

MGR in ABNJ: Clarifying terminology and constraining expectations

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Terminology

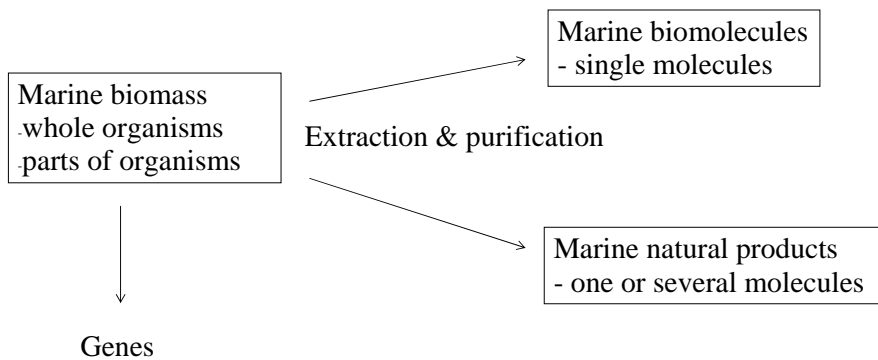
Marine biomass
- whole organisms
- parts of organisms

Extraction & purification

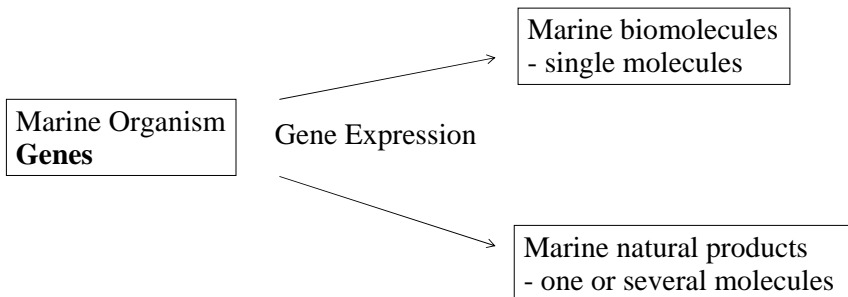
Marine biomolecules
- single molecules
- Compounds
- enzymes

Marine natural products
- one or several molecules

Terminology



Terminology



Pathway to MGR Commercialization Step 1 – Initial discoveries

New marine organisms
field expeditions

New genes and biomolecules
follow up lab analysis

Who makes initial discoveries?

New marine species

- academic and government researchers

New genes and biomolecules

- academic and government researchers
- limited industry initial discovery effort

New marine natural products

- initial descriptions by academic & government researchers
- value-adding recognition by industry

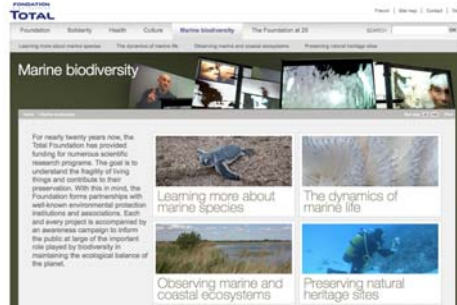
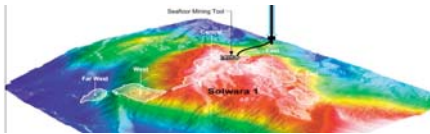
Funding for initial discoveries?

MGR field expeditions

- state agencies
- occasional private & NGO expeditions

Laboratory analysis

- state agencies
- industry

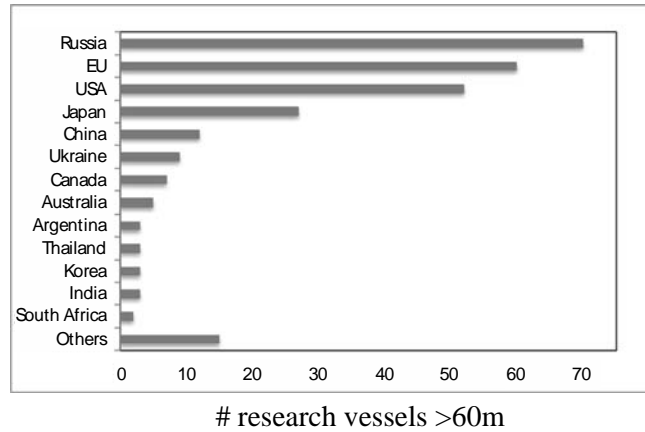


Access to MGR in ABNJ

- Finding and identifying new species requires
 - ocean going research vessels
 - expertise in species identification
- Biomolecular & genetic discoveries require
 - analytical facilities and expertise
 - biochemical analysis
 - genomic and metagenomic

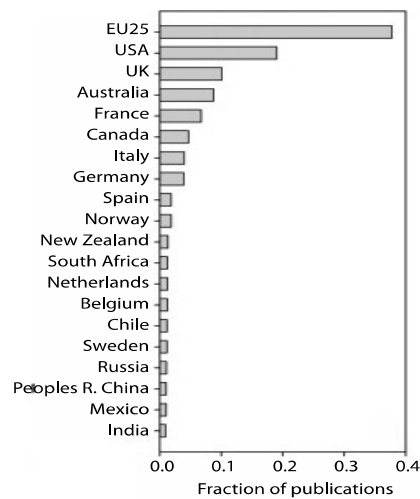
Access – Research vessels

- Research vessels over 60 metres in length required for expeditions in ABNJ
- Most large vessels owned by developed nations



Access - Biodiversity Expertise

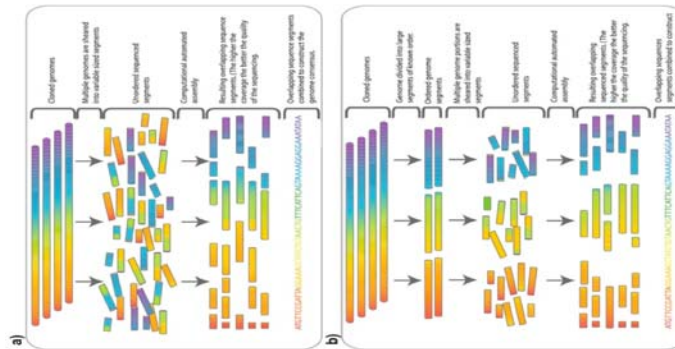
- affiliations of 1st authors of biodiversity publications (1987-2005)



Access – initial laboratory analysis

Commercial analytical facilities

- biochemical analysis
- sequencing and metagenomics
- increasingly common and accessible



Access – Analytical Facilities

Patent Claims for a Gene of Marine Origin

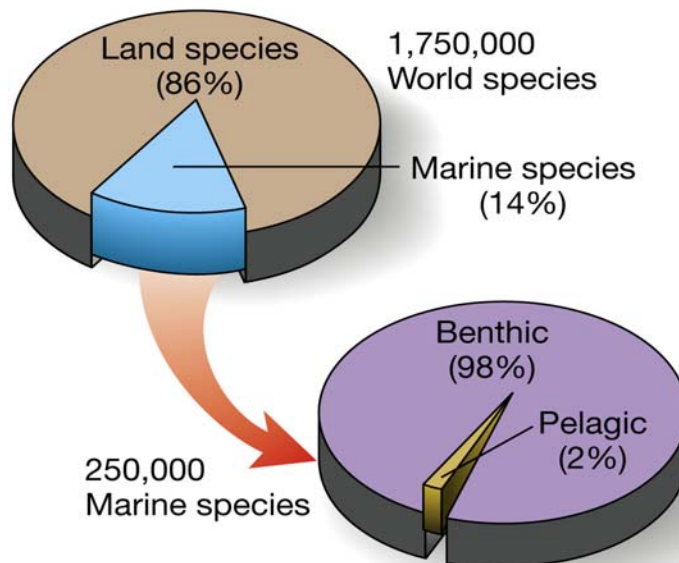
Country	Marine organism patent claims
USA	199
Germany	149
Japan	128
France	34
United Kingdom	33
Denmark	24
Belgium	17
Netherland	13
Switzerland	11
Norway	9

Ten countries own 90% of patents deposited,
with 70% in top three

State versus Private Sector Funding cont'd

- State funding critical to early laboratory studies of MGR
- "...a biotechnology-based industry cannot be established in a country unless there is a close relationship between the research establishment and the applied sector."
 - **Marine biotechnology and developing countries**, Raymond A. Zilinskas Carl Gustaf Lundin. 1993. The International Bank for Reconstruction and Development/THE WORLD BANK
 - IS THIS STILL THE CASE?
- State funding important to development of derived products (eg. fisheries waste)
- What about pharmaceuticals? At what point does the hand-off occur?

Biodiversity in the world ocean



Census of Marine Life (CoML)

- 10-year program (2000-2010) involving 80 nations
- Network of separate programs (seamounts, Antarctic, marine mammals, chemosynthetic ecosystems, etc)



Catalogued 246,000 species

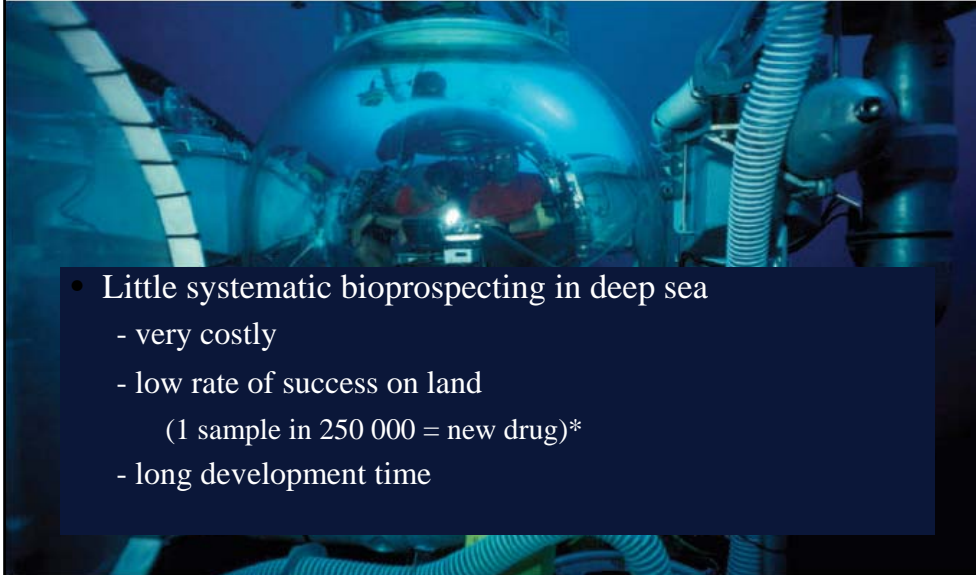
Genetic Resources of the Deep Sea – The Promise



*“... a source of new and viable wealth creation”**

* National strategy on marine bioprospecting, Norway, 2009

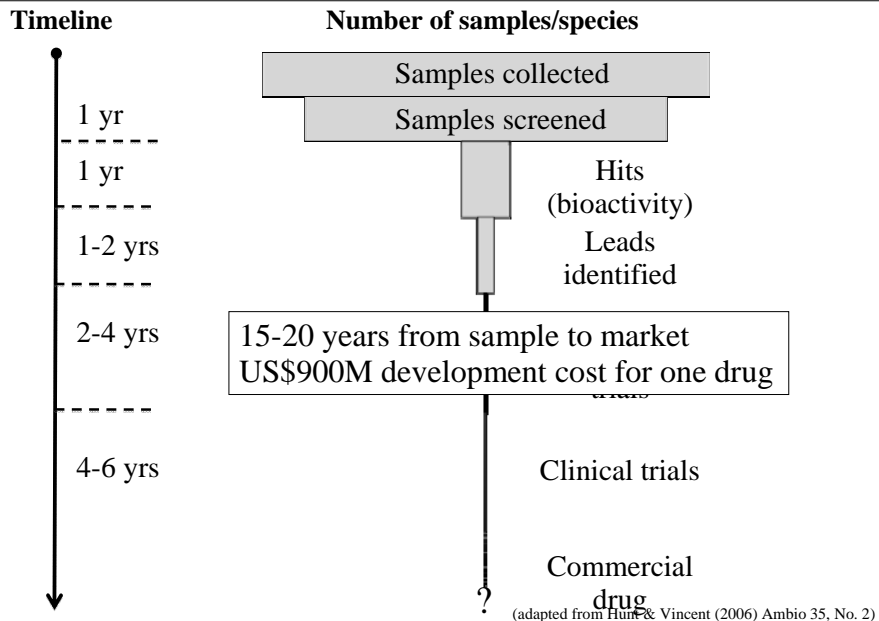
Bioprospecting in the deep sea - The Reality



- Little systematic bioprospecting in deep sea
 - very costly
 - low rate of success on land
(1 sample in 250 000 = new drug)*
 - long development time

* Nature (1998) 392, 535

Drug discovery and development from natural products



Drugs of marine origin currently in clinical trials (2006)

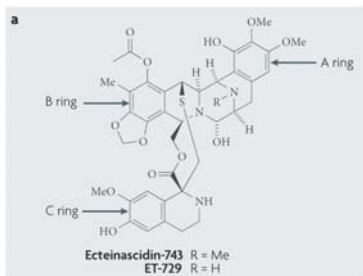
Drug/Compound	Source Organism	Phyla	Current Supply source	Phase of Clinical Trials	Therapeutic Activity
Prialt (ziconotide, ω -conotoxin MVIIA)	<i>Conus magus</i>	Mollusc	Synthetic	III	Pain
Bryostatin 1	<i>Bugula neritina</i>	Bryozoan	Wild harvest take (B2)	II	Anticancer
Yondelis (ecteinascidin 743)	<i>Ecteinascidia turbinata</i>	Urochordate	Semi-synthesis	III	Anticancer
Apilidin (aplidine)	<i>Apilidium albicans</i>	Urochordate	Synthetic	II	Anticancer
Kahalalide F	<i>Elysia rufescens/Bryopsis</i> sp.	Mollusc/Green Algae	Synthetic	II	Anticancer
Squalamine	<i>Squalus acanthias</i>	Chordate	Synthetic	II	Anticancer
KRN7000 (agelasphin derivative)	<i>Agelas mauritanus</i>	Sponge	Synthetic	I	Anticancer
Neovastat (AE-941)	Various "shark" species	Chordate	Wild harvest take	II/III	Anticancer
HTI-286 (hemiasterlin derivative)	<i>Cymbastella</i> sp.	Sponge	Synthetic	II	Anticancer
Discodermolide	<i>Discodermia dissoluta</i>	Sponge	Synthetic	I	Anticancer
E7389 (halichondrin B derivative)	<i>Lissodendoryx</i> sp.	Sponge	Synthetic	I	Anticancer
ES-285 (spisulosine)	<i>Spisula polyryma</i>	Mollusc	Wild harvest take (B3)	I	Anticancer
NVP-LAQ284 (psammaplin A derivative)	<i>Psammaphysilla</i> sp.	Sponge	Synthetic	I	Anticancer
ILX651 (synthatoxin, dolastin 15 derivative)	<i>Dolabella auricularia</i>	Mollusc	Synthetic	I/II	Anticancer
Cematodin (dolastatin 10 derivative)	<i>Dolabella auricularia</i>	Mollusc	Synthetic	I/II	Anticancer
TZT-1027 (dolastatin 10 derivative)	<i>Dolabella auricularia</i>	Mollusc	Synthetic	II	Anticancer
IPL-576,092 (contignasterol derivative)	<i>Petrosia contignata</i>	Sponge	Synthetic	II	Anticancer
IPL-512,602 (IPL-576092 derivative)	<i>Petrosia contignata</i>	Sponge	Synthetic	II	Anticancer
IPL-550,260 (IPL-576092 derivative)	<i>Petrosia contignata</i>	Sponge	Synthetic	I	Anticancer
GTS-21 (anabasine derivative)	<i>Pseudopterogorgia elisabethae</i>	Cnidarian	Synthetic	I	Alzheimer's/ Schizophrenia
CGX-1160 (contulakin G)	<i>Conus geographus</i>	Mollusc	Synthetic	I	Pain

Currently 7 DFA-approved drugs

Yondelis® (trabectedin)

Marine derived anti-tumoral agent discovered in the colonial tunicate *Ecteinascidia turbinata* and now produced synthetically by PharmaMar.

- Currently approved for treatment of ovarian cancer in 57 countries



Anti-cancer and analgesic drugs from marine invertebrates

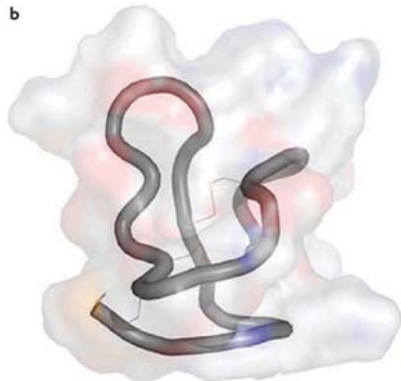
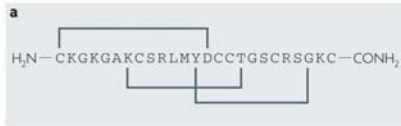
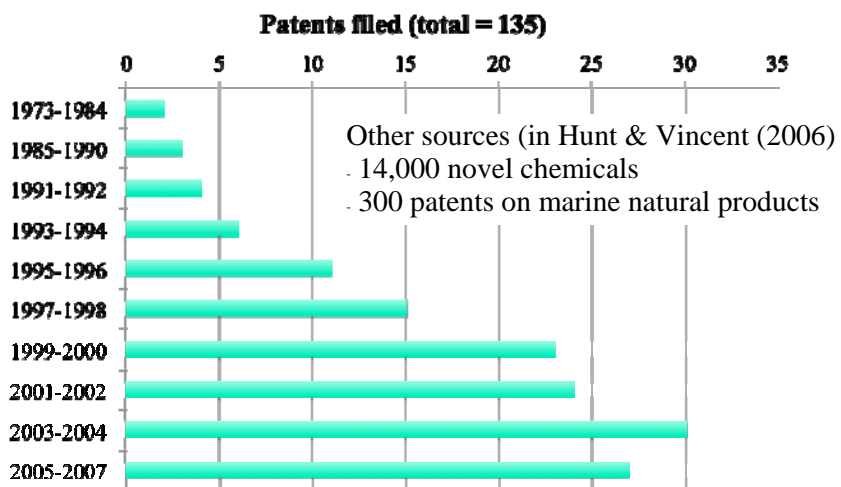


Figure 1 | α -Conotoxin VIIA. a | Amino-acid sequence



Figure 2 | Marine invertebrates producing anticancer and analgesic drugs. a | Textile cone snail *Conus magus*. b | The Caribbean sea-squirt *Ecteinascidia turbinata*. c | The Caribbean sea-squirt *Trididemnum solidum*. d | The sea hare *Dolabella auricularia*. e | The saccoglossan *Elysia rufescens* feeding on the red alga *Bryopsis* spp. f | The bryozoan *Bugula neritina*. Panel a, image reproduced with permission from Elan Pharmaceuticals, USA. Panel b, image courtesy of S. Lopez-Legintil, University of North Carolina, USA. Panel d, image reproduced with permission by W. B. Rudman, Sea Slug Forum, Australian Museum, Sydney, Australia. Panel e, image reproduced with permission by H. Floodrops, Sea Slug Forum, Australian Museum, Sydney, Australia. Panel f, image reproduced with permission by the California Academy of Sciences, USA.

Marine Genetic Resource Patents



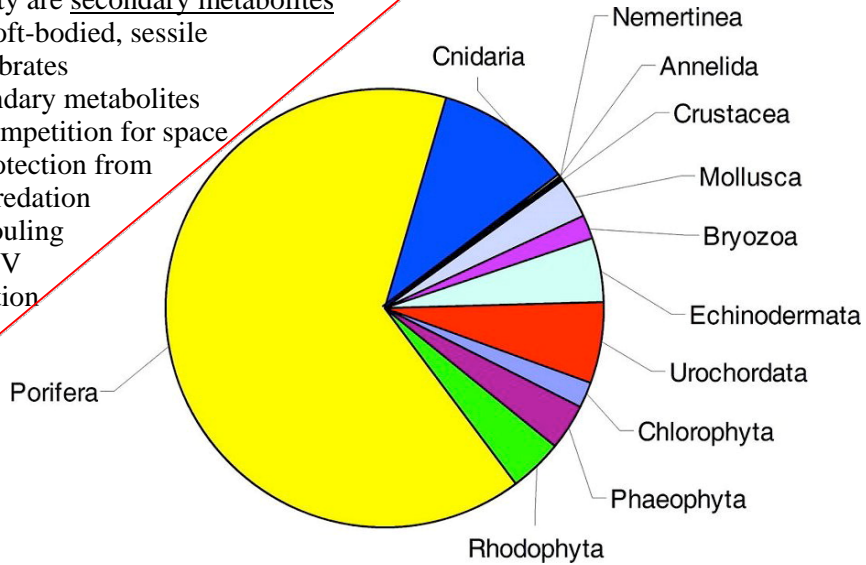
(adapted from Leary et al. (2009) Marine Policy 33, 183-194)

Novel marine compounds grouped by phyla

Majority are secondary metabolites from soft-bodied, sessile invertebrates

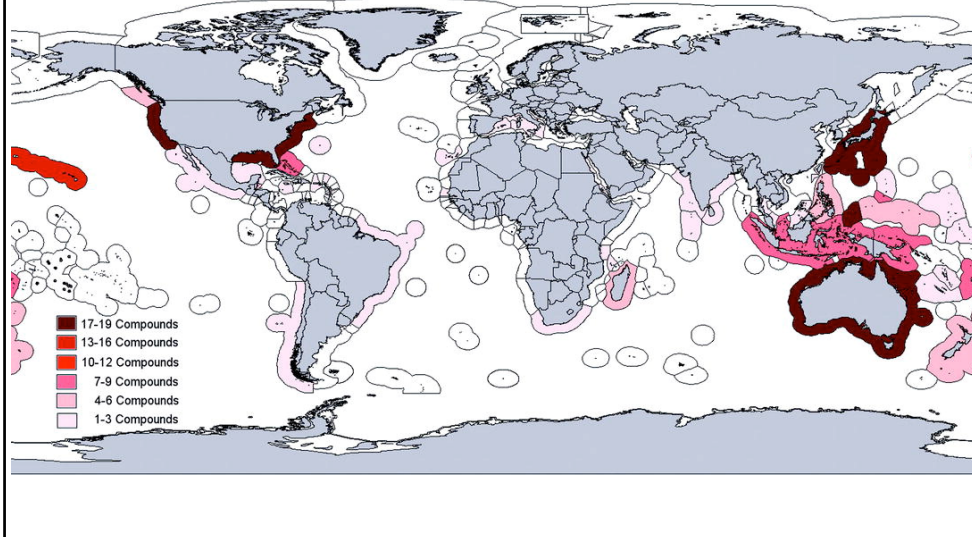
- Secondary metabolites
 - Competition for space
 - Protection from
 - ✓ predation
 - ✓ fouling
 - ✓ UV

Collection bias?



(from Hunt & Vincent (2006) Ambio 35, No. 2)

Geographic origins of novel marine compounds



Non-pharmaceutical areas of MGR research

- **Nutraceuticals**

- \$128 billion in 2010, projected to \$180 billion by 2017
- marine and algal Omega 3 ingredients = \$1.5 billion in 2009

http://www.nutraceuticalsworld.com/contents/view_online-exclusives/2012-01-23/all-signs-point-to-growth/



a better life with seafood

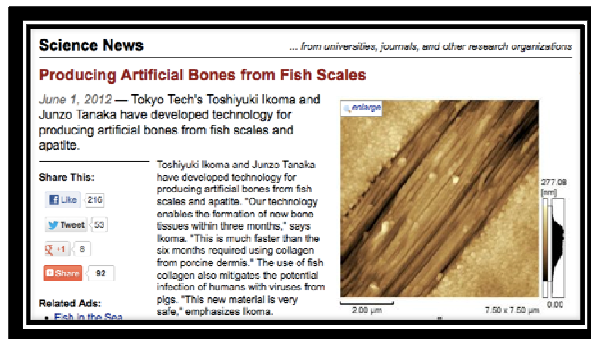
Nutraceuticals - should these included in MGR discussions?

- Collagen creams and other cosmetic/health products from waste fish skin
- Deep-sea mining industry examining bulk extraction of microbes and microbial products from ore prior to metallurgical processing



Natural products extracted from marine biomass

- Value added products can represent a real and economically viable crossover industry
- Outside of classic linear pipeline that begins with bioprospecting or field research and ends with commercialization of MGR products



Other non-pharmaceutical areas of MGR research

- Novel marine feed resources for aquaculture



ARCHIVED - New marine feed resources: Investigate the nutritional value of unutilized marine resources for use in fish diets

Source: NRC Institute for Marine Biosciences
Canada

Conclusions

- Need to clarify terminology
 - avoid ambiguity and confusion.
- Need for MSR capacity development
 - Unequal distribution of research capabilities
- Long, costly path from discovery to commercialization
- Few examples of commercialized MGR from ABNJ
- Important not to confuse or conflate potential of MGR from ABNJ with examples from coastal areas
- Should nutraceutical and biomass-based industries be included in MGR debate?