

CENTRE
SCIENTIFIQUE
DE MONACO

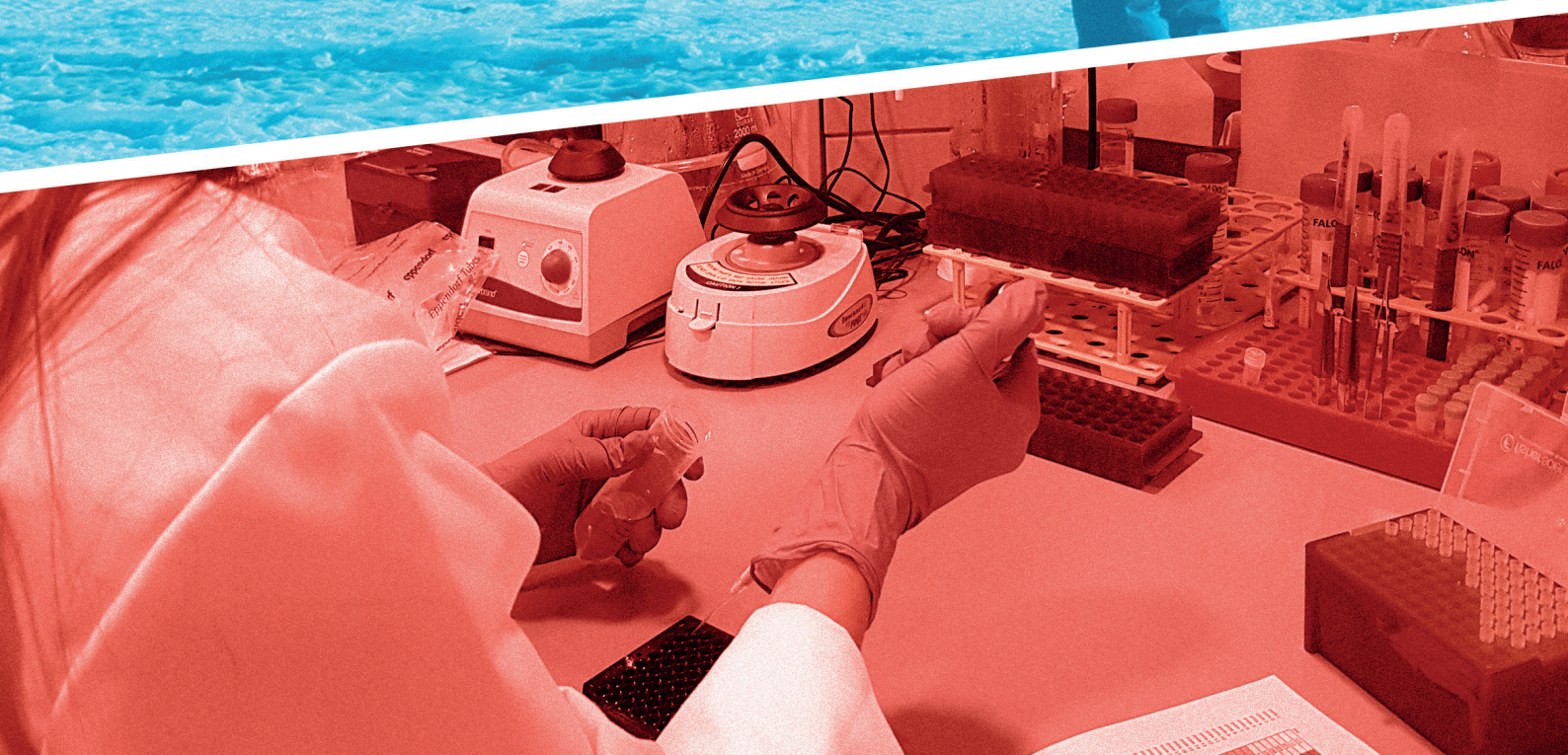


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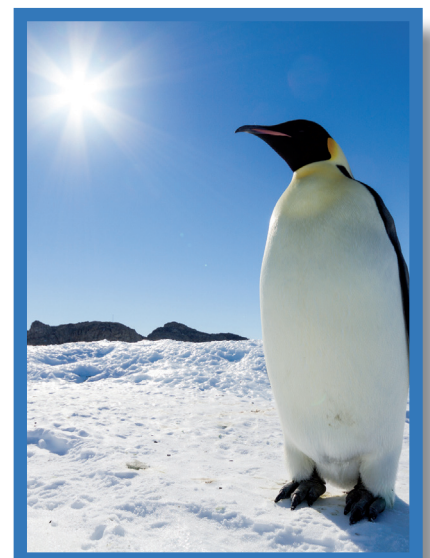
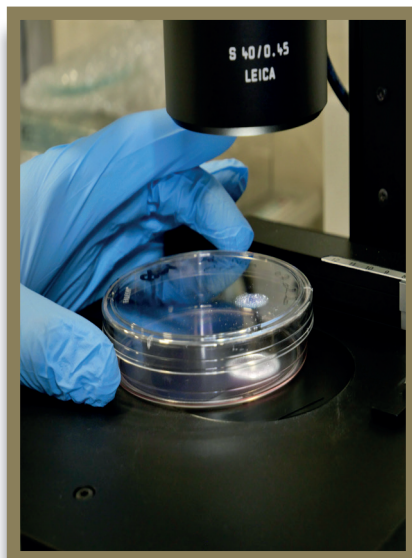
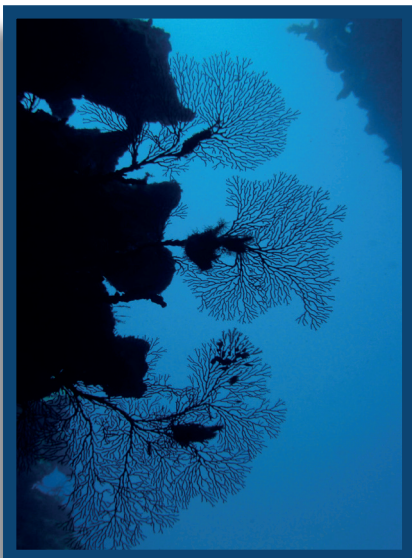
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THE MONACO SCIENTIFIC CENTRE



Founded in 1960 by Prince Rainier III, the Monaco Scientific Centre is now a world-renowned scientific research agency. Under the leadership of its President, the Centre's Scientific Director is responsible for maintaining multidisciplinary excellence in the fields of biology, environmental management and health.

Historically recognised for the quality of its work in the field of Marine Biology, the Monaco Scientific Centre focused its early years of research on the coral ecosystem and coral physiology, both excellent indicators of the state of health of the oceans.

The Marine Biology department now comprises two biology teams and an Environmental Economics team, enabling us to study coral reefs from the gene to socio-ecosystems. The Coral Physiology and Biochemistry team mainly studies biomineralisation in corals, the process that leads to the formation of their skeleton, while the Ecophysiology and Ecology team is mainly interested in the symbiotic relationships that exist between corals and the associated micro-organisms (dinoflagellates, bacteria, viruses) that form a holobiont, as well as the physiological/metabolic response of these holobionts to environmental disturbances.

Under the impetus of HSH Prince Albert II, two new departments have been added to the centre: a Polar Biology research department in 2010 and a department specialising in Medical Biology in 2013.

The Polar Biology department studies the behaviour, physiology and evolutionary capacities of certain species of South Pole penguins facing environmental change. Like coral reefs, sea ice is also an excellent indicator of the state of the planet and the environmental impact it is experiencing.

The Medical Biology department is developing both fundamental and applied research to enable data to be shared rapidly with clinical practice in the Principality: research into cancer, muscular dystrophy and the study of digestive ecosystems. Other areas are integrated into international programmes such as Monacord, a Eurocord project with the International Sickle Cell Observatory, which is studying the future of patients suffering from this disease. The department also has a Human Health Unit, which includes a funding agency for clinical research in the Principality, as well as a think tank focusing on the study of the consequences of environmental change for human health and the link between human health and ocean health in a One Health context.

The CSM is managed by a Board of Directors, whose President is appointed by HSH the Sovereign Prince. The Board is comprised of various representatives of the Prince's Government and qualified personalities. The CSM is managed on a day-to-day basis by a General Secretary and is assisted by its support services, made up of professionals who put their knowledge and expertise to work to achieve the Centre's general objectives by mobilising their skills and talents. The departments bring together different areas that are essential to the Centre's success: administrative and financial management, human resources management, quality, health and safety management, information systems and technical services. Their mission is to ensure the continuity and smooth running of the Scientific Centre, and to manage and support the operational teams in their missions. They represent around 20% of the total workforce. These strategic functions make the Centre more efficient and contribute to its performance.





CORAL PHYSIOLOGY AND BIOCHEMISTRY TEAM

MARINE BIOLOGY



Staff in 2024

- 1 Research Director
- 4 Research Scientists
- 1 Postdoctoral Researcher
- 1 Engineer
- 2 PhD students
- 2 Senior Technicians
- 2 Part-time Technicians

Research theme

The main theme of the Coral Physiology/Biochemistry team is the study of biomineralisation in corals, the process that leads to the formation of their skeleton. Our research aims to answer three major questions:

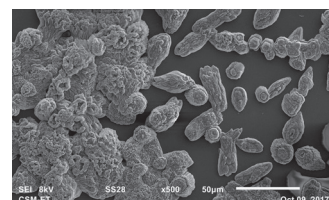
- A physiological question: what are the mechanisms involved in controlling biomineralisation?
- An evolutionary question: is biomineralisation the result of the development of specific tools and/or the use of common ancestral functions?
- An environmental question: how and why do corals respond to global changes, including ocean acidification, and why are some species more resistant than others?

Study models

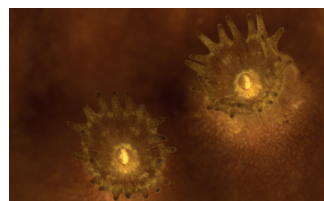
Our main study models are the tropical reef-building coral *Stylophora pistillata* and the Mediterranean red coral *Corallium rubrum*, for which we have been acquiring data for over 30 years. These corals belong respectively to the subclasses Hexacorallia and Octocorallia, two classes that diverged during evolution before the appearance of biomineralisation. Among the Hexacorallia, we are extending our study models to include other symbiotic corals (*Acropora* sp., *Pocillopora* sp.) and non-symbiotic corals (*Tubastrea* sp.). Our comparative studies range from the scale of the organism to the gene, via tissues, cells and molecules.



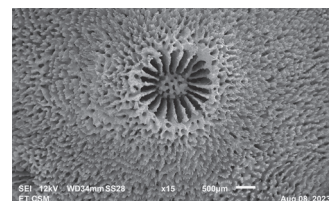
A bleached *Stylophora pistillata* polyp



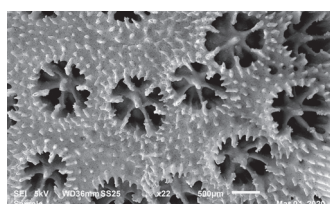
Aragonite crystals deposited by *Stylophora pistillata* on a glass slide



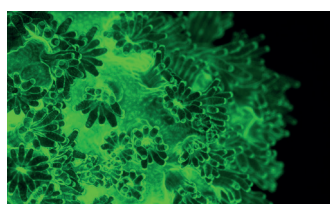
Turbinaria reniformis polyps



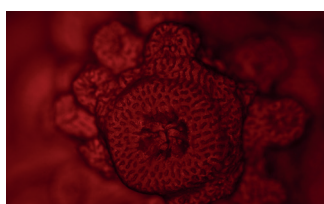
Calyx of *Turbinaria reniformis* observed with SEM



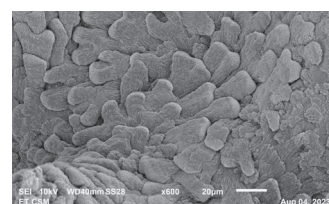
Skeleton of *Stylophora subseriata* (SEM observation)



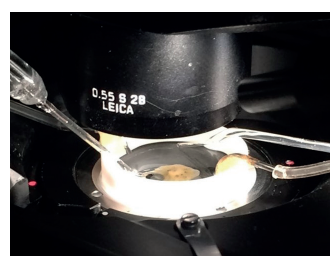
Pocillopora damicornis observed under blue light (natural fluorescence)



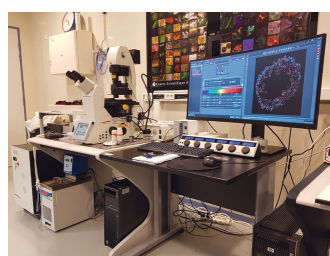
Acropora sp. observed under blue light (red fluorescence of zooxanthellae)



Detail of the skeleton of *Acropora* sp. observed with SEM



In vivo microelectrodes



Confocal microscope

Techniques used

Most of our experiments are carried out in the laboratory under controlled conditions, using a wide range of complementary techniques:

- Physiology: isotope kinetics, pharmacology, *in vivo* microelectrodes.
- Light and electron microscopy for ultrastructural studies.
- *In vivo* cell imaging, including confocal microscopy.
- Biochemistry, molecular biology, bioinformatics and genomics.

Our collaborations

In addition to collaborating with other CSM teams, we work closely with other international groups (France, Italy, Germany, United Kingdom, Saudi Arabia, USA, etc.).





CORAL ECOPHYSIOLOGY AND ECOLOGY TEAM

MARINE BIOLOGY



Staff in 2024

- 1 Research Director
- 4 Research Scientists
- 1 Postdoctoral Researcher
- 1 Engineer
- 2 PhD students
- 2 Senior Technicians
- 2 Part-time Technicians

The Coral Ecophysiology and Ecology team explores the intricate relationships between corals, their symbiotic micro-organisms and the surrounding environment. The team's research is divided into four key areas:

1. **Resilience of corals to environmental change:** this area of research focuses on identifying the factors that enable corals to resist the effects of climate change and pollution, including plastic waste and agricultural runoff. The findings from this work are important for the development of strategies for the conservation and restoration of coral reefs.

2. **Nutrient acquisition and exchange within the coral holobiont:** this area is concerned with the processes by which corals and their associated micro-organisms (bacteria, dinoflagellates, viruses, fungi, etc.) acquire and exchange nutrients. Understanding these symbiotic mechanisms is essential to unraveling how corals maintain their health and promote their growth. The complexity of this research lies in the fact that corals utilize a wide range of inorganic and organic micro- and macro-nutrients.

3. **The diversity of micro-organisms associated with corals:** this research area explores the diversity and key role of micro-organisms that live in symbiosis with corals. These micro-organisms are essential for coral health, resilience and overall ecological function of corals.

4. **Use of proxies to study past and predict future climate:** this area focuses on the use of proxies such as stable isotopes and trace elements to reconstruct past climate conditions and predict future climate trends. These analyses are crucial for a deeper understanding of the long-term impacts of climate variability on coral ecosystems.

To carry out its research, the team uses three different coral models:

1. Tropical corals

These corals require stable and relatively high temperatures, around 25°C, and plenty of light, due to their symbiosis with photosynthetic algae.

2. Temperate corals

Adapted to strong seasonal variations in temperature and light, these corals are highly resilient to environmental fluctuations.

3. Cold-water corals

Inhabiting the ocean depths, these corals live in darkness at very low temperatures, varying between 8°C and 12°C.

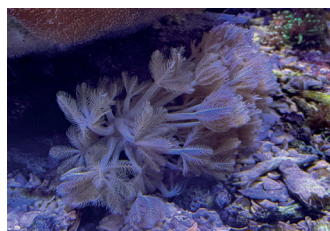


Paramuricea clavata gorgonian

The use of these different models enables the team to study a wide range of environmental conditions and to gain a better understanding of the mechanisms by which corals adapt and become resilient to environmental change.



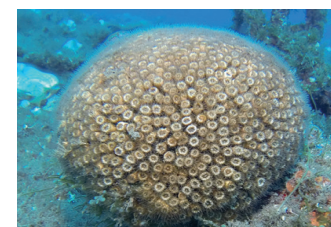
Stylophora pistillata coral



Xenia sp. soft coral



Dendrophyllia ramea deep-water coral



Mediterranean coral *Cladocora caespitosa*



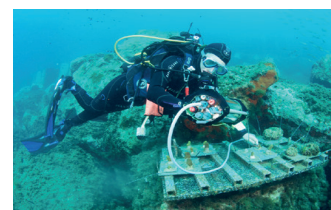
Coral culture room

We carry out experiments both on the field, under natural conditions, and in the laboratory, under controlled conditions. To do this, we use a variety of techniques, including :

- **Isotopes and trace elements:** to trace nutrient fluxes, investigate biogeochemical processes and trace past climate in coral skeletons.
- **PAM fluorimetry:** to measure the photosynthetic efficiency of symbiotic algae.
- **Biochemical and enzymatic analyses:** to evaluate the physiological responses of corals and their interactions with the environment.
- **Microbiology and molecular biology techniques combined with bioinformatics:** to study the microbial communities associated with corals and understand their role in reef health and resilience.

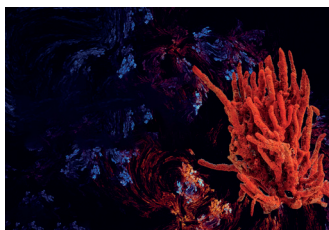
Our collaborations

In addition to collaborating with other CSM teams, we work closely with regional and national entities (International Atomic Energy Agency, Institut de la Mer de Villefranche, Observatoire Océanologique de Banyuls, CEA Paris-Saclay, etc.) and international groups (Italy, Spain, Denmark, United Kingdom, Israel, Saudi Arabia, Australia, United States, Brazil, etc.), strengthening our ability to conduct cutting-edge research and develop innovative solutions for coral reef conservation.



PAM (Pulse Amplitude Modulation) fluorimetry





CSM – CHANEL PRECIOUS CORAL BIOLOGY RESEARCH UNIT

MARINE BIOLOGY

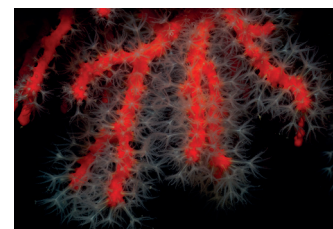


Staff in 2024

- 2 Research Scientists
- 2 Engineers
- 2 PhD students

In September 2019, the Monaco Scientific Centre and CHANEL signed a partnership agreement to set up the Precious Coral Biology Research Unit. This research unit is located at the interface between the Coral Physiology and Biochemistry and Coral Ecophysiology and Ecology teams. Its aim is to carry out basic research to gain fundamental knowledge of the biology of red coral, in order to propose innovative solutions for its conservation and optimise its use in jewellery.

Mediterranean red coral is an emblematic material for jewellery, and has been used in this field since ancient times. Its characteristic red colour distinguishes it from white tropical coral, and contributes to its preciousness and fascination. Long exploited and characterised by a very slow growth, red coral is now a natural treasure of the Mediterranean that must be protected.



Launched in 2019 for a period of 6 years, this scientific programme focuses on three fundamental research areas:

• Investigating coral growth and the control of calcification:

how do genes 'control' the shape of the skeleton?

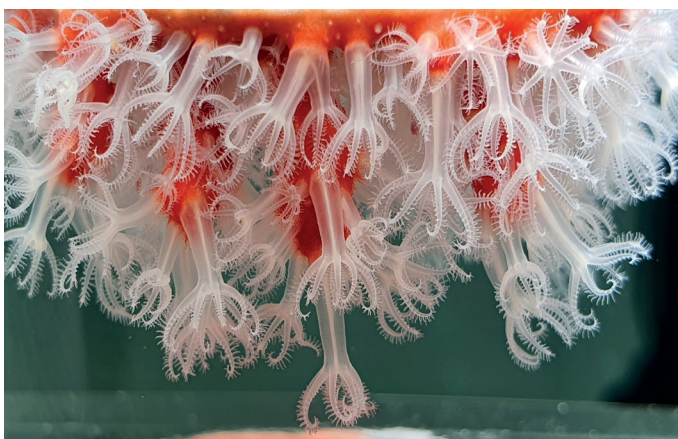
What role do external/internal factors play in controlling coral growth?

• The study of colour control in skeletal structures:

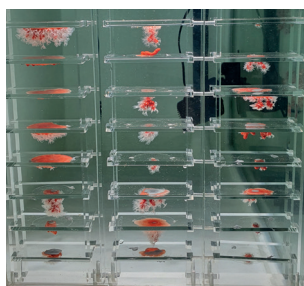
where do the carotenoids that give corals their precious red colour come from?

• The study of associated microorganisms (microbiota):

like all living organisms, red coral hosts a large number of organisms such as bacteria, fungi, protozoa and viruses. This microbiota plays a key role in the physiology of its host: which micro-organisms live in symbiosis with the coral? How do they develop? What role do they play in colour, stress resistance and nutrition? What impact does global warming have on this microbiota?



In addition to the three fundamental research areas, the programme also includes applied coral breeding research. Artificial 1 m³ coral caves have been set up off the coast of Monaco to study the factors that control the reproduction of red corals. Which sex ratio (male/female) produces the most larvae and for what density of adults? Which substrate provides the best breeding ground for the larvae? Which amount food maximises reproduction?



This work has led to the development of *in vitro* and *in situ* red coral culture applications and advances in biotechnology. To raise public awareness about the future of red coral and the importance of research, the Precious Coral Biology Research Unit is also developing various communication tools, such as publications, films, conferences, books and exhibitions.





ENVIRONMENTAL ECONOMICS

MARINE BIOLOGY



Staff in 2024

- 1 Research Scientist
- 1 Postdoctoral Researcher



Research in Environmental Economics focuses on three topics:

Socio-economic impacts of climate change and ocean acidification

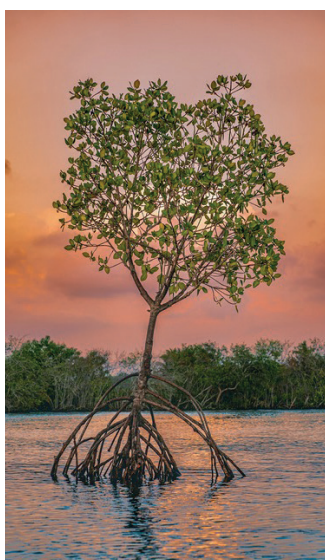
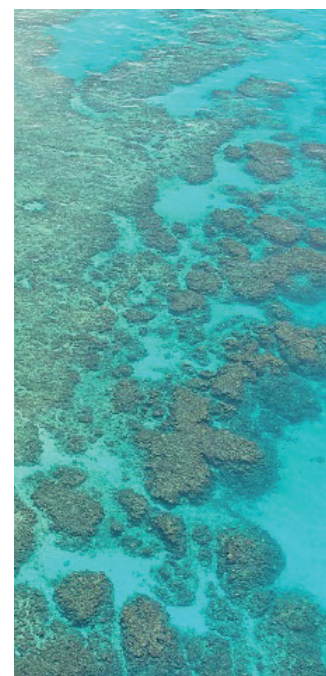
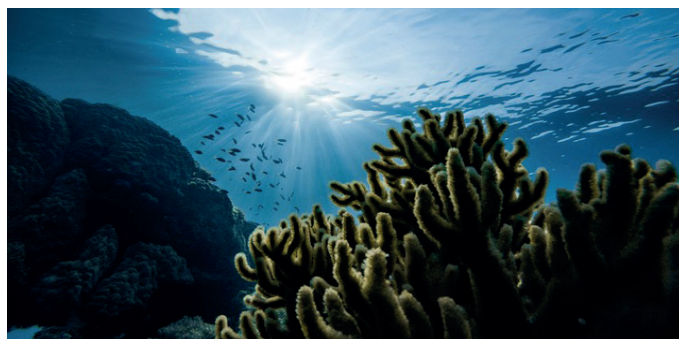
The CSM's environmental economics section focuses on the socio-economic impacts generated by CO₂ emissions, due to climate change or ocean acidification. This is also reflected in the series of multidisciplinary workshops «Bridging the gap between ocean acidification impacts and economic valuation» organised jointly by the CSM and the IAEA under the leadership of Dr Nathalie Hilmi.

Dr Hilmi was lead author of two IPCC reports in the 6th assessment cycle: the Special Report on the Ocean and Cryosphere in a Changing Climate and the 6th Assessment Report in the 2nd Working Group on Impacts, Adaptation and Vulnerability.

In order to connect nature conservation and sustainable finance, this topic includes studies on blue carbon ecosystems.

Assessing and valuing coral reefs

In tropical environments, particular attention has been paid to studying methods for assessing the systemic services provided by coral reefs. Collaboration with experts in the humanities and social sciences has enabled economic, social and cultural aspects to be taken into account in an ecosystemic approach. Several of the United Nations' Sustainable Development Goals (SDGs) are concerned with the good health of coral reefs (food security, the fight against poverty, human health, etc.). In addition, governance issues are crucial when it comes to managing natural capital and conserving environmental resources. There are many players involved in the protection or resilience process. Decisions are taken at different levels, from local to global, by a multitude of stakeholders. Communication is essential if research is to reach all levels of decision-making.



Economic policies and sustainable development

When it comes to environmental policies, the notion of sustainable development is essential because it encompasses three pillars: economic, social and environmental. Environmental policies are a component of broader economic policies, and without an understanding of the macroeconomic and social context in which countries find themselves, it is impossible to make appropriate policy recommendations for a paradigm shift towards a regenerative economy that is positive for nature. In a world marked by local and global fragilities and instabilities of all kinds (political, social, economic and financial), an environmental disaster can have particularly devastating economic and human effects. By taking a macroeconomic approach, the environmental economics section is able to address the major global issues and give them the political and international dimension needed to make them comprehensible to political decision-makers.





Staff in 2024

- 1 Research Director
- 1 Research Engineer
- 1 PhD student

Main study species

Our research focuses on 3 penguin species (king, Adélie and emperor penguins). Two of our field sites are located on the Antarctic continent (Adélie Land and Queen Maud Land), and two other on sub-Antarctic archipelagos (Crozet and Kerguelen Islands).



Robot and radiotracking system used in penguin colonies



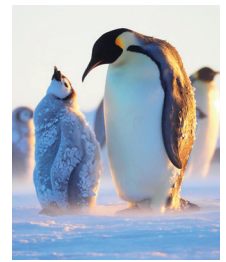
Installation of a detection antenna



King penguin



Adélie penguin



Emperor penguin

Research axes

We are interested in the adaptive capacities of penguins to environmental changes through :

1. The study of individual responses to environmental conditions
2. The projection of population dynamics as a function of climate change scenarios
3. The development of non-intrusive observation methods in natural environments
4. The elaboration of practical tools for implementing biodiversity conservation strategies alongside international organisations (Antarctic Treaty, CCAMLR)

Life Observatories

In partnership with the CNRS and the programmes of the French (IPEV) and German (AWI) Polar Institutes, our department is setting up long-term monitoring of undisturbed penguin populations. Implanting electronic chips (0.8 g) under penguins' skin and deploying detection antennas on the access paths to breeding colonies enables detailed, non-intrusive monitoring of these birds throughout their lives.

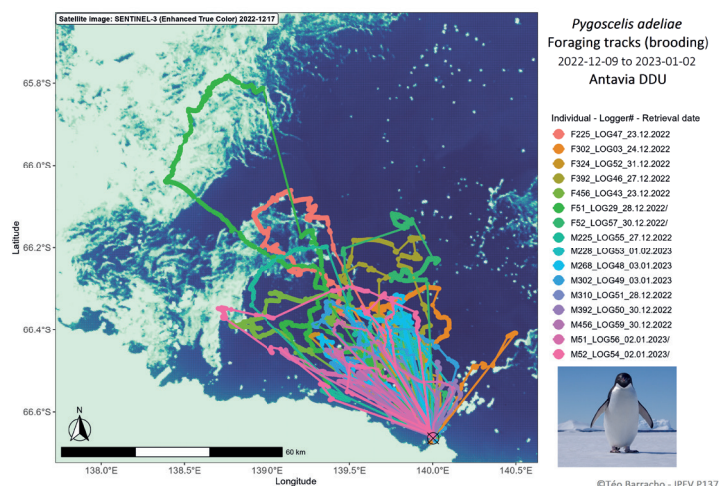
The tagging of more than 30,000 penguins since 1998 and their continuous monitoring have enabled us to build up a database that is unique in the world. In collaboration with a number of international teams (e.g. France, Germany, USA, Finland, Italy, Canada...), this database allows us to measure the impact of climate change on polar ecosystems and doing so, to help define areas that it would be crucial to preserve in the form of Marine Protected Areas.

Technological innovations

We use and develop several innovative technologies to minimise the impact of our observations on our study species, such as automatic identification and weighing systems, or cameras recording the movements and activities of individuals in the colony. By using robots to enter the colony or miniaturised on-board sensors (GPS, Argos, temperature and pressure sensors, accelerometers) to track the penguins' movements, we have revealed unexpected features of their biology and ecology. To manage and analyse the huge amount of data, we are using artificial intelligence and machine-learning techniques.

Our collaborations

We work closely with international groups in France, Germany, USA, Italy, Finland and Canada.





STEM CELLS AND BRAIN TUMOURS TEAM

MEDICAL BIOLOGY



Staff in 2024

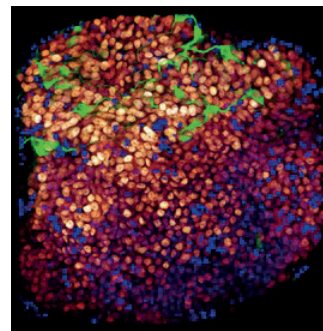
- 3 Research Scientists
- 1 Engineer
- 2 Senior Technicians
- 2 PhD students

Our team is interested in high-grade brain tumours. These tumours are largely composed of cells comparable to embryonic cells of the nervous system. This characteristic is particularly significant in paediatric cancers, which appear to be caused by the abnormal persistence of proliferative embryonic cells. This embryonic/stem cell identity deeply influences their metabolism, and in particular the way in which they use intracellular iron, as well as their sensitivity to conventional treatments such as radiotherapy. However, no current treatment takes these peculiarities into account, and our aim is to better understand them in order to detect new vulnerabilities in cancer cells.

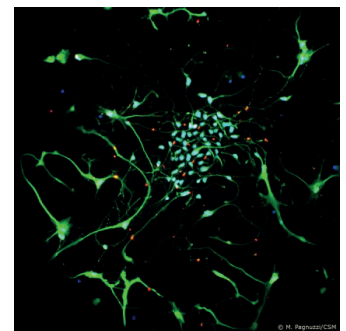
Preclinical approaches: repositioning of molecules and sensitisation to radiotherapy

Paediatric brain cancers are currently systematically treated using methods developed for adult cancers that have been adapted for children, particularly in terms of dose. Our work in this field has given rise to a clinical trial called MEPENDAX, in which 36 children with relapsed brain cancers will receive a targeted therapy currently validated only in adults. The first results of this study in real-life conditions are very promising and fully explain why we continue to explore this new therapeutic path.

We have also shown that techniques for sensitising tumours to radiotherapy and the use of internal vectorised radiotherapy techniques could be effective in treating paediatric brain cancers. These studies, carried out in partnership with the Princess Grace Hospital in Monaco, could also lead to improvements in the treatment of paediatric cancers.



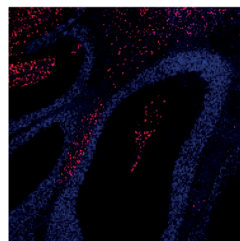
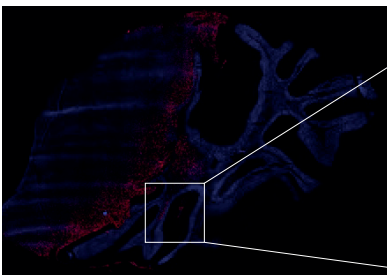
Embryonic tumour generated *in vitro* (embryonic cells in orange and neurons in green)



Neurons (in green) and cancer cells (in blue) cultured *in vitro*

Fundamental research: gaining a better understanding of cancers to discover new treatments.

Our team develops research models that accurately reproduce the mechanisms of tumour induction during embryonic development. We focus on how tumours form by blocking embryonic/stem cells in a proliferative state. These research models include tumour induction in sea anemone embryos and in cerebral organoids, genuine mini-brains manufactured *in vitro*. Using these models enables us to work on the development of specific treatments for these very particular cancers. We are especially using methods to influence the metabolic properties of cancer cells, in order to make them more sensitive to conventional treatments, mainly radiotherapy.



Invasive embryonal tumour: tumour cells (in red) invade normal tissue adjacent to the tumour (in blue)

Our collaborations

In addition to collaborating with other CSM teams, we work with:

- The Princess Grace Hospital (Monaco) and several French hospitals (Nice, Marseille, Grenoble)
- Other research teams (Nice, Grenoble, Uppsala...)
- International consortia and thematic networks (PETRA Network, Reac4Kids, SUNRISE, etc.)





ECOSYSTEMS AND IMMUNITY TEAM

MEDICAL BIOLOGY



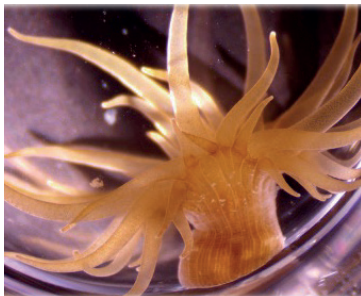
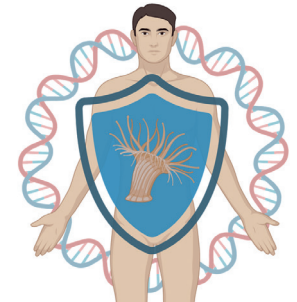
Staff in 2024

- 1 Research Director
- 1 Research Scientist
- 1 Engineer
- 1 PhD student

The expansion of antibiotic resistance represents a real public health problem, prompting research into new strategies to tackle bacterial infections. In addition, climate change is causing oceans' warming, leading not only to their deterioration but also to the emergence of new bacteria that are pathogenic to humans and/or marine animals.

Research theme

Innate immunity, the first defence line in the digestive tract, plays a key role in pathogen recognition. In our team, we work on infection-induced immune responses in human and mouse myeloid cell models. Comparative studies on the responses to infection of a marine invertebrate, the sea anemone *Exaiptasia pallida* (*E. pallida*), are enabling us to draw parallels with humans and discover new defence mechanisms. The hypothesis is that certain aspects of immunity are maintained between humans and cnidarians.

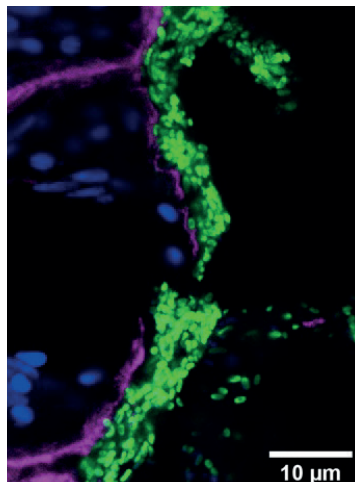


Symbiotic *Exaiptasia pallida* CC7

Immune response in vertebrates: the role of intestinal microflora

The concept of a 'trained' innate immune memory has recently emerged, which states that a first exposure to a non-pathogenic organism can amplify pro-inflammatory responses of the 'protective' type during a second exposure to a pathogen. It is in this context that one of our team's research areas focuses on the effect of the medicinal probiotic yeast *Saccharomyces boulardii* CNCM I-745 (*S. boulardii*) on the innate immune response triggered by infections of the digestive tract.

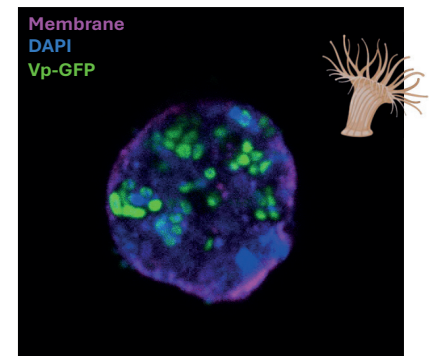
The gastrointestinal microflora or 'microbiota' is an extremely complex ecosystem that coexists in equilibrium with the host and plays a vital role in the proper functioning of the innate digestive immune system. The role of the microbiota as an immunomodulator in various cancers is a promising approach for improving patient survival. It is in this context that we have conducted a study in collaboration with MBRU University in Dubai on the effect of the microbiota on the immune response during chemotherapy treatment in breast cancer patients.



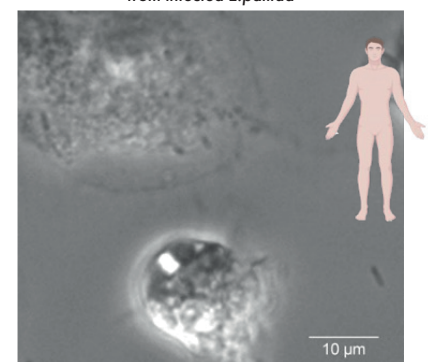
Colocalization between mucus and Vp-GFP on the surface of *E. pallida*

Immune response in an invertebrate model: effect of global warming

Global warming, and consequently the rise in sea surface water temperature, has the effect of: on the one hand, increasing the spread of bacterial species that are pathogenic for humans and marine organisms, and on the other hand, affecting the host of similarities in the immune response conserved between anemones and humans. Using a spectral cytometry approach, we have identified 'amebocyte-like' cells in *E. pallida* infected with *Vibrio parahaemolyticus* (Vp), which phagocytose the bacteria and also display a spectrum similar to human monocyte cells. We have also identified new pathways involving NLRs in the response of *E. pallida* to Vp infection. As part of this work, the team is participating in a research project aimed at identifying pharmacological targets inspired by molluscs and cnidarians for the treatment of inflammatory diseases.



Amebocyte-like phagocytic cells isolated from infected *E. pallida*



Human monocyte that phagocytoses pathogenic bacteria

The aim of our studies is to gain a better understanding of the host/pathogen relationship, which will enable to define new strategies for combating infections in humans. This work should also lead to gain insight on the responses of sea anemones to human pathogens originating from the sea, and to a better understanding of certain coral diseases. The results of these studies will have an impact not only on the environment, but also on human pathologies linked to infections.

Our collaborations

- Management of LIA-ROPSE (International Associate Laboratory - Responses of Organisms and Populations to Environmental Stress)
- Regional collaborations: L. Boyer C3M team, O. Croce IRCAN Côte d'Azur University bioinformatics platform
- International collaborations: MBRU Dubai





BIOTHERAPIES APPLIED TO NEUROMUSCULAR DISABILITIES TEAM

MEDICAL BIOLOGY



Staff in 2024

- 1 Research Director
- 1 Engineer

Since 2013, the creation of the International Associated Laboratory (LIA) Biotherapies Applied to Neuromuscular Disabilities (BAHN) between the Monaco Scientific Centre (CSM) and the University of Versailles Saint-Quentin-en-Yvelines (UVSQ) has enabled the development and validation of various therapeutic strategies based on gene transfer and/or modulation of messenger RNA (mRNA) splicing in the context of genetic diseases affecting the neuromuscular system.

Innovative biotherapies for Duchenne muscular dystrophy (DMD)

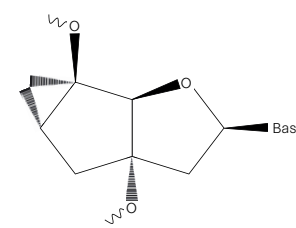
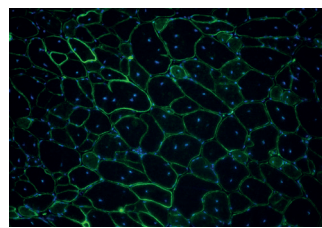
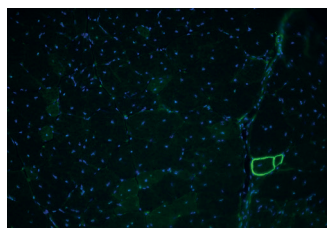
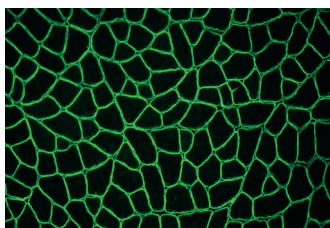
DMD is the most emblematic of neuromuscular diseases of genetic origins. It is caused by mutations in the DMD gene coding for Dystrophin, a protein essential for maintaining the structure and function of muscle fibres. This particularly severe and incapacitating myopathy currently has no satisfactory treatment.

Faced with this curative void, and thanks to the financial support of the Monaco Muscular Dystrophy Association (AMM), various innovative therapeutic strategies have been investigated by LIA-BAHN in recent years to restore expression of the Dystrophin protein and thus limit muscle deterioration. These include modulation of mRNA splicing by exon skipping.



Tricyclo-DNA (tcDNA), a new generation of synthetic nucleotide analogues for splicing modulation approaches

Compared with 2 different ASO (antisense oligonucleotide) chemistries already approved for clinical use by the FDA, tcDNA rapidly demonstrated its superiority for the re-expression of Dystrophin by exon skipping of DMD in different mouse models. With the clinic as its objective, LIA-BAHN then continued to enhance the efficacy of tcDNAs by adding new chemical modifications and/or conjugation, while taking care to limit the risks of toxicity.

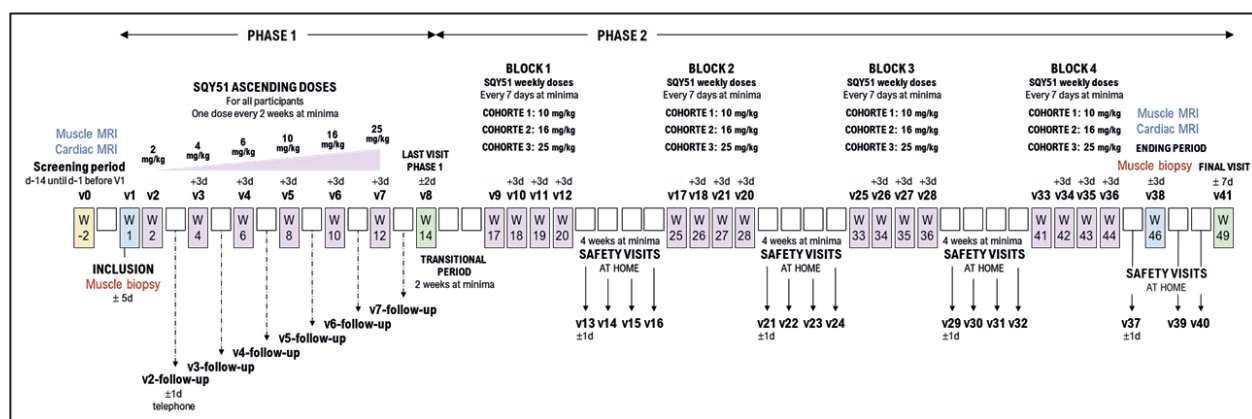


Visualisation of Dystrophin protein expression by immunofluorescence on transverse sections of muscle tissue (triceps) from healthy mice (left), DMD patients (middle) and DMD patients after 8 weeks of tcDNA treatment (right).

Chemical structure of tcDNA

« Bench to bedside »

All of these works have led to the selection of a tcDNA drug candidate called SQY51, which has been tested since June 2023 in the AVANCE1 study conducted by SQY Therapeutics. This phase 1/2a study includes 12 paediatric and adult patients and is designed to assess the safety, pharmacokinetics and pharmacodynamics of SQY51.



Experimental pattern of the phase 1/2a AVANCE 1 clinical trial

Optimising tcDNA efficiency through combined strategies

While new chemical modifications and/or conjugations will undoubtedly further improve the efficacy of tcDNAs, ASO technology in general is still coming up against certain limiting points that will have to be fixed if this approach is to achieve its maximum potential in a therapeutic context. This is why, alongside the validation of new tcDNA designs, LIA-BAHN is currently working on overcoming 4 different obstacles through approaches combining the use of tcDNA with that of therapeutic molecules that have already been validated as positive levers for these pathways.



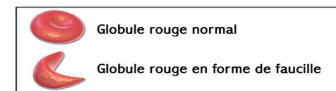


Staff in 2024

- 1 Research Director
- 2 Research Scientists

Sickle cell disease is a severe hereditary haemoglobin disease affecting mainly people from sub-Saharan Africa. However, sickle cell anaemia has spread far beyond its geographical origins, and is now found in many countries due to the worldwide migration of the population.

Sickle cell patients suffer from symptoms such as anaemia, vaso-occlusive crises and cerebrovascular accidents, resulting in poor quality of life and limited life expectancy. The only curative treatments are haematopoietic stem cell transplantation and, more recently, gene therapy.



Monacord has won major international recognition for its scientific studies based in particular on :

- stem cell transplantation from HLA-identical siblings as a definitive curative treatment for sickle cell disease,
- the development of cellular therapies, including transplantation using umbilical cord blood cells from family donors or unrelated non-HLA-identical donors from international umbilical cord blood banks,
- umbilical cord blood banks for sickle cell families,
- disseminating knowledge on this subject, particularly in African countries,
- the study of immunogenetic factors in sickle-cell patients, which has led to a better definition of this heterogeneous disease.

Monacord's future projects will focus on :

- identifying the immunogenetic characteristics of the donor that may influence the outcome of the transplant, in order to optimise the choice of donor,
- analysing the contribution of inter-individual immunogenetic diversity to the development of complications in sickle cell disease, in order to gain a better understanding of the molecular mechanisms involved, with a view to establishing clinical prognostic criteria and ultimately contributing to better management of sickle cell patients,
- the formulation of clinical recommendations for the management of sickle cell disease, including indications for haematopoietic stem cell transplantation and other innovative therapies such as gene therapy,
- developing and coordinating actions to promote the diagnosis and treatment of sickle cell disease in Africa.

Our collaborations

- Eurocord, Saint-Louis Hospital - Paris, France,
- San Raffaele del Monte Tabor Hospital - Milan, Italy
- Sao Paulo University - Brazil
- Sickle Cell Disease Research and Ambulatory Care Centre of Gaston Berger University - Saint-Louis, Senegal
- Kyoto University - Kyoto, Japan
- Fred Hutchinson Cancer Center - Seattle, USA
- Cordons de Vie, Monaco Scientific Association - Monaco

International registries :

- EBMT (European Society for Blood and Marrow Transplantation)
- CIBMTR (Center for International Blood and Marrow Transplant Research)
- Japanese Data Center for Hematopoietic Cell Transplantation - Nagakute, Japan.





HUMAN HEALTH UNIT

MEDICAL BIOLOGY



Staff in 2024

- 1 Delegate Physician
- 1 Project Manager

The CSM's Human Health Unit comprises :

- Activities to evaluate, support and fund institutional clinical research in the Principality of Monaco, set up in 2009 through an annual call for projects;
- «Health & Environment» activities, launched in 2012 and focusing on the impact of environmental change on human health.

Environmental Health theme:

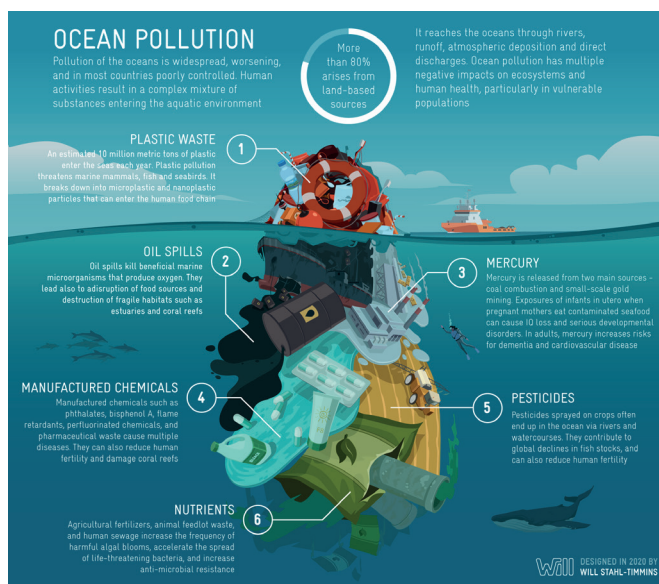
Launched in 2012, this axis consists in teaching, training, publications and scientific and general public communications on the consequences of environmental change for human health, with two main themes:

- The study of the benefits and risks to human health of the oceans, in particular climate change and pollution.
- The environmental and human health impacts of the production, use and disposal of plastics and their chemical additives.

The Human Health Unit has coordinated two synthesis reports on this topic:

In 2020, Human Health and Ocean Pollution (<https://tinyurl.com/HumanHealthOceanPollution>)

In 2023, The Minderoo-Monaco Commission on Plastics and Human Health (<https://tinyurl.com/HumanHealthOceanPollution>)



Ocean pollution, a complex phenomenon (from the report published in 2020)
Credit: Will Stahl Timmins

Clinical Research theme :

Its activities essentially consist in an annual call for proposals aimed at funding clinical research projects taking place in healthcare facilities of the Principality of Monaco, with the following objectives:

- Support and boost Monegasque clinical research to promote medical progress,
- Helping to improve the quality of care by evaluating new diagnostic and therapeutic methods,
- Scientifically validate new medical knowledge,
- Encourage collaboration between health professionals and between healthcare facilities.

Calls for proposals are «open» and cover all areas of clinical research. Projects may concern therapeutic evaluation, assessment of technologies and innovations, prevention, diagnostic strategies, quality of care and risk analysis, in all medical or surgical disciplines. However, priority is given to projects dealing with ageing and/or cancer and, since 2024, to projects involving the CSM's research teams.

The Human Health Unit provides financial, methodological and regulatory support to project leaders, assists teams in implementing their projects and regularly monitors their progress, both scientifically and in terms of the use of the funds allocated. It is the contact point for the healthcare institutions involved (CHPG, CCM, IM2S, CHPM).

Since 2009, this activity has attracted sustained interest from the Monegasque medical community, thanks to the number of clinical research projects funded (in 15 years, the CSM has received 80 projects and funded 50 of them), as well as enabling the implementation of partnerships of excellence in collaborative projects with other institutions (Cancer Centers, University Hospitals) and research organizations (CNRS, INSERM).

Our collaborations

- Global Observatory on Planetary Health of the Boston College, USA
- Minderoo Foundation, Australia
- Woods Hole Oceanographic Institute, USA
- Heidelberg Institute of Global Health, Germany
- Princess Grace Hospital (CHPG), Monaco
- Monaco Institute of Sports Medicine and Surgery (IM2S)
- Monaco Cardiothoracic Centre (CCM)





MOLECULAR BIOLOGY PLATFORM

Staff in 2024

- 1 Project Manager
- 1 Bioinformatician
- 1 Quality Engineer
- 2 Technicians

The Molecular Biology platform was set up during the pandemic. In order to track mutations in the virus, a MiSeq from Illumina (M) and a Gridion from Nanopore (G) have been installed.

Illumina sequencing uses a PCR-based technique in which one fluorescent nucleotide is analysed at a time. On the other hand, Nanopore sequencing uses 'protein nanopores' to detect changes in the flow of a DNA or RNA molecule as it passes through the pore.

Today, the Molecular Biology platform has the human and technical resources to best meet the needs of the centre's researchers. The sequencer used will depend on the various analysis required, for example:

- Genomic analysis of complete bacterial and viral micro-organisms, and antibiotic resistance (M);
- Study of the microbiome in environmental, intestinal and oral samples, etc. (M);
- Targeted sequencing of specific genes or regions (M);
- Long genome sequencing, comparative genomics studies, detection of structural variants, RNA sequencing and transcriptomics (G).

Marine Biology :

- **Corals project**

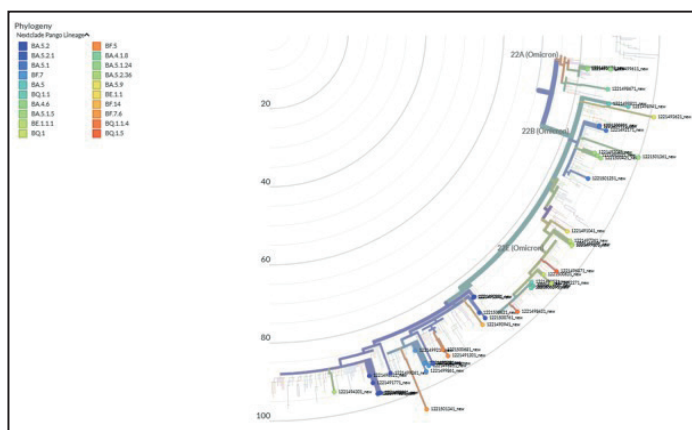
Purpose: To study microbial interactions and their role in coral health.

Method: Sequencing of the 16S region for bacteria and ITS2 for zooxanthellae.

- **Elasmobranchii project**

Purpose: Understanding the migratory movements of large marine vertebrates under threat in the Mediterranean, particularly rays and sharks.

Method: Analysis of DNA samples to confirm species identification and study the relationships between individuals.



Example of COVID sequencing results



Medical Biology :

- **Brain tumours**

Purpose: To analyse gene expression profiles of tumour stem cells.

Method: Identification of biological pathways, of tumorigenesis-regulating genes and study of epigenetic modifications (e.g. DNA methylation).

- **Microbiota and breast cancer**

Collaboration between the Ecosystems and Immunity team (CSM) and the Mohammed Bin Rashid University of Medicine and Health Sciences (Dubai)

Purpose: To analyse the intestinal microbiota and skin flora of the breasts of women with breast cancer.

Method: « Shotgun » sequencing of stool and skin flora samples.

Public health :

- **Search for transmissible agents (arboviroses)**

Purpose: Monitor zoonoses transmitted by mosquitos, for their potential impact on public health.

Method: PCR tests to detect the presence of arboviruses carried by *Aedes albopictus* mosquitos.

- **Microbiological monitoring of waste water**

Purpose: Anticipate the appearance of clusters in humans by identifying pathogenic microbiological species.

Method: Analysis and sequencing of pathogens from sewage samples.



GENERAL SECRETARIAT AND SUPPORT SERVICES

Administrative and financial management and secretariat for the Presidency

It ensures the Centre's development and continuity and provides information to the Board of Directors to facilitate decision-making.

The general secretariat coordinates administrative management and organises the meetings of the Board of Directors. It monitors donations from foundations, associations and/or individuals and grants from the State.

It helps to draw up and monitor budgets. It also acts as secretary to the President and to the Association of Friends of the Monaco Scientific Centre.

- 1 Accounting Officer
- 1 Accounting Secretary
- 1 Administrative Attaché

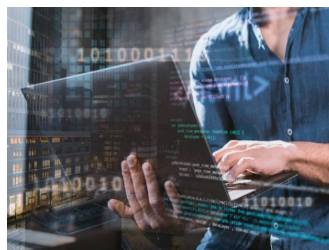
The IT team

The IT team provides all staff with the tools they need to carry out their work, and monitors technological developments to ensure that they are optimised. It also provides technical assistance to users.

Finally, it must protect the CSM's systems, data and networks against any form of digital attack or threat that could paralyse the Centre. The CSM handles valuable and often confidential data. Security aims to preserve the integrity and confidentiality of this data, which is of paramount importance.

The IT and maintenance teams work together with the same objective in mind: to ensure optimal and secure operation of all systems, equipment and facilities.

- 1 IT specialist / Team Manager
- 1 Systems and Networks Administrator
- 1 Run / Helpdesk Technician
- 1 Project Manager



Quality

- 1 Quality Engineer

In order to optimise the CSM's operations and meet the need to harmonise procedures, a Quality mission was created in January 2024. Its aim is to ensure the reliability of data and activities by implementing a methodology based on benchmarks. It ensures the sustainability of know-how, the transfer of skills and the traceability of data. It ensures effective monitoring of information.

The Quality approach concerns all the CSM's activities.

Communication

Media coverage of the CSM is based on a multitude of practices and approaches, such as written and audiovisual press, as well as social networks, all of which serve the common objective of reconnecting the world of science with the general public. The CSM responds to numerous interviews with journalists from various media and drafts press releases that are relayed by the Principality's Communications Department.



Human resources management

- 1 HR Manager
- 1 HR Secretary

Human Resources play a central role at the CSM, as human capital is a key strategic factor in the smooth running of the organisation. Within the CSM, the Human Resources department implements a policy in the service of science, encouraging the fulfilment, development and creativity of its staff. The head of the department is a key contact for all members of staff at the Centre. She is responsible for the expertise and management of the main HR areas and processes: monitoring payroll and the wage bill, maintaining skills, career development, training, social action and workforce control.

The head of department is also the benchmark for labour law.

- 1 HSE Technician
- 1 Service Technician

Building Maintenance Team Health, Safety & Environment

The maintenance team is responsible for a range of activities, including ensuring the safety of the premises, monitoring work to adapt and fit out workstations, environmental risks, etc., all of which are essential to the CSM's research activities.

This team is responsible for the technical operation and maintenance of the facility.

The smooth running and lifespan of equipment, goods and facilities is crucial, as it has an impact on the work carried out at the Centre. The stakes are high at a time when equipment and technologies are becoming increasingly complex and expensive.

The Health, Safety and Environment (HSE) activity plays an essential role. It ensures employee safety by preventing and correcting any malfunctions in equipment that could cause injury to users. It is closely linked to Quality.



ASSOCIATION OF THE FRIENDS OF THE MONACO SCIENTIFIC CENTRE



This non-profit Monegasque association has two main objectives:

- Develop scientific knowledge and culture in the Principality by providing our members with information on the activities of the Monaco Scientific Centre and by organising conferences for the general public, debates and visits to scientific sites,
- Help the Monaco Scientific Centre expand its scientific activities by providing financial support in addition to government grants for research programmes, teaching programmes or study grants for doctoral or post-doctoral students.



"My intention is to give a new impetus to the Scientific Centre. I wish to complement the research activity performed in the field of marine environment with the development of biomedical and polar research programmes. These multidisciplinary scientific programmes will help to pool talent and consolidate a strong and unique reality: that of a Principality of Monaco focused on excellence and the future."

Extract from the speech by HSH Prince Albert II at the inauguration of the CSM's new premises on October 1st, 2013.

To achieve these goals, we need you to develop our actions.

Support our projects and make a donation !





ASSOCIATION DES AMIS
DU CENTRE SCIENTIFIQUE
DE MONACO ♦♦♦



Gouvernement Princier
PRINCIPAUTÉ DE MONACO

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