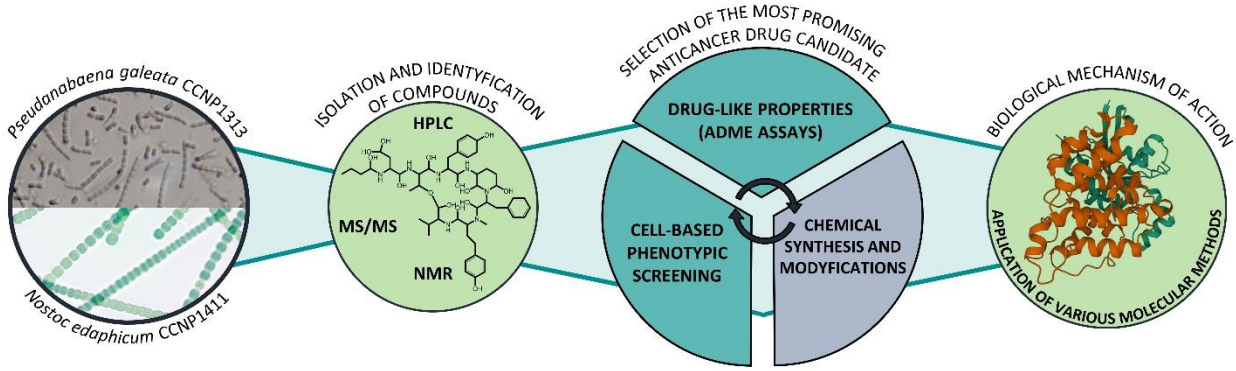
Anticancer drug candidates from *Nostoc edaphicum* CCNP1411 and *Pseudanabaena galeata* CCNP1313 (CYANOCRAB)

Globally, cancer is the second most common, and at the same time the most lethal disease. The applied chemotherapies are frequently associated with multiple side effects and are poorly tolerated in patients. Therefore, efforts are being made to develop new, effective and safer treatment methods. Since ancient times, plants and animals have been a basic source of medicinal substances. Even today, more than 60% of the drugs in clinical use are of natural origin. Among marine organisms, cyanobacteria were found to be one of the richest sources of secondary metabolites with pharmaceutical potential. Four cyanobacteria-derived compounds were approved as anticancer drugs, and many others are in different stages of pre-clinical and clinical trials.

In this project, we will explore the therapeutic value of secondary metabolites produced by the Baltic cyanobacteria. We will focus on two filamentous strains, *Nostoc edaphicum* CCNP1411 and *Pseudanabaena galeata* CCNP1313, which (as we found) produce more than sixty new peptides and peptide-like structures. The *in vitro* anticancer activities of the compounds, or the activity of separated chromatographic fractions containing the compounds, were documented. To make further progress in the studies, we scaled-up the cultures and started collecting higher cyanobacterial biomass.



In this project, the activity of the newly isolated compounds against at least five cell lines (cancer and normal cells) will be assessed. The results of the *in vitro* tests and also the studies into the drug-like properties of the compounds will provide basis for the selection of the most promising anticancer drug candidates. In the new project, we will test the effects of the selected compounds on cytoskeleton function, vacuolar transport, cell cycle, DNA replication, lysosomes and mitochondria function, apoptosis, autophagy, ferroptosis and the changes in transcripts and protein profiles. The obtained results will allow for hypothesis generation on the biological mechanism of action of the tested compounds. The method of chemical synthesis and structure modification of the most promising anticancer agent will be elaborated. Chemical synthesis might be a more effective method for the anticancer compound supply for further studies.

The successful implementation of the project tasks will significantly increase the international recognition of the consortium and place it among the leading research groups working on the pharmaceutical potential of marine resources.