

The Quarterly Newsletter of OMIC-Engine Q1 2019

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Editorial

Synthetic Biology and the Greek National Research Infrastructure OMIC-Engine

By Prof. Kostas Mathiopoulos

Synthetic Biology (SB) is an exciting multidisciplinary research area that bridges biology with engineering. The aim of SB is to reprogram cell systems so that they make products beneficial to humans and society. To do so in an effective and predictable way, it uses principles of engineering and tools of systematic design. The idea of SB was originally based on recombinant DNA technologies developed since the 1970s, i.e. the ability to clone and express DNA fragments in plasmids. However, a huge impetus to SB has been the revolution of "omic" technologies, i.e. the technologies that led to the sequencing of the entire genome of an organism (genomics), to the determination of all RNA transcripts (transcriptomics), to the determination of all the proteins of a cell (proteomics). These biological innovations have been supplemented by engineering approaches so that there is an easier, repeatable and predictable systematic design and construction of new biological systems and cells, thus accelerating the development of new applications in biotechnology. Given these tools and this logic, the synthesis of a biological system is carried out from bottom up by standard parts. Systems that perform integrated tasks (e.g., measurement and control functions) result from the assembly of bioparts (with encoded biological functions) and devices (made from a collection of different bioparts) and encode manufacturer-defined functions (e.g., biosensors, logical gates). Synthetic biology already finds applications in areas such as health, energy, the environment, agriculture and livestock, the development of biomaterials and others.

Recently, the Greek General Secretariat for Research and Technology financed a National Infrastructure in Synthetic Biology in the field of agro-biotechnology, to support the development of SB and the coordination of many important but fragmented efforts in our country. This infrastructure, under the name OMIC-Engine, is coordinated by the Department of Biochemistry and Biotechnology of the University of Thessaly and encompass 8 more partners shown in Figure 1.

Among the OMIC-Engine research directions are:

- Omic analyses towards the understanding of particular product properties
- Biosensors for the effective detection of viruses
- Construction of specially programmed cells with specific functions
- Construction of specially programmed organisms with special functions

- Construction of specially designed synthetic substrates with special functions

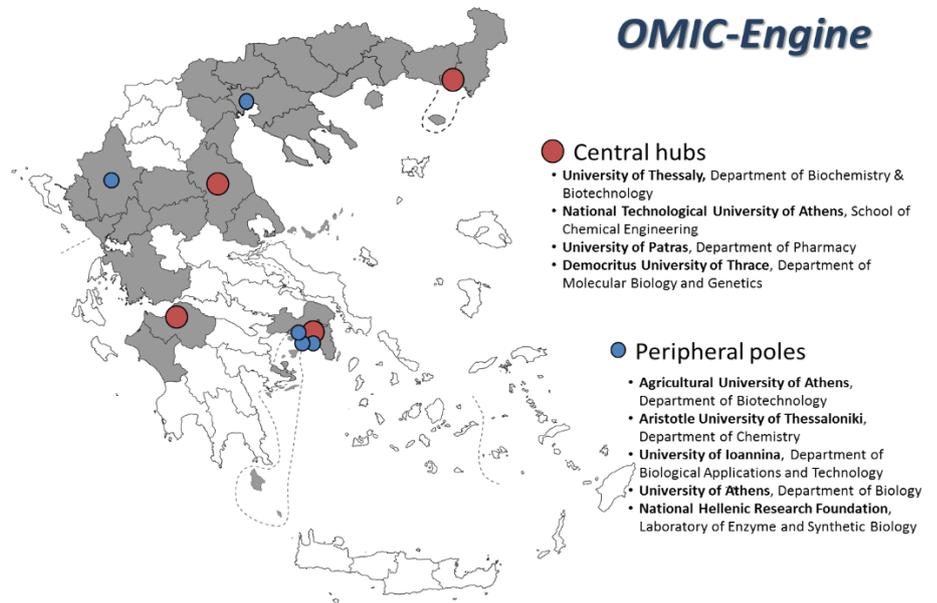


Figure 1. The structure and the partners of the OMIC-Engine RI

OMIC-Engine also provides scientific and technological support to the scientific community and the industry in the exploitation of SB through small research projects selected according to their scientific merit. In this context, OMIC-Engine offers services and scientific support to industry in areas such as seed, crop, animal feed, animal disease diagnosis, food quality control, food additives and others. Furthermore, OMIC-Engine makes a special effort to get in direct communication with the agro-industry sector, to identify the problems in the need of technological solutions and to launch strategic actions to solve them.

Finally, OMIC-Engine supports students' efforts to enter the field of Synthetic Biology, particularly the young iGEM teams. iGEM (International Genetically Engineered Machine) is a competition that arose from the lab work of students of the renowned Massachusetts Institute of Technology in Boston in 2003 and within a few years has developed into an international competition for high school, undergraduate or postgraduate University students from all over the world. This year, 4 Greek teams participate in the competition and different OMIC-Engine members and labs offer support to these teams.

All this is indicative of the quality of scientists and their interest in Synthetic Biology, as well as the infrastructures that are slowly being built in our country.



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Interviewing OMIC-Engine Researchers



Dr Eleni Galliopoulou holds a degree in Molecular Biology & Genetics from Democritus University of Thrace, an MSc in Molecular Genetics and a PhD from the University of Thessaly. She was recruited by OMIC-Engine infrastructure as a post-doctoral researcher in synthetic biology working on the development of a synthetic cellular system to produce constitutively European sea bass (*D. labrax*) digestive enzymes. **Email: galliopoulou@gmail.com**

Question: Eleni tell us a few words about the research project you are working on in OMIC-Engine?

My research is focused on the development of a synthetic cellular system that will constitutively produce a series of European sea bass digestive enzymes, namely two different trypsin isoforms and amylase. The synthetic system will ultimately secrete digestive enzymes in the culture medium in an attempt to reduce the isolation and purification steps of the products to a minimum. This approach enables us to obtain expertise on the design of synthetic secretory systems for the production of the whole range of digestive enzymes in the emblematic Mediterranean species, the European sea bass and the gilthead sea bream that we will target at a following stage.

Question: What do you think will be the impact of OMIC-Engine in your future career?

My participation in OMIC-Engine has broadened my horizons regarding the way I view the future of science. It is quite remarkable how by using basic molecular techniques, we can create a controllable functional system that integrates elements from different organisms to complete the work of many different cell types in an organism. This know-how will offer me alternative ways of analyzing scientific questions in my next research steps. The application of the products of this system is also inspiring as it connects cutting edge research with fish farming, a fast-growing sector and key to food security. Also, OMIC-Engine has been a great vehicle for interaction with other researchers, at different career stages, all work in the same field. Exchange of ideas, problems seeking solutions that synthetic biology can offer and possible applications are major outcomes of this interaction.

Question: What do you think will be the main contribution of OMIC-Engine in Greece?

OMIC-Engine contributes in achieving scientific excellency by recruiting many universities to come in unity in order to produce innovative, cutting edge systems in the light of synthetic biology. The infrastructure aims to create new services and products that upgrade economic fields such as agriculture, aquaculture and pharmaceuticals. An important output of OMIC-Engine is the scientific community that it is weaved through the operation of the infrastructure. Facilitating interaction is a great asset and a major aim of OMIC-Engine; the OMIC-Engine community can be inspiring and act as a multiplier even outside the project boundaries.

Question: Where do you see yourself in 5 years?

As a post-doctoral researcher, my scientific interests focus on molecular genetics in the field of marine aquaculture. Greece is the main country producer of the popular Mediterranean species, sea bass and sea bream. In five years, I would like to see myself as a researcher in synthetic biology and applications that contribute to the Mediterranean fish farming sector. Synthetic biology has a lot to offer in this field and a great deal of resourcing is still required before synthetic biology fully develop its potential in aquaculture.

Meet the OMIC-Engine Research Groups - University of Patras Hub

The **University of Patras** is located in Western Greece and is one of the four main Hubs of the OMIC-Engine Research Infrastructure. It is composed of four Research Laboratories: (a) the Laboratory of NMR and Biomolecular Simulations (Professor. G. Spyroulias) (b) the Laboratory of Molecular Biology and Immunology (Associate Professor. K. Poulas) (c) the Laboratory of Pharmacogenomics and Pharmaceutical Biotechnology (Professor G. Patrinos) (d) the Laboratory of Hygiene (Professor A. Vandarakis).

Professor G. Spyroulias is the research coordinator of the Hub of the University of Patras. His laboratory



belongs to the Department of Pharmacy and participates in OMIC-Engine by providing expertise in metabolomics (Figure 2), which combines biochemical pathways, analytical techniques and a variety of statistical analysis methods to provide useful data in areas such as toxicology, cancer research, nutrition, natural products, pharmaceutical, quality control and in the determination and the examination of products for geographical origin prediction (PDO).

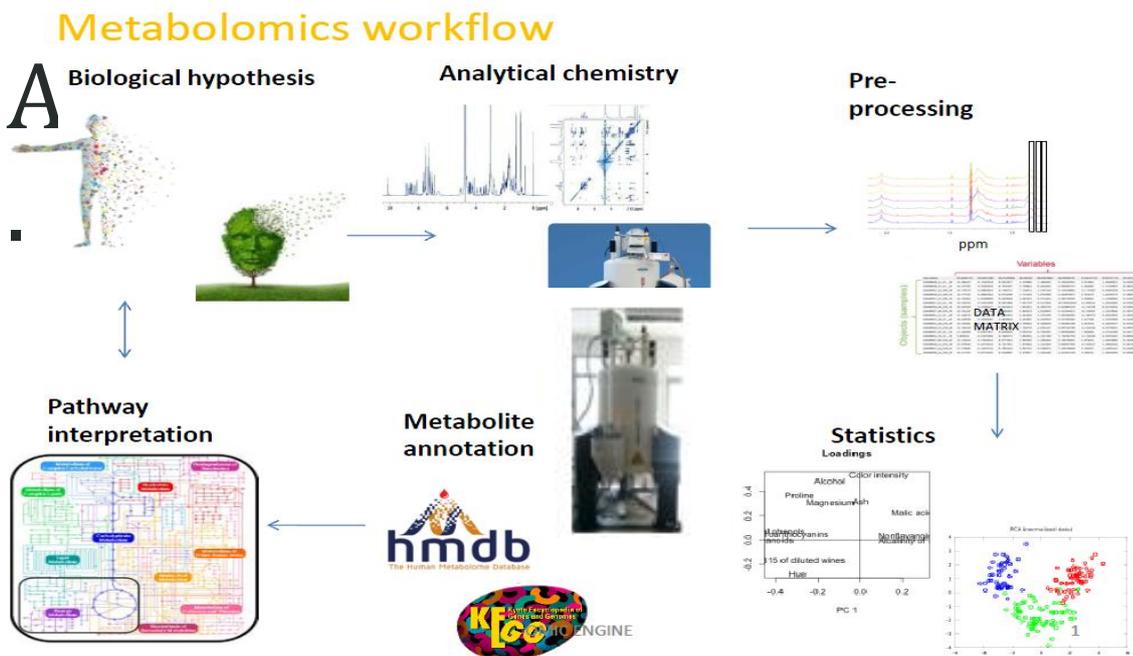


Figure 2. Metabolomics Workflow

Webpage: <http://bionmr.upatras.gr/>

E-mail: G.A.Spyroulias@upatras.gr

Professor G. Patrinos (left) and **Associate Professor K. Poulas** (right) are Principal Investigators of the Hub of the University of Patras. Their Laboratories belong to the Department of Pharmacy. Their expertise lies in heterologous protein expression for proteins prone insufficient expression levels or poor quality (unfolded or insoluble protein, inclusion body formation etc.).



Their available strategies for optimization of protein expression include:

- Assessment of different expression systems
- Test of various tags (NH₂- & COOH- terminal, 6xHis etc).
- Investigation of various conditions, such as temperature, cofactors and expression rates.
- **Protein-coding gene modification**, either **rational** (expression of certain protein domains, substitution of single amino acids and protein domains) or **random** (mutagenesis and screening).

They have developed an optimization protocol of protein-coding gene modification, based on the principles of directed evolution and random mutagenesis (Figure 3).

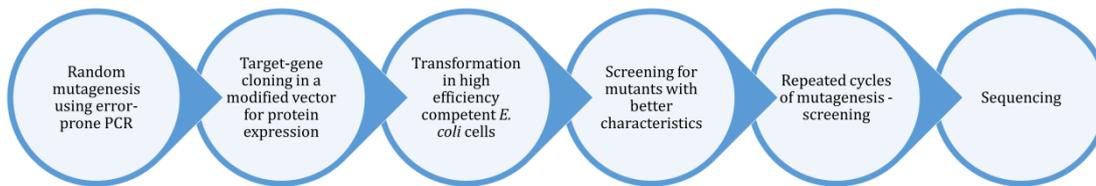
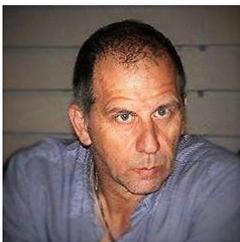


Figure 3

Webpage: <http://www.pharmacy.upatras.gr/index.php/el/personell/meli-dep/-mainmenu-41/81-patrinos-giorgos> , <http://www.pharmacy.upatras.gr/index.php/el/personell/meli-dep/-mainmenu-40/35-poulas-konstantinos>

E-mails: gpatrinos@upatras.gr, kpoulas@upatras.gr



Professor A. Vantarakis is Principal Investigator of the Hub of the University of Patras. His Laboratory belong to the Faculty of Medicine. The expertise of his group lies in molecular diagnostics of pathogens in food and water as well as to risk assessment of food quality. The laboratory is accredited by ESYD for their testing methods. The Center is supported by scientific staff consisted of 4 full-time researchers. The Center serves needs in the following areas:

- Food quality control and risk assessment
- Water Quality control and risk assessment

Website: www.iwaterfood.gr, Contact: info@iwaterfood.gr, avanta@upatras.gr

In the frame of OMIC-Engine, the Hub of the University of Patras has employed one Post-Doc and six PhD students, thus far.

New Projects from the OMIC-Engine Hubs

- **BIOTEC-01-2018-H2020** "*Fostering Synthetic Biology standardization through international collaboration (BioRoboost)*"

A consortium of 27 Universities, Research Centers and private companies (15 European, 4 from USA, China, India, Singapore). Engine participates under the coordination of the University of Thessaly with five labs (University of Thessaly, National Hellenic Research Foundation, University of Athens and National Technological University of Athens). The main objective of BioRoboost is to solve technical difficulties in Synthetic Biology by i) gathering the most relevant stakeholders of all the aspects of standardisation in synthetic biology in Europe; ii) by empirically testing cultural (lab-centric) standardisation practices and by promoting a consensus conceptual and technical redefinition of biological standards; and, finally, iii) by fostering a realistic and flexible toolbox of standard biological parts, including a reduced set of specialised chassis for specific applications as well as a renewed conceptual framework to inform policy makers, scientific and other societal actors.

- **ERC Consolidator Grant** "*A unified drug discovery platform for protein misfolding diseases (ProMiDis)*"
Coordinator Dr Georgios Skretas, National Hellenic Research Foundation, Athens, Greece.

The project will develop engineered bacteria that will function as a stand-alone, high-performance, living drug discovery platform against protein misfolding diseases (PMDs). By applying principles of synthetic biology and molecular evolution, Georgios Skretas will develop a bacterial early drug discovery platform against PMDs which: will be widely applicable to potentially every protein misfolding disease, will target the misfolding of both soluble & membrane proteins, will allow the investigation of chemical libraries with greatly expanded diversities containing billions of different test compounds, will be very simple to use, fast and cheap, will deliver lead therapeutic compounds against four major PMDs: Huntington's disease, light chain amyloidosis, dialysis-related amyloidosis and retinitis pigmentosa. Dr Skretas was awarded this prestigious and high competitive Grant which is expected to start in March 2019

- **PRIMA 2018** "*Innovative Tools to Combat Crop Pests in the Mediterranean (INTOMED)*" Coordinator: Dr Kalliope Papadopoulou, University of Thessaly, Department of Biochemistry and Biotechnology, Lab of Plant and Environmental Biotechnology.

The overall objective of INTOMED is to identify, develop, validate and promote effective and sustainable Integrated Pest Management (IPM) tools by (a) exploiting beneficial interactions between plants and soil-borne microbes and (b) identifying naturally derived key molecules (peptides, metabolites and RNAs) to enhance the resistance of economically important Mediterranean crops against major agricultural arthropod pests and pathogens, as well as by (c) assessing the social acceptability of the proposed tools by end-users. The consortium includes 9 academic and industrial partners from Greece, Spain, France, Morocco, Portugal and Tunisia. INTOMED will generate new knowledge on plant-microbe-pest interactions and develop novel

sustainable tools to prevent outbreaks of economically important pests and pathogens in the Mediterranean. INTOMED was just selected for funded and it is expected to start in the next few months.

- The **Emblematic Action** of the Hellenic Ministry of Education "*The Routes of the Olive Tree*", University of Thessaly.

OMIC-Engine is participating in this Emblematic Action through the Laboratory of Plant and Environmental Biotechnology (Dr K. Papadopoulou & Dr D. Karpouzas) and the Laboratory of Molecular Biology and Genomics (Dr K. Mathiopoulos) which have undertaken the tasks of (a) looking at the composition and the functional role of the microbiome in selected Greek varieties of olive trees (b) working on innovative biotechnology-based methods to control olive fruit fly. This project started in November 2018 and will last for 24 months.

- **SFS-23-2016-H2020**, "*Consumer Driven Production: Integrating Innovative Approaches for Competitive and Sustainable Performance across the Mediterranean Aquaculture Value Chain (PerformFISH)*"
Coordinator: Dr. Katerina Moutou, University of Thessaly. Website: <http://performfish.eu/>

The overall objective of PerformFISH is to increase the competitiveness of the Mediterranean aquaculture sector by tackling biological, technical and operational weaknesses, while addressing social and environmental responsibility and contributing to Blue Growth and Food Security. PerformFISH brings together 28 partners and 13 Linked Third parties from 10 European countries. Five national Fish Farming Associations from Spain, France, Italy, Croatia and Greece, representing 92.8% of sea bream and sea bass EU production, participate in the PerformFISH consortium together with distinguished scientists and pioneering SMEs in aquaculture services and consultancy. PerformFISH integrates an array of approaches, technologies and methodologies to generate outputs for the industry as well as for the consumers, the environment and to serve robust policy implementation; validated tools for genomic selection; robust indicators of larval and juvenile quality for commercial hatcheries, egg and larval programming protocols; husbandry practices to respond to disease challenges and welfare demands by the consumer through efficient diagnostic, prevention and treatment tools, novel pharmacologically active substances, new and improved vaccines and vaccination schemes, and operational welfare indicators; threshold of micro- and macro-nutritional quality for MMFF feeds and sustainable, cost-effective fish feeds of low ecological footprint and high performance linked to genetic optimization and technology for improved feed management; common marketing strategies for European sea bass and sea bream products and new methods of consumer outreach on the target markets; robust benchmarking system based on Key Performance Indicators; revisited Code of Conduct to safeguard quality along the product line and of the final product, establish proper and responsible practices to serve the vision of economic and ecological sustainability that ensure food security and lay the foundation for a respected contract with the consumer and society; knowledge transfer plans for individual knowledge outputs and training courses; exploitation plans and contribution to policy and research initiatives. PerformFISH started in May 2017 and will last for 5 years.

OMIC-Engine Seminars



On Wednesday 13th of February 2019, Dr Konstantinos Vavitsas visited the Department of Biochemistry and Biotechnology in the University of Thessaly and gave a presentation on the use of Cyanobacteria as very promising platform for the production of high-value chemicals combining photosynthetic growth with simple cellular organization. In his presentation, he elaborated on the potential of using plants and cyanobacteria as biosynthetic vessels by linking productivity directly and indirectly on photosynthesis, with a focus on terpenoid production. He also presented the effects of introducing two heterologous biosynthetic pathways in the cyanobacterium *Synechocystis* sp. PCC 6803, using targeted metabolite analysis and computational modeling. Dr Vavitsas will join the group of Dr Hatzinikolaou in the National University of Athens which participates in OMIC-Engine, Email: konvavitsas@gmail.com

Upcoming Seminar in OMIC-Engine

- Date: 6 March 2019, Venue: Department of Biochemistry and Biotechnology, University of Thessaly, Larissa, Speaker: Associate Prof. Kriton Kalantidis, University of Crete, Department of Biology – FORTH, Institute of Molecular Biology and Biotechnology



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