilities (includes Aquaria and mesocosms)
 - Research Platforms and Workflows (includes 'Omics)
 - Cultures
 - Information Systems and Data
 - Training & Education



Service Offer

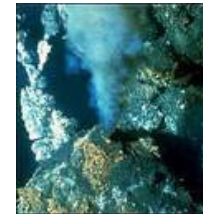
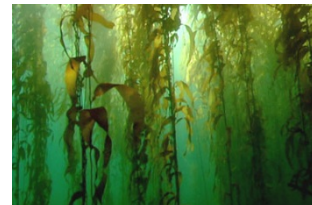
Level of externalisation

- 1. All-in-one (for industrial users only):** externalization of the project to EMBRC, from the definition of the research protocol to the running of the experiments
- 2. Co-produced service (custom):** EMBRC team helps the user to define the research protocol and may conduct experiments with industrial / academic research team
- 3. Delegated service (custom):** The user defines the research protocol. Experiments conducted solely by EMBRC team with no intervention from initial industrial / academic research team (mutant...)
- 4. Delegated service (off the shelf):** The user is choosing in a catalogue of services or biological resources. Experiments conducted solely by EMBRC team with no intervention from initial industrial / academic research team
- 5. Sole use of facilities:** Access to ecosystems and marine biological resources, to experimental aquaria and mesocosms...
- 6. Scientific expertise:** EMBRC team brings scientific expertise on specific aspects (taxonomy, 'omics, imaging, protein structure...)
- 7. Training:** General education, training regarding the use of facilities, ...
- 8. Remote access to e-infrastructure and large datasets**

Inventory of ecosystems readily accessible to shore-based marine stations

- Fjords
- Estuaries
- Mud flats
- Sea grass beds
- Kelp forests
- Volcanic seeps
- Coral reefs
- Megatidal seas
- Deep sea environments

Latitudinal range, regional seas



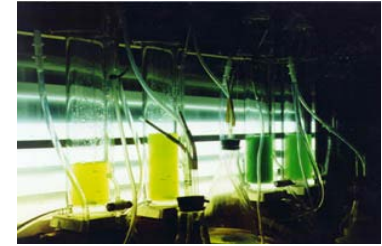
Inventory of access platforms

Coastal research vessels, remote operated vehicles, tethered buoys, scientific diving, and animal borne sensors



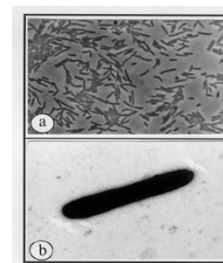
Inventory of aquaria

Seawater supply, cold and warm water aquaria, environmental control (pH, CO₂, temperature, light, salinity), plankton and invertebrate feed culture, mesocosms



Inventory of biological resources (culture)

Model species, genotypes, mutant strains including transgenics, genomic resources (e.g. BAC libraries), type culture collections, antibodies





EMBRC
EUROPEAN
MARINE
BIOLOGICAL
RESOURCE
CENTRE

Vision

**EMBRC will be the Global Reference
Research Infrastructure
for Marine Biology and Ecology**

RI Clusters

1. European Marine Biological Research Infrastructure Cluster (EMBRIC)

Connected by the Cluster:

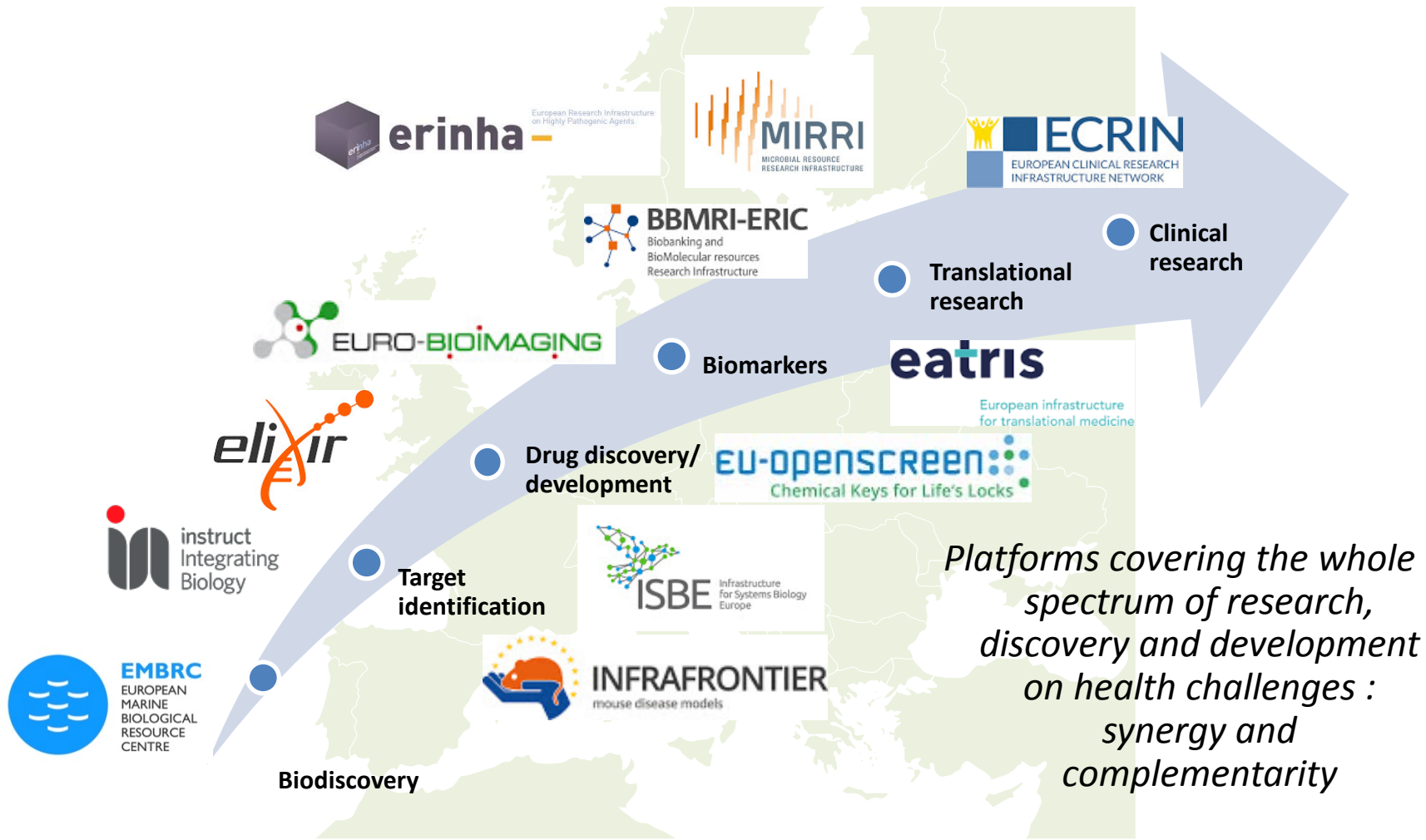
The EMBRIC consortium connects **6 Existing European Research Infrastructures**.

Four ESFRI Research Infrastructures (EMBRC, MIRRI, EU-OPENSREEN, ELIXIR) and two Integrating Activity projects (AQUAEXCEL and RISIS).



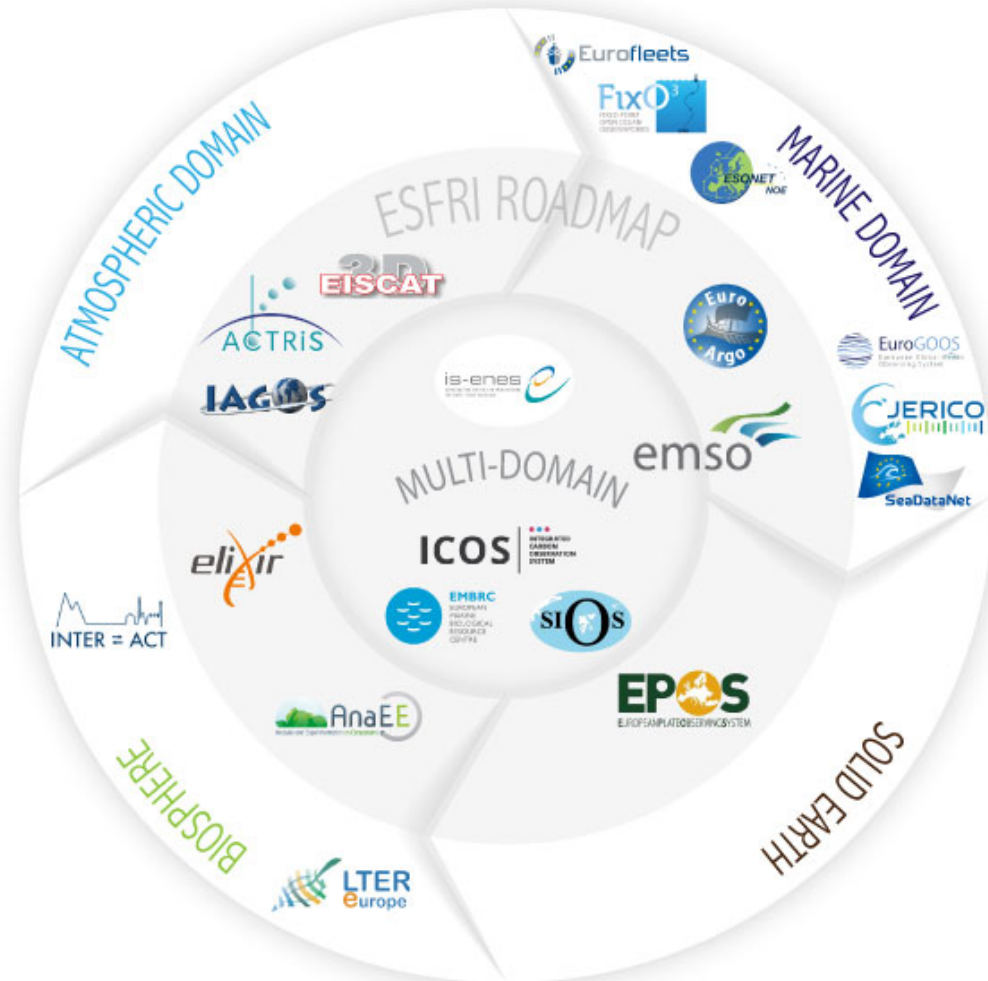
RI Clusters

2. Corbel - Coordinated RIs Building Enduring Life-science Services

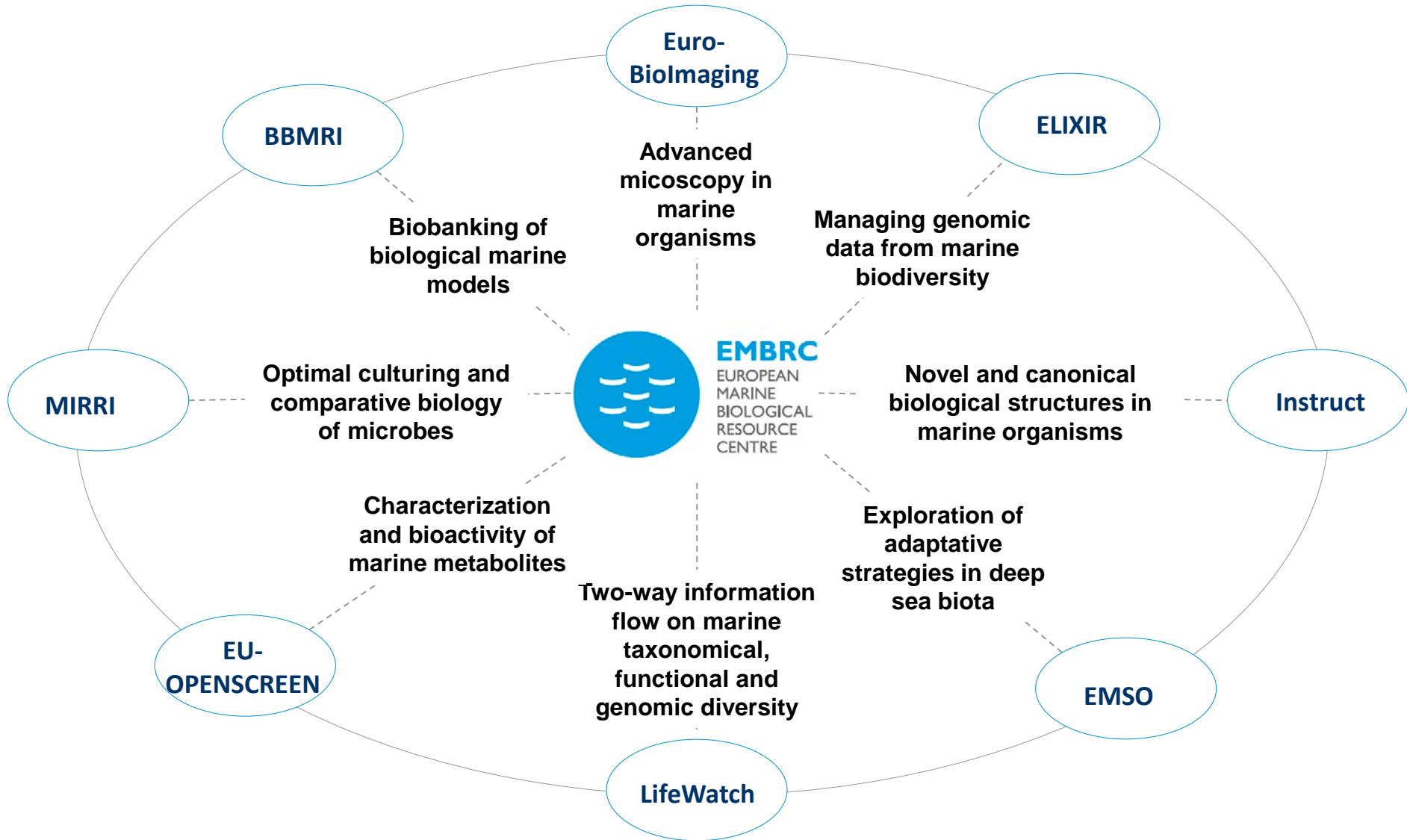


RI Clusters

3. ENVRI Plus – Supporting Environmental research with integrated Solutions



The Future Research Infrastructure Environment



**The EMBRC Headquarters are hosted at the
University P.M. Curie - Paris 6, Paris.**

WWW.EMBRC.EU

info@embrc.eu