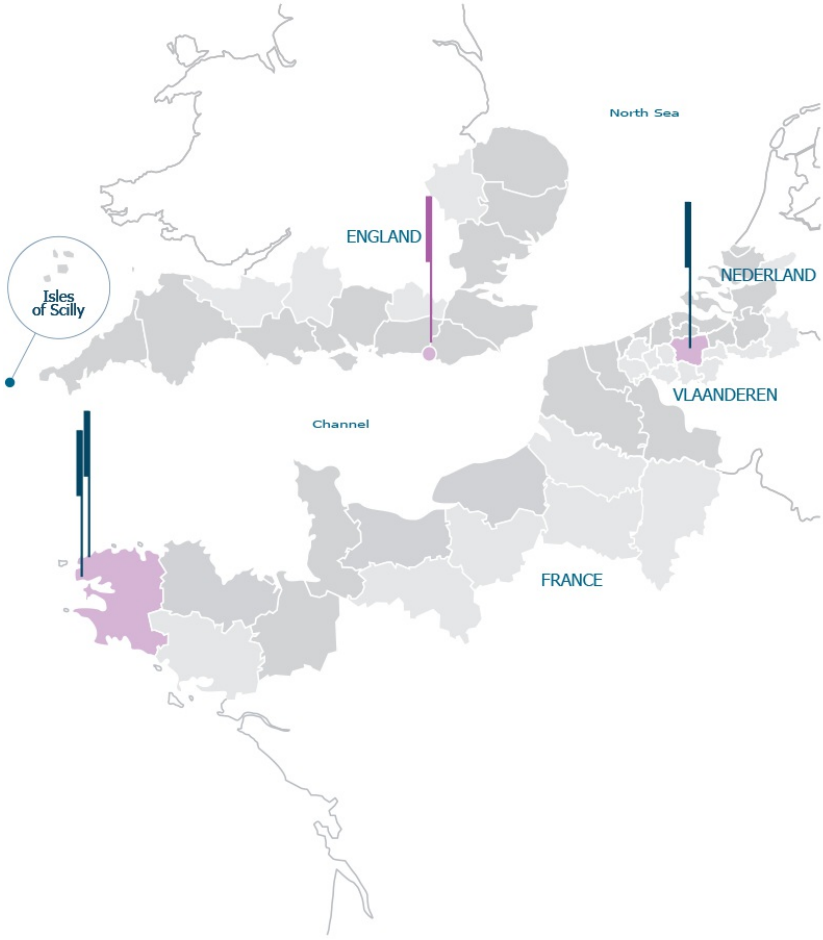
# BioCare

## Biomolecules of the sea for environmental remediation and healthcare

### ■ Project summary




BioCare will build a cross-border network of expertise in identifiying and utilising marine biomolecules, found in the 2 Seas area, for the benefit of its inhabitants' health and the environment in which they live. BioCare will gather together partners from universities, research centres and the Private sector. This network will implement research and development activities and develop new products using our regional marine resources. BioCare's objectives are to identify, isolate and collect marine biomolecules of medical interest or those that can be applicable in pollution reduction processes. The identified applications concern human dermal tissue regeneration (treatment of chronic wounds, reconstruction of burn injuries...) or metal capture-systems applied to biomedicine in the detoxification of blood and tissues. It will also concern the sector of bioremediation of polluted environs such as post-industrial sites and ground-waters. Through the identification of 2 Seas region-specific biomolecules, with a commercial potential, the BioCare project will generate a sustainable approach to this cross-border research, offering an economic imperative to protect the marine environment.

### ■ Activities

**What was the project trying to achieve?**

The aim of the project was to initiate a cross-border network of excellence in the research, development of novel products for health and the environment using our shared regional marine resources. Our objectives were: 1) To identify, isolate and characterise marine biomolecules of medical, pharmaceutical or biomedical interest e.g. antimicrobial

polysaccharides and peptides produced by marine bacteria and macro-algae. 2) To functionalise marine biomolecules by presenting them in forms suitable for their intended use, such as; a) polymer hydrogel dressings that allow controlled release of a drug to its target; b) as porous matrices that support a high flow-rate of wastewater for metal capture; c) as porous scaffolds that have the necessary geometry and surface characteristics to allow the infiltration of cells for human dermal tissue regeneration (e.g. for the treatment of burn injuries). 3) To communicate our findings to instigate further research and development by academia and industry within the region, and to assist with the local realisation of the commercial potential of this emerging field. Stakeholders were not only from academia and industry; we aimed to engage local authorities, healthcare and environmental bodies to raise the profile and valuation of the off-shore environment in the context of emerging scientific applications for community benefit.

### What were the activities implemented?

Activity 1 was concerned with the identification, isolation and evaluation of novel marine antimicrobial agents, including their potential for incorporation as slow-release agents into marine-based biomaterials. Thus, an extensive batch of putative antimicrobials was screened for antimicrobial activity against the pathogenic bacterial species E. coli, S.aureus and P.aeruginosa. In parallel, a range of marine polysaccharides was chemically characterised. The most promising were modified chemically to make them responsive to environmental conditions such that they could release antimicrobials infused within them in a predictable manner. Thin films of biodegradable agarose from seaweed were also evaluated as a means to deliver antimicrobials. Activity 2 was concerned with the development of tissue regeneration matrices for the regeneration and reconstruction of chronic wounds and burn injuries. Fish gelatin and agarose from seaweed was made into highly porous sponge-like cryogel form, including for the first time a dual layer arrangement, consisting of an agarose backbone with a fish gelatin surface. These were evaluated for a capacity to accommodate the infiltration of human dermal cells in vitro with a view to their future adoption for clinical practice. Another novel development was the cross-linking of fish gelatin using a non-toxic method that included the use of UV light. In a further development, certain bacterial polysaccharides were found to have chemical similarity to those found in the extra-cellular matrix of human skin. These were further modified to make them more stable in the human body. A preliminary screen of the reaction of human skin cells to these polymers was undertaken. Activity 3 was concerned with creating metal capture systems using marine bacterial polysaccharides. A range of polysacchardies were screened for their ability to bind metals. These were incorporated into hydrogels and cryogels which also included agarose (or fish gelatin). Metal solutions were passed through these matrices and their ability to remove the metals from solution quantified.

## ■ Results

### What were the key results of the project?

Extracellular polysaccharides (EPS) produced by marine bacteria were modified to enhance their ability to be solubilised and cross-linked – a process that can allow them to be mixed and chemically bonded with other materials, to be more stable when implanted in the body, and to be degraded in a predictable manner. Shellfish and crustaceans were found to contain peptides

that had antimicrobial activity against pathogenic bacteria. Agarose (from seaweed) in the form of a film was found to be a useful means of delivering antimicrobial agents. High surface area, macroporous cryogels made from marine agarose and fish gelatin were tested for their ability to support the growth of human skin cells. A primary structure of agarose coated with a secondary layer of gelatin was found to be amenable to cellular infiltration. In addition, a selection of native and partner-modified EPS was tested (including highly sulphated forms with a similar structure to human glycosaminoglycans found in the extracellular matrix of skin) for an ability to enhance the growth of human skin cells. These could have the potential to speed the regeneration of time-critical dermal wounds (when imbued within a tissue regeneration matrix material) such as those found with burn injuries. One isolate of EPS was identified with favourable activity in terms of potentiating the proliferation of human skin cells. For the first time fish gelatin was cross-linked (stabilised) using a non-toxic UV curing process which could be used to make highly porous cryogels as a basis for a tissue regeneration matrix. The presence of stabilised EPS cross-linked with itself or within a carrier material (such as agarose or fish gelatin), allows production of a high surface area matrix that could pull metals out of solutions that pass across its surface.

**Did all partners and territories benefit from the results?**

The target groups were the healthcare sector, marine industry related to the use of sustainable biological resources, regional research and development institutions, including universities, and the environmental sector. Healthcare was benefited by new knowledge generated and disseminated at our events (and ultimately through scientific publications). The healthcare sector was contacted via our dissemination activities including via direct discussions with the Blonde McIndoe Research Foundation (presented at Sea Life, and Final event) (which is part of the Queen Victoria Hospital, East Grinstead, one of Europe’s leading burns treatment centres). The LP gave a presentation of Biocare Marine at the Royal Institution (the most famous lecture theatre in the world with two Nobel prize winners in attendance and other world leading healthcare experts) as part of the International Conference on Repair, Regeneration and Reconstruction on 26th September 2014. Further, the LP showed the film and presented the project at the Gatwick Diamond, UK, (45, 000 members including Life Sciences, Health Technologies and Medical Devices), Innovations in Healthcare Event, in July 2014. Of note to the healthcare sector were new methods in which to create potential tissue regeneration matrices for the treatment of dermal wounds. Biocare made cryogel forms of these which comprised of fish gelatin cross-linked using a UV light curing process. It also developed dual-layer cryogels consisting of an agarose structural core with fish gelatin providing a biocompatible outer layer - favourable for cell attachment and infiltration (as would be required to form new skin in these materials).

**What were the effects / outcomes for the territories involved?**

All territories will share in the benefits since they all possess the potential for harvest of marine resources for healthcare advancement which in turn can stimulate economic and social benefits. The project initiates what we believe will be a regional critical mass in researching and developing marine resources for healthcare. Each member of the consortium will continue to work in this field and already new ways to collaborate with one another are being investigated. New additional partners with similar or complimentary expertise are being brought in to our network for new projects which will build upon the new knowledge created by Biocare - again

towards achieving critical mass. By working together and pooling our talents there brings a better chance of innovation and the tangible benefits this brings to the area. The common priority area has the key combination of special natural marine resources and the technological expertise in utilising these to make the region a global leader in advancing healthcare provision. Biocare has tried to raise the profile of this potential and the consortium members intend to pursue this goal beyond the project. By doing so, and encouraging others, the population will ultimately benefit.

## ■ Distinctiveness

**What was the real added-value of doing this cross-border project?**

Our French partners worked to produce a unique and extremely interesting stock of marine molecules which the other two partners did not have. The latter were able to bring their own unique expertise to modify and apply these materials towards improved healthcare solutions.

**Have any synergies been developed with other projects or networks?**

Biocare was invited to present at two events held by the Interreg Channel (France-England) "Bridge" project. This project focused on realising the potential of the expertise in green materials held in that region. Biocare members also developed a relationship with the Unesco Brighton Biosphere project with a view to future collaborations.

**What are the key messages , key lessons learned you would like to share?**

## Project Information

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| **Title** | Biomolecules of the sea for environmental remediation and healthcare |
| **Total project budget** | € 2 007 294 |
| **ERDF** | € 1 003 647 |
| **Priority & objective** | Priority 4 a. Promote cross-border cooperation issues and implement joint actions on issues of common interest throughout the whole area, and in particular those with a maritime dimension |
| **Timeframe** | 2011-06-01 - 2014-09-30 |
| **Lead partner** | University of Brighton |
| **Project Coordinator** | Iain John Allan(i.u.allan@brighton.ac.uk) |