ARISTOTLE UNIVERSITY OF THESSALONIKI

“iGEM Thessaloniki through the years”



by iGEM Thessaloniki

Team’s message (iGEM Thessaloniki 2026)

Throughout our journey toward the iGEM Grand Jamboree 2026, we often found ourselves looking back: at the projects that came before us, at the students who built them, and at the history that iGEM Thessaloniki has created throughout the years. In moments of difficulty, uncertainty, and countless brainstorming sessions, we were reminded that the spark of curiosity, creativity, and persistence that drives us today is the same spirit that has shaped every iGEM Thessaloniki team before us.

This book was born from a simple yet meaningful idea shared by our members: to honor the teams who paved the way for us while also creating a resource to introduce new audiences to the world of synthetic biology. Each project presented in these pages is more than a scientific idea. It is a story of students identifying a problem, imagining a biological solution, learning through challenges, and working together to turn an ambitious concept into something real.

Through this book, we hope to make synthetic biology more approachable, especially for students, educators, future iGEMers, and anyone encountering the field for the first time. By presenting the projects of iGEM Thessaloniki as real case studies, we aim to show how science can begin with curiosity, grow through collaboration, and become a tool for addressing real-world challenges.

To every former member of iGEM Thessaloniki, this book is our way of saying thank you. Thank you for building the foundations on which we now stand, for inspiring us through your ideas and dedication, and for leaving behind a legacy that continues to guide new generations of students.

And to every reader who opens this book, we hope these pages remind you that science is not only about experiments, results, and medals. It is also about people coming together, asking bold questions, learning from one another, and believing that even the craziest ideas can come to life through teamwork, persistence, and imagination.

We invite you to explore this journey through iGEM Thessaloniki's projects so far. More than a collection of summaries, this book is a celebration of our past, a learning tool for the present, and an invitation to imagine the future of synthetic biology.

Introduction

What is the iGEM Competition?

iGEM (International Genetically Engineered Machine competition)is the world's largest synthetic biology competition for students.

It began at MIT in 2003 as an independent study course, grew into a summer competition with a handful of teams in 2004, and opened to international participants in 2005. It is now run by the iGEM Foundation, an independent non-profit. Today, over 400 student teams from more than 50 countries take part each year, converging on the Grand Jamboree in Paris,an event that gathers over 5,000 researchers, industry representatives, startup founders, investors and policymakers, and where projects are grouped into thematic Villages.

The premise is simple and unusually demanding: a team of students identifies a real problem, designs a biological system to address it, builds and tests that system over the course of roughly a year, and presents the result to an international panel of judges.

For students, iGEM is often the first time they design a research project rather than execute one, the first time they raise their own funding, manage their own timeline, and answer for their own choices.

That experience is the real prize!

SubTeams

An iGEM project is far too large for any one person, or any one discipline, to carry. Our team is therefore organised into subteams, each responsible for a different dimension of the project, and each dependent on the others.

Wet Lab: Designs and runs the experiments. Cloning, expression, assays, troubleshooting, and the long hours that turn a design on paper into data.

Dry Lab: Builds the computational side of the project: mathematical models that predict how the system will behave, bioinformatic analyses, and any software or hardware the project requires. Modelling guides the Wet Lab as much as it follows it.

Human Practices: Takes the project out into the world. Meets with experts, clinicians, patients, industry and regulators, and brings their feedback back into the design. Responsible for ensuring the project is safe, useful and wanted.

Fundraising: Secures the sponsorships, grants and partnerships that make everything else possible, from reagents to registration fees to the trip to Paris.

Wiki: Builds and maintains the team wiki, the complete public documentation of the year's work and the primary artefact the judges assess. Everything every other subteam does eventually has to live here - which makes the Wiki team the last one standing before the deadline.
Graphics: Creates the team's visual identity: logo, project artwork, figures, posters, presentation design and everything that gives the year a recognisable face. Turns complex science into images people actually understand.

Social Media: Runs the team's public voice online. Builds the audience that our outreach, fundraising and collaborations all depend on, documents the season as it happens, and keeps the team visible to sponsors, other iGEM teams and the wider community.

Special Prizes: Beyond the medal criteria, iGEM awards a series of Special Prizes for excellence in specific areas, such as education, software, hardware, entrepreneurship, sustainable development, inclusivity and more. Each carries its own requirements and deliverables. This subteam identifies which prizes fit the year's project, coordinates the work across the other subteams, and makes sure nothing that deserves recognition goes undocumented.

“iGEM 2017„

IGEM Team: Greece 2017

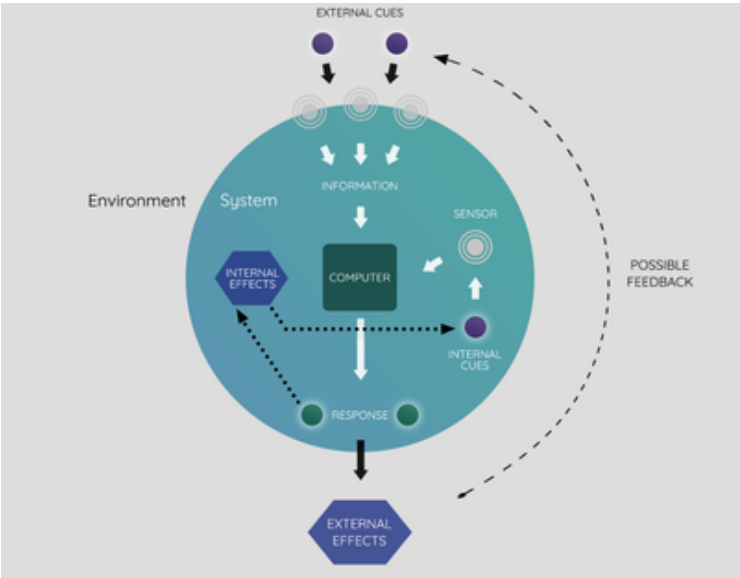
Project Name: pANDORRA

Team Members: Eugene Ballhisa, Thomas Nikopoulos, Asteris Arabatzis, Charis Giannitsis, Constantine Akritidis, Konstantinos Samaras-Tsakiris, Elissavet Sandaltzopoulou, Angeliki Papadimitriou, Thanasis Theocharis, Nausica Papaioannou, Charis Komodromos*

Advisors: Eleni Gounari, John S. Aristeidakis, Angeliki Malamidou, Christina Salpingidou, Handakas Vagelis, Nikolaos Bekas

Principal Investigators: George Koliakos, George Mosialos, Dimitra Dafou, Dimosthenis Sarigiannis

Instructors: Spyros Petrakis, Paul Hadweh, Fotis E. Psomopoulos, Elisavet Lioulia, Athanasios Sachinidis

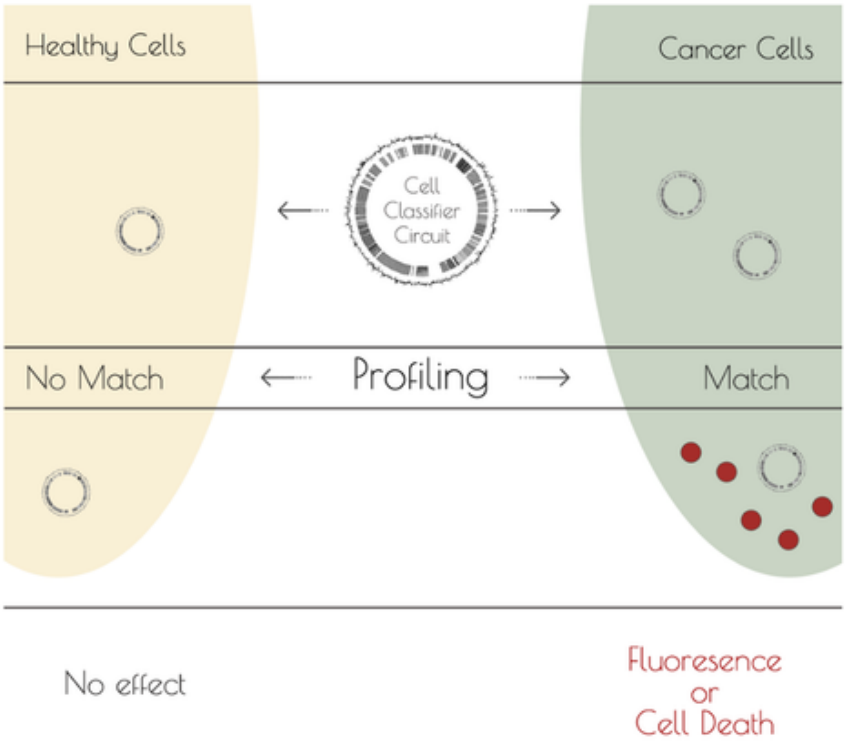


The Problem: Traditional cancer treatments often function as biological sledgehammers. Because they cannot reliably distinguish between a malignant cancer cell and a perfectly healthy one, they kill both indiscriminately. This leads to severe toxicity, painful side effects, and compromised patient health. In the case of colorectal cancer, the medical field desperately needs smart, localized therapeutics. The ideal

solution is a treatment that can accurately read the molecular signature of a cell, verify whether it is genuinely cancerous, and only pull the trigger on a therapeutic payload when it is completely certain it has found a target.

Why: Colorectomy and systemic therapies represent significant physical and psychological trauma for patients. Cancer cells bypass normal cellular regulations because their internal programming is corrupted. However, this corruption leaves behind distinct clues, for instance highly specific profiles of microRNAs (miRNAs) that are radically different from those found in healthy tissue. By reading these biological signatures, it becomes possible to build a personalized defense system. Unfortunately, building these multi-layered genetic circuits has historically faced massive technical bottlenecks. The design rules are incredibly complex, and biological parts are rarely standardized or easy to swap out. Furthermore, introducing genetically engineered systems into the human body triggers intense public concern and valid biosafety questions. To shift cancer therapy away from invasive surgeries and toxic drugs, two major hurdles stand in the way: the medical and scientific community requires an open-source, easily accessible toolkit to construct these smart biological systems, alongside an unshakeable, bulletproof biosafety protocol to make them acceptable to the public.

How: The team created pANDORRA (Programmable AND/OR RNAi-based Antitumer Apparatus), a biological computer designed to accurately classify cell types and selectively destroy colorectal cancer cells while leaving healthy tissue completely untouched. The project tackled this ambitious goal through an integrated approach combining biological computing and modular hardware parts.



The Biological Computer (RNAi-Classifiers). The core of pANDORRA relies on multi-layered RNA interference (RNAi) logic circuits. These circuits operate like cellular software. They sample the internal miRNA environment of a cell. By setting specific

"AND" and "OR" logical gates, the circuit measures the levels of internal miRNAs. If the specific combination matches a predefined colorectal cancer profile, the circuit evaluates the cell as "Malignant." Once the biological computer identifies a cancer cell, it triggers a response. To address health and environmental safety risks raised during expert consultations, the team incorporated Apoptin strictly in cancer cells. They wrapped the entire architecture in a multi-star serial fail-safe system to guarantee the circuit would never fire by mistake in healthy tissue.

To democratize this design and bypass existing technical complexities, the team standardized their biological parts. They built pANDORRA into a universal, open-source toolkit complete with basic parts deposited in the iGEM Registry. This enables future researchers to easily swap out target sequences and build custom classifiers for other types of cancer.

Jamboree Results: Team Greece 2017 was awarded a Gold Medal and earned a prestigious nomination for the Best Therapeutics Project Award at Jamboree in Boston.

“iGEM 2018„

Project Name: GALENE



Team members:

- Yvoni Giannoula
- Yvonni Xesfiggi
- Pantelis Kiriakidis
- Panagiotis Karatakis
- Alexandros Giannopoulos Dimitriou
- Grigorios Kyrpizidis
- Ioannis Alexopoulos

Principal Investigators (PIs):

- Professor George Mosialos
- Associate Professor Ioannis Vizirianakis

Advisors:

- Androulla Miliotou
- Stefanos Tsiftsoglou
- Maxim Gavriilidis
- Ilias Dimitriadis

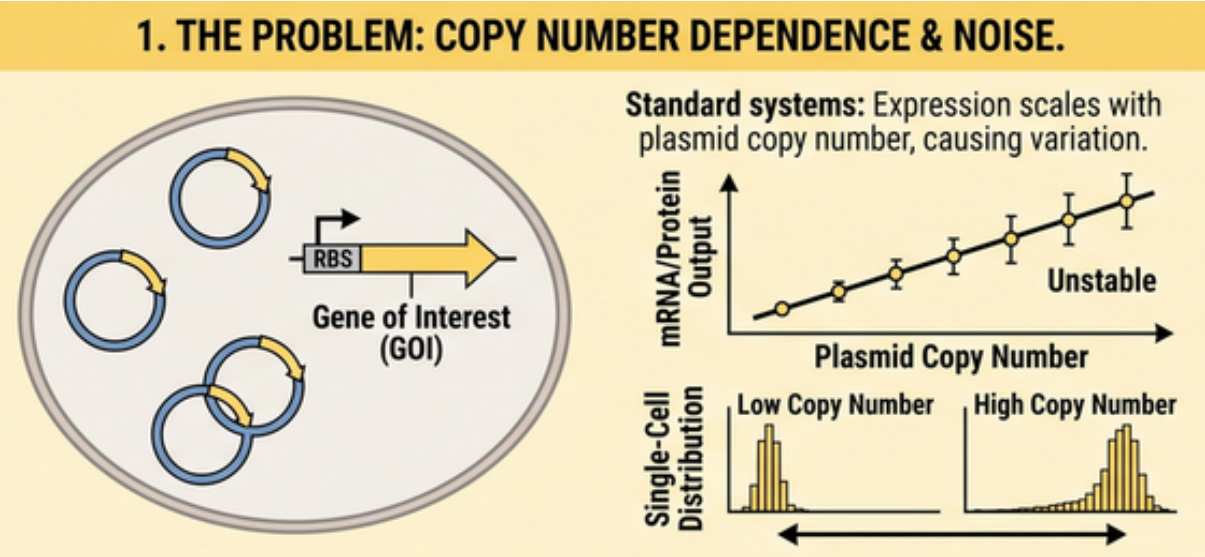
The Problem

Gene expression is unpredictable, noisy, and prone to perturbations, thus posing a challenge towards designing reliable and functional systems. One of the most decisive factors affecting the functionality of synthetic biological systems is gene copy number variation, which gives rise to variability in gene expression.

Why

Despite the fact that copy number is usually regarded as being constant, many factors related to the internal and external environment of the cell contribute to copy number variation both over time and between different cells. Gene expression is characterized by a positive correlation with the plasmid copy number. Thus, variations in copy number lead to variations in gene expression, affecting the function of the system.

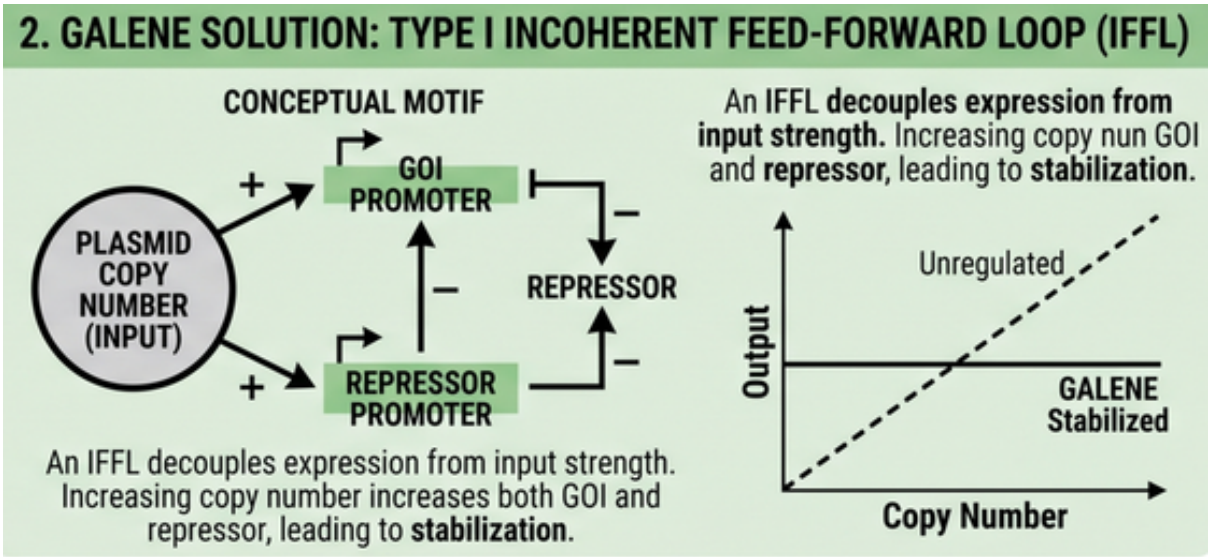
Particularly in complex systems that require high precision, such as metabolic pathways and multi-input logic gates, the accumulation of perturbations caused by variations in their individual parts greatly affects the functionality of said system. Regulating expression strength is usually achieved via the replacement of regulatory elements such as RBSs and Promoters. Still, this does not ensure predictable behavior over different genetic contexts. Therefore, constant re-tuning is mandatory to maintain the system's proper function.



Approach

The team created GALENE, a genetic toolbox that enhances the stability of biological systems by disassociating transcription from gene copy number and provides translational control of protein production.

They achieved this by engineering stabilized promoters which produce the same output regardless of their biological context in order to render synthetic biological systems more predictable and reliable. Building upon the work of Shapiro et al., the team implemented an incoherent Feed-Forward Loop (iFFL) network motif. This motif consists of a regulatory element which compensates for changes in copy number, thus stabilizing the promoter.

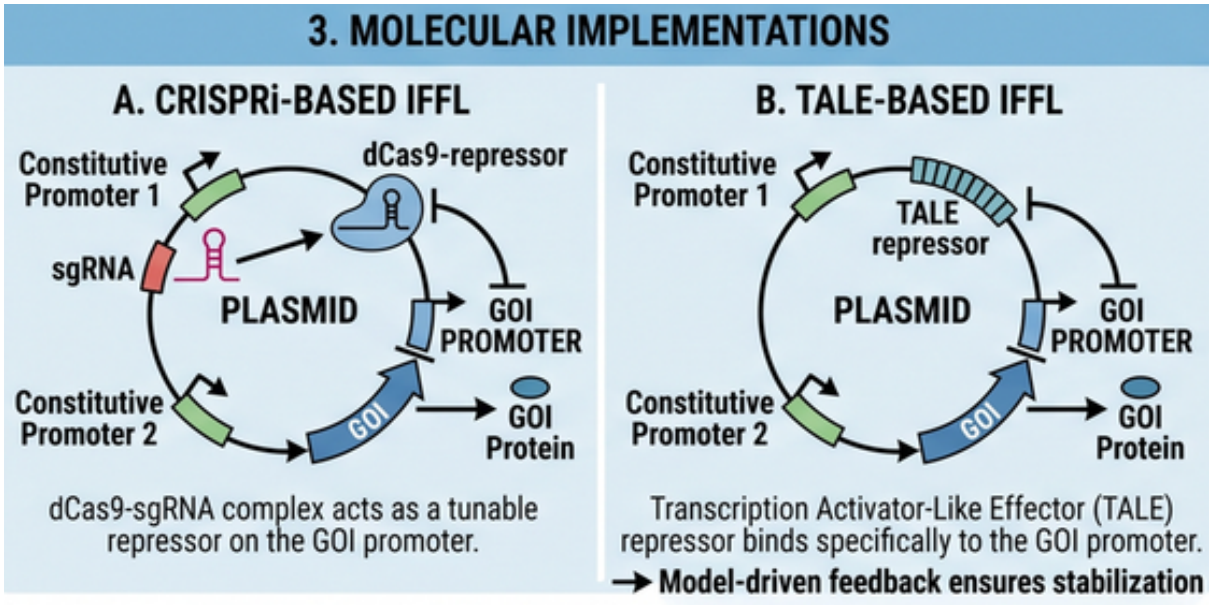


Implementation

Through model-driven feedback, the team accomplished promoter stabilization using two distinct systems, each with its own advantages:

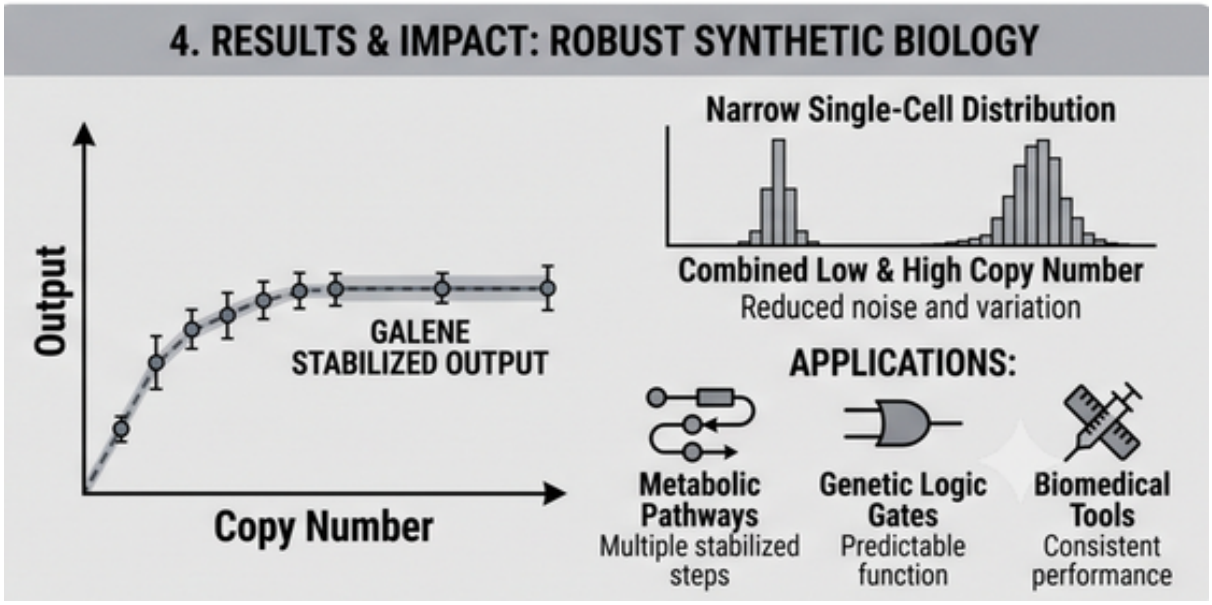
1. TAL Effectors: To achieve tight, error-free repression based on specific recognition sites.
2. CRISPR interference: Utilizing dCas9 for targeted transcriptional repression.

In addition to these, the team designed and simulated a third stabilization system using Attenuator-interacting sRNA regulators. Wanting to expand on the stabilized promoters system, they also designed a theophylline Riboswitch. This allowed, on top of the stabilization of a promoter, its induction and activation to a specific, desired expression level.



The team also outlined several crucial real-world applications for these stabilized promoters:

1. Genome Insertion: Maintaining a genetic circuit's level of expression independent of the position of the inserted gene relative to the Origin of Replication (ORI).
2. Medicine: Introducing predictability and increasing specificity in contemporary therapeutic methods, such as gene and cancer therapies.
3. Toxic Protein Production: Allowing for tight control of gene expression so that sufficient expression can be achieved before toxicity in the host cells comes into play.
4. Metabolic Engineering: Functioning as regulatory tools for the expression of genes participating in metabolic pathways, increasing the system's robustness and stoichiometric performance.
5. Large Scale Production: Controlling fermentation-related genes in organisms used for industrial production (e.g., Saccharomyces cerevisiae) to cope with varying bioreactor conditions and improve the quality of the final product.



Jamboree Results

iGEM Thessaloniki 2018 was awarded a Silver Medal at the Global iGEM Competition in Boston.

“iGEM 2019”

Project name: Poseidon



Team Members:

Students
Platon Megagianis
Sofia Moysiadou
Kristine Chanagkian
Kyriaki Karavan
Ioannis Maliousis
Aliki Anastasiadou
Charalampos Malathounis
Apostolos - Stefanos Ioannidis

PIs
Aivaliotis Michail
Mosialos George

Advisors
Kozalakis Konstantinos
Malousi Antigoni
Vizirianakis Ioannis

Mentors
Arampatzis Asteris
Ballhysa Eugene
Giannitsis Charis
Lioulia Elisavet
Lioulia Elisavet

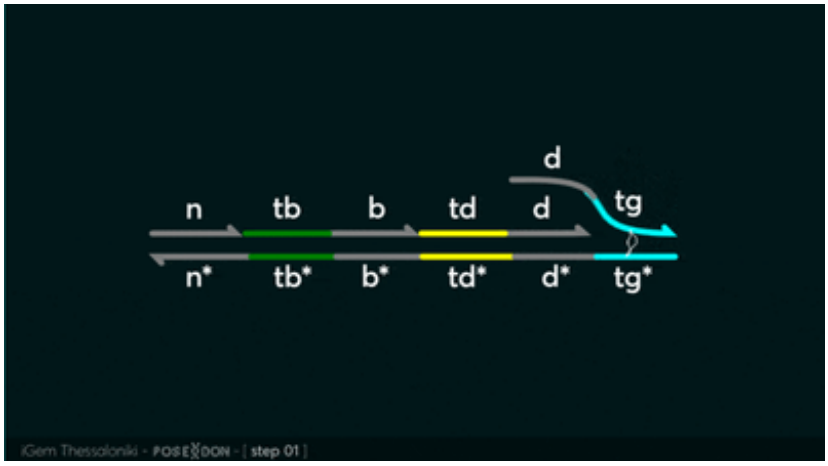
Problem which the team tried to solve
DNA Computing has vigorously emerged in science, taking nucleic acids outside their biological context and constructing molecular motifs of autonomous self-assembly, capable of information processing. DNA circuitry builds on the nucleic acids' intrinsic ability to convert molecular networks into computational layouts. Moreover, the cornerstones of DNA, nucleobases, are capable of constructing proficient programming languages that can integrate limitless mathematically defined operations into biological systems. Hence, DNA Computing proves to be a promising tool for the construction of programmable networks with computational proficiency, feasible in an abundance of research fields.

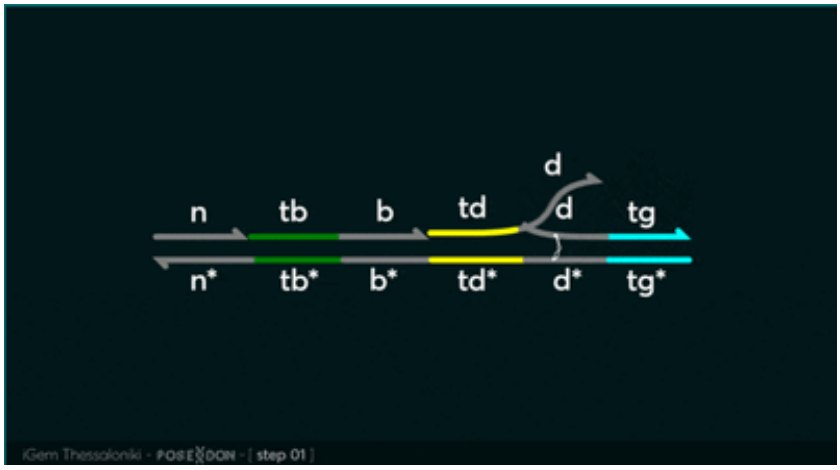
Why
Molecular networks are the fundamental units through which a cell can process information and mediate primary operations regarding its integrity. Fundamental processes that keep the cell alive are consistently mediated by a myriad of molecules that connect and form perplexing networks of interaction.

Such chemical grids prove to be especially sensitive and their malfunction is the prevailing cause of cell defect and the process of malignancy. In particular, DNA-Protein interactions have major effects upon many phenotypic features, such as gene regulation and protein maturation that rely on the identification of target sites in the genome containing distinct sequences. Elucidation of these interactions and the conditions under which they are dissociated are of major importance for a plethora of future applications that concern disease diagnosis, therapeutics, drug discovery and many more. To this day, most assays directed towards the characterization of such intracellular interactions are limited to qualitative identification, while those performing quantitative measurements tend to be rather costly. Most importantly, the majority of information concerning a wide variety of proteins come from in silico predictions that meet no immediate validation from in vitro experiments and, therefore, there is an immediate need for novel methodologies of DNA-Protein interaction examination.

How

Introducing POSEIDON; our team deploys the first DNA Computer able of quantifying DNA-Protein interactions. Using toehold-mediated DNA Strand Displacement, we design multilayer molecular circuits that examine a protein's properties and quantify its binding affinity towards a particular sequence. After running through the molecular processing algorithm, an output signal in the form of fluorescence is produced making the signal acquisition obtainable by a variety of laboratory equipment. To that extend, our team developed an alternative method of reporting measurements based on an electrochemical assay where a gold sensing pad is able to distinguish between the active and inactive states of our molecular circuit.





Implementation
The team tried to find a novel way to make use of the aptitudes of molecular programming to intensify advances in basic fields of biological research. The terrain of DNA-protein interactions was a perfect match. The soaring need to elucidate such interactions in the fields of diagnostics, therapeutics as well as cell and systems biology, rendered the need for their quantitative study of utmost importance. In that accord, we sought out to entangle DNA-protein interactions into the molecular computation performed through nucleic acid molecules, in the form of a novel formal Chemical Reaction Network (CRN) that takes both DNA molecules and DNA-binding proteins as inputs while producing measurable output.

Jamboree Results
Gold Medal

“iGEM 2020.21”

Project Name: Metis



Team members:
Charalampos Anagnostakis
Anna Anastasiou
Anna Varvari
Danai Eleni Vergini
Anastasia Theodosiadou
Maria Kosmidou
Dimitris Trygoniaris
Alexandros Tsigilis
Konstantina Tsouderou
Emmanouil Chatzichristofis

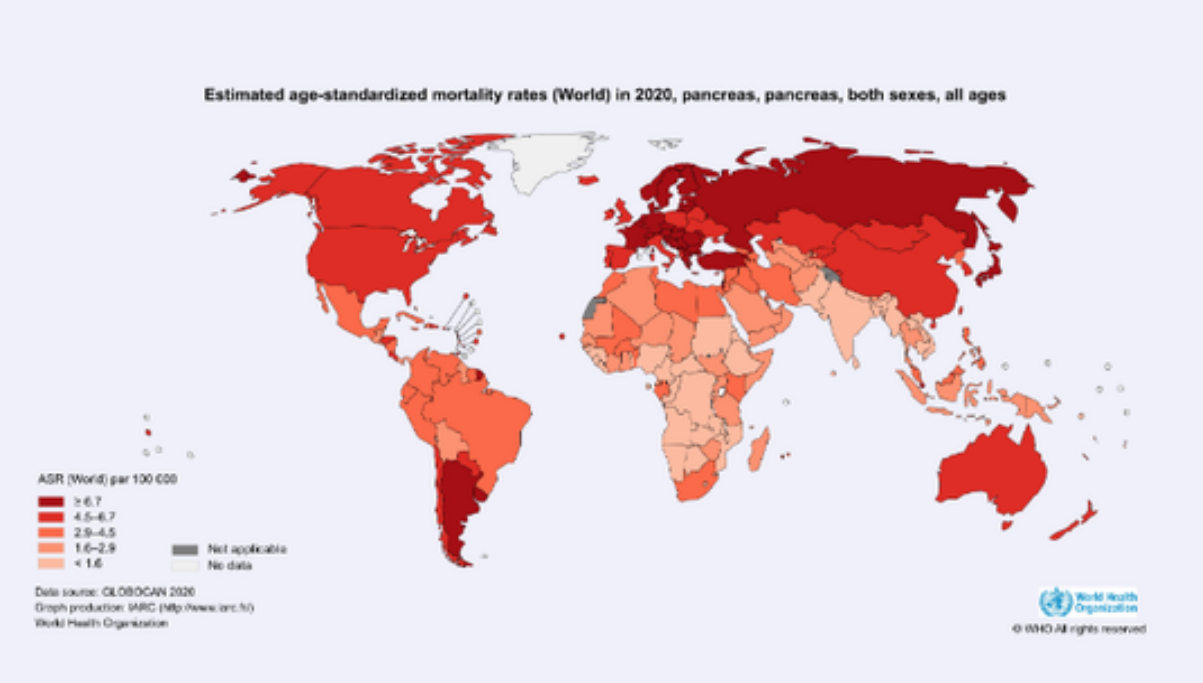
Advisors
Panagiotis Valatsos

Mentors
Asteris Arampatzis
Panagiotis - Nikolaos Lalagkas
Aris Sionakidis

PI
Ioannis S. Vizirianakis

METIS, a cost-effective, non-invasive diagnostic tool for Pancreatic Ductal Adenocarcinoma.
METIS deploys Toehold Switches, a kind of synthetic riboswitches, to detect upregulated miRNAs in urine.

Why
Pancreatic Ductal Adenocarcinoma (PDAC) is the most common type of pancreatic cancer and it is estimated that it affects 13.2 people out of 100,000 every year worldwide. Although PDAC is a relatively rare cancer, it is associated with a very poor prognosis, with approximately a 10% 5-year survival rate, which is the poorest prognosis among the solid types of cancers.



It is considered that this dismal outcome might be improved through the earlier diagnosis of the disease, which will allow both a more efficient therapeutic intervention before the onset of migration of cancer cells to other tissues and nodes, as well as a better understanding of the pathogenesis of the disease.

The high mortality of PDAC can be attributed to some of the characteristics of this type of cancer: The anatomical situation of the pancreas which hinders the detection of the tumor, the presence of vessels that are often surrounded by malignant cells, making the surgical resection impossible, as well as the aggressive nature and high metastatic propensity of this cancer, are some of the features that affect the prognostic factors that are taken into account for the determination of the stage and the treatment.

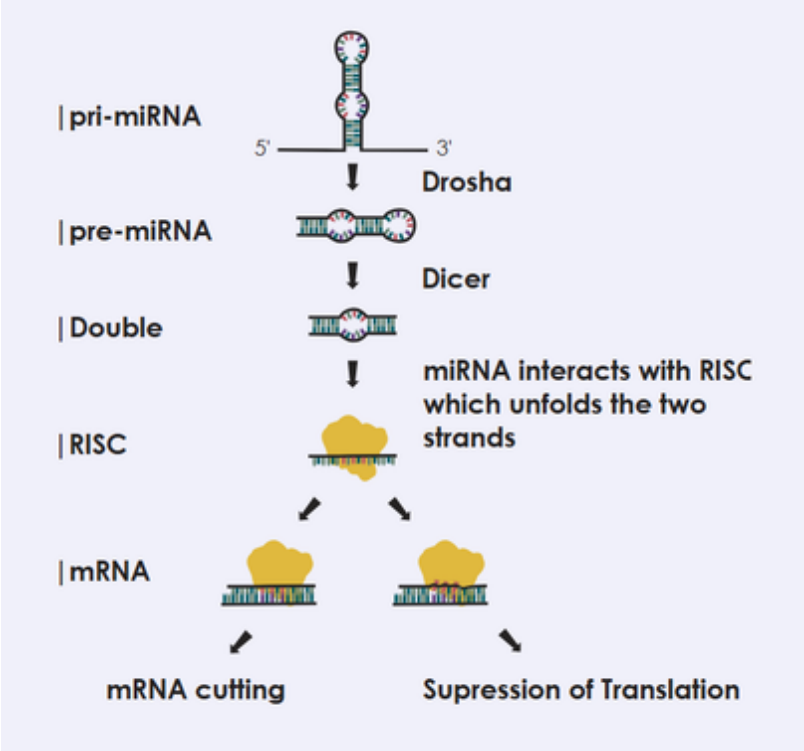
The lack of symptoms, during the first stages of PDAC, renders the screening even of seemingly healthy populations vital [8]. At present, the diagnosis of PDAC, depends, primarily, on imaging techniques and biopsy. Imaging techniques include methods such as Computed Tomography (CT), Magnetic Resonance Imaging (MRI), Positron Emission Tomography with Computed Tomography (PET/CT) and Endoscopic Ultrasound (EUS).

Both imaging and biopsy pose several limitations for the early diagnosis of the disease. On the one hand, imaging methods are incapable of detecting the early-lesions and on the other hand, biopsy is an invasive procedure and hence, the possible benefit for the patient does not exceed the risk.
To overcome these issues, non-invasive biomarkers have been proposed. However, CA-19-9, the only blood biomarker approved by FDA, has been proven inefficient due to its low specificity and sensitivity.

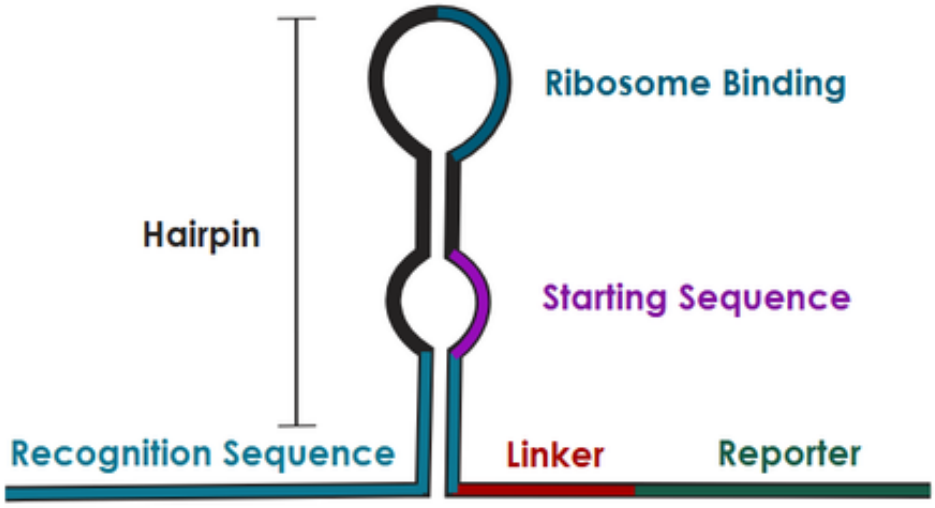
HOW

miRNAs are small, non-coding RNA molecules that play an essential role in the regulation of gene expression at the post-transcriptional level. More specifically, miRNAs are incorporated into the RISC complex and bind to a complementary sequence of an mRNA molecule, leading to the inhibition of translation or the degradation of the target.

Many miRNAs contribute to the regulation of cell growth and proliferation by inhibiting the expression of genes crucial for the cell cycle, migration, or apoptotic signals. Thus, the dysregulation of these molecules is proposed to be involved in the initiation and development of cancer. Indeed, in many neoplasms, several miRNAs are either downregulated or upregulated in different samples, such as blood, serum, saliva and urine. The different miRNAs profile that occurs in different cancer types holds potential as a diagnostic or prognostic biomarker and thus, can be employed in new diagnostic tools.



METIS utilizes a kind of synthetic riboswitches, called Toehold Switches; RNA molecules that consist of a hairpin-like structure and a reporter gene, expressed when a trigger molecule causes the unfolding of the hairpin structure. In the absence of the trigger, the hairpin inhibits the binding of the ribosomes and hence, the expression of the gene.



We chose three miRNAs to function as triggers.
We determined that hsa-miR-143-3p, hsa-miR-30e-5p and hsa-miR-1246 are the most suitable for this purpose, due to their high specificity and sensitivity. In addition, they are upregulated in urine of patients with PDAC at stages I and II, which allows an early and non-invasive detection.
These three miRNAs are excreted in urine exosomes in small quantities. Therefore, the exosomal RNA should be isolated from the sample and then, the triggers should be amplified. We decided to use an EXPAR-like amplification method, which is an isothermal technique, in order to reduce the cost and the equipment needed to the minimum – that is a simple incubator.
The amplified miRNAs bind to a complementary sequence, within the loop, leading to the reconfiguration of the toehold and the production of the reporter gene. As a reporter, we used eGFP, a well-characterized protein that produces fluorescence, when excitated. The fluorescence can be measured with a variety of commonly used equipment, such as a fluorometer. The miRNAs can be quantified through the intensity of the fluorescence produced by the system.
Since in greek diagnostic centers there is not always specialized equipment for fluorescence measurements, we decided to design a portable fluorometer device which functions as a cost-effective tool. After conducting the necessary research in the field of entrepreneurship we concluded that the device will not only decrease the cost of diagnosis but will also increase the accessibility of it.
Our device should be able to solve basic problems existing in labs given the following characteristics:

- **Plug-and-Play Software:** in order for the device to operate, it has to be plugged into a PC. The PC allows the usage of a graphical interface which maps the locations of the biological material in the wells of the testing plate at the beginning of the process and provides the measurements to the user correspondingly to the wells.
- **Hardware:** the device uses two computational units (Arduino and Raspberry Pi) for the control of the conditions (light and temperature) under which the reactions take place (Toehold-miRNA binding, eGFP expression).

Implementation

METIS is a diagnostic kit for the screening for Pancreatic Ductal Adenocarcinoma at the first two stages of the disease. Its function is based on the detection of specific miRNAs in urine samples with a safe, cheap, and user-friendly procedure. We suggest that this tool can be used in a variety of different settings, such as hospitals and diagnostic centers without any expensive equipment.
Through literature research, we found that one of the most important challenges, related to the late diagnosis, is the inconsistency of the symptoms. Most of the patients are either asymptomatic at the onset of the disease or present non-specific symptoms such as weight loss, jaundice, anorexia, or diarrhea, leading to a delay of the diagnosis of the disease. For this reason, we decided to design a diagnostic tool for the screening of both symptomatic and healthy populations.



The workflow of our method consists of three main parts: First of all, the sample should be collected and the whole RNA should be isolated by ultracentrifugation. The next step is the amplification of the selected miRNAs specifically and finally, the reaction of the amplification product with the toehold switches and the measurement of fluorescence.
The fluorescence is easy to measure and interrelate with the quantity of the biomarkers. For the measurement of the fluorescence, we are designing a user-friendly device, to minimize the errors that could happen due to the different equipment of labs and handling of the personnel.
Many factors, both genetic and modifiable, have been identified to be related to the development of PDAC. In 10% of PDAC cases a genetic background is identified, related with mutations in BRCA1 and BRCA2, STK11/LKB1 and other genes commonly involved in other types of cancer as well. On the other hand, modifiable factors include smoking, excessive alcohol use, chronic pancreatitis, obesity or diabetes.



Another important factor affecting the incidence of PDAC is age: It has been shown that the risk of developing PDAC increases with age. More specifically, according to the SEER program, the incidence of PDAC starts rising from approximately the age of 50. Based on this fact, we suggest that our diagnostic test can be included in a regular check-up for high-risk populations after the age of 60.

Jamboree results:

Gold medal

During development, the project won the prestigious **iGEM Impact Grant** from the iGEM Headquarters, validating its clinical value and potential real-world market implementation

“iGEM 2022”

Project Name: THERIAC: Theranostics using RNA interference with applications in cancer



Team PIs:
PI: Michalis Aivaliotis
Secondary PI: Alexandros Kiparissides, Eleni Nikolakaki

Student Team Members:
Aikaterini Sofia Leonida
Anna Anastasiou
Despoina Papadopoulou
Ellie Peitsini
Ioanna Choustoulaki
Markos Mathioudakis
Stylianos Sfondylis
Elias Pilianidis

Advisors:
Anna Nikolaidou
Konstantinos Kozalakis
Stylianos Kokkas

Instructors:
Dorothea Evmorfidou
Konstantina Psatha

Other:
Lydia Despoina Angelou
Panagiota Papadopoulou
Styliani Kioutsiki

Problem:
Glioblastoma (GBM), while a rare cancer overall, is the most common type of brain tumor and one of the most aggressive malignancies. Classified as a grade IV tumor, it originates in astrocytes, a type of glial cell located in the brain and spinal cord. Known for its highly lethal nature, glioblastoma features cancer cells that multiply rapidly, allowing the disease to quickly invade and destroy healthy surrounding tissue. (external sources: https://my.clevelandclinic.org/health/diseases/17032-glioblastoma)

Why:
Statistics of GBM show it is the most common malignant tumour in an adult's brain. GBM has the lowest survival rate among all types of cancer and only 5–6 out of 100 glioblastoma patients survive 5 years after diagnosis. A patient is usually expected to live for about 15 months. This short life expectancy can affect the patient’s physical and mental health, so it is a dual problem.

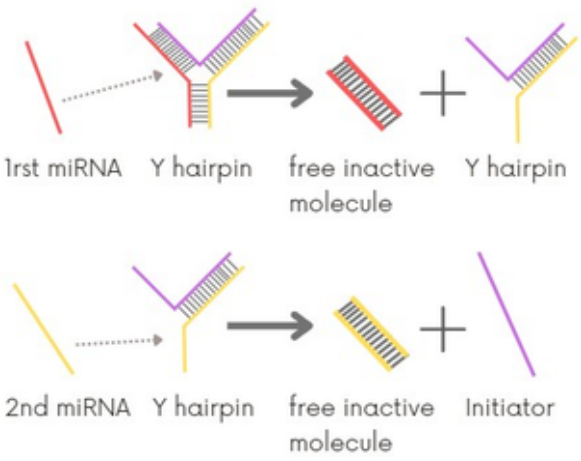
Glioblastoma concerns 3 per 100,000 people around the world every year (Ostrom et al. 2018), so it is a rare type of cancer.

The current methods of treatment are surgery, radiotherapy, and chemotherapy. Surgery cannot be perfect. It is difficult for the neurosurgeon to distinguish between tumor cells and healthy tissue. So, the tumor cannot be completely removed, which leads to local recurrence. Chemotherapy and radiotherapy often cause chemoresistance and burdening side effects (Grochans et al. 2022). Moreover, GBM patients often suffer a relapse because of ineffective treatments. This is equivalent to a worse prognosis (Mirzaei et al. 2021).

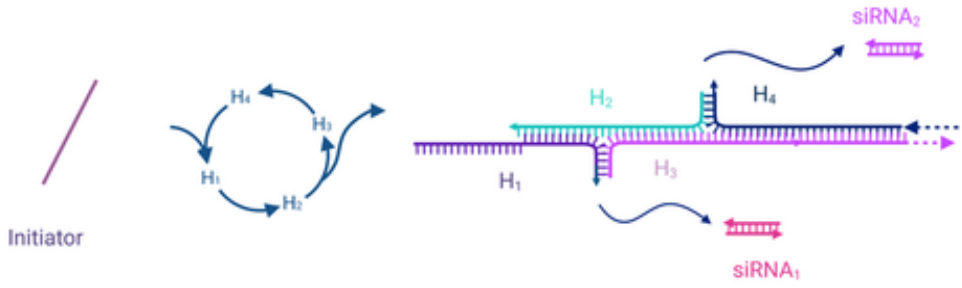
Significant efforts have been made toward cancer therapy, however, research remains stationary. The fact that statistics and prognosis are continuously worsening, makes the situation dire. Consequently, exploring new therapeutic approaches is crucial.

How/Approach/Solution:
Theriac is a molecular theranostic tool that aims to specifically detect and kill GBM cells. It consists of two types of DNA molecules. These molecules remain inactive in absence of cancer, but, when cancer cells are detected, they are activated and release two therapeutic molecules. This molecular machinery will be uploaded to a nanocarrier so it can easily reach all brain areas. The brain is protected by a wall called the "blood brain barrier". To avoid this wall, Theriac will be administered through the nose. When released in cancer cells, Theriac will act therapeutically in two distinct ways. Consequently, it will stop cancer proliferation and cause tumour suppression with minimum or even none side effects. It will also enable better and real-time MRI monitoring of the patients, through our approach employing artificial intelligence methods.

More analytically, Theriac is a two-step theranostic approach. It consists of two types of DNA molecules called hairpins. The first hairpin (Y-shaped) is made of three DNA strands and detects two different cancer biomarkers simultaneously. These biomarkers are microRNAs, specifically miR-21 and miR-10b, and they are co-overexpressed in glioblastoma cancer cells.This detection releases an initiator strand, which changes the secondary structure of the downstream hairpins via an enzyme-free, isothermal Hybridization Chain Reaction (HCR). The initiator is complementary to the 5′ toehold of the first hairpin (H1). After hybridization between H1 and the initiator, H1 unfolds and binds to the H2 hairpin, which in turn binds H3. Once unfolded, H3 binds with H4, which then triggers the unfolding of the next H1, continuing the process as a chain reaction. For every completed H1-H4 assembly cycle, two small interfering RNA (siRNA) molecules are released to selectively downregulate oncogenic targets.



Y Mechanism

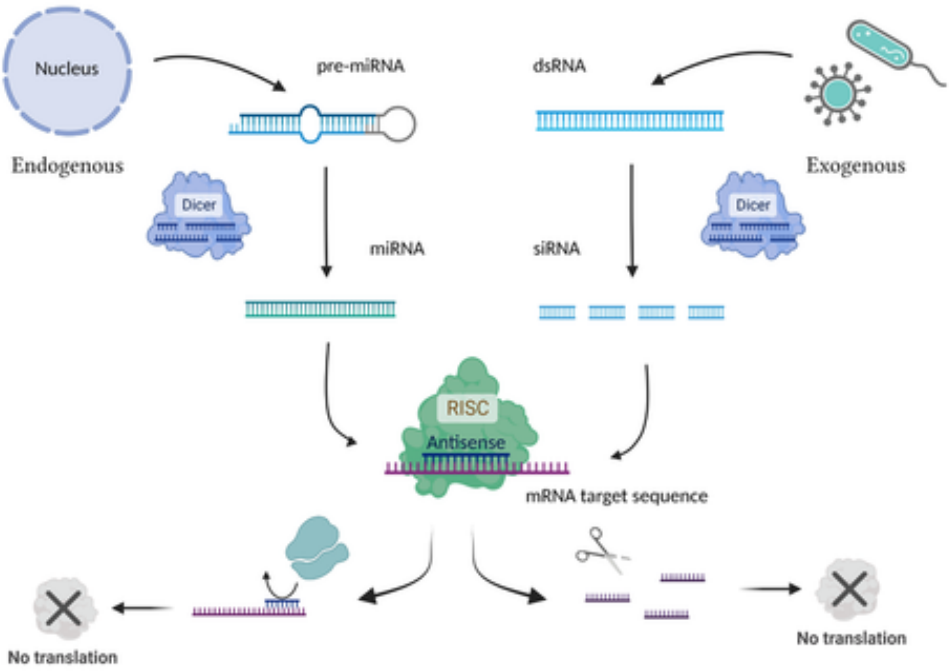


HCR Mechanism

siRNAs are double stranded nucleotide molecules consisting of 21–23 nucleotides. These molecules are bound to the RNA induced silencing complex

(RISC) and are unwounded into single-stranded RNAs by Argonaut 2 (AGO2) that bind to the complementary mRNA sequence (unnecessary strands are degraded). The pairing causes cleavage at the targeted area, which prevents the targeted mRNA from being translated and causes its degradation. When the paired mRNAs are cleaved, RISC and single-stranded siRNAs are free to bind to other mRNAs to lower protein expression level (Kim et al. 2019).

The mRNAs chosen for their synergistic anti-tumor efficacy and complementary interactions with the miRNA sensing domain were STAT3, HIF-1α and PLK1.



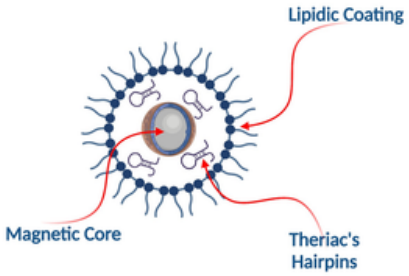
We aim to load our molecular mechanism to a nanocarrier so that it reaches metastatic cells in areas of the brain the surgeon cannot. Apart from that, the nanocarrier could amplify the magnetic resonance imaging (MRI) signal, helping the process of monitoring.

To deliver this molecular machinery safely and efficiently across the blood–brain barrier, the entire HCR-hairpin system is loaded onto a specialized nanocarrier platform.

Implementation:

Molecular Mechanism:

Theriac consists of two types of hairpins, the first hairpin (Y-shaped) detects at the same time two different cancer biomarkers (miR-21 and miR-10b). In this way, cancer cells are differentiated from healthy ones. At the same time, by attaching the two microRNAs, Theriac prevents them from acting in favor of cancer cells, achieving a first-to-go attempt of therapy. Inhibition of miR-21 and miR-10b in GBM cancer cells could lead to inhibition of metastasis and cancer cells' death. Only after the detection of both microRNAs, and through changes in the secondary structure, the final and more specialized therapeutic molecules will be released. This procedure is called HCR and leads to the release of two siRNAs that target key molecules of cancer cells' metabolism. Through this intervention, Theriac will cause apoptosis to both cancer cells and cancer stem cells, reducing the size of the tumour and minimizing the possibility of recurrence.



Administration:

Theriac hairpins will be uploaded to a nanocarrier, with a magnetic core surrounded by a lipid membrane. The composition of the lipid membrane will be similar to those of glial cells to achieve better recognition of GBM cancer cells. The magnetic core will enhance the MRI signal giving the opportunity for real-time monitoring, detection of distant tumor loci, and treatment regiment adjustment.

Theriac will be administered in the form of aerosol intranasally. The brain is protected by the blood-brain barrier (BBB) which doesn't allow most of the therapeutic molecules to reach GBM tumours. Nose-to-brain delivery offers a promising alternative to systemic delivery. It enables the direct transfer of therapeutic drugs to the CNS via the trigeminal or olfactory nerves, avoiding the BBB.

Theriac will be administered after surgery (if that possible) or, instead of it, in cases where surgery is not feasible. If surgery is successful, Theriac will not be activated because there will not be any cancer cells left. Unfortunately, in most cases, due to the high metastasized profile of the GBM cells, the surgery is not successful and a lot of cancer cells are left behind. In those cases, due to overexpression of the microRNAs, Theriac will be activated and kill the cancer cells and cancer stem cells left behind.

Neural Network:
We also developed a software tool to monitor the patient in real-time and assist the medical professional using Theriac. Our neural network is trained to identify MRI images from patients with GBM, evaluate the current stage of the disease, and possibly, the effect of a potential treatment. Our nanocarriers, due to their Ferrum oxide core, will enhance the MRI signal in the areas they reach. Common therapies are causing false images in MRI scans called pseudoprogression due to edema caused by damage to near healthy cells. Theriac has a high specificity for GBM cells thus, no pseudoprogression will occur.

Outcome
In total, Theriac will offer a personalized theranostic approach with a high safety profile. A more accurate and well-tolerated therapy accompanied by better monitoring techniques, according to bibliography, can increase the 5-year survival rate from up to 15% percent, saving many lives. It will take many years and financial resources for such a product to enter the market. An integral part of Theriac's future implementation is the founding of Theriac's platform. Our dream and passion are to make breakthrough research possible and accessible by everyone.

Jamboree results:
Silver Medal, Nomination for Best Supporting Entrepreneurship, Undergraduate

“iGEM 2023”

Community mentor:
Konstantinos Ragios
Project name: **Euphoresis: a synbio soil-ution for forest conservation**



Team members:
Markos Mathioudakis
Artemis Savva
Aggeliki Maria Papapanou
Thetis Tsinoglou
Ioanna Gerogianni
Aggeliki Savvopoulou Tzakopoulou
Stefanos Anagnostopoulos
Nefeli Makri
Rafail Andreou
Asimenia Ioannidou
Michaela Ververi
Soultana Delizisi
Panagiota Baka
Efstathiou Niki

Instructors & Advisors
Christos Giannakopoulos
Rigini Papi
Konstantina Psatha
Ioanna Koumentakou

Principal Investigators
Michalis Aivaliotis
Spyros Gkelis

Euphoresis is a, as minimally invasive as possible, solution to ecosystem destruction caused by fire, aiming to strengthen the regenerative mechanisms of the soil by changing the soil's characteristics after a strong fire so, that water runoff and erosion are limited, soil fertility is enhanced, and the soil promotes its own forest's regeneration.

Why
Wildfires are always unforeseen phenomena, brought on by human action or natural causes, that devastate the environment and human well-being.It is indicative that 119 million hectares (1 hectare = 10.000 m2) of trees were

reportedly lost due to fire over a period of twenty years, making fire responsible for 27% of tree cover loss worldwide.
Every year, in our country, Greece, wildfires are a common phenomenon, especially during the summer period. Our country has ranked in Europe’s second place, regarding the percentage of burned area from 2008 up until 2022.

Moreover, data shows that the number of wildfires in Greece increased by approximately 60%. This translates to more than 46 fires breaking out every year and more than 30,000 hectares of land being burned.
Nevertheless, the summer of 2023, was a catastrophic period compared to 2008-2022, with multiple wildfires in numerous places, making Greece take Europe's first place in 2023.

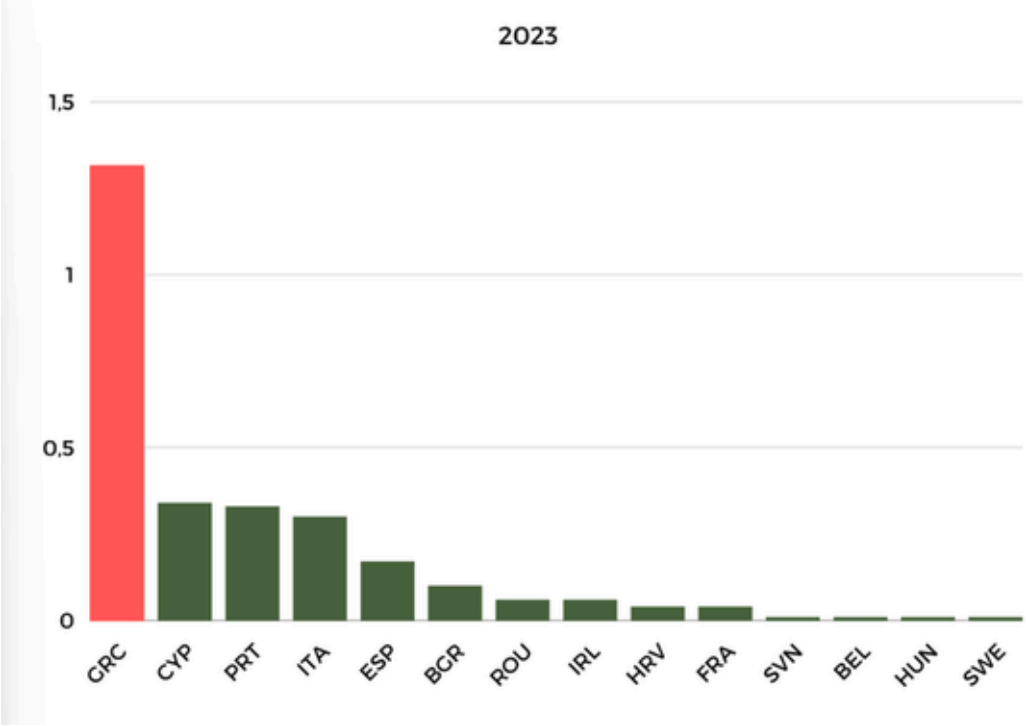


Figure 1: Percentage of country’s land burnt in year 2023

Soil quality restoration is one of the fundamental issues brought on by wildfires and a component of forest restoration failure. Numerous organic and inorganic compounds can burn and volatilize as a result of the massive consequences of a strong fire, resulting in a significant loss of soil organic matter and nutrients.To the same extent, a sizable loss of biomass has been found in the soil microorganisms that are involved in the life cycle of the forests.The degradation of the root system, soil disaggregation, and its increased hydrophobicity after a wildfire can lead to soil erosion. As a result, floods, landslides, rockfalls, and debris flows, all of which are linked to erosion and the consequential soil’s inability to absorb water, can contribute to additional mass movement and soil loss.

These factors establish an inhospitable setting for the growth of new vegetation. Upon our bibliographic research, we found that, in a 5-year span, 46% of burned areas in the Mediterranean showed a lower plant cover compared to the situation before the fires because of soil erosion, harsh conditions, and repetitive wildfires in the spots of interest.This poses, now more than ever before, the threat of a permanent desertification of once-alive and perfectly balanced ecosystems if things continue to be the way they are.

How

Euphoresis, our proposed solution, involves a three-level approach: a biodegradable hydrogel host hosting a bacterial consortium while also encapsulating plant seeds.

The Hydrogel

Realizing that one of our first priorities should be to solve the problem of hydrophobicity of the soil, we focused our research on polymeric resins, specifically in the category of hydrogels, and decided to create a hydrogel-forming biopolymer. Our polymer will exhibit a high swelling capacity, enabling it to absorb rainwater effectively, thus mitigating water runoff and contributing to improved resistance against erosion.

Our hydrogel formulation matrix consists of three ingredients: two polysaccharides, pectin and chitosan, and a synthetically engineered antimicrobial peptide serving as a crosslinker agent.

This unique combination will ensure the stability and safety of our product.

We used an existing peptide with antimicrobial properties against gram-positive bacteria as a template and designed our own peptide to be physically crosslinked via charge interaction with chitosan, while it can also form "covalent dimers" via the cysteines in its structure. By choosing an antimicrobial peptide, we are aiming to add an extra biosafety layer as a complementary step to the other biosafety measures against the release of our GMMs (Genetically Modified Microorganisms).

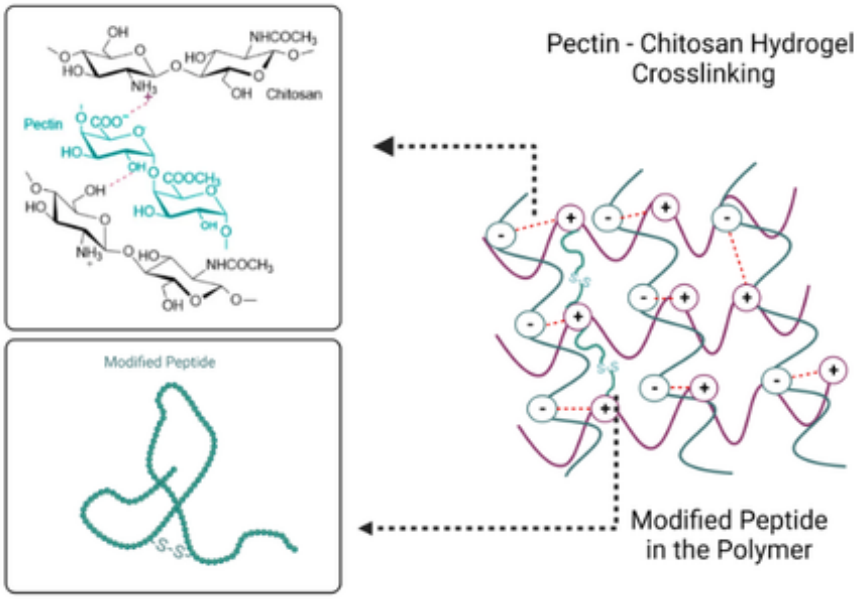


Figure 2: The final bio-copolymer with crosslink between chitosan, pectin and the engineered peptide

Microbial Consortium

The bacterial consortium within our hydrogel comprises two distinct species: WB800N, a strain of *Bacillus subtilis*, and *Nostoc Oryzae* TAU-MAC 2710, a strain of filamentous cyanobacteria. These bacteria have been carefully engineered to communicate with each other using a quorum-sensing system. This mechanism ensures harmonious coordination among the bacteria, allowing them to function co-dependently while controlling the kill switch system and

safeguarding against leaks from the hydrogel.

We have also built a system of microspheres that are trapped inside our hydrogel and serve as hosts for our bacterial consortium. They consist of alginate and pectin, a co-polymeric system that has been previously used for bacteria encapsulation with adjustable pore sizes, which depend on the ratio of the two polysaccharides. By changing the pore sizes, we can permit the release of the desired enzymes while preventing bacterial leakage.These microspheres thus serve a dual purpose by improving the biosafety measures of our suggested material and fostering a favorable microenvironment for the bacterial consortium.

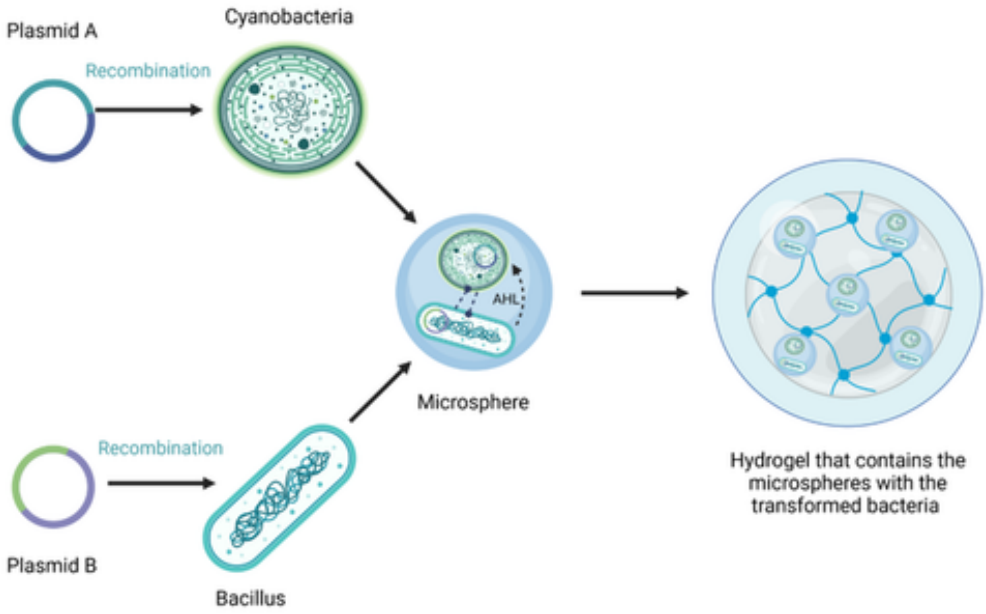


Figure 3: The microbial consortium that communicates through a quorum-sensing mechanism inside the microspheres

Seeds

In the final stage of our project, we made an effort to make each situation's solution more comprehensive. We decided to include a variety of local or endemic species' seeds, chosen carefully for each environment, to ensure the maintenance of biodiversity and raise the success rate of vegetation rehabilitation. The plan would have a mosaic pattern, in order for the new forest to include plants more resistant to fires, ensuring in this way their protection from this phenomenon.

Implementation

Euphoresis - the original

This is the core version of our product, aiming to deal with soil erosion, increase soil organic matter, and enrich soil with nitrogenous compounds.

Euphoric plus - seeds in action

Our second version will carry the same elements as the original Euphoresis product. The main difference will be the addition of seeds, putting our enriched Euphoresis product into the reforestation game . Euphoresis plus will be useful in forests that have been burned twice in a period of ten to fifteen years, and where seeds have been eliminated.

Euphoric hydryad - a step to the future

In recent years, some attempts have been made to introduce Genetically Modified trees in forests or in agriculture to promote faster growth, or to absorb greenhouse gases. Those ideas could potentially match with the Euphoresis project, to create Euphoresis hydryad, the ultimate SynBio version of our product that will contain GMO seeds, carefully engineered to promote, for instance, a more effective reforestation and enhanced forest fire resistance.

Other applications

- Urban green spaces: Greece occupies the last place in Europe when it comes to urban green spaces, with just 2 m2 to 10 m2 per capita. Euphoresis can increase soil stability and water absorption in urban areas as well, resulting in less use of water, rapid growth, and enhanced preservation of the plants that make our cities beautiful and sustainable. Moreover, cyanobacteria are capable of capturing CO2 emissions, and with further engineering.

- UFORESIS - Getting ready for colonization of Mars: Cyanobacteria could thrive in the extreme Martian conditions, requiring just CO2, water, nitrogen, and the Martian regolith to survive. If engineered correctly, they could provide in exchange oxygen, nitrogenous compounds, fuel, and even

food and building materials. On the other hand, it has been proven in research that hydrogels could promote efficient plant growth in Martian conditions. These two combined prove that Euphoresis could stand as an ideal Martian startup kit and start conquering the uUniverse**.**

- Agriculture: Hydrogels have been used in agriculture over the past decades, while both cyanobacteria and *Bacillus subtilis* strains have been successfully studied for their potential use in sustainable agricultural units. Euphoresis unites their powers in one single particle, which we hope can reach the agricultural market and be recognized as a versatile product that aims for sustainable crop development.

Jamboree results:
Silver medal
The team earned a highly prestigious global nomination for **Best Sustainable Development Impact** in the Undergraduate division.

“*iGEM 2024*”

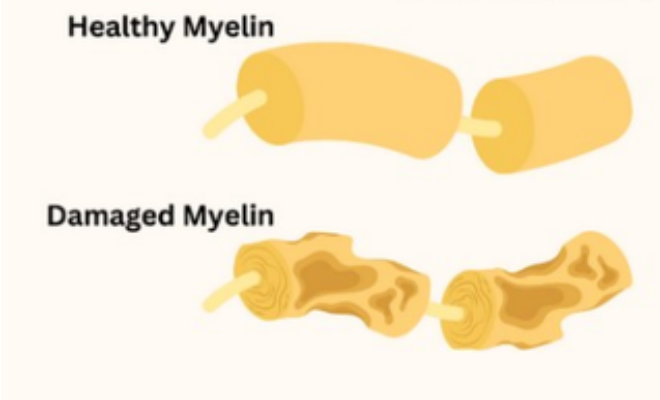
Project name
NeuroMuSceteer



Team members
Students
Ilias Pilianidis
Panagiotis Boutos
Eva Chasekidou
Antonios Tsiorvas
Maria Kefala
Maria Christina Tsilia
Ioanna Karampela
Anastasia Trygouti
Vasilis Panagiotis Theocharopoulos
Louiza Takatzoglou
PIs
Michail Aivaliotis - PI
Anastasia Papadopoulou-coPI
Nikoleta Psatha-coPI
Evangelia Yannaki-coPI
Instructors
Konstantina Psatha
Stefania Maniatsi
Alexandros Liatsos
Advisors
Kallisti St John
Ioanna Choustoulaki
Stathis Pateras

Problem which the team tried to solve

Multiple Sclerosis



Multiple Sclerosis (MS), an autoimmune disease where CD4+ T cells target the central nervous system (CNS), leading to cytokine/antibody storms, demyelination, and irreversible destruction of oligodendrocytes and neurons

Why



Multiple sclerosis is a particularly pressing issue in the local region, Thessaloniki, Greece, due to higher prevalence rates than in other parts of the country. According to studies, northern Greece, including Thessaloniki, has one of the highest MS incidences in Europe, most likely due to genetic, environmental, and lifestyle factors unique to the region. This increased prevalence could be attributed to specific genetic markers found more frequently in northern Greek populations, as well as environmental triggers such as vitamin D deficiency .

How

In brief, our project proposes a dual-targeted approach to tackle the neuroinflammation and demyelination associated with MS. By modifying T cells to act as regulatory agents and employing nanoparticles for miRNA delivery, we aim to provide a comprehensive and effective therapeutic strategy for MS patients

Pillar 1: T-Cell Modification (CRISPR and CAAR)

Overview

The first part of our approach focuses on the modification of T-immune cells derived from MS patients. By leveraging CRISPR technology, we aim to convert these cells into regulatory T cells (T-regs), expressing the transcription factor Foxp3. This conversion is crucial, as T-regs play a vital role in maintaining immune homeostasis and preventing excessive inflammation.

Pillar 2: miRNAs Delivery

Overview

The second component of our solution involves the introduction of microRNAs (miRNAs) encapsulated in nanoparticles. This method is inspired by previous proposals, mainly iGEM Thessaloniki 2022 Project “Theriac” . As an administration route, the olfactory nerve is recommended for targeted delivery .

Implementation

Methodology

1. **Epigenetic CRISPR Modification**: We utilize a lentiviral vector system to introduce a dCas9-VPR epigenetic tool into the T cells to effectively activate Foxp3 expression and switch conventional T cells into T regulatory cells (Tregs). This step is supported by studies demonstrating the efficacy of CRISPR in enhancing T-reg cell populations .
2. **CAAR Construction**: Following T-reg conversion, we integrate a specific Chimeric Auto-Antibody Receptor (CAAR) construct into Treg cells, targeting key epitopes involved in MS pathogenesis, particularly Myelin Basic Protein (MBP) and Myelin Oligodendrocyte Glycoprotein (MOG) . These epitopes are critical as they are often recognized by autoimmune B cells, leading to demyelination. The binding of these autoimmune B cells to modified CAAR T-regs can help modulate the autoimmune response by by-passing the detrimental binding of myelin proteins to auto-antibodies.
3. **Blood-Brain Barrier (BBB) Modifications**: The passage of CAAR Treg cells across the BBB when they are administered intravenously, is expected based on their documented migratory capabilities. Recent studies have shown that engineered T cells can effectively cross the BBB, which in case of MS could be further facilitated by the active CNS inflammation leading to partial BBB disruption . Intrathecal administration should also be taken into consideration, provided that modified CAR-T cells are unable to sparkle inflammatory reactions in the CNS .

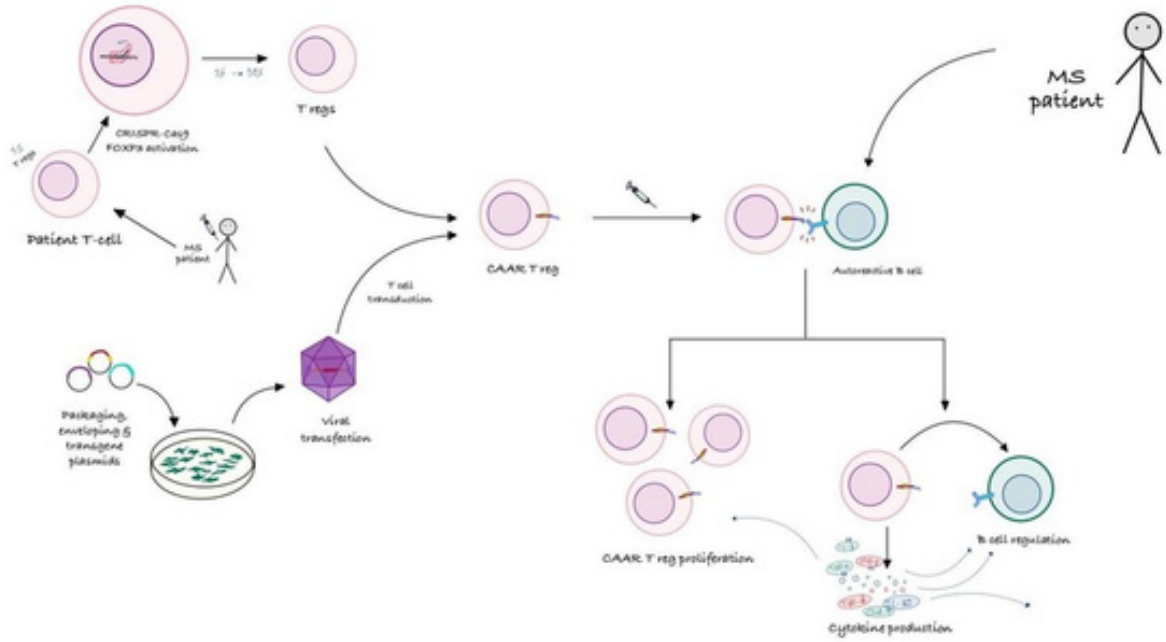


Figure 2: T-Cell modification.

miRNA Selection and Function

We focus on a cluster of four miRNAs, strategically chosen for their roles in MS pathogenesis:

- **Identifier miRNAs: miR-27a** and **miR-125a-3p** are upregulated in MS plaques, specifically in oligodendrocyte lineage cells. Their identification within these lesions underscores their potential as biomarkers.
- **Therapeutic miRNAs: miR-219** and **miR-338** have been shown to promote remyelination and protect against myelin sheath damage. By delivering these miRNAs to targeted MS lesions, we aim to reverse the demyelination process

Mechanism of Action

The proposed mechanism involves the activation of a series of reactions known as Hybridization Chain Reaction (HCR) upon the targeted release of the therapeutic miRNAs at the identified MS plaque sites. This approach ensures localized remyelination while minimizing potential off-target effects, thereby enhancing safety and efficacy.

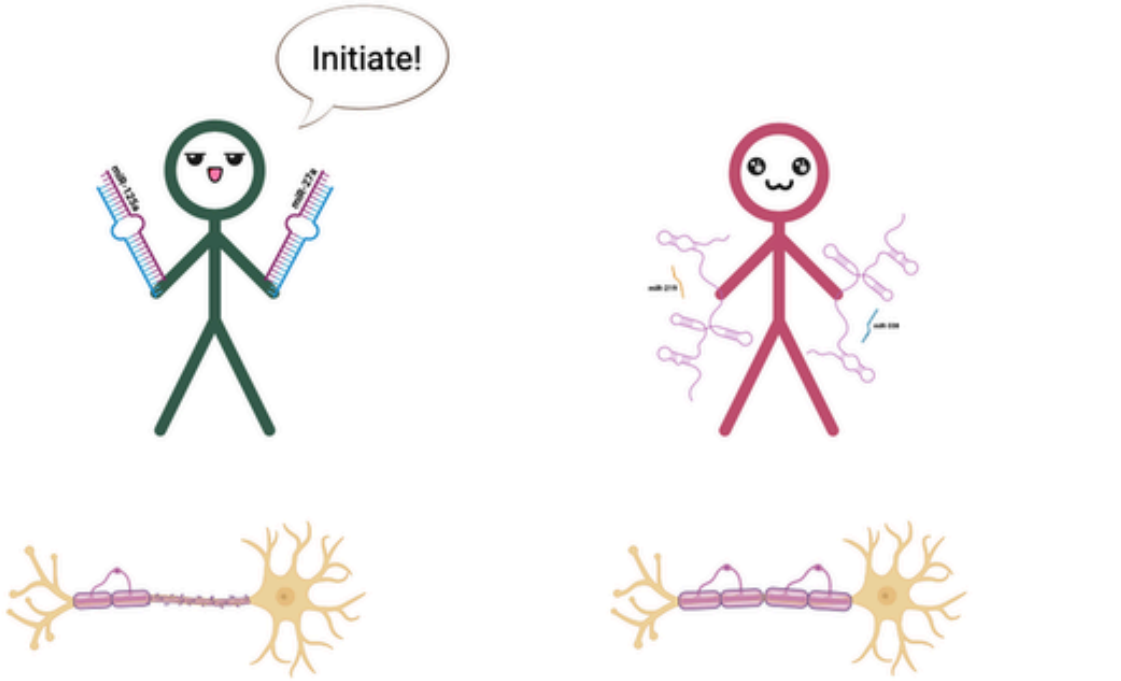


Figure 3: microRNA delivery.

Jamboree results
Silver Medal

“iGEM 2025”

Project Name: siREN



Team Members
Students:
Antonis Tsiorvas
Ioanna Karampela
Aggeliki Iordanidou
Margarita Papastergiou
Errika Sylai
Erriketti-Theodora Moumka
Marianna Rafailia Palieraki
Olga Anna Skarlatou
Georgios Zekas
Georgios Maroulis-Bousmalis
Kyriakos Marios Papamanolis

PI:
Michalis Aivaliotis

Instructors:
Konstantina Psatha
Stefania Maniatsi
Eleftheria Girousi
Dimosthenis Tzimotoudis

What problem did the team try to solve?

Chronic Lymphocytic Leukemia (CLL) is a chronic malignancy of mature B-lymphocytes accumulating within the blood, bone marrow, lymph nodes, and spleen: eventually overtaking normal blood cells and preventing their normal respiratory, coagulatory, and immune functions.

Why?

Chronic Lymphocytic Leukemia is the most common type of Leukemia in adults in Western countries. Despite therapeutic advances, CLL remains incurable, often with significant treatment side effects, high relapse rates, and drug resistance, which challenge both the patients and the doctors entrusted with their care.



How?

siREN proposes a dual-targeted RNA interference (RNAi)-based therapeutic strategy for Chronic Lymphocytic Leukemia (CLL). By simultaneously silencing the BCL-2 and BTK genes using small interfering RNAs (siRNAs) and delivering them selectively to malignant CLL cells through selective lipid nanoparticles (LNPs), the team aimed to induce apoptosis, inhibit leukemic cell proliferation, and minimize off-target effects.

Pillar 1: Dual Gene Silencing (BCL-2 and BTK)

The first pillar focuses on targeting the two major drivers of CLL progression: BCL-2, which protects leukemic cells from apoptosis, and Bruton's Tyrosine Kinase (BTK), a central mediator of B-cell receptor signaling that promotes cell proliferation and survival.

Small interfering RNAs (siRNAs) are short double-stranded RNA molecules (20–24 nucleotides) that mediate gene silencing through the RNA interference (RNAi) pathway. After entering the cell, one strand of the siRNA is incorporated into the RNA-induced silencing complex (RISC), while the other strand is discarded. Guided by the siRNA sequence, RISC recognizes complementary messenger RNA (mRNA), and its catalytic component, Argonaute-2 (Ago2), cleaves the target mRNA. The degraded mRNA can no longer be translated into protein, resulting in efficient and highly specific silencing of the target gene.

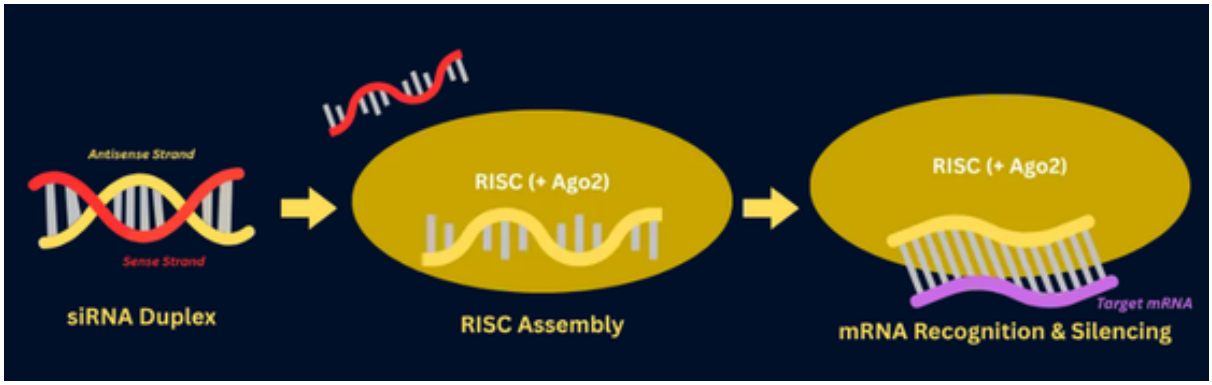


Figure 1: Mechanism of action of the siRNA-RISC complex

By designing siRNAs against both target genes, this strategy aims to simultaneously dismantle the anti-apoptotic and proliferative mechanisms that sustain CLL, providing a more effective treatment than targeting either pathway alone.

Pillar 2: Targeted Lipid Nanoparticle Delivery

The second pillar involves the encapsulation of therapeutic siRNAs within engineered lipid nanoparticles (LNPs). These nanoparticles are designed to protect siRNAs from degradation, facilitate intracellular delivery, and selectively target CLL cells through tissue-specific targeting, and through antibody fragments specific for ROR1: a transmembrane protein almost exclusive to CLL cells. This targeted delivery system seeks to maximize therapeutic efficacy while reducing systemic toxicity and off-target gene silencing.

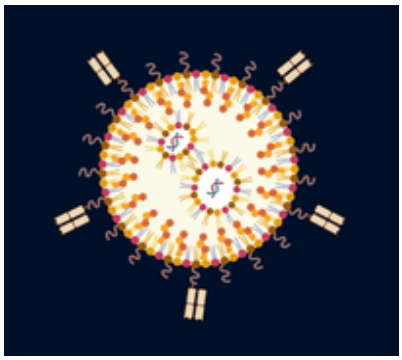


Figure 2: Structure of the designed Lipid Nanoparticle functionalized with ROR1-specific antibody fragments, and shown encapsulating the siRNA payload.

Implementation

Regarding project implementation, this therapy will require parenteral administration: either intravenous (IV) or intramuscular (IM). IV administration enables rapid systemic delivery to circulating and lymphoid CLL cells but requires careful monitoring due to the risk of infusion-related reactions and systemic off-target effects. In contrast, IM administration offers slower, sustained release with improved tolerability, although it may cause localized injection-site reactions.

Early stage in vitro experiments showed that siRNA targeting BCL2 are able to induce cell cycle arrest in CLL cell lines such as MEC1, and thus slow their proliferation. This attribute could be explored in the context of co-administration with other common CLL drugs, where it is expected that this targeted approach can selectively weaken the pathological cells to prime them for stronger drugs. This way, necessary treatment doses can be lowered, and thus the safety profile of many drugs used today might improve. This is especially important in CLL, because the majority of patients, i.e. recipients of therapy, face challenges such as immunocompromization, comorbidities, and frailty related to their illness or to old age.

After future preclinical (in vitro and in vivo) and clinical trials show good results and good safety data, this therapeutic approach might reach the shelves of hospital pharmacies, and provide CLL patients with an additional treatment offering less side effects and better efficacy in battling this incurable disease.

Jamboree Results

Gold Medal
Nomination for Best Integrated Human Practices, Undergraduate
Nomination for Inclusivity Award, Undergraduate
Nomination for Best Oncology Project, Undergraduate and Overgraduate
local people solving local problems
iGEM

“

Local people solving local problems

iGEM



ARISTOTLE
UNIVERSITY
OF THESSALONIKI



