



Current challenges and opportunities in marine biotechnology and marine biodiscovery

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eCOAST
MARINE RESEARCH



PHARMASEA

**Increasing Value and Flow in the Marine
Biodiscovery Pipeline**

Call for Proposals

- **KBBE.2012.3.2-01: Innovative marine biodiscovery pipelines for novel industrial products. Call: FP7-KBBE-2012-6**
- Marine organisms represent an almost inexhaustible source of bioactive compounds and of novel molecules and materials for industrial applications (e.g. chemicals, pharmaceuticals, biomaterials, cosmetics, etc.) which we are only now starting to understand and investigate. In order to unveil novel and interesting products and processes, thus properly exploiting the potential of marine biotechnology, comprehensive and integrated efforts are needed that focus on industry's requirements.
- EUR 24 Million
- More than 1 consortium will be funded
- 25% Industry

- **Increasing Value and Flow in the Marine Biodiscovery Pipeline**
- EU Framework Programme 7 Consortium funded at EUR 9.5 million
- 24 Partners
- Norway, Denmark, UK, Belgium, Germany, Spain, Italy, Republic of Ireland, Chile, South Africa, China, New Zealand, Costa Rica
- *To improve the quality, volume and value of active agents discovered in the marine environment and increase the speed at which they can be delivered to the marketplace, by addressing bottlenecks and restrictions and adding technical booster-pumps*
- Start date 01/10/2012; Duration 48 months (& 6 extension)
- Project Coordinator Camila Esguerra/Peter de Witte, KU Leuven, Belgium

PHARMASEA

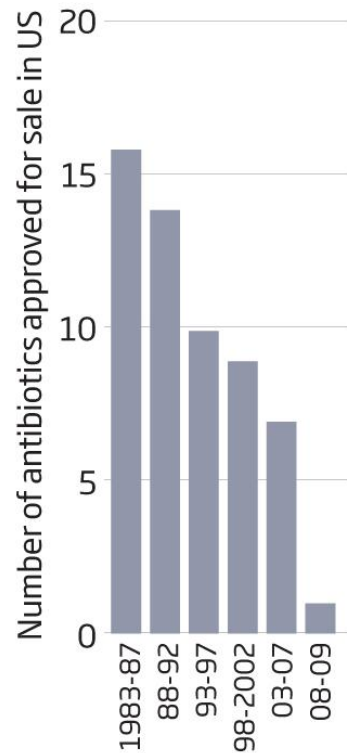
★ UniAbdn, DeepTek
★ ACDLabs, RSC, BioBridge
★ KULeuven, eCoast
★ SeaLife Pharma



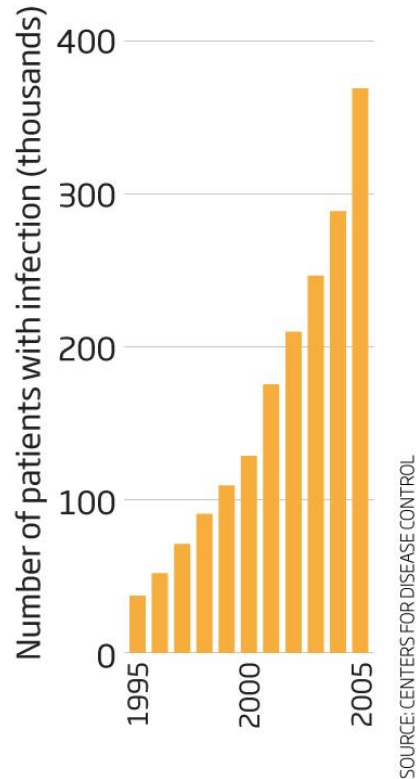
Access to both poles, the world's deepest trenches and thermal vents

Why PharmaSea?

Decline in new approved antibiotics



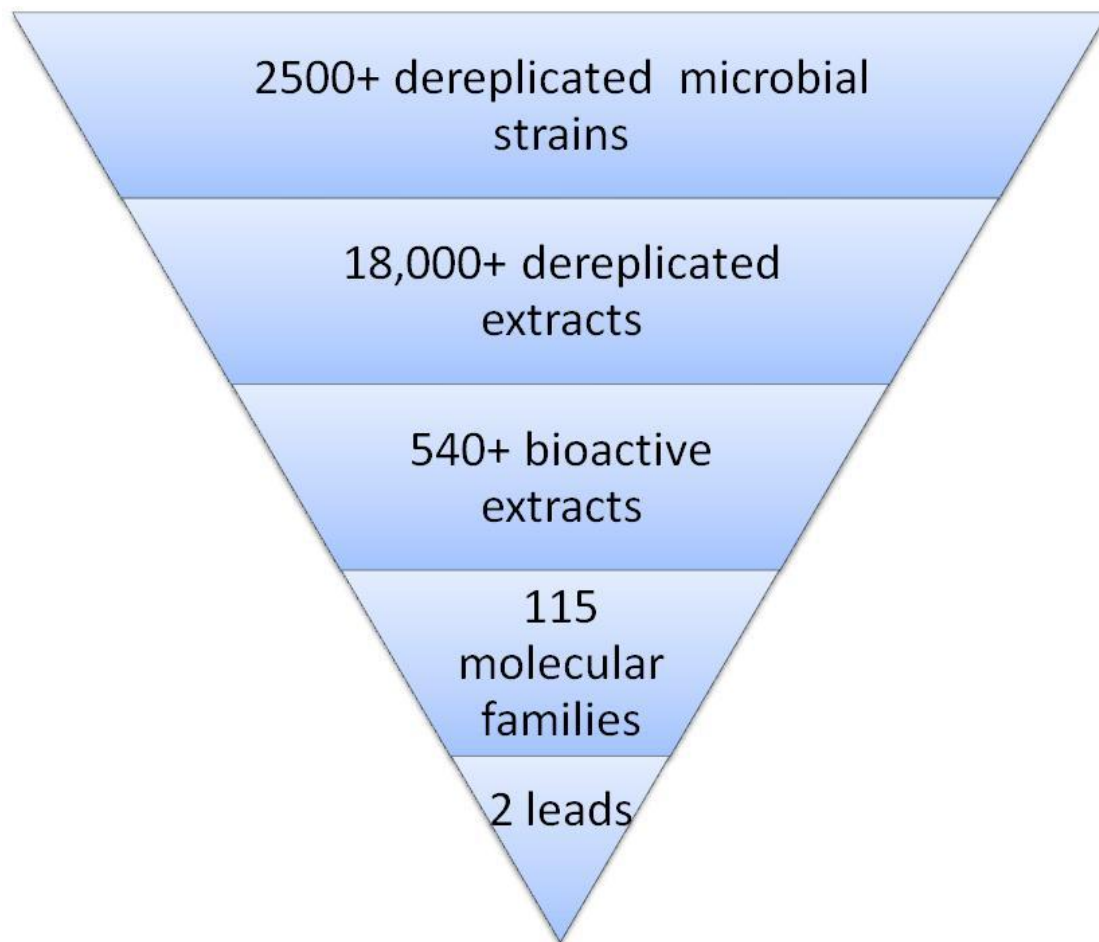
Increase in hospital MRSA infections

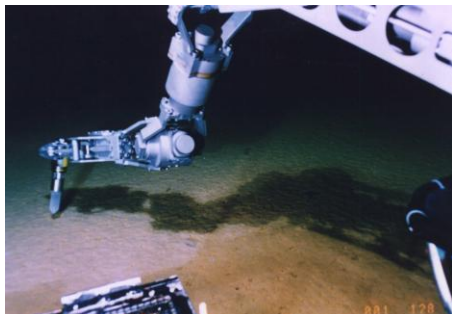


- New therapeutics for microbial infections and CNS diseases
- Widen bottlenecks in marine biodiscovery pipeline
- Develop mechanisms to transfer marine biotechnology to end users
- Make marine bioproducts more attractive to develop for industry

Source: New Scientist

Discovery Funnel

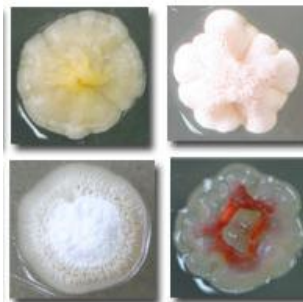




Extreme Environment

Legal Access

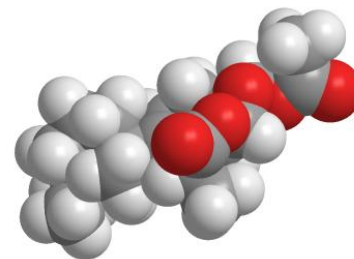
Physical Access



Novel Biology

Isolation/identification

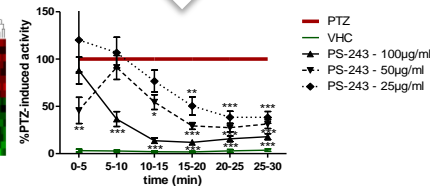
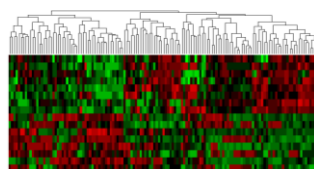
Chemical talent



Novel Chemistry

Chemical novelty

Datamining



Product

Scale-up

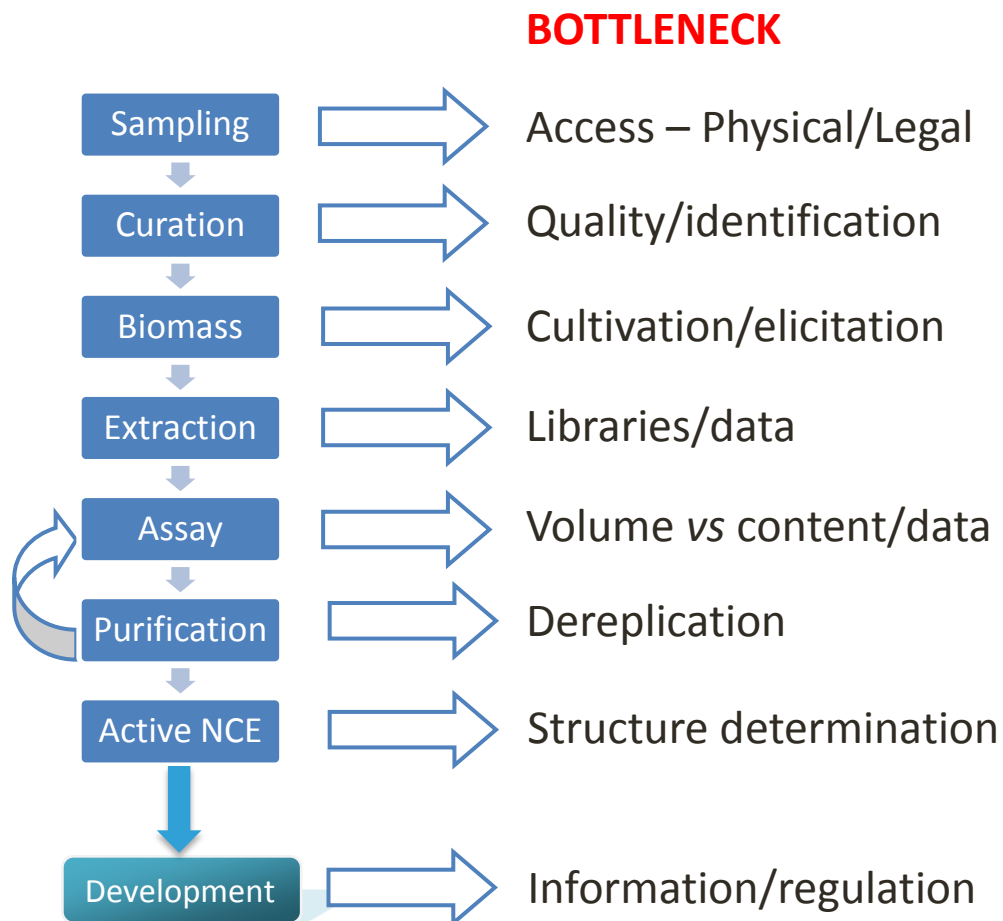
Knowledge transfer

Novel Activity

Mechanism of action

Toxicity

Bottlenecks in the Marine Biodiscovery Process



Create Science/Policy Interface

MGR Practitioners
Research /
Industry



Legal Experts &
Policy Makers

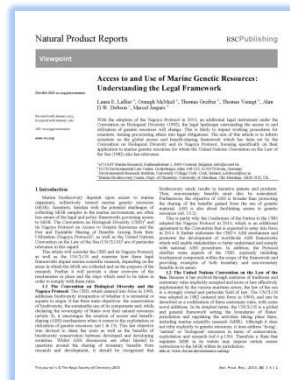
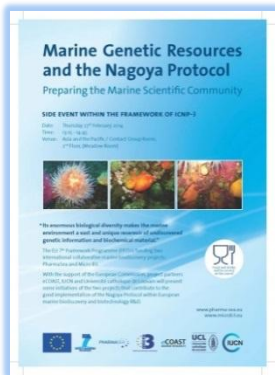
EC (DG MARE & DG ENV),
UNDOALOS, CBD Secretariat,
CIESM, ISA, CMS Secretariat



Inform Policy

Awareness
Raising

Share best practice



Obtaining Marine Genetic Resources with Legal Certainty

Changes in Convention on Biodiversity/Nagoya Protocol (ratified by EU mid Oct 2014) mean:

- All MGR collected with prior informed consent and under mutually agreed terms

- Permits deposited with CBD clearing house

- Benefit sharing obligations

- Traceability for 20 years (inc. change of use)

- Legal sanctions

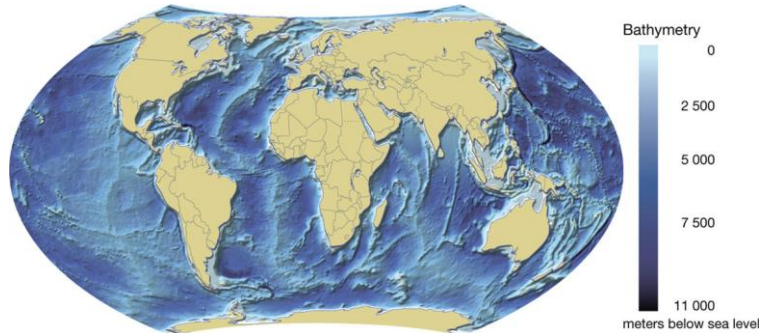
UN Convention on Laws of the Sea (areas beyond national jurisdiction)

- MGR not specified in UNCLOS

- Incompatibility between UNCLOS and IP law

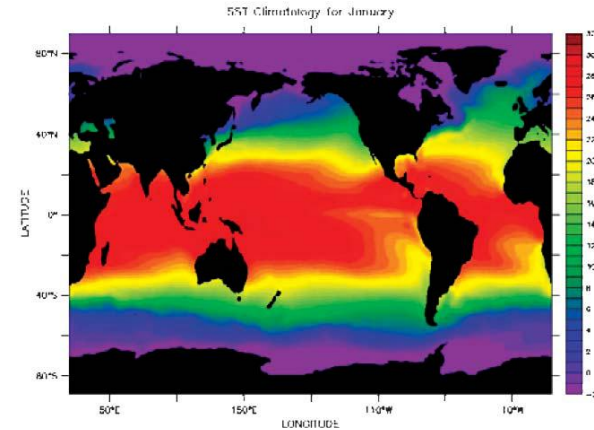
Low level of scientist awareness of obligations

Extreme Marine Environments



Deep Oceans

95 % > 1000 m deep
50 % > 3000 m deep
Average depth = 3790 m



Cold Oceans



Thermal Vents

WP1 Strain Collections (n = 13,689)

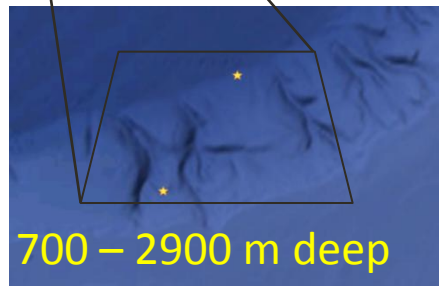


Legacy Collections: Arctic, Antarctic, Republic of Ireland, South Africa and Argentina

New Collections: Antarctic, South Africa

Scheduled Collections: South Shetland Trench (-5200 m)

WP1 Deep Sea Sampling



RV Celtic Explorer



ROV
Holland I



Live HD Video
of sampling



*Inflatella
pellicula*

750/2900 m



*Lissodendoryx
diversichela*

1,350 m



*Stelletta
normani*

1,350 m



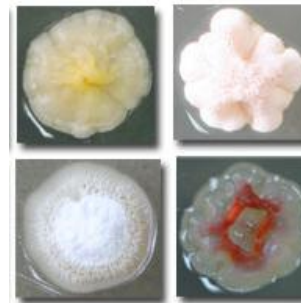
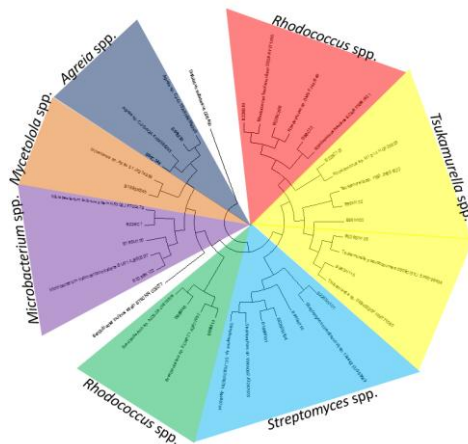
*Poecillastra
compressa*

2,100 m



Sediments

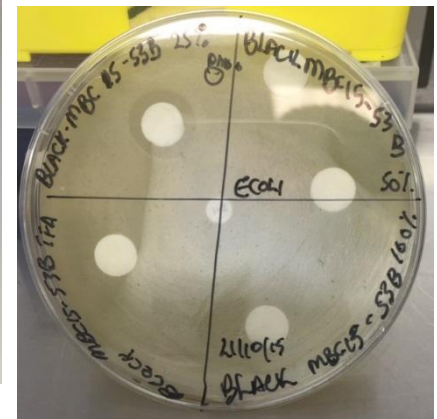
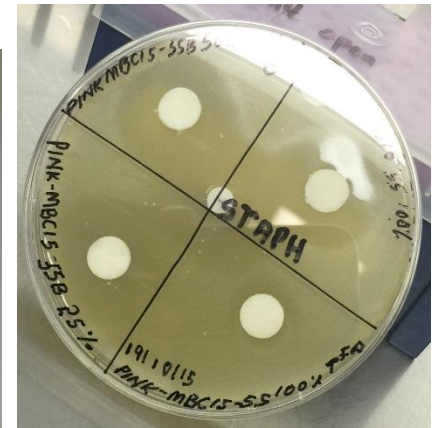
750 m – 2,900 m



WP1 New Environments

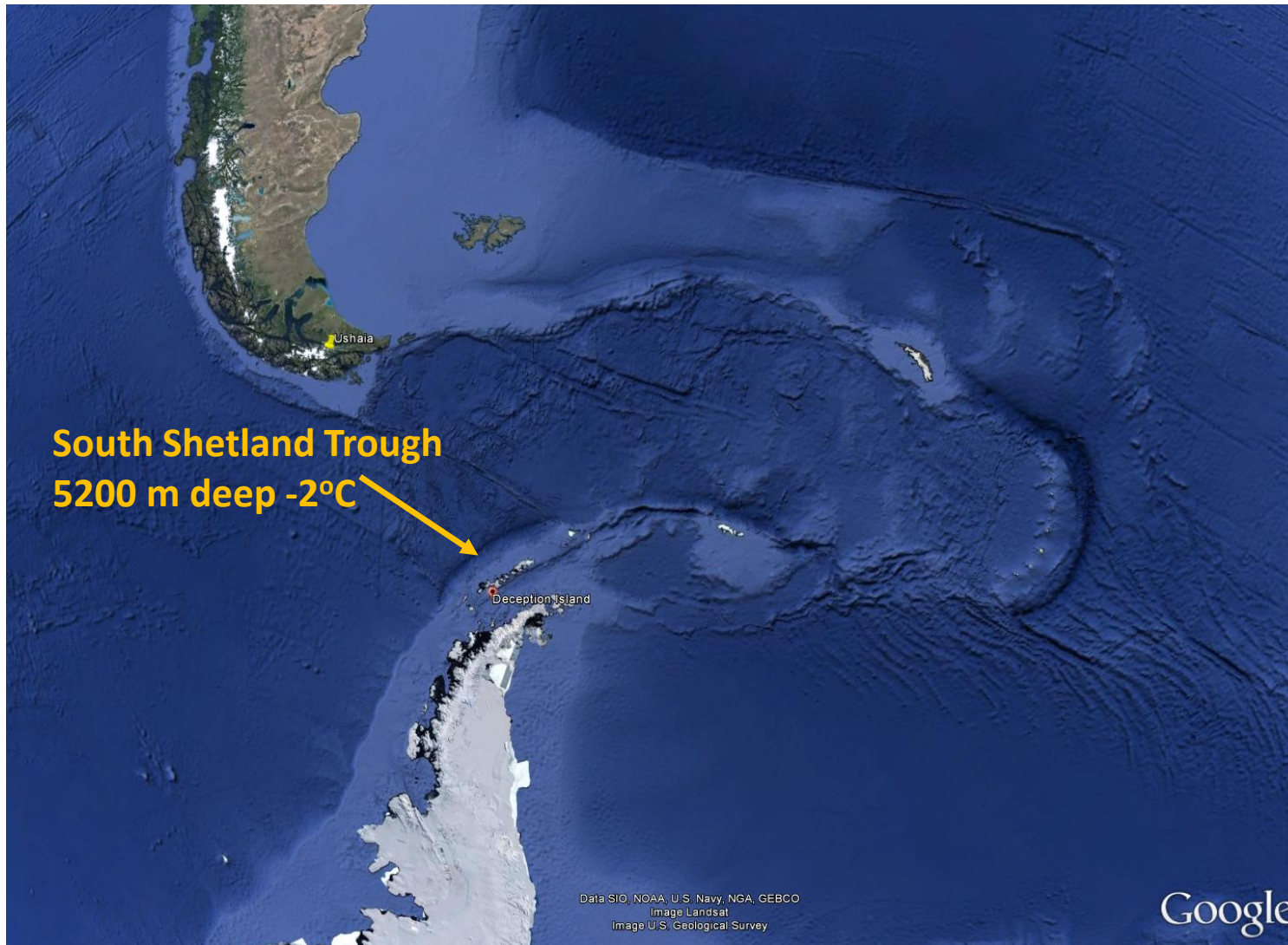


WP1 Recent Deep Sea Collections

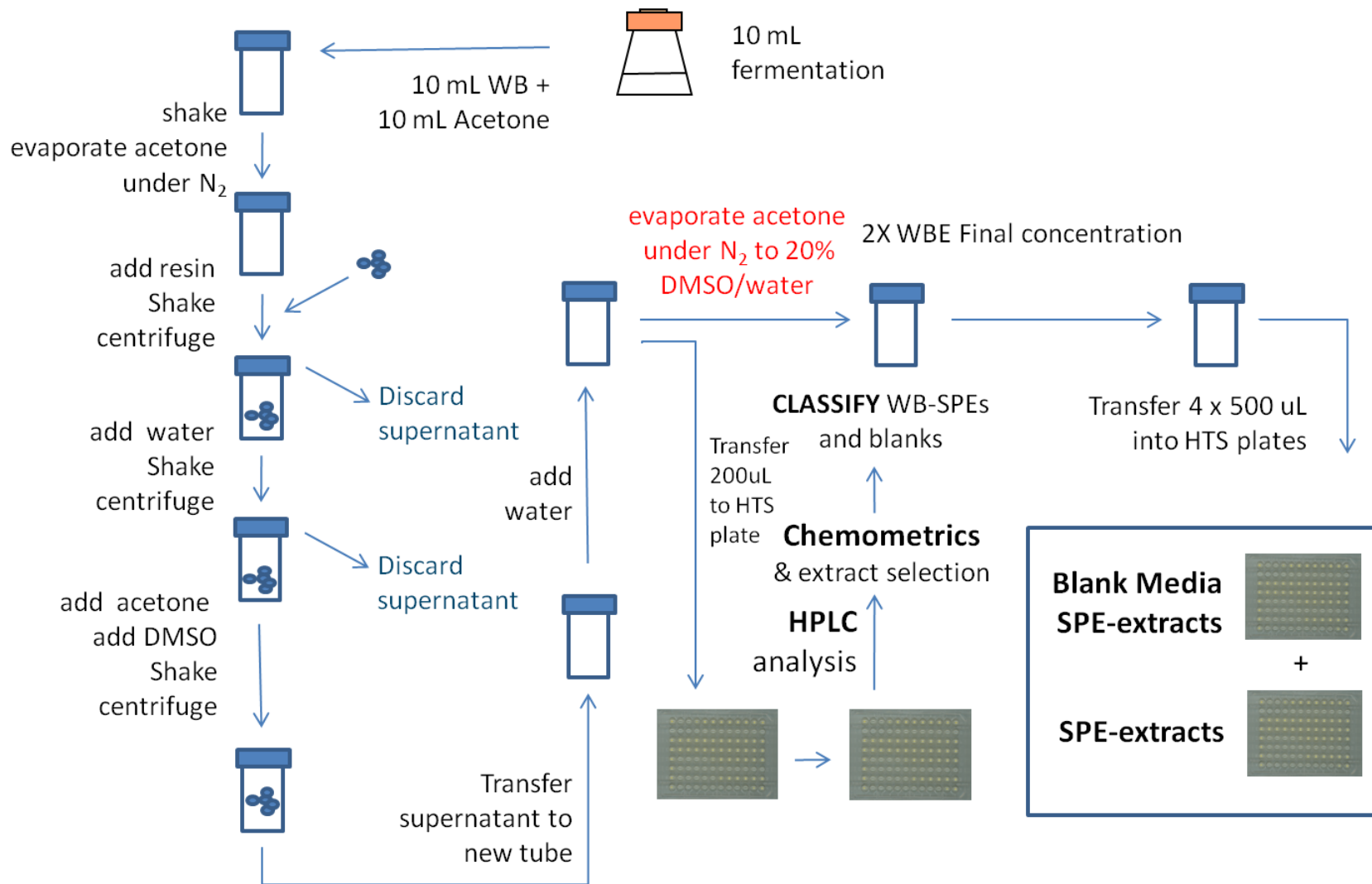


Alan Jamieson
Larry Mweetwa

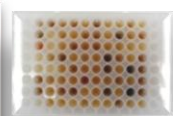
WP1 Planned PharmaDeep Expedition December 2015



WP2 Standardised Fermentation and Extraction Protocols



WP3 PharmaSea Anti-infective assays



Crude extracts or fractions



MULTIDROP



ULTRA TECAN

Incubation
18-20 h 37°C
(7-14 days
Anti-TB)



ULTRA TECAN

Absorbance /
Resazurin dye
0.002%

Incubation
2 h 37°C

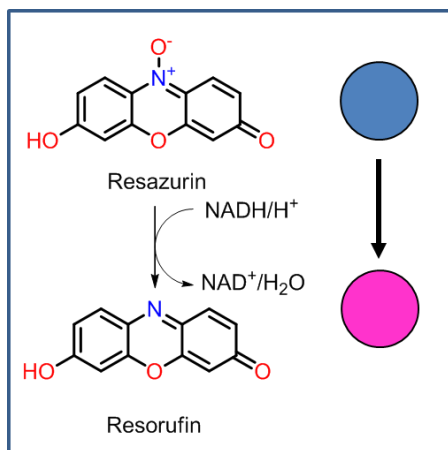
Inoculum assay

TO absorbance

TF absorbance

612 nm

612 nm



Data analysis
Screener Program

HIT SELECTION



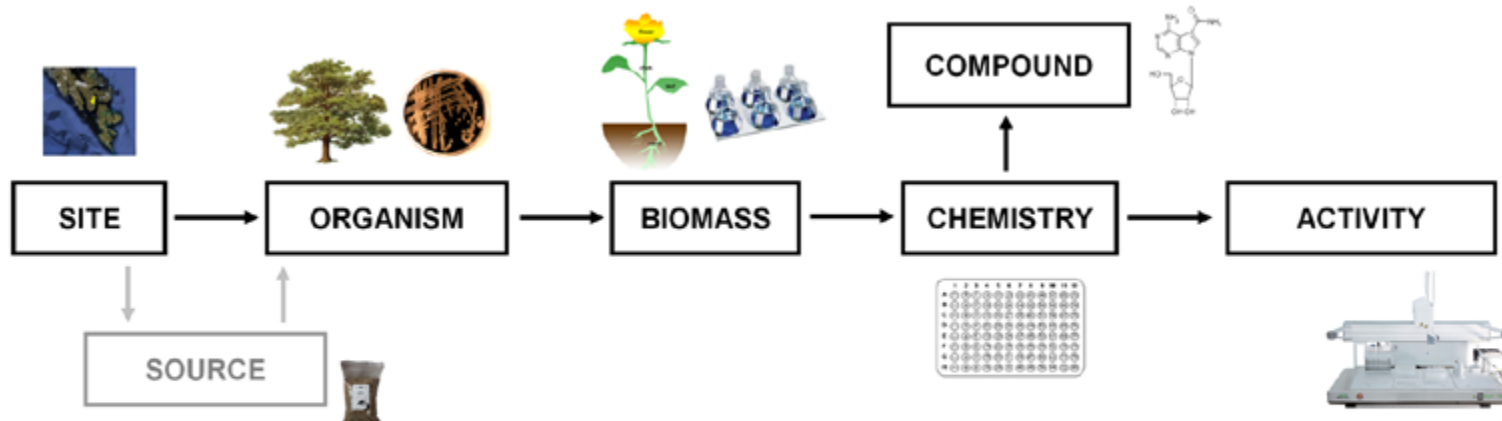
Fluorescence

570 nm excitation/600 nm
emission



Active extracts Non active extracts

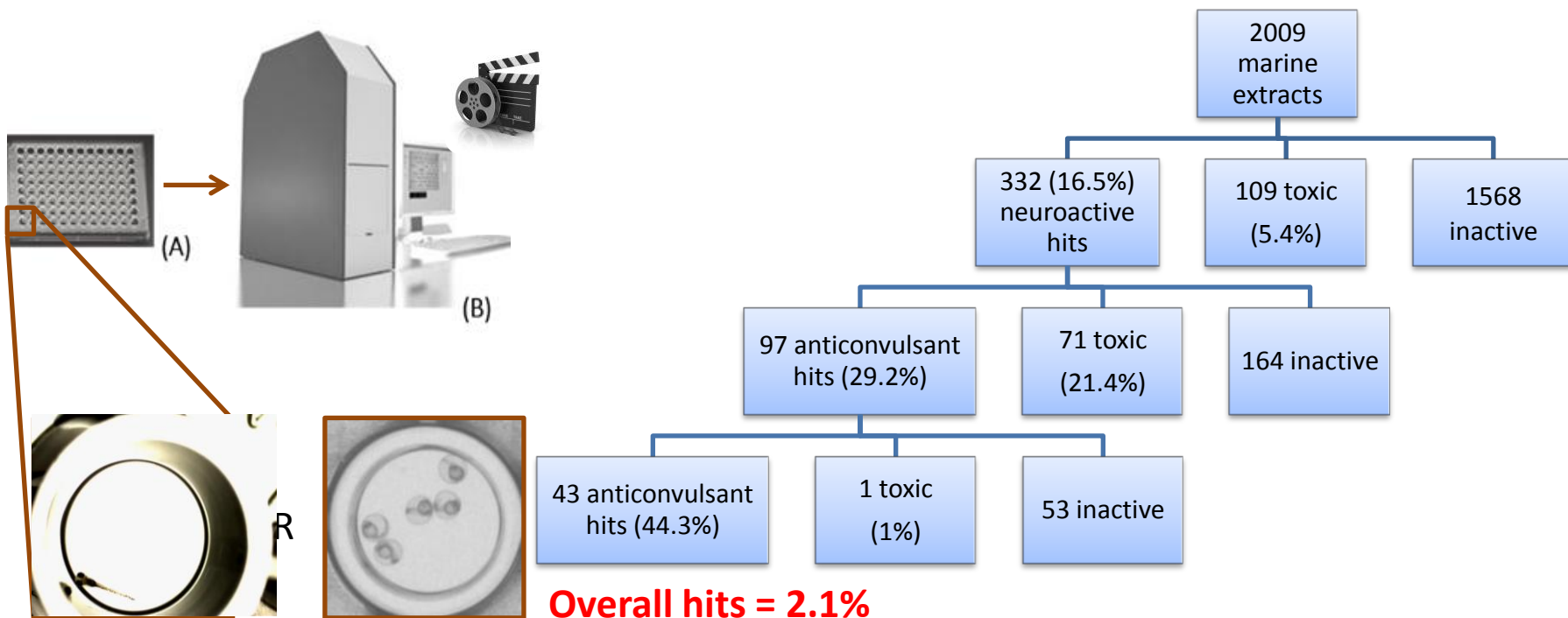
WP2/3 Data Management



OpenNAPIS™
Functional Design

White Point Systems, Inc.
20100626

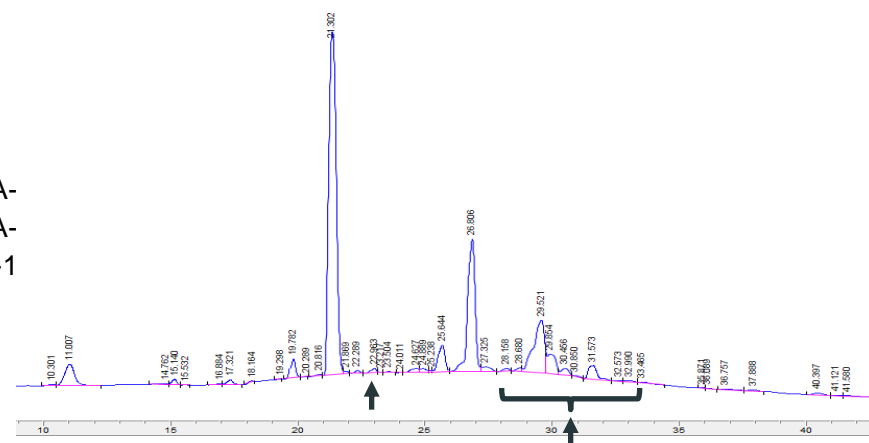
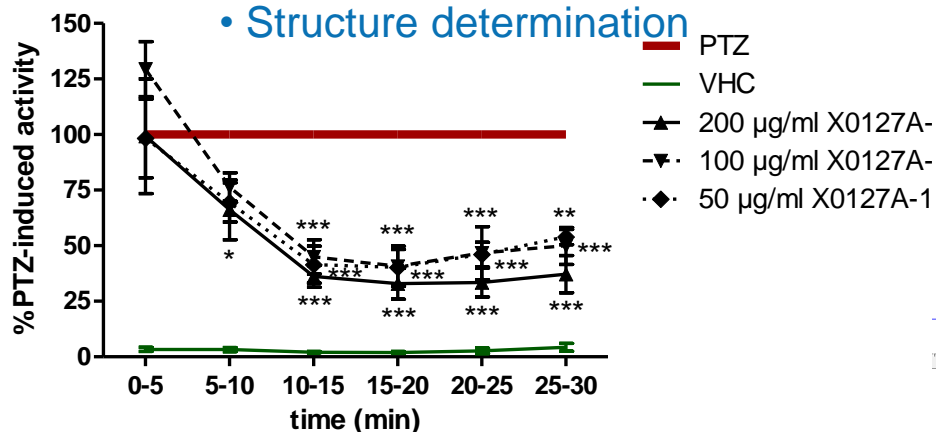
WP4 CNS Assay Cascade



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

WP3/4/5 Identification of the Anticonvulsant Hit X0127A-1-04

- University of Tromsø
 - isolation of the marine microorganism
 - fermentation and extraction
 - pre-fractionation of the extract for bioactivity analysis
- KU Leuven
 - neuroactive and anticonvulsant screening
 - toxicity analysis
 - confirmation of anticonvulsant activity in three independent experiments
- University of Aberdeen
 - Purification step
 - Structure determination



WP3/4/5 Function-based purification of X0127A-1-04

- SealifePharma

- scale-up of X0127A-1-04

- University of Aberdeen

- purification of final scale-up SPE100%
 - identification of one pure compound (novel small molecule)
 - purification of the peptides is ongoing

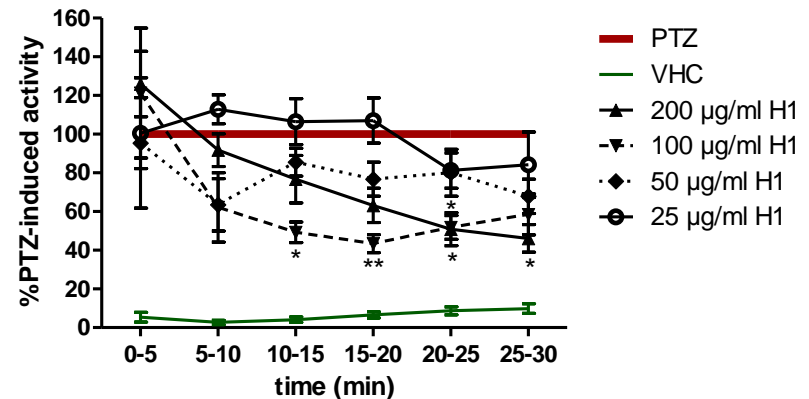
- KU Leuven

- activity analysis

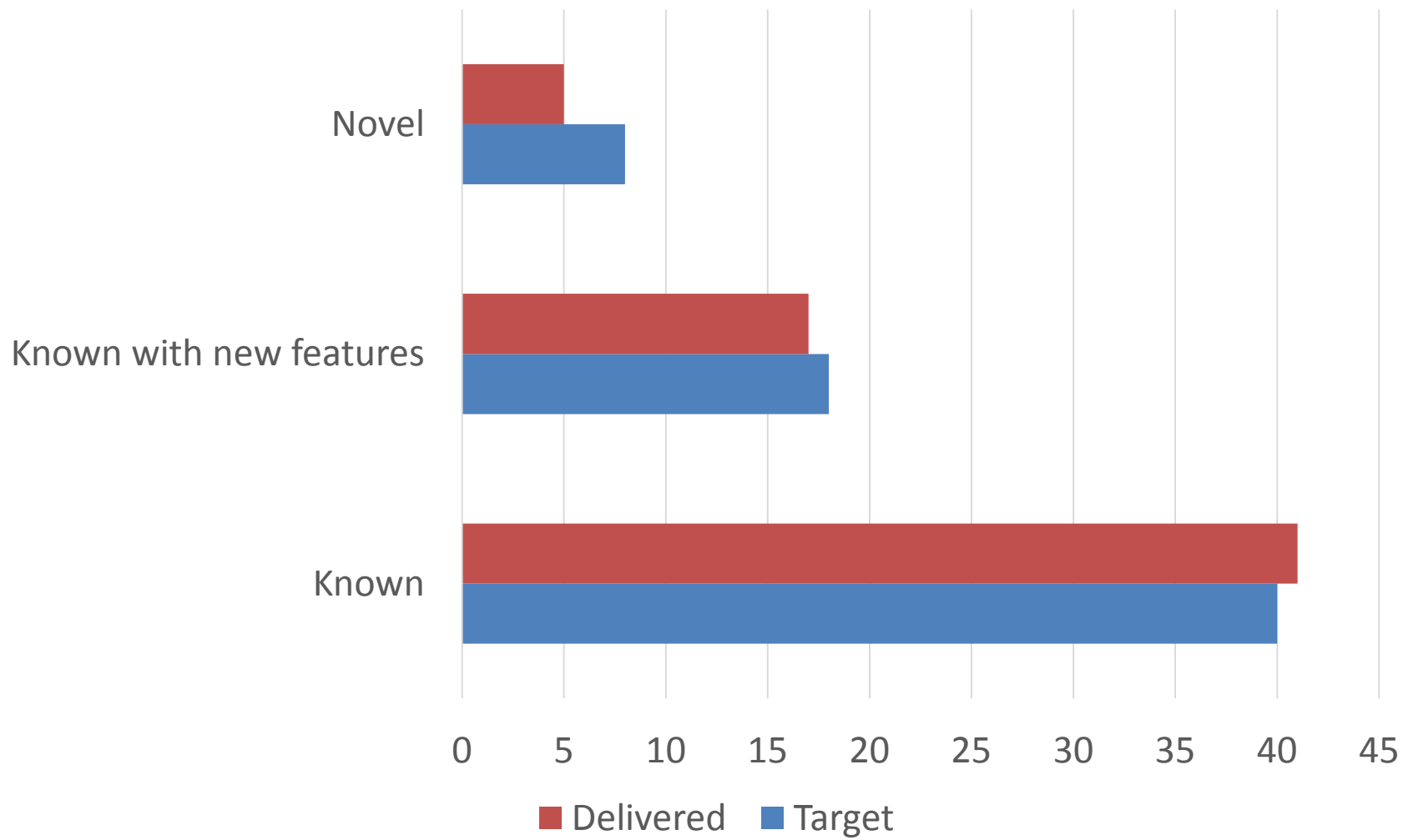
- challenge: small molecule has anticonvulsant effect, but efficacy is lower than X0127A-1-04
- analysis of the peptides will be initiated

- next level analysis of anticonvulsant activity

- investigate effect of active pure compound(s) also on other seizure markers than seizure behaviour



WP4 Structural Families Isolated (from 668 chemically dereplicated active extracts)



WP1-4 Assembling the Marine Biodiscovery Pipeline



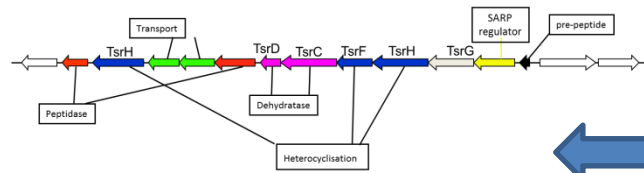
Stelletta normani
(1,300m)



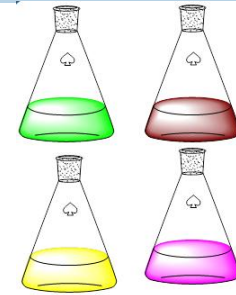
Lissodendoryx diversichela
(1,300m)



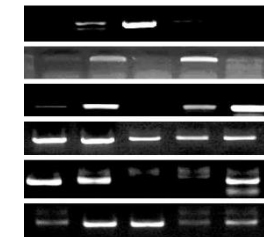
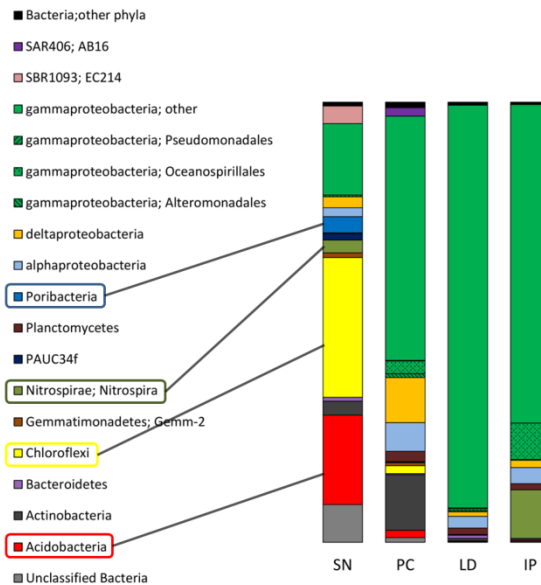
Inflatella pellicula
(2,900m)



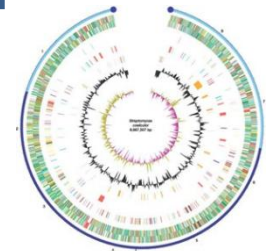
Discovery of new genes
giving new products



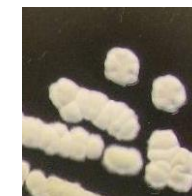
Fermentation under
different conditions



Gene expression
analysis



Genome
sequencing



Isolation
of bacteria

Bacterial diversity in sponges

WP7 Communication and dissemination



WP7 Communication and dissemination: Radio and news articles



BBC: Drugs in dirt – Scientists appeal for help

US scientists are asking the public to join them in their quest to mine the Earth's soil for compounds that could be turned into vital new drugs...

» [\(read\)](#)

Copyright: <http://www.bbc.com>
20.01.2015



New Scientist: "Antibiotic abyss – the extreme quest for new medicines"

As antibiotic resistance increases, audacious expeditions are taking the quest to the ocean depths, and not a moment too soon...

» [\(read\)](#)

Copyright: www.newscientist.com



CNN: Arctic waters could hold secret to creating life-saving drugs

It is early afternoon on board the "Helmer Hanssen," and the Arctic sun is already starting to set. Near the back of the ship, two people dressed in orange rain slickers are anxiously waiting... » [\(watch\)](#)

Copyright: <http://edition.cnn.com>



BBC Radio 4 Shared Planet: Medicinal Planet

Radio interview with PharmaSea's Project Leader Marcel Jaspars (Duration: 28 minutes)

In recent years some conventional medicines such as antibiotics have become less effective in treating diseases and infections. With an increasing human population worldwide, the need to discover new medicines for the benefit of human health will... [listen](#).



Reuters: Extreme medicine – The search for new antibiotics

Marcel Jaspars, a professor of organic chemistry at Britain's University of Aberdeen, is leading a dive deep into the unknown to search for bacteria that have, quite literally, never before seen the light of day... » [\(read\)](#)

Copyright: www.reuters.com
17.08.2014



Welt Online: Neue Antibiotika schlummern in der Tiefsee

Antibiotika-Resistenzen breiten sich zunehmend aus. Um neue Wirkstoffe gegen die Superbakterien zu finden, starten Wissenschaftler jetzt eine Expedition zu den tiefsten Stellen der Tiefsee. ...» [read](#)

Copyright: Welt Online

WP7 Communication and dissemination: TV shows

“Vital Signs” on CNN



WP7 Communication and dissemination: TV shows

“The cure” on Al Jazeera



WP7 Communication and dissemination

PharmaSea was awarded at the **CommNet Impact Awards** in Brussels, Belgium on December 3rd, 2014 in the category "Engaging Citizens". The CommNet awards honour projects working across the bioeconomy, that have demonstrated excellence in communicating to European citizens, policy-makers, industry or young people.



PharmaSea Progress to Date



45%

From existing partner collections

>110,000 screening events

> 700 active dereplicated extracts

Active, non toxic, novel chemistry

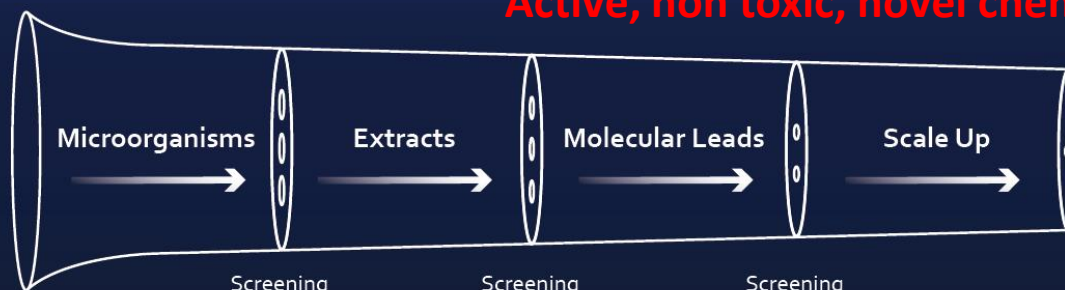


55%

New samples from cold/hot/deep habitats

At 48 Months:

Up to -6,000 metres



2
Drug Leads

Screening
↓
Microbial Library

Screening
↓
Extract Library

Screening
↓
Molecular Families

13,689
Strains

>14,000
Active
Extracts

>80
Active
Compounds

1
Drug
Lead

Conclusions

- PharmaSea will make marine biodiscovery more attractive for industry to adopt.
- PharmaSea is widening the bottlenecks
 - High quality biodiversity
 - Streamlined biodiscovery pipeline
 - New chemistry with new activity
- PharmaSea will provide mechanisms to transfer findings to end users whilst acknowledging:
 - Need for legal certainty over marine biodiversity collection.
 - Regulatory stress on companies.
 - Lack of risk taking by companies due to shareholder pressure.

PHARMASEA

<http://pharma-sea.eu/>



“The research leading to these results has received funding from the European Union's Seventh Framework Programme (FP7/2007-2013 under grant agreement n^o 312184)”

