



Loriano Ballarin

Department of Biology, University of Padova

**Maristem—Stem Cells of Marine/Aquatic Invertebrates:
from Basic Research to Innovative Applications**

Why marine/aquatic marine invertebrates?

Marine/aquatic invertebrates represent the widest eukaryotic phylogenetic radiation on Earth, with more than 2,000,000 species formally described.



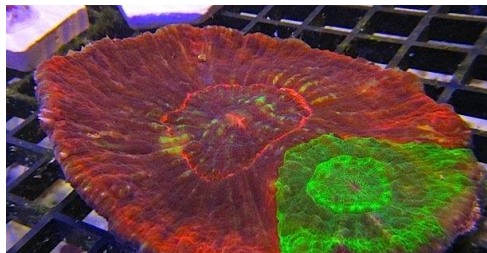
Why marine/aquatic invertebrates?

Marine/aquatic invertebrates contributed to the elucidation of various biological problems related to:

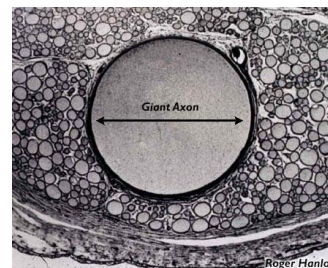
- natural immunity



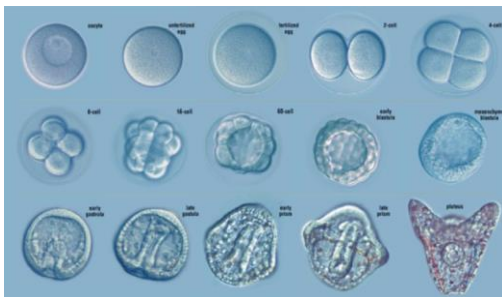
- chimerism



- nerve conduction

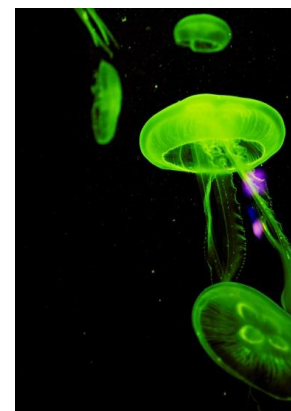
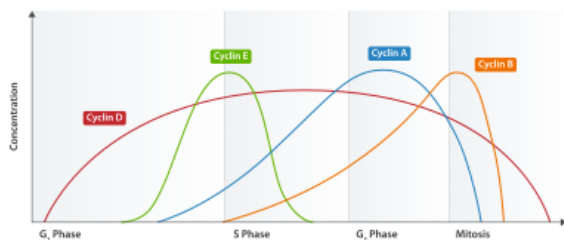


- developmental biology



- discovery of new laboratory tools (e.g., green fluorescent protein)

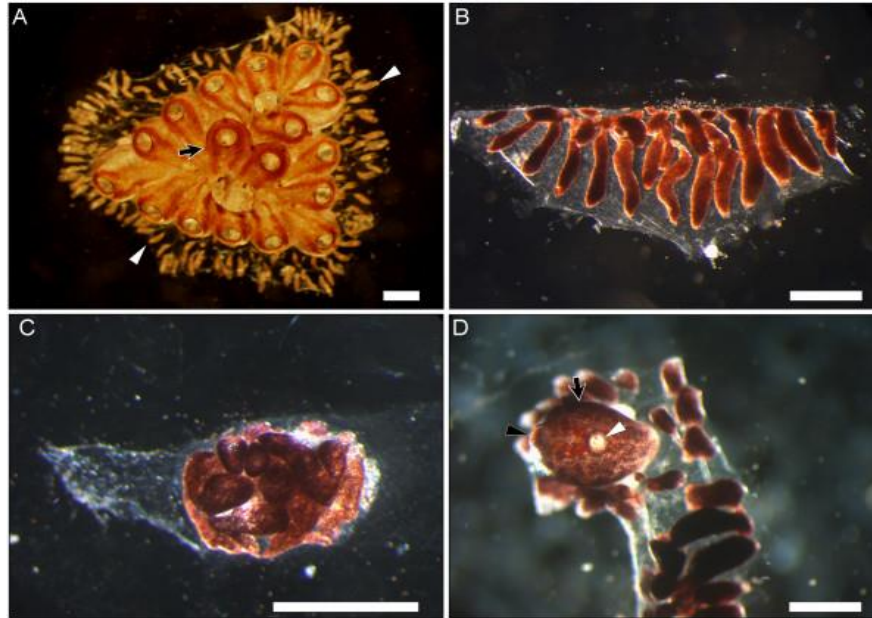
- gene regulatory networks (e.g., cyclins)



Why marine/aquatic invertebrate stem cells (MISCs)?

They have a central role in many biological processes and can help the understanding of fundamental biological processes.

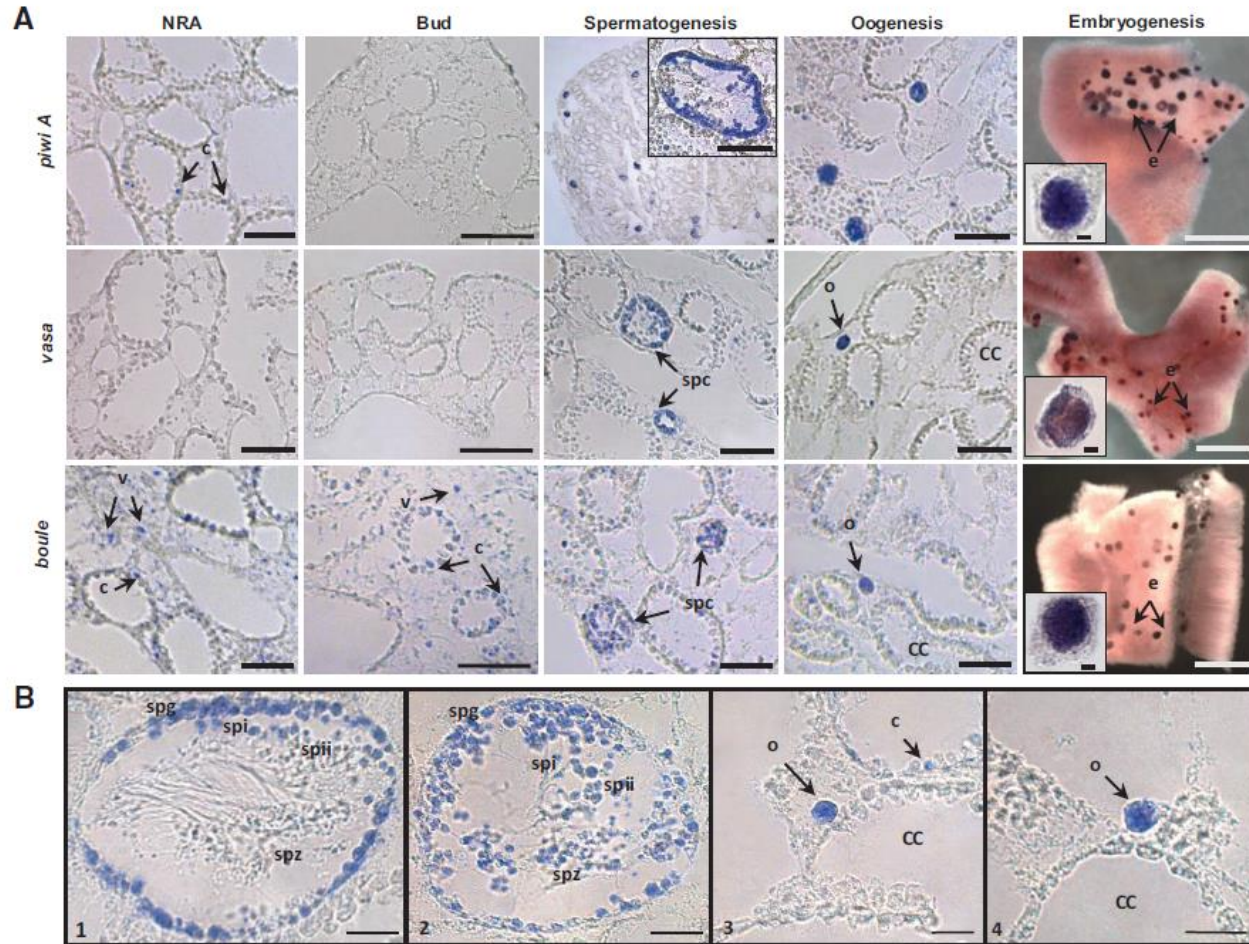
-adult marine/aquatic invertebrate stem cells (MISCs) are pluripotent cells, capable of generating both the germ line and the somatic tissues.



Rinkevich et al., BMC Developmental Biology 8: 100
(2008)

Why MISCs?

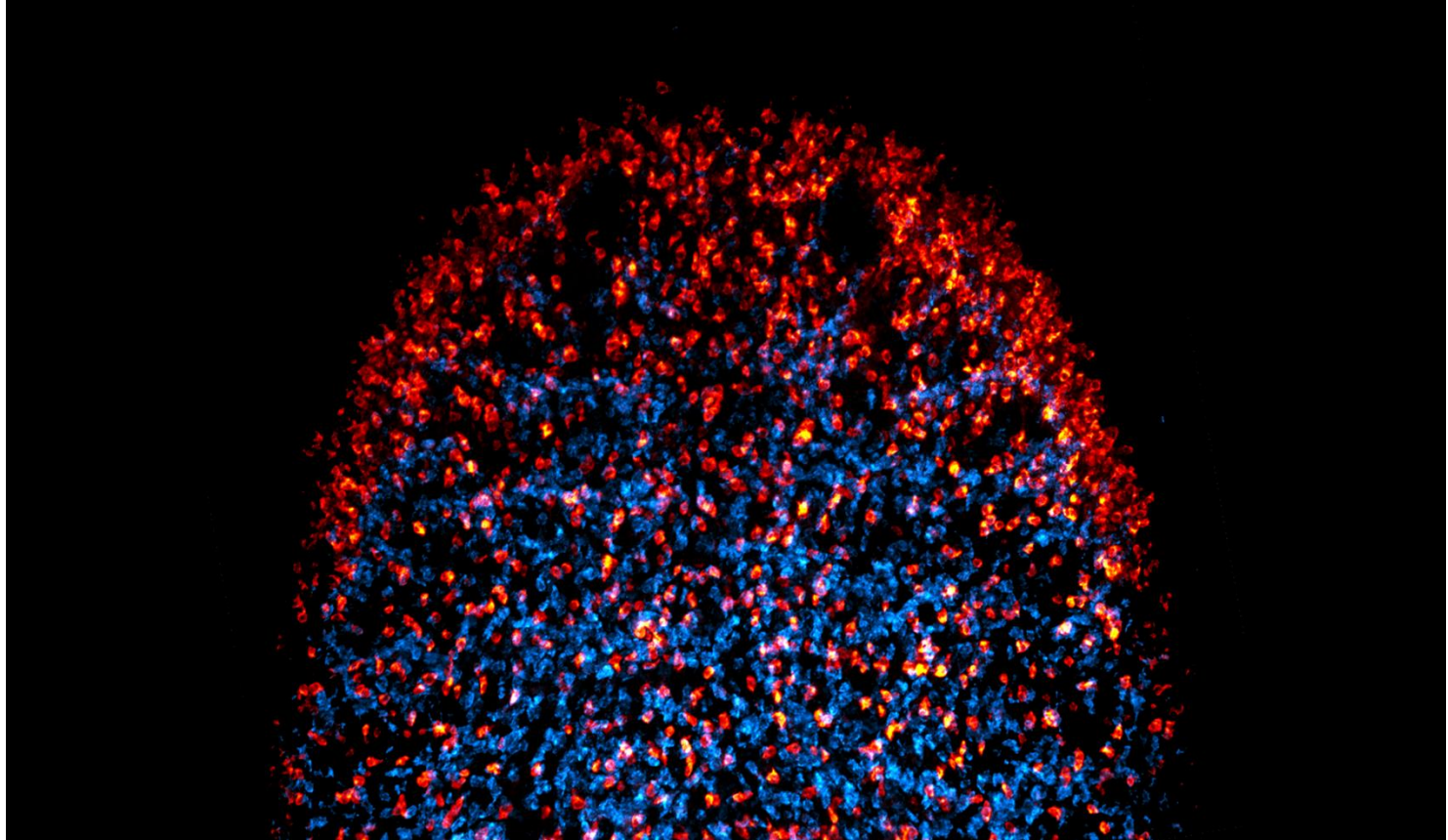
- aquatic invertebrates exhibit multiple cell types with stem cell attributes.



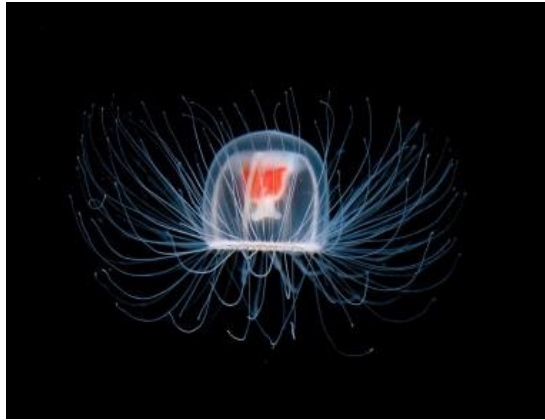
Fierro-Constain et al., 2016

Why MISCs?

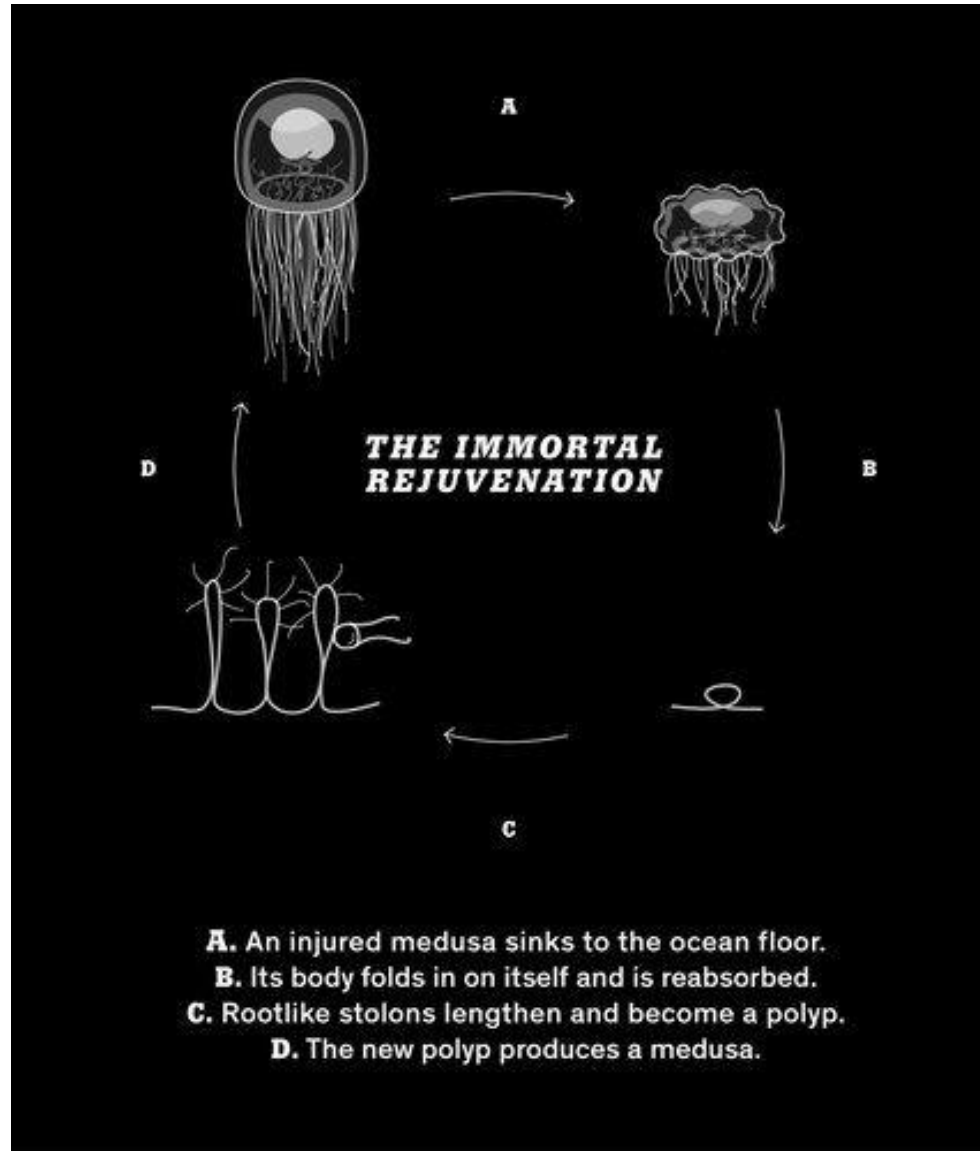
- Unlike vertebrates, in aquatic/marine invertebrates, stem cells are disseminated and widespread inside the animal body, i.e., not associated with a regulatory microenvironment (niche).



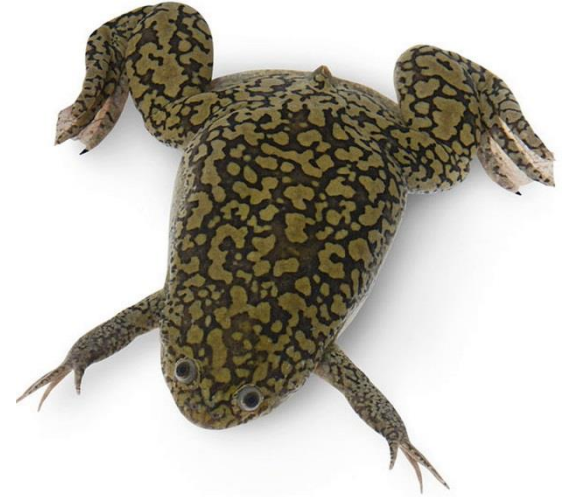
MISCs challenge the concepts of genetic and epigenetic control of stem cell differentiation



Turritopsis dohrnii

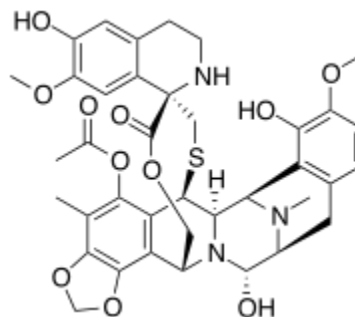


The use of vertebrate stem cells raises ethical concerns (see 2010/63/EU directive on the protection of animals used for scientific purposes).



MISCs can be important for biomedical and biotechnology industries

Marine/aquatic invertebrates produce a variety of bioactive molecules with applications in various fields, such as nutraceuticals, cosmetics, antibiotics, disease-fighting drugs, antifouling products, biomaterials, and more.



Trabectedin from *Ecteinascidia turbinata* (therapy of soft tissue sarcoma)

Workshop

Stem cells of marine invertebrates: from basic research to innovative applications

Padova (Italy), March 9-10, 2016

Aula Magna, Department of Biology, University of Padova

Organizing committee:

Loriano Ballarin, University of Padova, Italy

Anne-Marie Genevrière, CNRS, France

Valeria Matranga, CNR, Palermo, Italy

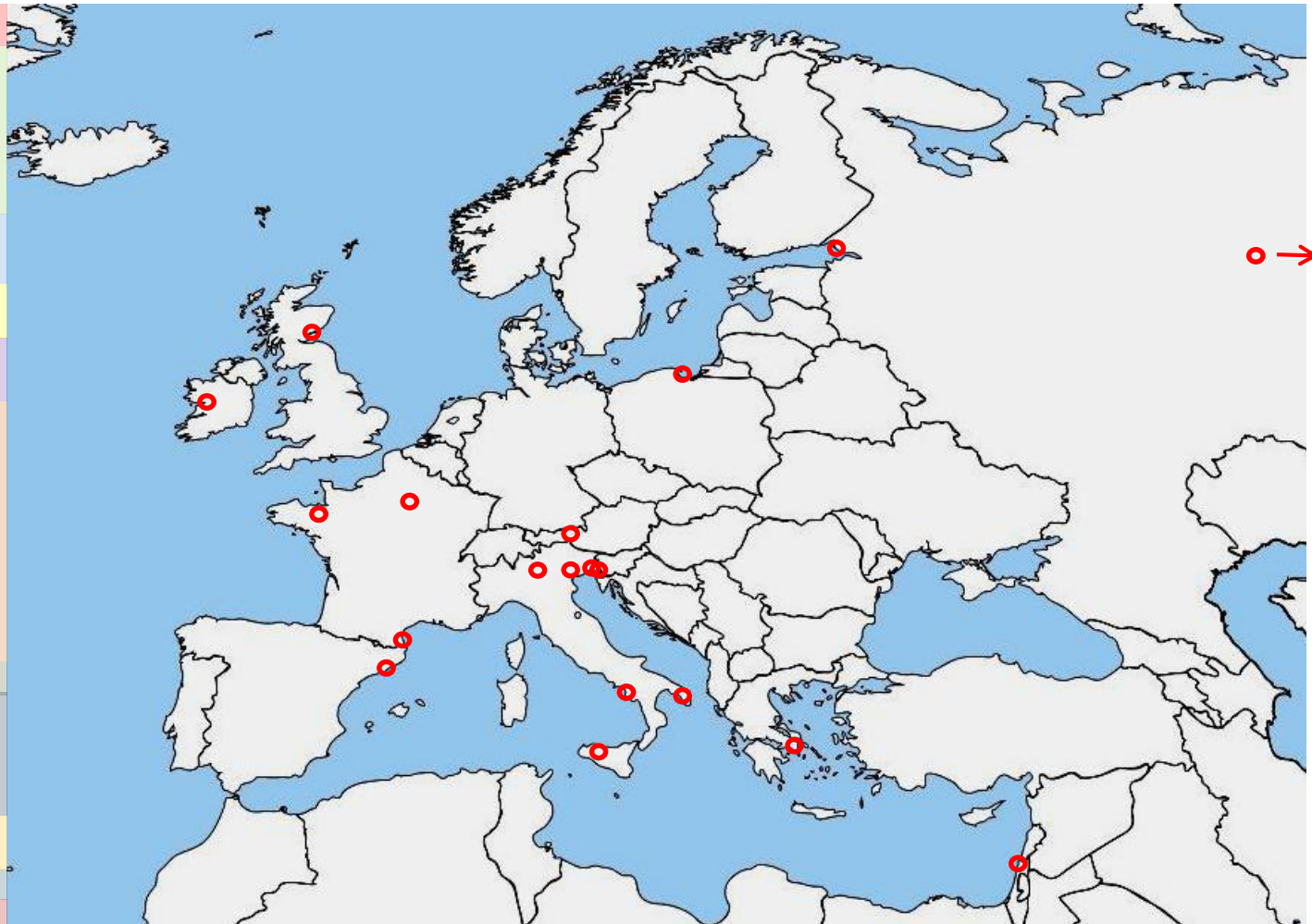
Andreja Ramšak NIB, Slovenia

Buki Rinkevich, IOLR, Israel

Uri Frank, NUI Galway, Ireland

32 participants, from 11 countries and 20 research institutions:

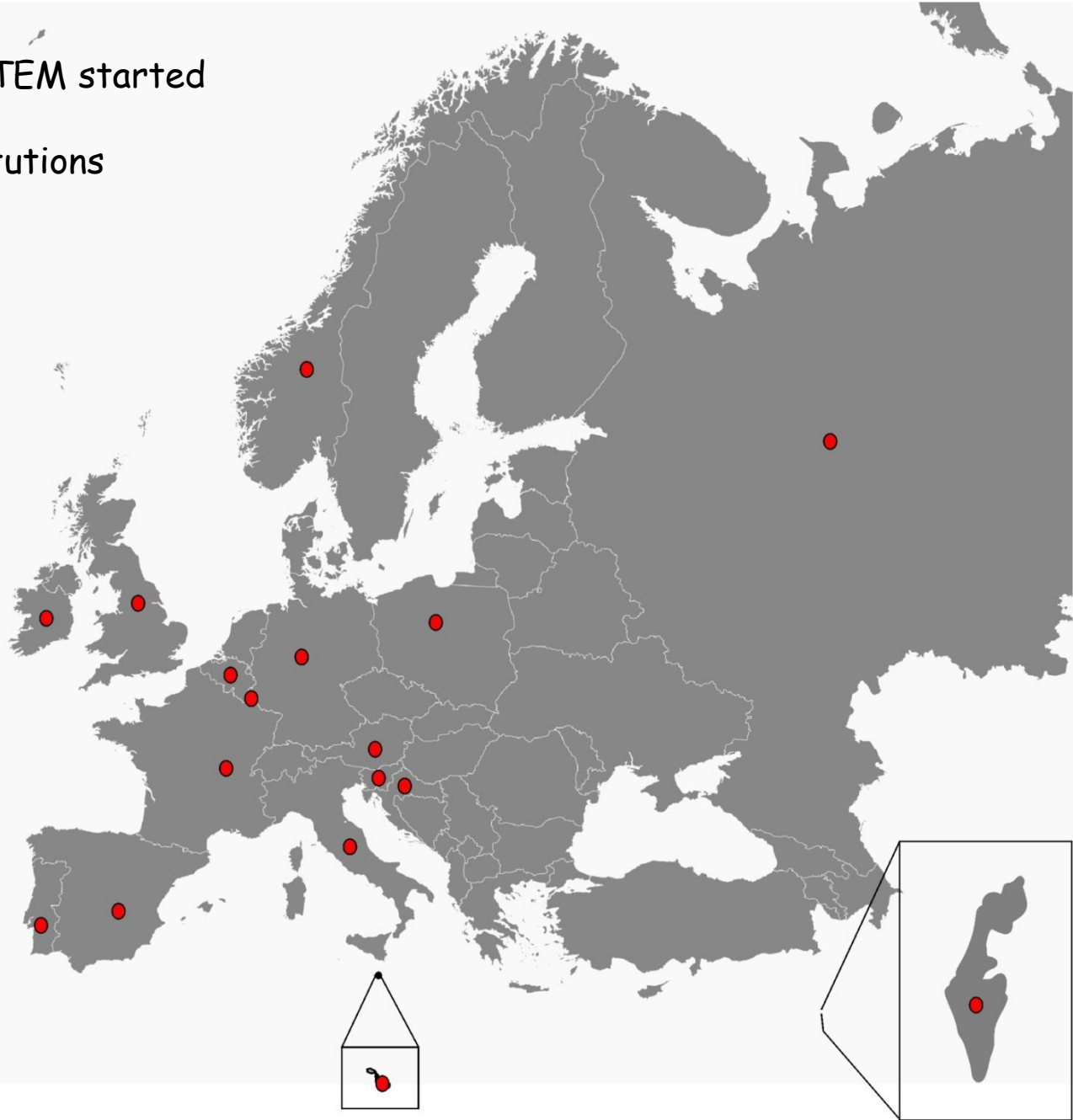
1. University of Innsbruck, Austria
2. Museum National d'Histoire Naturelle, Paris, France
3. Observatoire Océanologique, Banyuls-sur-Mer, France
4. Université de Caen-Normandie, France
5. Hellenic Centre for Marine Research, Greece
6. National University of Ireland, Galway, Ireland
7. National Institute of Oceanography, Haifa, Israel
8. CNR, Palermo, Italy
9. Stazione Zoologica, Napoli, Italy
10. University of Milano, Italy
11. University of Padova, Italy
12. University of Palermo, Italy
13. University of Salento, Lecce, Italy
14. University of Trieste, Italy
15. Institute of Oceanology, Poland
16. Institute of Marine Biology, Vladivostok, Russia
17. Russian Academy of Sciences, St. Petersburg, Russia
18. University of St Andrews, Scotland
19. University of Barcelona, Spain
20. National Institute of Biology, Slovenia



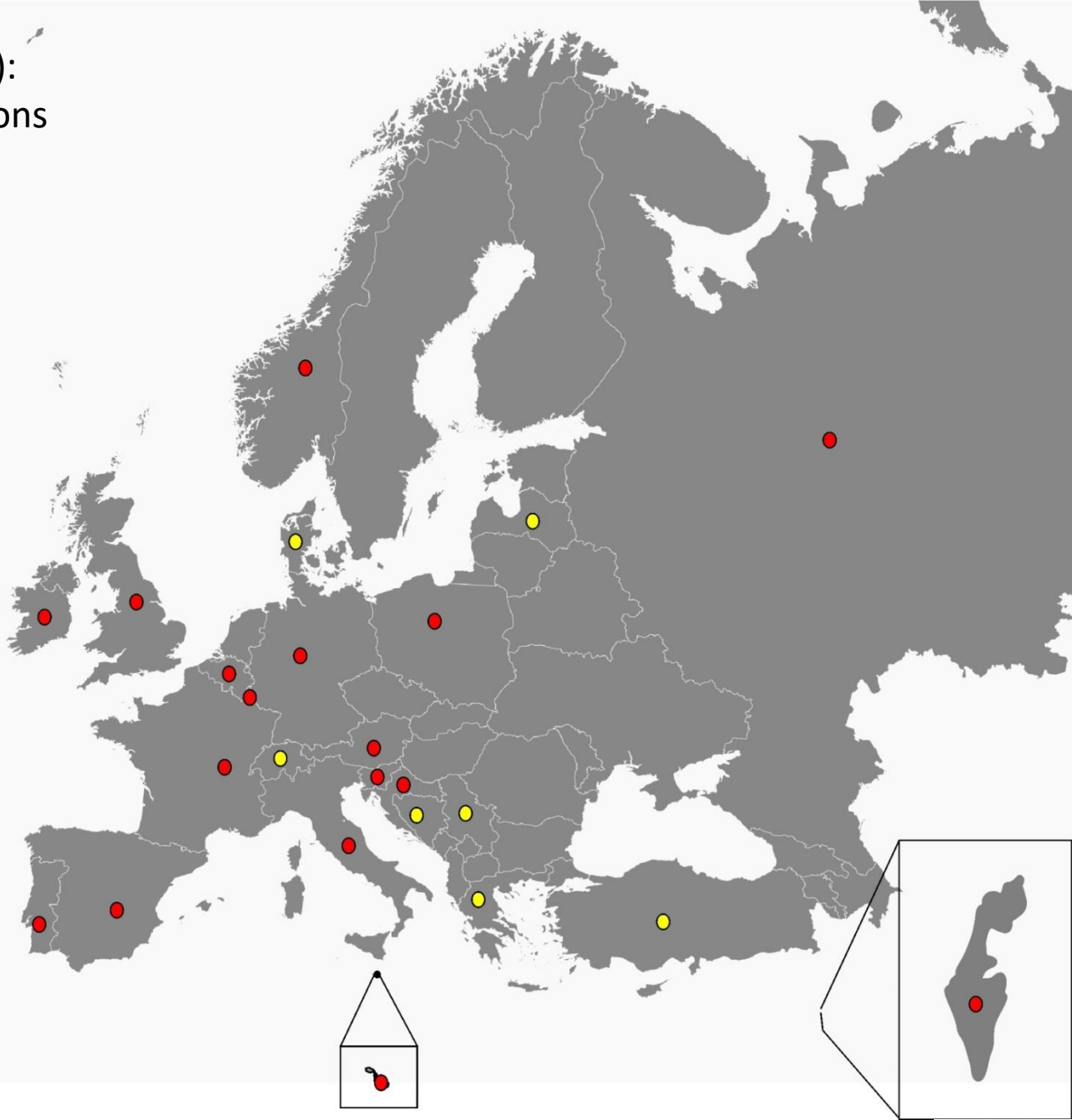
11 countries: 9 COST member countries (2 inclusiveness target country; ITC)
1 COST cooperating state
1 COST near neighbour country (NNC)

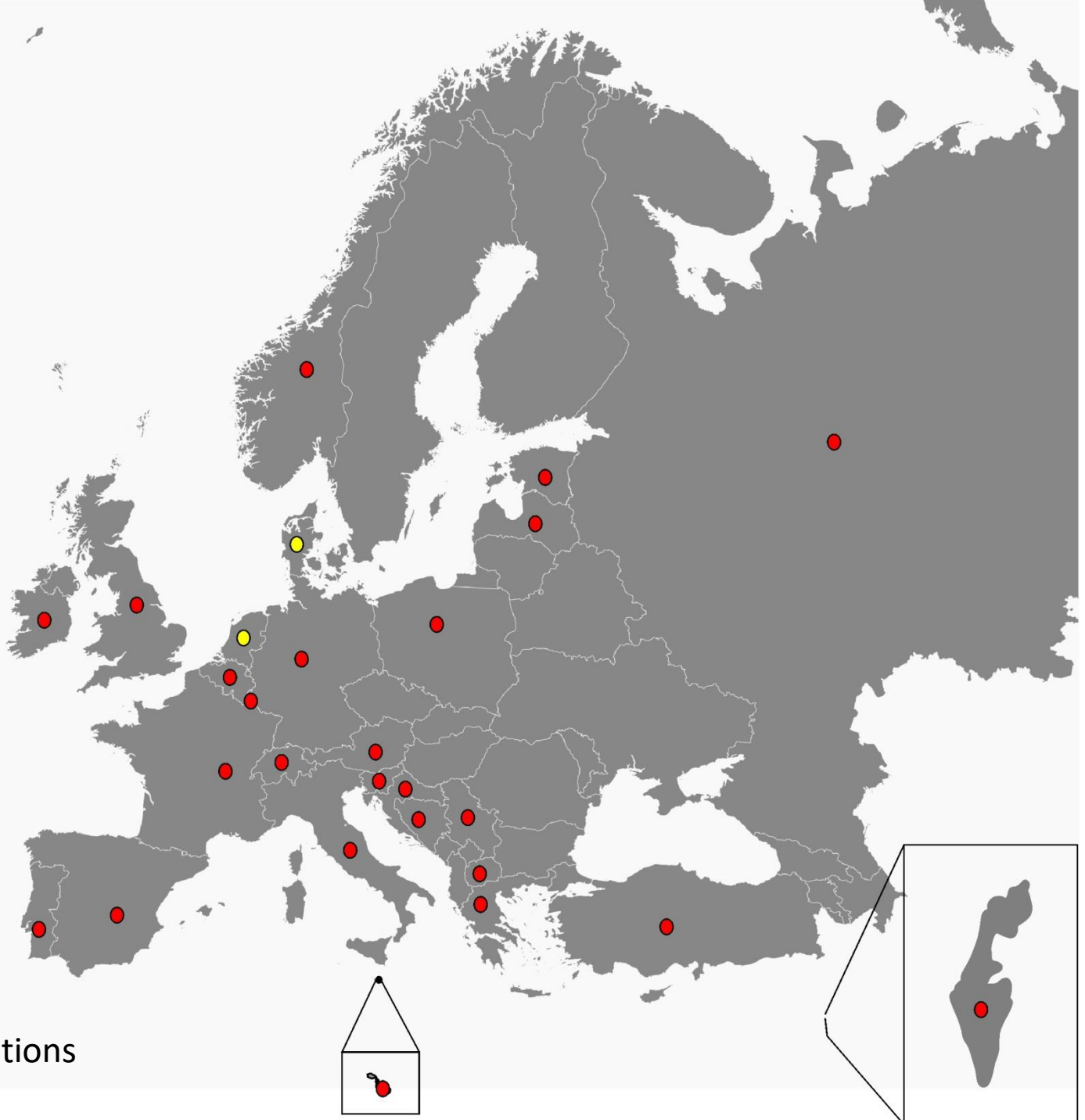
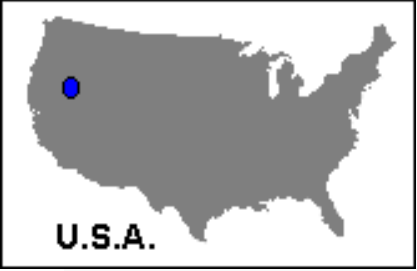
November, 1, 2017
COST Action MARISTEM started

17 countries, 26 institutions

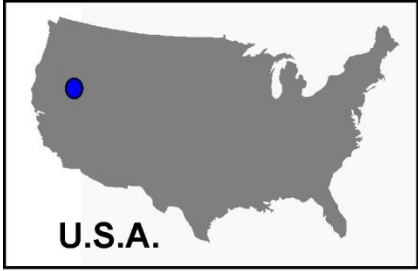


Banyuls (November 2018):
24 countries, 35 institutions

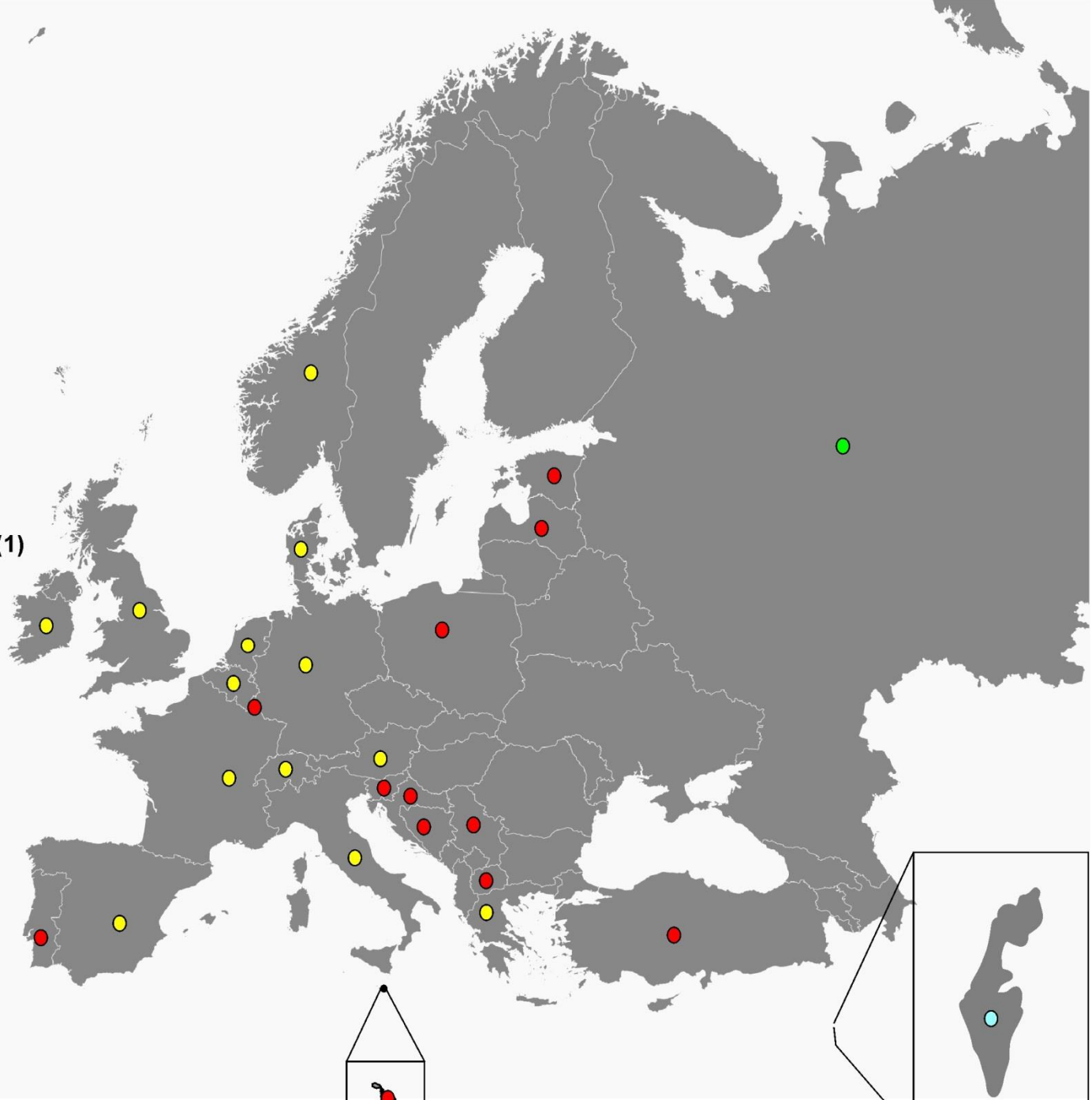




Today:
27 countries, 39 institutions



- COST full members (24)
- ITC (12)
- COST cooperating member (1)
- NNC (1)
- IPC (1)



Challenge

Foster the study of marine/aquatic invertebrate stem cells (MISCs) for innovative ideas relevant to various biomedical disciplines. The Action aims at **consolidating and strengthening the fragmented European MISC community**, and integrating the MISC field with biomedical disciplines

MoU objectives

- Research Coordination 1 **Consolidation of the European community of scientists involved in marine/aquatic invertebrate stem cell research.**
- Research Coordination 2 **Coordination of marine/aquatic invertebrate stem cell research**, sharing of methodologies/databases used in marine/aquatic invertebrate stem cell research in various European countries and updating of scientific and technical guidelines for standardisation of methods, techniques and protocols, to maximise the extent and the quality of the results.
- Research Coordination 3 **Establishing collaborations with industry** for technology transfer and the exploitation of marine/aquatic stem cells in the fields of biomedicine and biotechnology.
- Research Coordination 4 Coordinate collaborative and scientific ties, at international level, with scientists working on marine/aquatic invertebrate stem cells.
- Capacity Building 1 **Strengthening the European Community on marine/aquatic invertebrate stem cells** through data sharing, setting up new collaborations among participants.
- Capacity Building 2 **Promoting interactions of Action members** in order to establish a defined identity and profile in the European field of marine/aquatic invertebrate stem cells and **establish ties with European networks and scientific societies/institutions** in related fields.
- Capacity Building 3 Stimulating contacts and the development of a joint research agenda in order to strengthen future research on MISC.

DELIVERABLES

Deliverable 1	Overview publication on MARISTEM action on marine/aquatic invertebrate stem cells, as 'Research Ideas & Outcomes'.	Month 6
Deliverable 2	Creation of an Open website to offer accessible knowledge to the general public.	Month 6
Deliverable 3	Report listing the reference laboratories, institutions, marine stations for the supplying of marine/aquatic invertebrates.	Month 12
Deliverable 4	Report on identified stockholders interested in marine/aquatic invertebrate stem cells in COST countries.	Month 18
Deliverable 5	Publication (review) on the use of marine/aquatic invertebrate cells and stem cells in ecotoxicology.	Month 24
Deliverable 6	Report on biochemical and biomolecular stem cell markers for aquatic invertebrate organisms.	Month 30
Deliverable 7	Publication on genes, signal transduction pathways, proteins involved in development, senescence, regeneration, prevention/induction of cancer of marine/aquatic invertebrate stem cells.	Month 36
Deliverable 8	Comparative report on -omics data of marine/aquatic invertebrate stem cells.	Month 36
Deliverable 9	Report on functional role of endosymbiosis in MISC.	Month 36
Deliverable 10	Report on bioactive compounds (antimicrobials, anticancer, opsonins, enzymes) in marine/aquatic invertebrates of potential use in human health, pharmaceuticals, nutraceuticals, cosmetics, antifouling paint formulation.	Month 36
Deliverable 11	Report on evolutionary perspectives of regenerative potential across the animal kingdom.	Month 42
Deliverable 12	Protocols for marine/aquatic invertebrate stem cell identification, isolation, enrichment, immortalisation, rearing, storage.	Month 48
Deliverable 13	Report detailing the strategies for “manipulating” marine/aquatic invertebrate cells (knockdown, CRISPR, transgenesis, etc.).	Month 48
Deliverable 14	Scientific book, edited by MARISTEM, focused on marine/aquatic invertebrate stem cells and/or regenerative biology.	Month 48

DISSEMINATION / EXPLOITATION PLAN

Scientific community

- writing collaborative review articles on MISC research in peer-reviewed, high impact (possibly open access) scientific journals;
- editing a scientific book focused on MISC and/or regenerative biology;
- exploiting courses/workshops/meetings to disseminate the main outcomes of the Action among scientists;
- promoting workshops/teaching activities on MISC in the European universities through the initiative of the participants of this COST Action;
- promoting interuniversity agreements aimed to an International PhD program on MISC;
- addressing students, in mentoring activity, to research on MISC for their degree thesis;
- creating new networks, within the MISC community, research proposals/projects resulting from the networking activities that will occur under this Action;
- participating to international conferences on stem cells. This will provide good opportunities to share the results obtained within this COST Action with a wider scientist network.



STEM CELLS OF MARINE/AQUATIC INVERTEBRATES: FROM BASIC RESEARCH TO INNOVATIVE APPLICATIONS

Marine and aquatic invertebrates as a whole show the largest biodiversity on Earth and illustrate a kaleidoscope of stem cell-based phenomena of significant interest for human welfare. While stem cell research represents one of the most dynamic areas in biology and biomedicine, the study of marine and aquatic invertebrate stem cell (MISC) has not been pursued vigorously.

The goal of this action is to foster the study of MISCs by strengthening the European research community, and to integrate it with biomedical disciplines for innovative applications



Working *groups*



Working group 1

Developing protocols for raising marine/aquatic invertebrate stem cells under *in vitro* conditions



Working group 2

"omics" to characterize the MISC phenotypes



Working group 3

Blue technology: MISCs as model systems for the study of fundamental biological processes related to stem cells.



Working group 4

Networking with stakeholders

MARISTEM ACTION ORGANS

Core group (chair, vice-chair, WG leaders)

Management committee: all the MC members (2 for each countries)

Dissemination committee

STSM committee

What we have done

Meetings

- 1st general and WG meeting (Piran, February, 4-6, 2017)
- 2nd general and WG meeting (Banyuls, November, 28-30, 2018)
- 3rd general and WG meeting (Ankara, December, 2-5, 2019)

Workshops

- Use of MISCs in ecotoxicology (Banyuls, November, 27, 2018)
- Adult stem cells (ASC) from marine/aquatic invertebrates (Oberurgl, Marc, 29-31, 2019)
- OMICS approaches to identify and characterise MISCs (Peniche, April, 8-10, 2019)
- Defining ageing in long-living/immortal aquatic animals (Nice, December, 16-17, 2019)
- Aquatic invertebrate models in stem cells research (Lille, March 5-6, 2020)

Training schools

- An integrated approach to marine invertebrate biodiversity: evolutionary and functional adaptations (Tricase, October, 1-6, 2018)
- An integrated approach to marine invertebrate biodiversity: evolutionary and functional adaptations (Chioggia, September, 16-20, 2019)

STSMs

- 9 in the 1st grant period
- 9 in the 2nd grant period
- 2 forecasted in the 3rd grant period

Dissemination

- Ballarin et al., 2018. Maristem - stem cells of marine/aquatic invertebrates: from basic research to innovative applications. *Sustainability* **10**: 526. doi: 10.3390/su10020526;

