

Drugs from the Deep

An Overview of the Marine Biodiscovery Process

Professor Marcel Jaspars

Director, Marine Biodiscovery Centre

University of Aberdeen

Scotland, UK

m.jaspars@abdn.ac.uk

Drugs From Nature – Modern Cancer Treatments



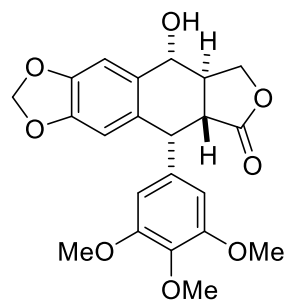
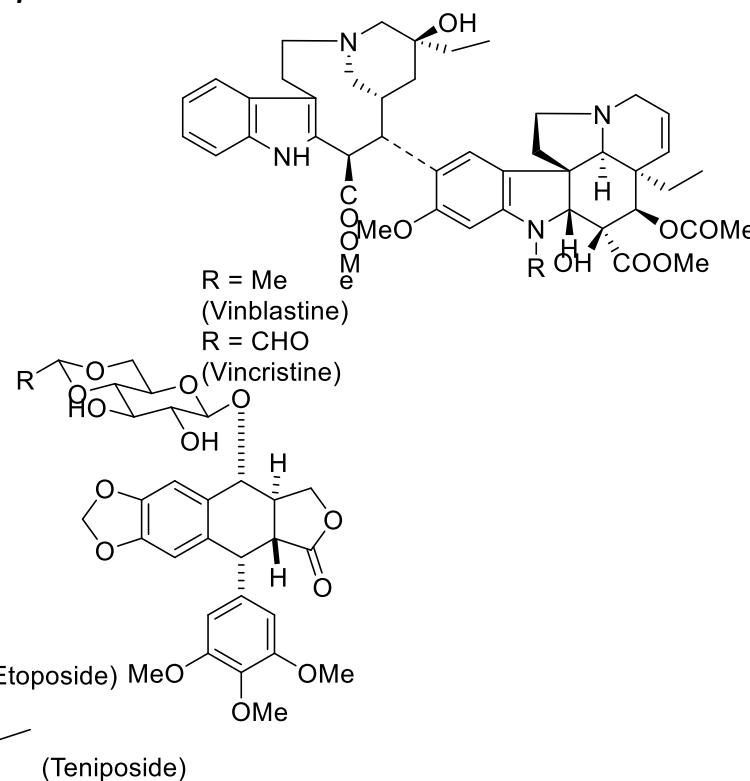
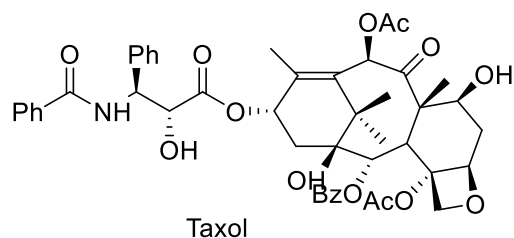
Taxus brevifolia



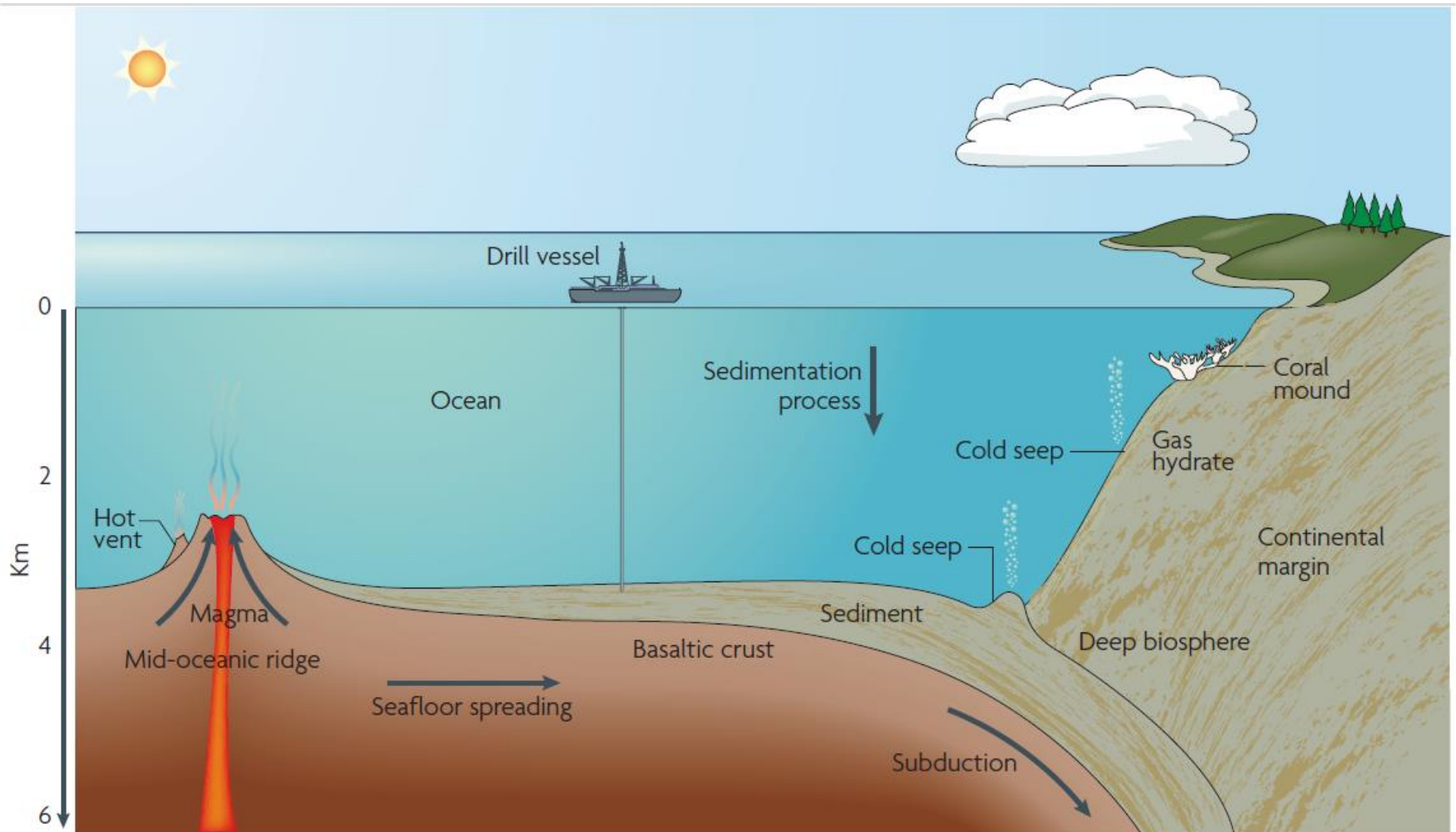
Podophyllum peltatum



Catharanthus roseus



Marine Environments





05 CORAL REEFS

Coral reefs are diverse underwater ecosystems held together by calcium carbonate structures secreted by corals. Coral reefs are built by colonies of tiny animals found in marine waters that contain few nutrients.

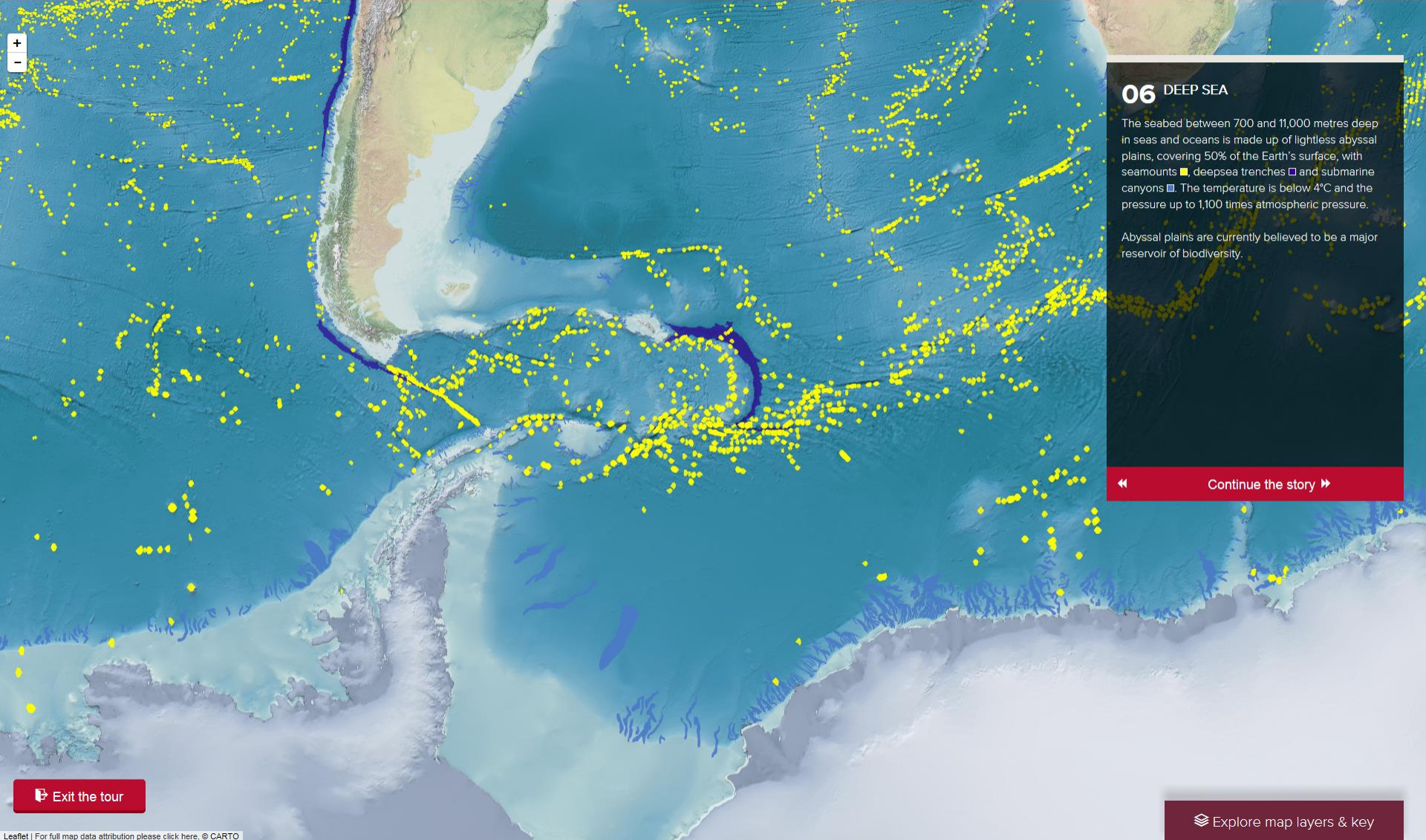
Tropical corals provide a home for at least 25% of all marine species including fish, molluscs, worms, crustaceans and sponges.



Continue the story ▶

Exit the tour

Map layers and explore the key



06 DEEP SEA

The seabed between 700 and 11,000 metres deep in seas and oceans is made up of lightless abyssal plains, covering 50% of the Earth's surface, with seamounts ■, deepsea trenches □ and submarine canyons ▨. The temperature is below 4°C and the pressure up to 1,100 times atmospheric pressure.

Abyssal plains are currently believed to be a major reservoir of biodiversity.

◀ Continue the story ▶

Exit the tour

Explore map layers & key

Benefits of Marine Biodiscovery

Offers advantage over comparable

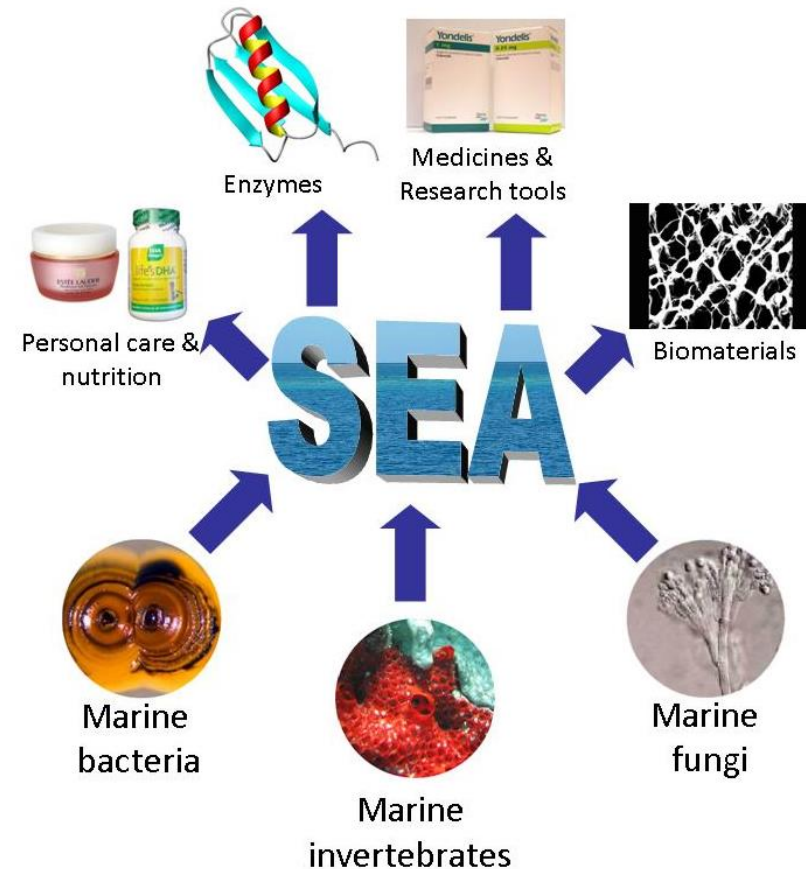
terrestrial resource:

- Superior performance
- Better economics

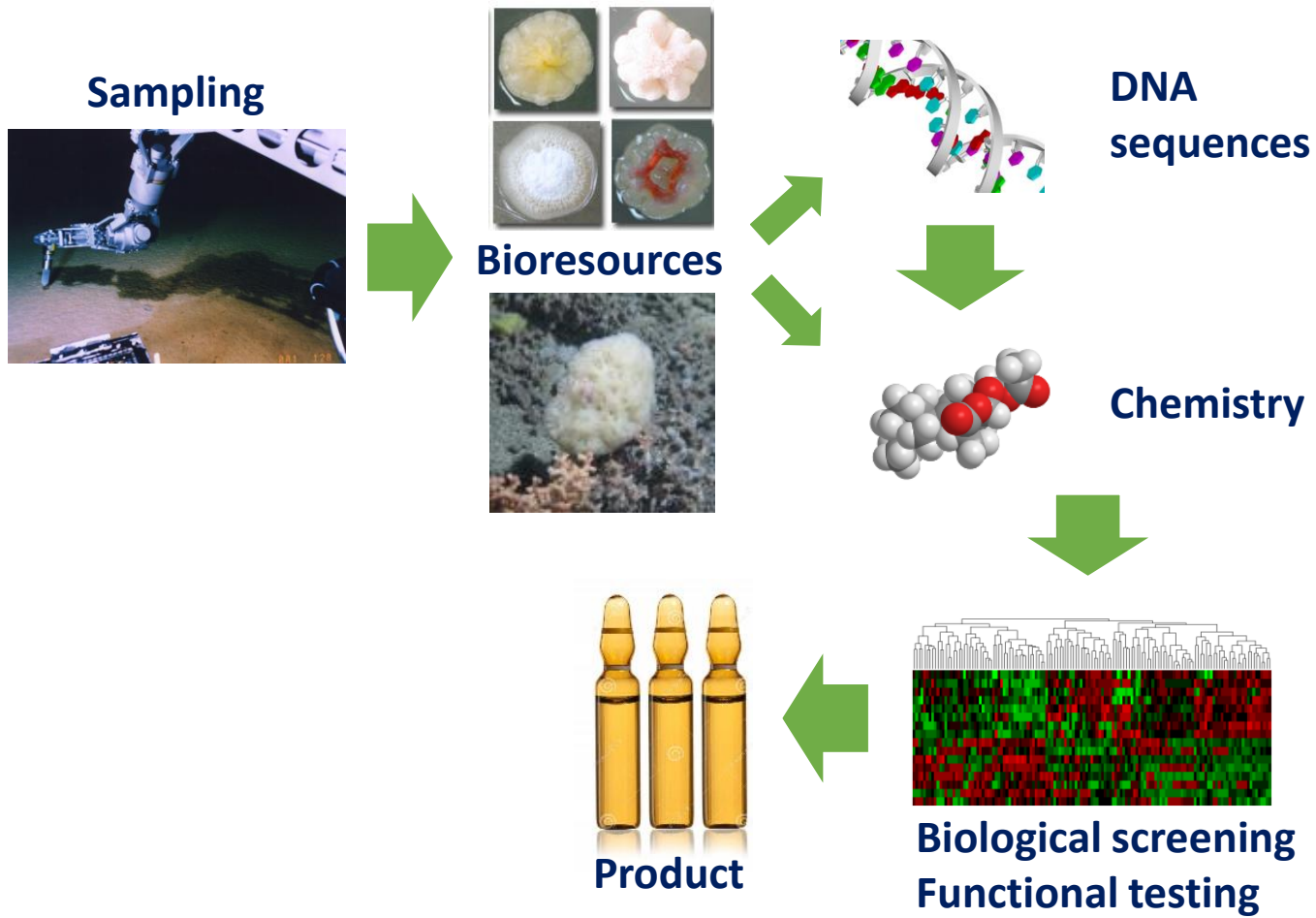
Unprecedented activity in particular

application:

- Enzymes: new reactivity/new biotransformation
- Small molecules: novel chemical structures & new mechanism of action
- Materials: new properties



The Process of Marine Biodiscovery



Collecting Materials

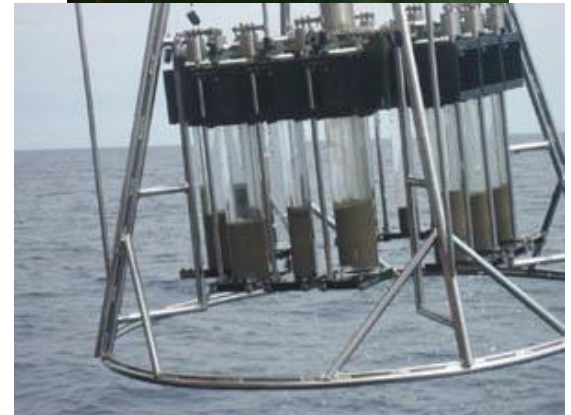
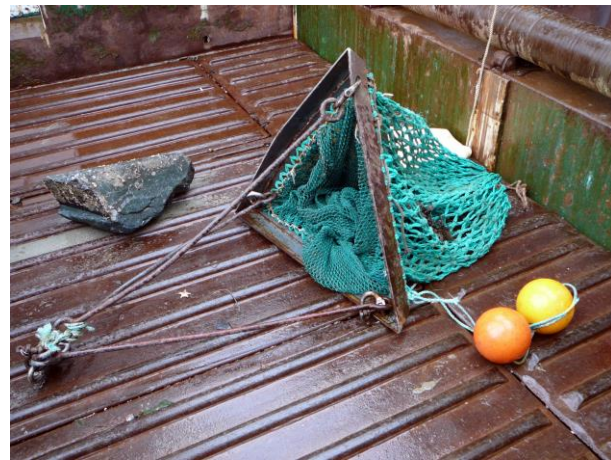


RRS Discovery (UK)



ROV Isis (UK) (6500 m)

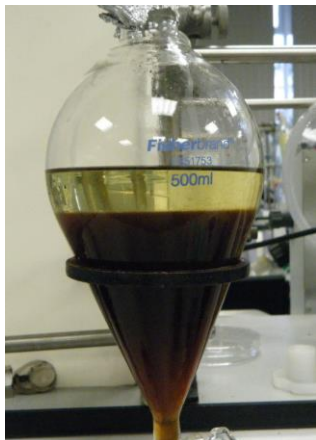
Sampling Devices



Biomass – Invertebrates and Microorganisms



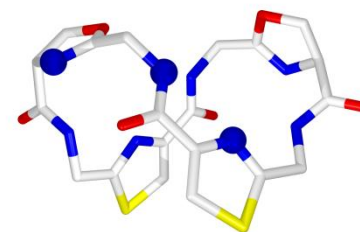
Chemistry



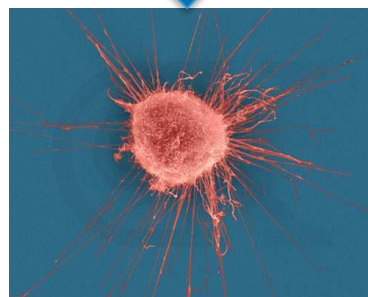
Extraction



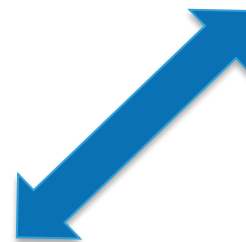
Compound Isolation



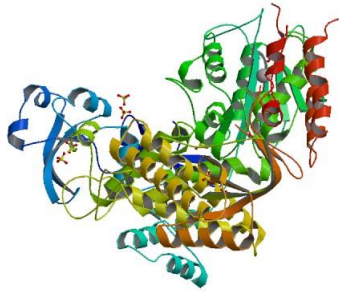
Compound Identification



Biological Testing



Non-Pharma Marine Derived Products on the Market



Vent Polymerase – for DNA amplification

Origin: Vent bacterium (Naples, Italy)

Production: Recombinant

Owner: New England Biolabs



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: Unilever

Marine 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



Ara-A (vidarabine)
antiviral

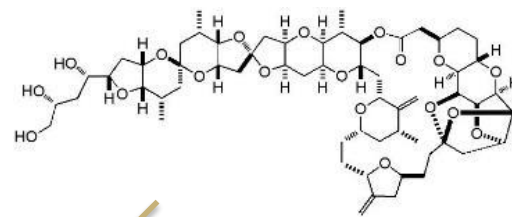
Case Study: Halaven (Eisai)



Bioprospecting

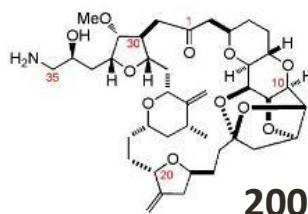


Pre 1986: Screening
Isolation & Structure



Halichondrin B

1996: Synthesis



E7389 Eribulin

2001: Derivative synthesis

Laboratory
tests and
clinical trials

2010:
approval by
US FDA



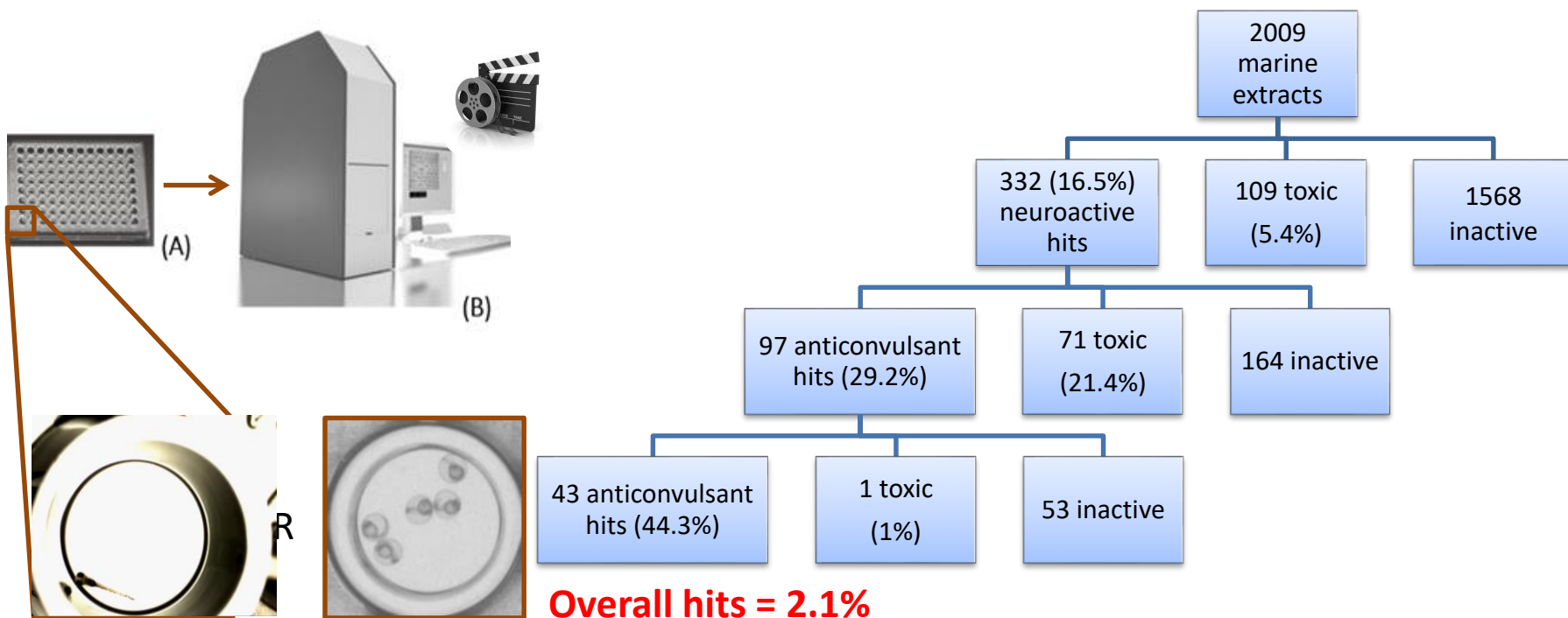
Case Study: Epilepsy

- 65 million people suffer from epilepsy worldwide.
- 2.4 million are diagnosed each year.
- There are 25 anti-seizure drugs on the market.

But:

- Current anti-seizure drugs fail to control seizures in 30% of the patients due to drug-resistance.

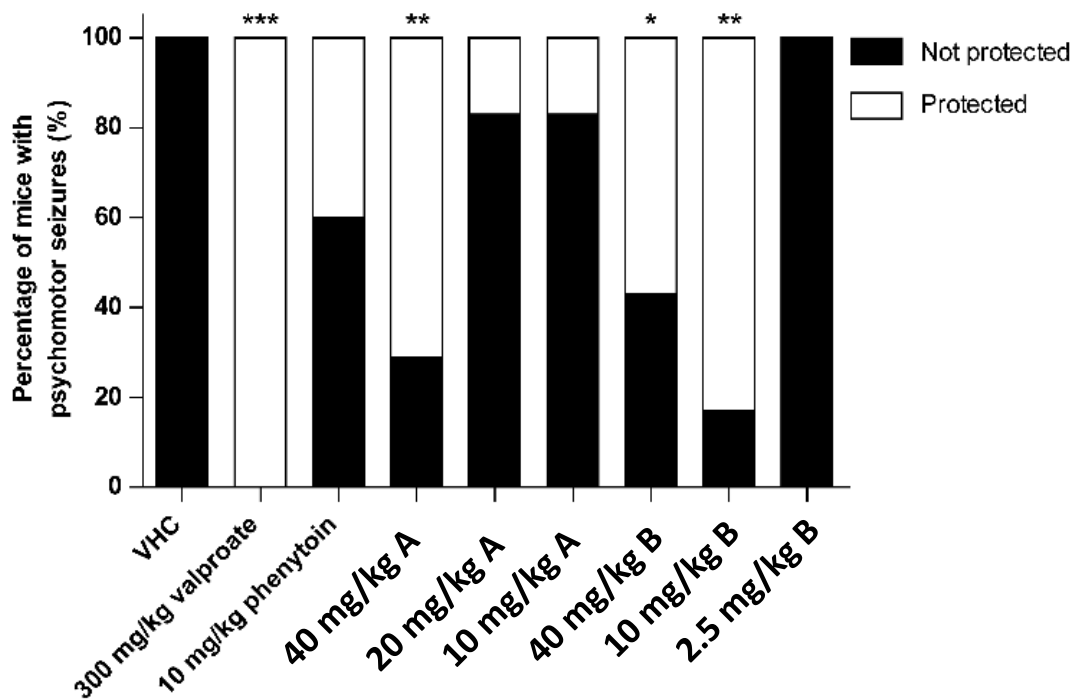
Case Study: Epilepsy Drug Discovery in PharmaSea



- **Primary Screen:** Photomotor response assay: neuroactive hits
- **Secondary Screens 1/2:** Epilepsy seizure model: anticonvulsant hits
- **Toxicity:** Maximum Tolerated Concentration (MTC) analysis

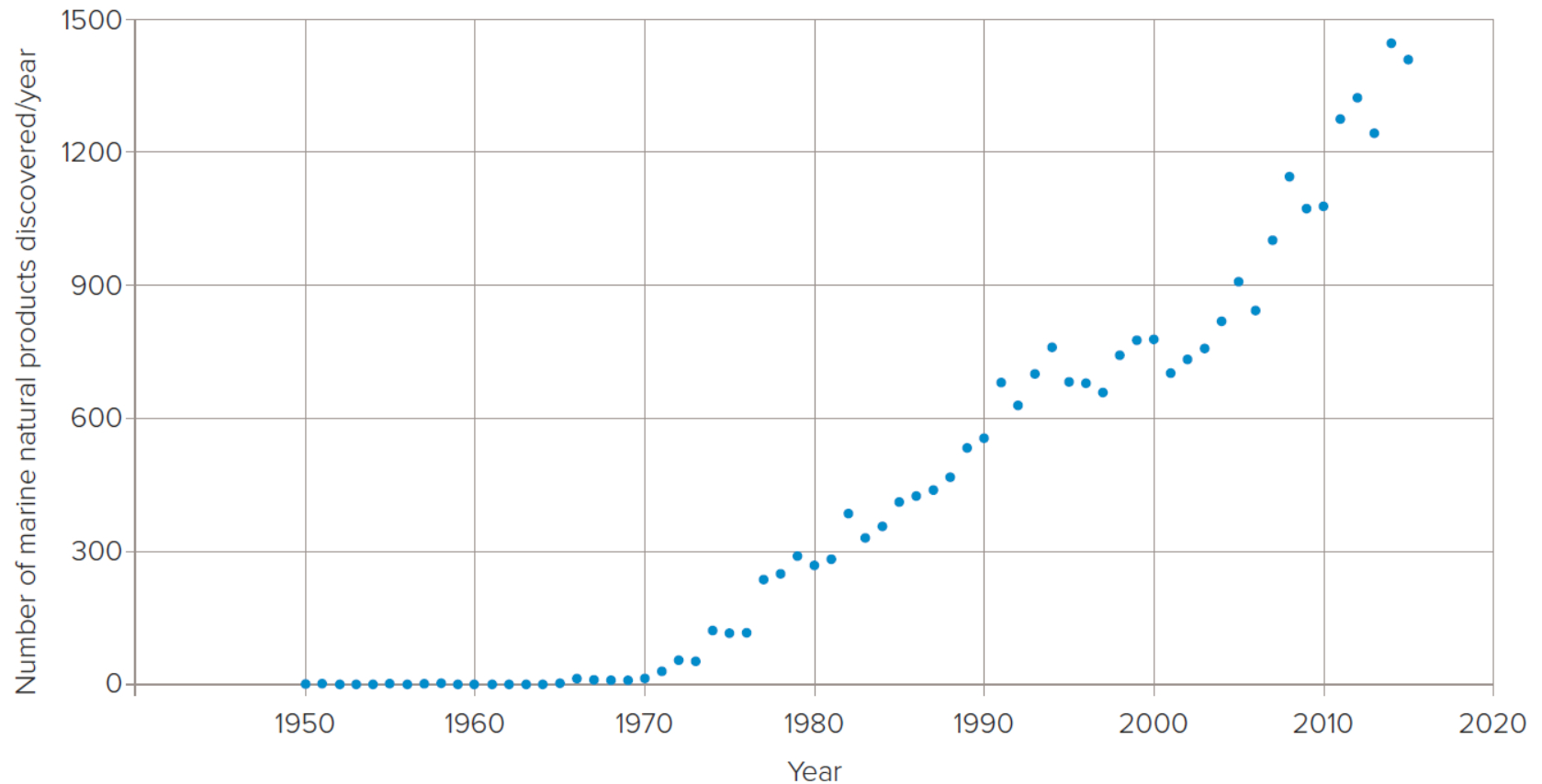
Case Study: Epilepsy Drug Discovery in PharmaSea

- Two marine fungal compounds demonstrated activity in zebrafish larvae.
- This activity was confirmed in the mouse 6-Hz seizure model.
- Both show excellent 'drug-like' profiles.



Increase in New Compounds Being Discovered

Annual number of newly discovered distinct natural products from marine organisms.



Source: RSC MarinLit database, February 2017.

The Marine Pharmaceutical Pipeline



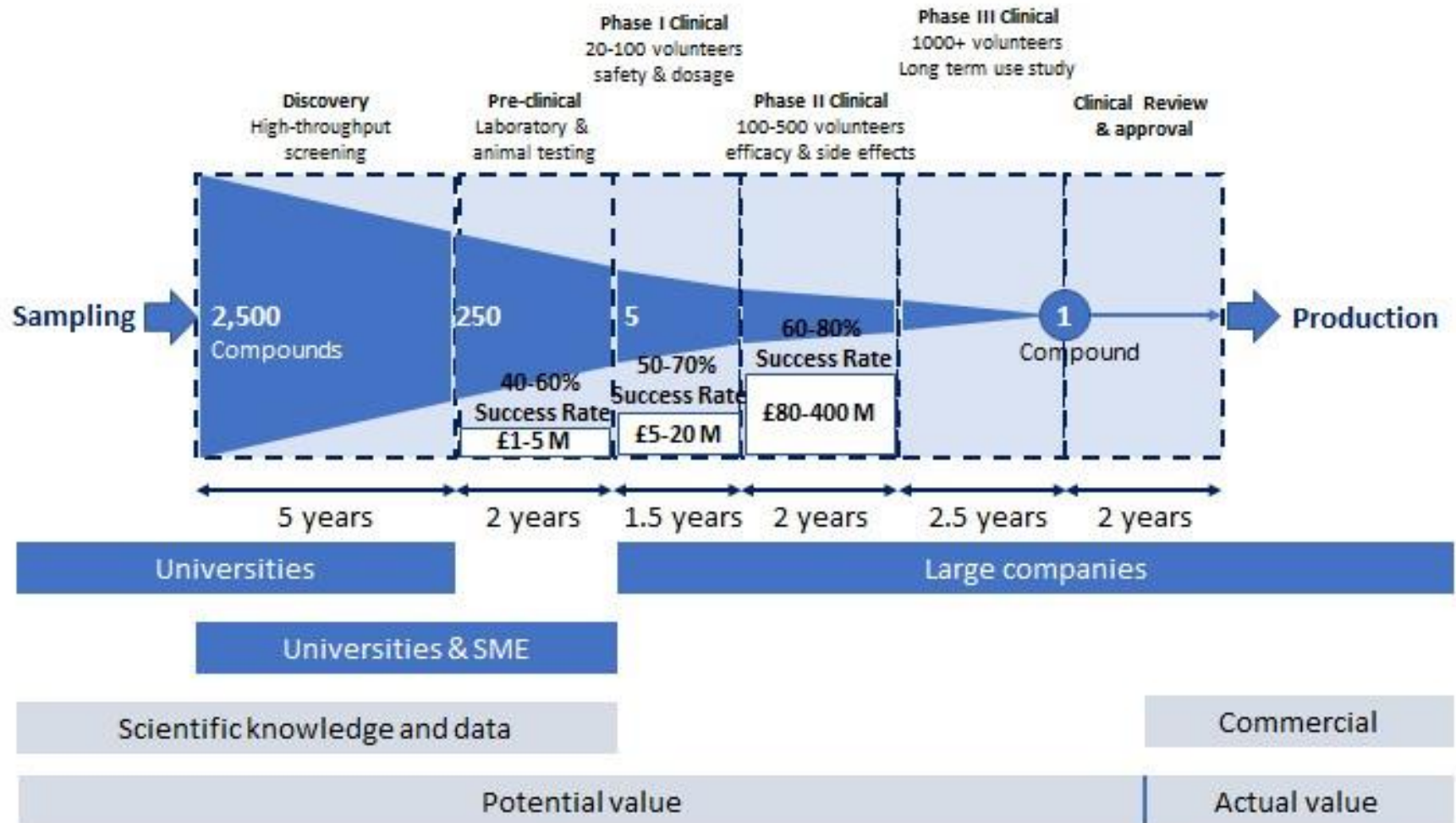
Mainly derived from shallow reef dwelling organisms

Mainly anti-cancer with a few analgesics and antivirals

Mainly start-ups at early stage with large pharma at late stage

<http://marinepharmacology.midwestern.edu/>

The Natural Product Pharmaceutical Discovery Pipeline



Environmental Considerations

- Only small amounts of whole organisms are collected (1-2 kg is sufficient)
- For commercial production these compounds are not obtained from these organisms but are produced by:
 - Chemical synthesis
 - Biotechnology
- Current emphasis is on the use of microorganisms from marine sediments

Future Prospects

- Pipeline of marine biotechnology products beginning to flow
 - New medicines
 - New processes
 - New materials
- If done correctly, little environmental impact
- Challenges
 - Understanding of marine biodiversity
 - Physical access to deep sea marine bioresources
 - Legal clarification of UNCLOS
 - Commercialisation – scale up/industry interest
 - Training researchers with right mix of skills