
The Oceans and Human Health: Drugs from the Deep

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Nature as a source of drugs

☆ Over 50% of the marketed drugs today are either extracted from natural sources or produced by synthesis using natural products as templates or starting materials.

☆ Some examples:

☆ penicillin

☆ aspirin

☆ morphine

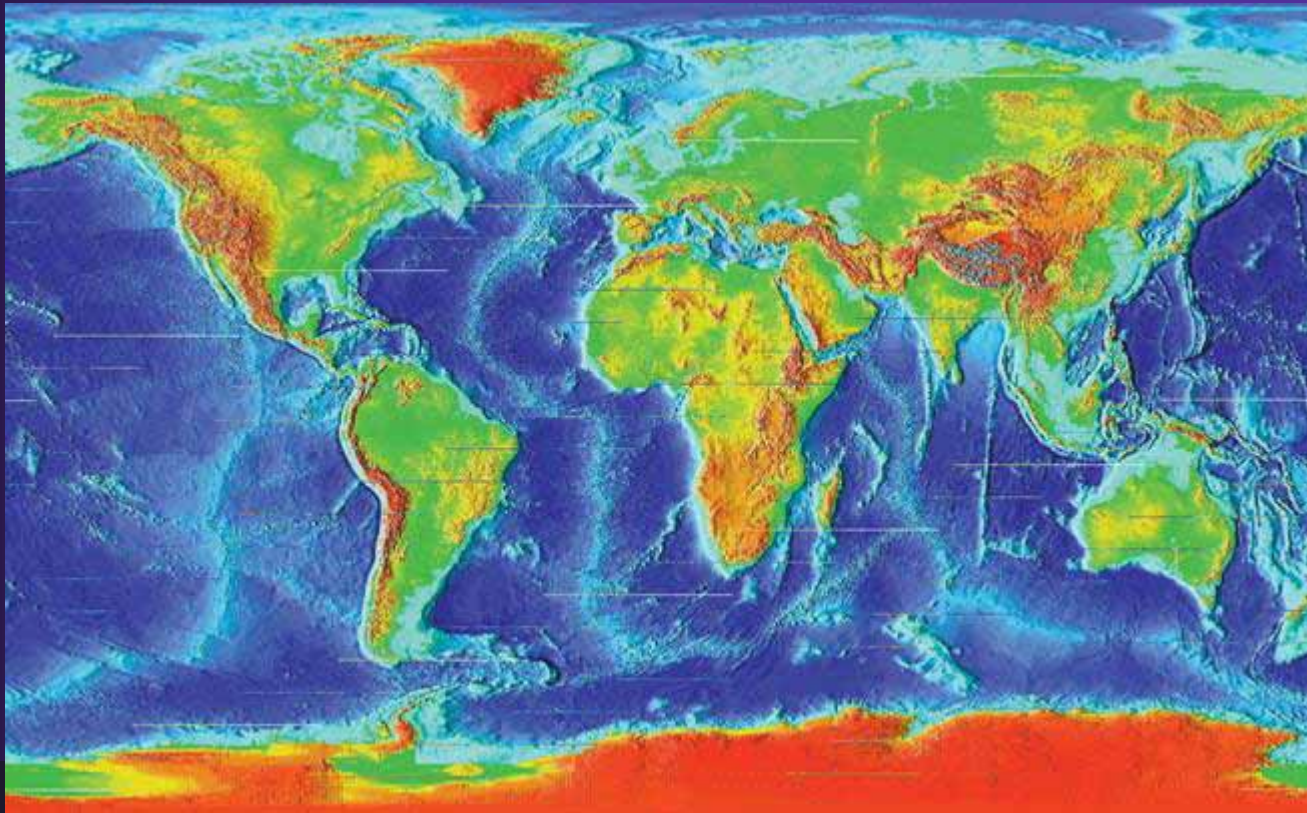
☆ cyclosporine

☆ Taxol[®]



Why explore the ocean for new medicines?

- The oceans cover more than 70% of the earth's surface.



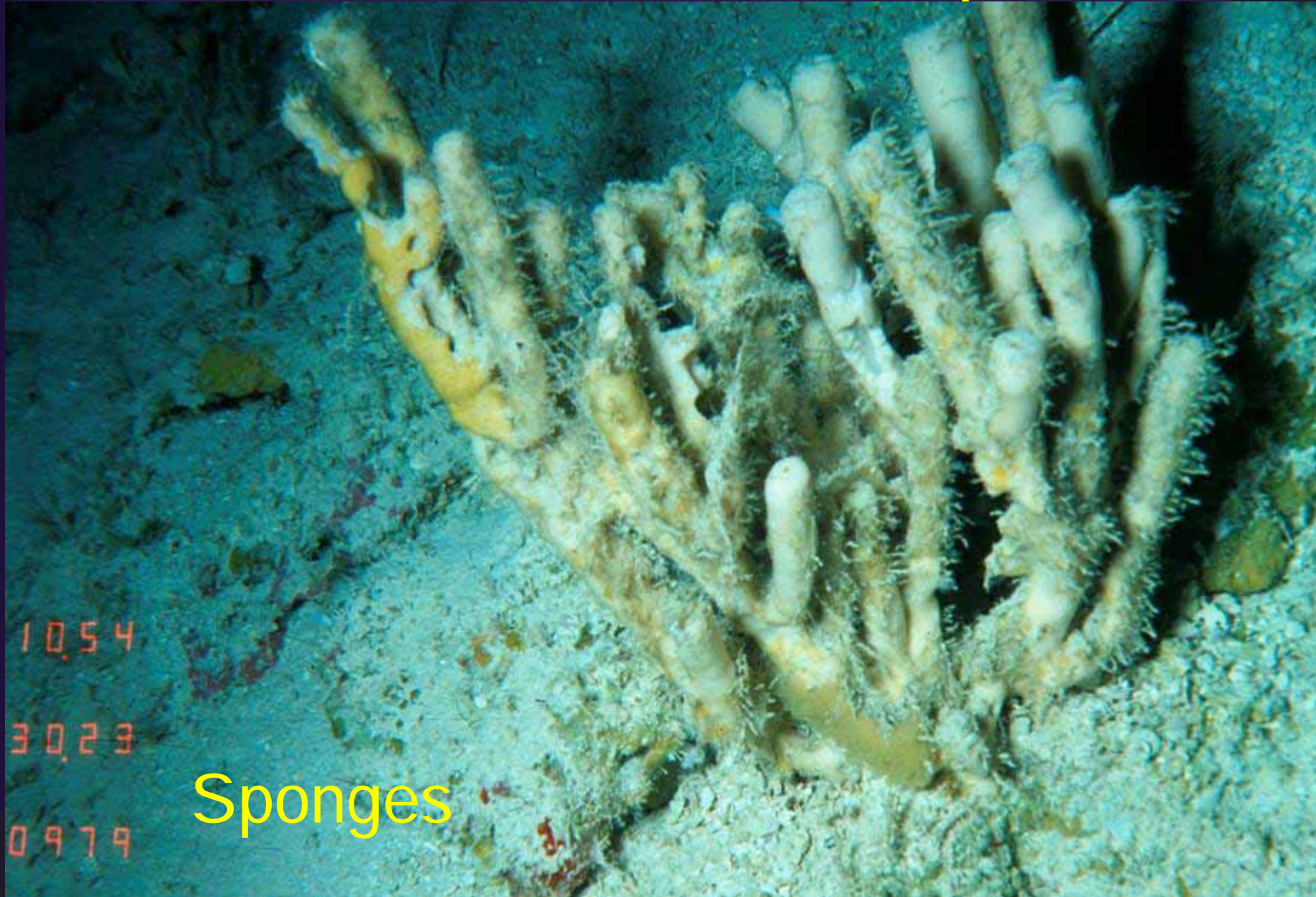
The oceans are a rich source of biological diversity.



Biological
diversity =
chemical
diversity
= potential for
discovery of
novel drugs

Slide courtesy of Dr. Russell Kerr,
Florida Atlantic University

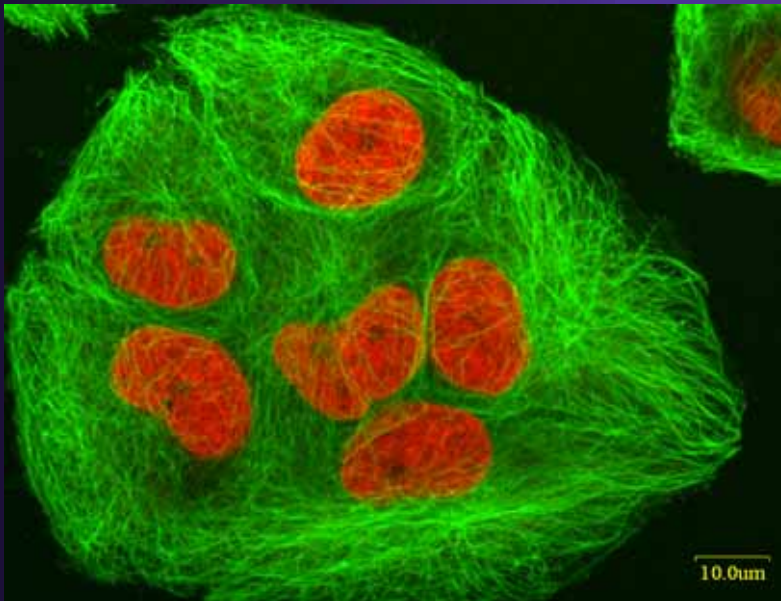
Sources of bioactive compounds



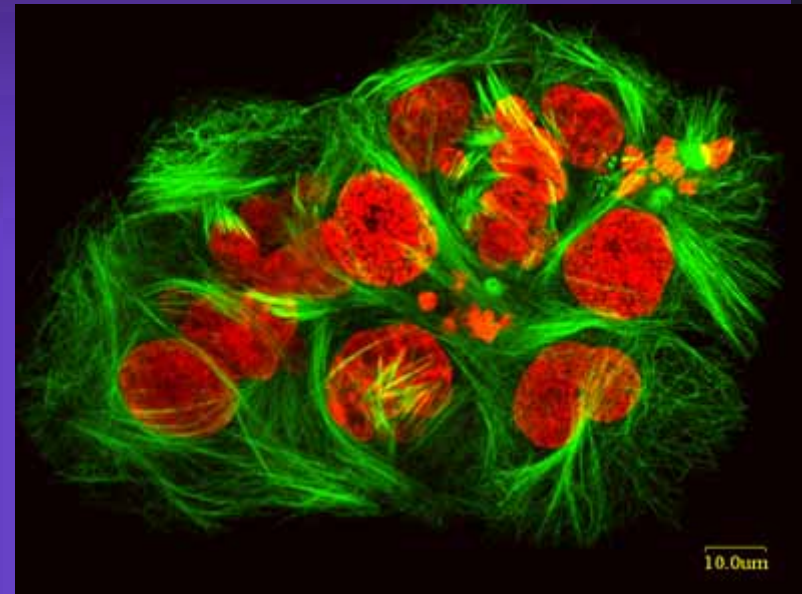
Sponges

DISCODERMOLIDE: a drug from a deep water sponge

Untreated cancer cells



Cancer cells treated with
discodermolide

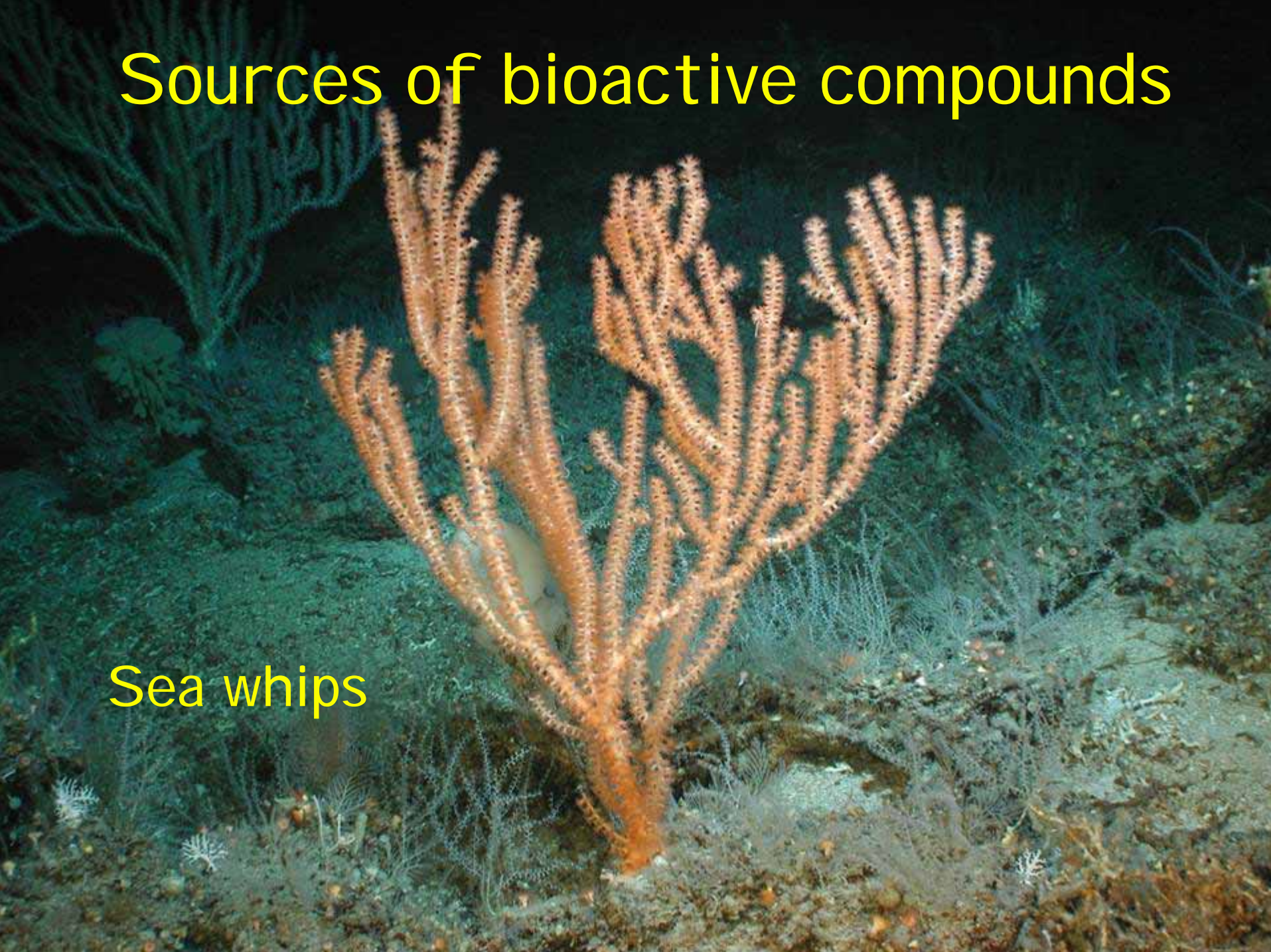


Red = nuclei

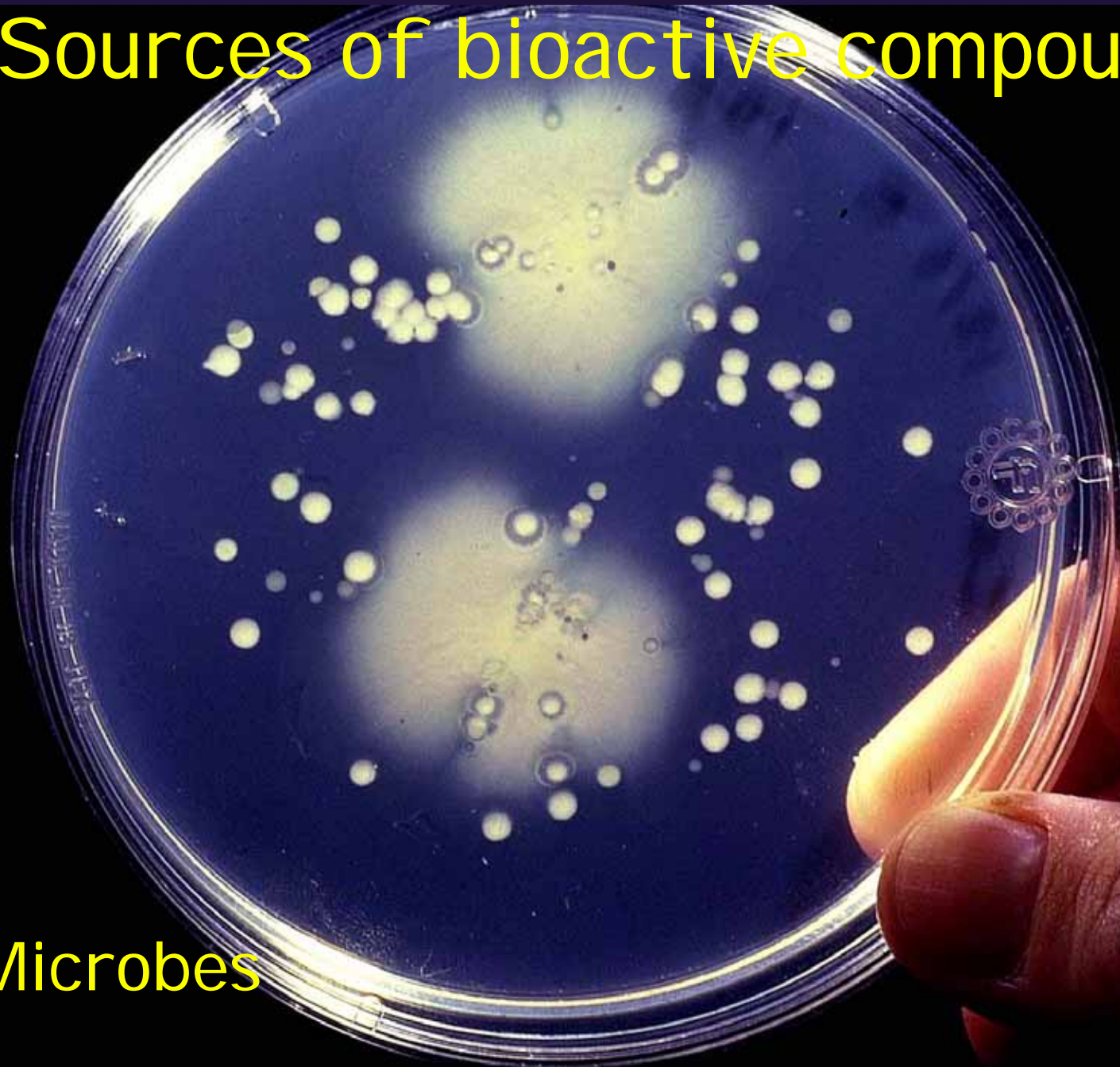
Green = microtubules

Sources of bioactive compounds

Sea whips



Sources of bioactive compounds

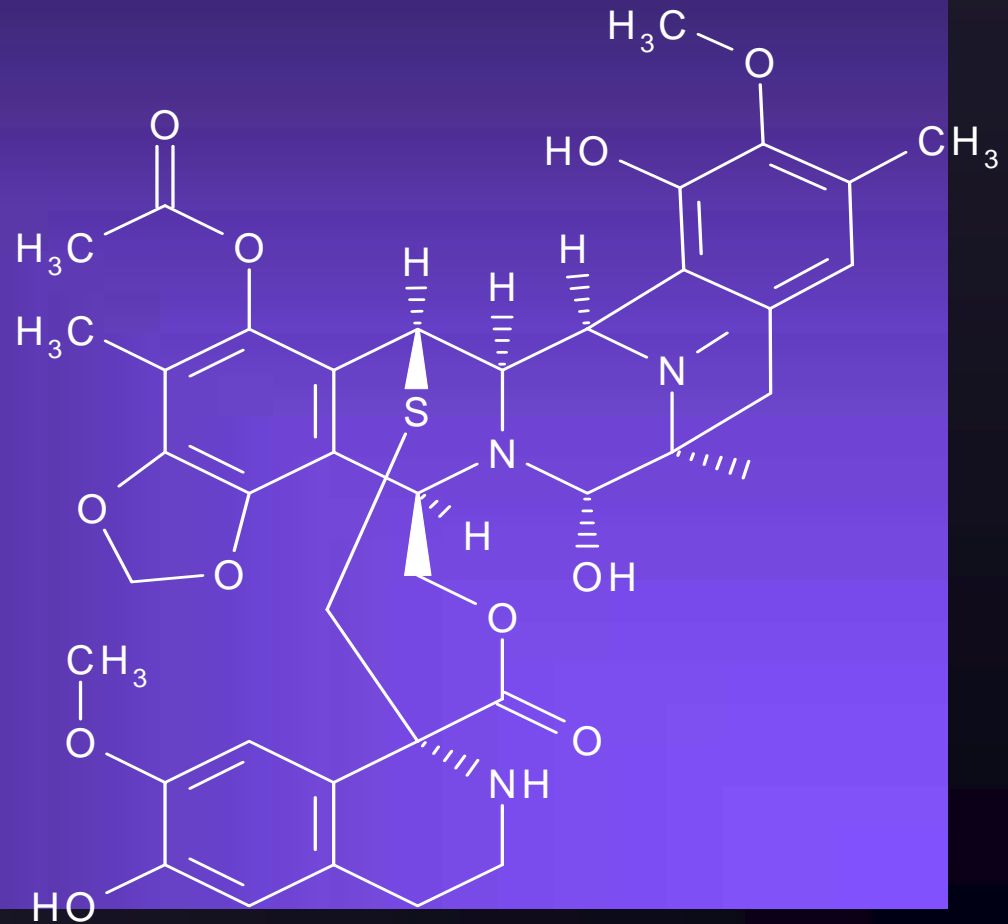


Microbes

ECTEINASCIDIN 743: "Yondelis"



In Phase III clinical trials for
treatment of cancer.
PharmaMar S.A.

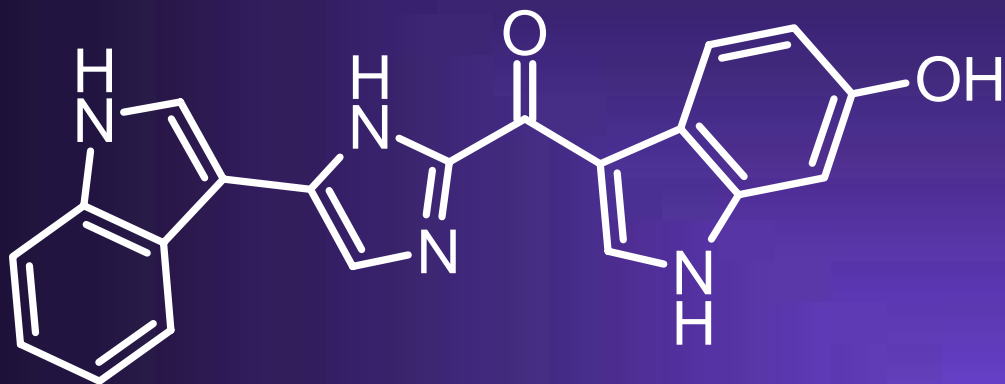


Marine-derived anti-cancer compounds currently licensed for development

Drug	Marine Source	Current Status
Bryostatin 1	Bryozoan	Clinical trials
Dolastatin 10	Mollusc	Clinical trials
Ecteinascidin 743	Ascidian	Clinical trials
Aplidine	Tunicate	Advanced preclinical trials
Kahalalide F	Mollusc	Advanced preclinical trials
Discodermolide	Sponge	Clinical trials
Isohomo-halichondrin B	Sponge	Advanced preclinical trials
Thiocoraline	Microorganism	Advanced preclinical trials
Isogranulatimide	Ascidian	Licensed
Bengamide	Sponge	Clinical trials
Hemiasterelins A & B	Sponge	Licensed
Girolline	Sponge	Licensed

data courtesy of Dr. David J. Newman, NIH, National Cancer Institute, Natural Products Branch

TOPSENTINS



- ❖ Potent anti-inflammatory compounds
- ❖ Therapeutic areas: Allergic reactions, burns, arthritis, inflammatory bowel disease
- ❖ Under investigation by multiple parties for both over-the-counter and prescription drug use

Challenges in Discovery and Development of Marine-Derived Drugs

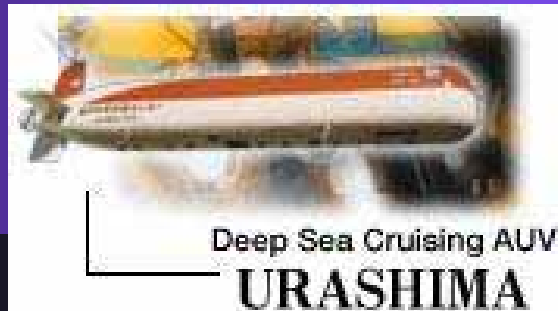
- Exploring the unknown
- New tools and platforms for discovery
- New pharmacological models for testing bioactivity
- Compliance with national and international regulations
- Benefit sharing
- Sustainable use of marine resources

Challenges: Exploring the Unknown

New environments

- shallow tropical habitats
 - Have we reached the point of diminishing return?
- the deep sea
 - Cost/benefit?
 - What tools do we need to sample from extreme environments?





Deep Sea Cruising AUV
URASHIMA



Challenges: Accessing New Genetic Materials

New species

-marine microbes

- Are there novel approaches to the issue of the "uncultureds"?



-Marine macro's

- Are there groups that we haven't adequately explored?



The Supply Problem

- It is not feasible to rely on large-scale collections for supply of marine natural products.
- Unless an organism can be cultured, or the compound can be synthesized using an economically feasible, industrial-scale process, adequate supply of bulk amounts to support pre-clinical and clinical development will be an issue.

What are some options for sustainable use of marine resources?

- Chemical synthesis
- Controlled harvesting
- Aquaculture
- In vitro production
- Microbial fermentation
- Transgenic or enzymatic production

Challenges: Regulatory Constraints

- ❖ complying with regulations related to the rights of a country to its natural resources
- ❖ fair and equitable sharing of technologies and revenues resulting from commercialization of products from marine resources

Financial constraints

- ❖ the cost of accessing new environments and new samples
 - ❖ Ship & submersible costs: \$20-30K/day
- ❖ the cost of development of pharmaceuticals
 - ❖ 5-7 yrs, \$15-25M for medical devices
 - ❖ longer and more expensive (up to \$200 M) for drugs

Ocean Exploration & Drug Discovery in the 21st Century: Needs

- A greater focus--and both private and federal funding for research--on marine organisms as a source of pharmaceuticals
 - Research in disease areas other than cancer.
 - Development of a new suite of tools, sensors, and platforms that will allow us ...
 - to explore habitats that are currently beyond our reach
 - to identify, conserve, and use resources with medicinal potential



Funding:

NIH/National Cancer Institute

NOAA Sea Grant

National Science Foundation

NOAA Office of Ocean Exploration

Exploring the Oceans for the Benefit of Mankind

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