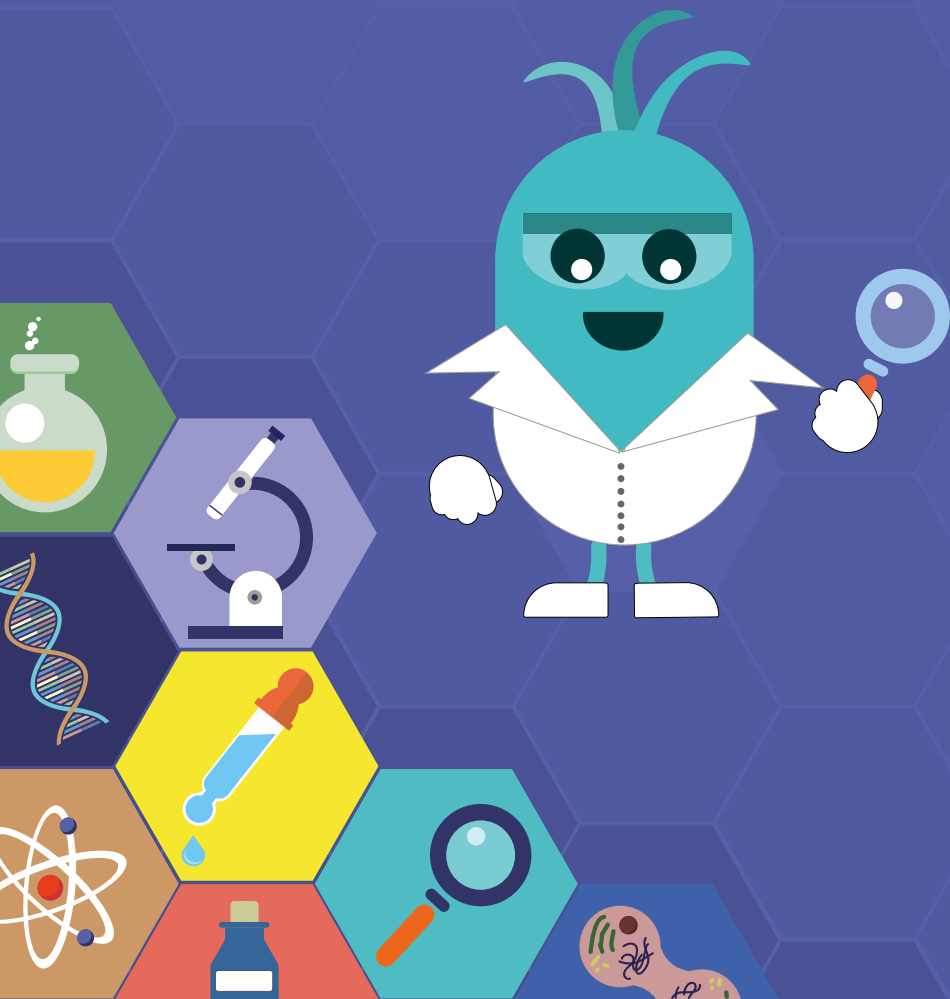


Dr. Coli`s adventures

and other incredible stories
on how synthetic biology
saves the world



This comic book is the result of an international collaboration of student research teams, all working on projects on how to solve problems of humanity with the help of synthetic biology.

Therefore, we cannot guarantee the correctness and completeness of the content.

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**Dr. Coli's Adventures and Other
Incredible Stories on how
Synthetic Biology Can Save the
World**

For you

Synthetic Biology can save the world and this book is dedicated to explaining how for you.

For you, who does not know what Synthetic Biology is.

For you, who wants to know more about what you can achieve with Synthetic Biology.

For you, who hardly knows anything about Biology.

For you, who knows much about Biology.

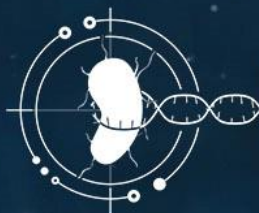
11 science projects in the field of Synthetic Biology are explained for everyone to understand.

Illustrations demonstrate the principles of the project. The abstract following each comic shows you the details of the project and if you would like to dive even deeper into the topic, links to the website of the research teams are provided.

We wish you an enjoyable and educational read!

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DIANE
Diagnosis is Now Easier



iGEM
PASTEUR
PARIS
2019



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...Mommy ? Does the doctor know what I have yet ?



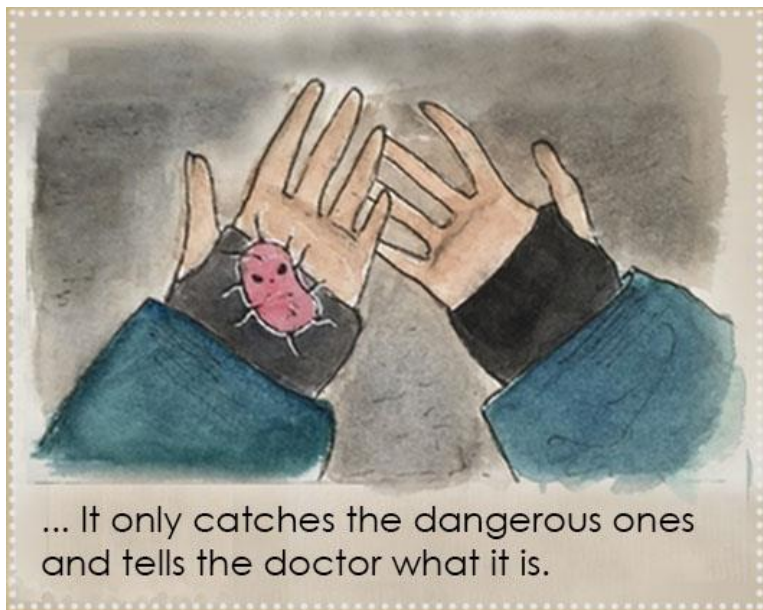
Don't worry sweetie, the results will be here soon, they are using Diane !



The doctor told me it's like an archer
who's bow & arrows are made out of DNA



It strikes fast and never misses its target.
From all the bacteria in your body...



... It only catches the dangerous ones and tells the doctor what it is.



Thanks to Diane, the doctor can then chose the right medicine that will cure you !

Abstract

Infectious diseases are one of the leading causes of death around the world, especially in developing countries. Worldwide, infectious diseases account for 40% of the total 50 million annual estimated deaths. 700 000 of these deaths are due to infections caused by resistant bacteria, with up to 25 000 in Europe alone [1]. Antimicrobial resistance is a major concern as the excessive use of antimicrobial drugs is not only making the microorganisms resistant, but as a result also causing severe infections, which are becoming harder to treat. Current diagnostic methods often require bacterial culture¹, implying at least 24 hours of incubation, which is not ideal for time sensitive clinical cases. In this context, improving the speed, sensitivity, and specificity of bacterial detection is crucial. Our project aims to create a portable, precise and rapid device for diagnosis, in order to detect pathogens by using an aptamer²-based sensing electrode³.



¹Bacterial culture: develops when microorganisms are cultivated. The microorganisms grow by cell division in media (a substance containing nutrients).

²Aptamer: RNA – sequence that can bind a specific molecule. Once this molecule binds to the aptamer the product can be synthesized by the cell. If this molecule isn't bound to the aptamer, the aptamer prevents the synthesis of the product.

³Electrode: electrical conductor.

Reference:

[1] INSERM, "Résistance aux antibiotiques", INSERM, online since the 22/03/18, available on:

www.inserm.fr/information-en-sante/dossiers-information/resistance-antibiotiques, visited the 11/04/19

Team Pasteur Paris



Team members

CAMBON Elise, DELAMARE Clara, Fournier Tara, Durix Léa,
MOSAGNA Quentin, SABATOU Marie, SAVERAT Vincent,
SOUDY Ronan, VIGNE Laurence, ZIDAT Alexandre

Coach members: CHARENDOFF Chloe, MAZZUOLI Maria
Vittoria, DE JODE Mathieu, PI GOPAUL Deshmukh

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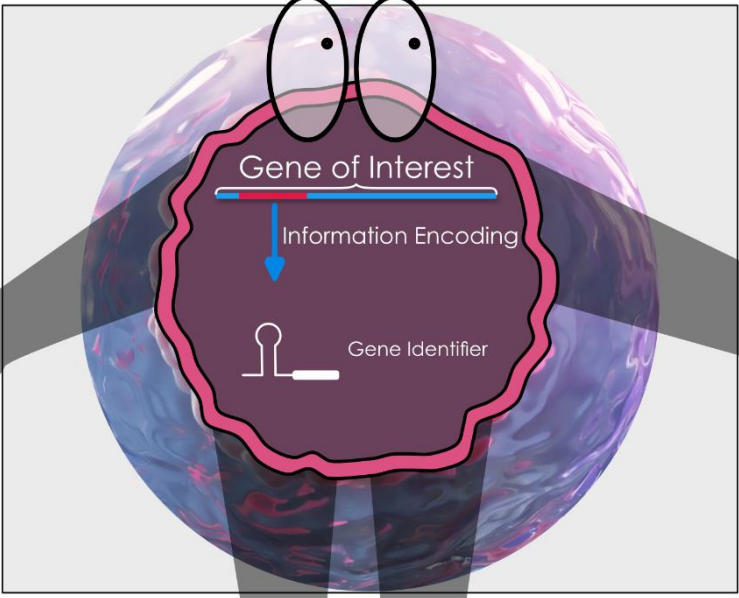
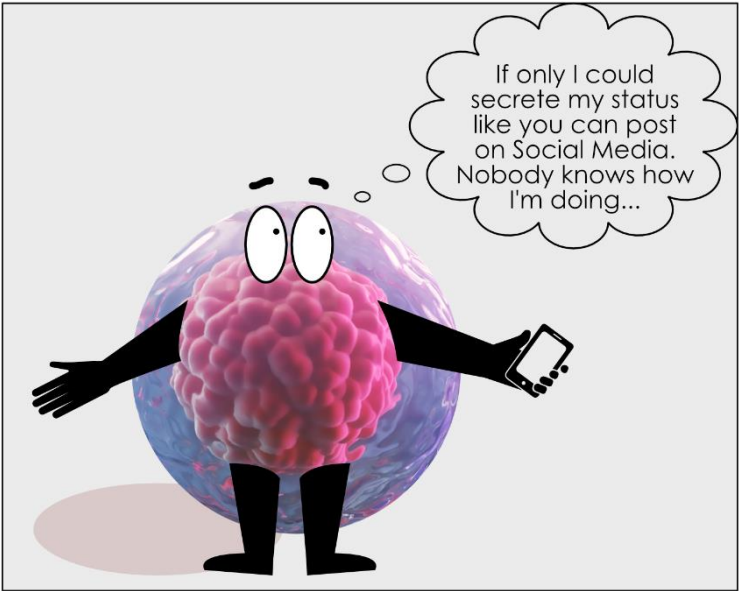


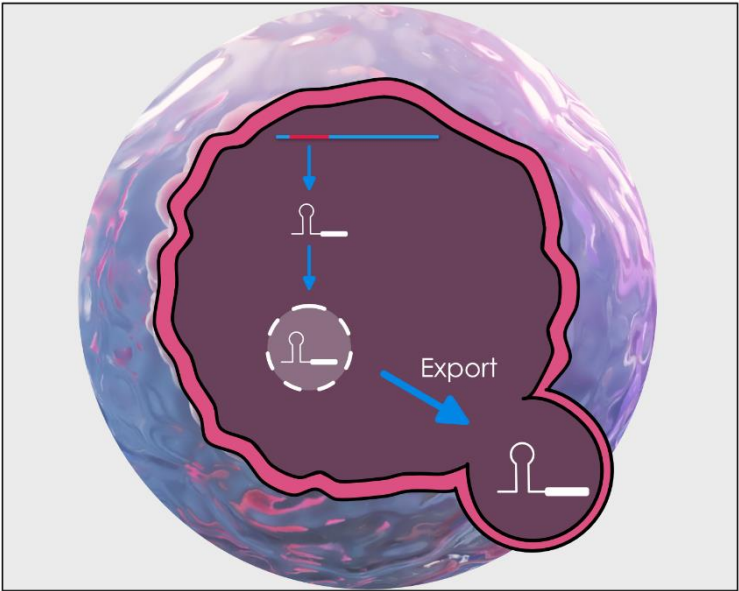
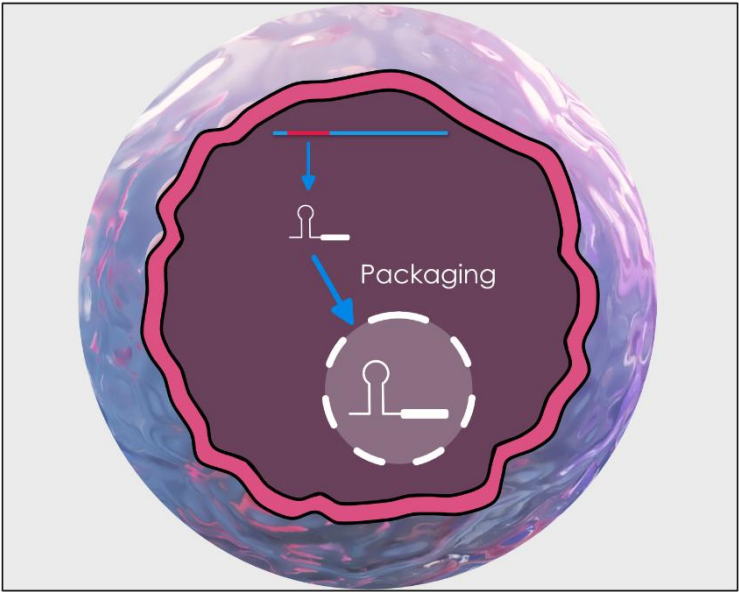
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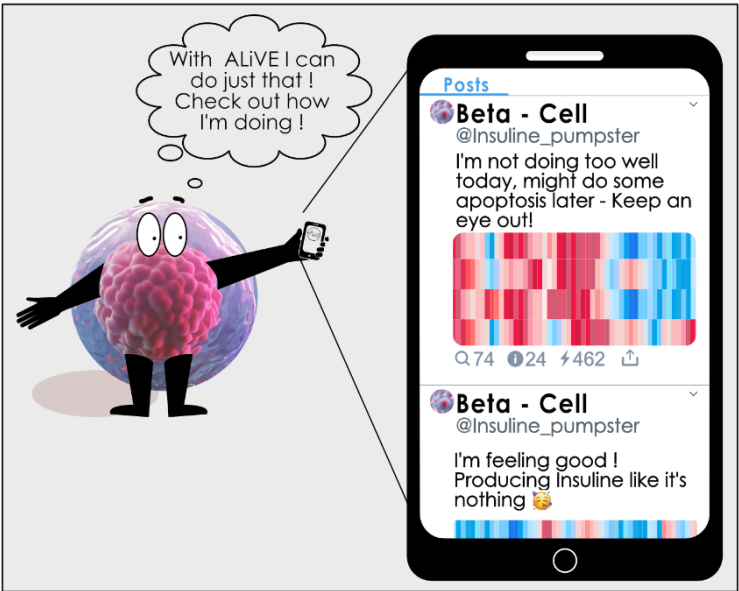
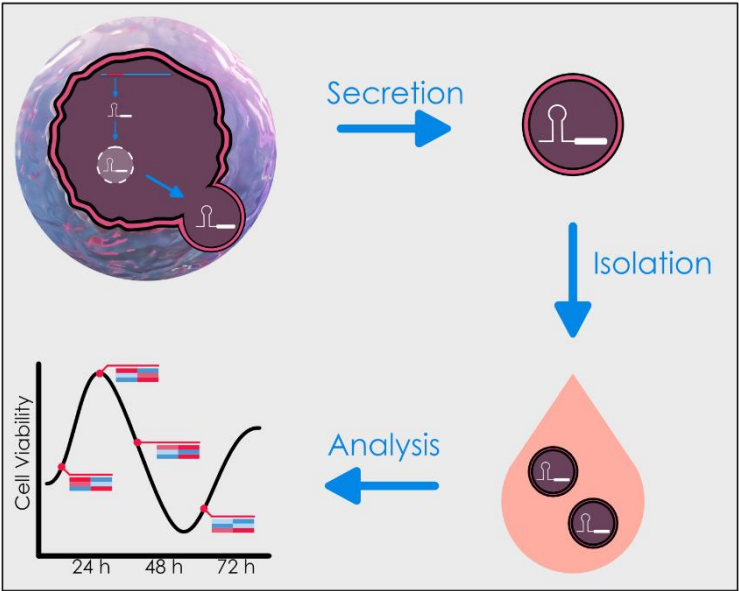
ALiVE



Analysis of Living cells by Vesicular Export







Abstract

New therapeutic methods like CAR-T cell therapy¹ have great potential for treating patients, who have cancer, but also brings new problems to research. Transplanting engineered cells² into a patient requires monitoring of these cells to make sure they fulfill their correct function and don't mutate or go rogue. Until now, monitoring the cells' status requires their destruction which is not optimal as the cells are the therapeutic agents in this kind of therapy. The new modular platform we are developing tackles this problem by enabling non-invasive monitoring of the state of a cell at different points in time while leaving the cells alive. In order to achieve this, we engineer cells to pack specific information in form of mRNA³ into vesicles⁴. The vesicles are then secreted and purified from the extracellular fluids, allowing continuous long-term monitoring of the cells' status over transcriptome⁵ analysis.



¹CAR-T-cell therapy: Chimeric antigen receptor T cell therapy, in which T-cells (cells of the immune system) have been engineered to kill specific cells e.g. cancer cells.

²Engineered cells: cells that are changed to do a user-based task.

³mRNA: a gene – a DNA sequence is transcribed (synthesized) into mRNA. mRNA is translated (synthesized) into a protein via the ribosome, a ribozyme consisting of RNA and proteins. mRNA is therefore the bridge between DNA and proteins.

⁴Vesicles: a structure inside or outside a cell enclosed by a coat (lipids) and containing liquid and different compounds.

⁵Transcriptome: is the set of all RNA molecules in one cell or population of cells. The name stems from transcription, meaning the synthesis of RNA from an DNA template.

Team Munich



Team members

Alejandro Salinas Illarena, Alexander Henrici,
Anja Domadenik, Annika Elimelech, Johann Körner,
Johanna Wallner, Joshua Hesse, Moritz Hocher,
Richard Koll, Sarah Brajkovic, Theresa Keil

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Instagram: [igem.munich](https://www.instagram.com/igem.munich)



VOTRUM

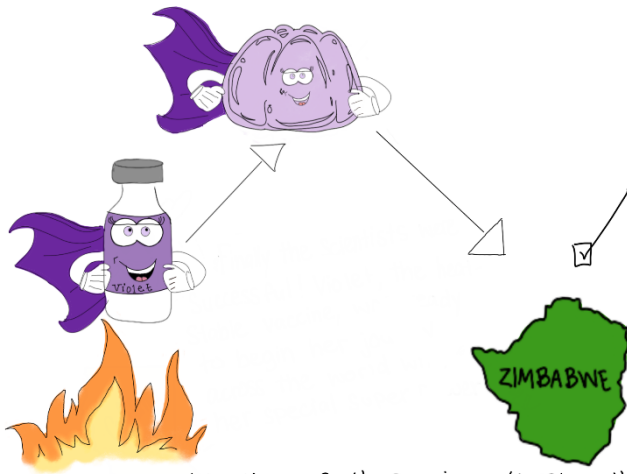
UCSC iGEM 2019



Once there was a Team of 16 undergraduates that wanted to use science to send medicine around the world.



They worked day and night for nine months to develop a vaccine formulation strong enough to survive worldly conditions and Break the cold chain.



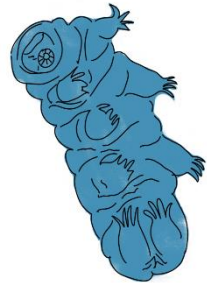
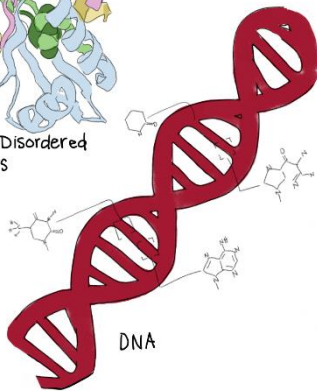
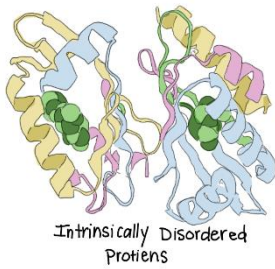
Through the combination of these ingredients the scientists created violet, the super vaccine, able to resist denaturation from high temperatures by taking on a gelatinous form.



Violet arrived to the Zimbabwe Animal Hospital where she sat on the shelf for over 12 months as seasons changed just waiting to do her job.



The scientists used :



Abstract

Around the world, many people lack access to vaccines as a result of the cold chain¹. To alleviate this issue, the University of California, Santa Cruz (UCSC) 2019 iGEM team, Vitrum, is developing a heat-stable vaccine formulation. Our novel approach uses intrinsically disordered proteins² (IDPs) to protect the LaSota vaccine strain for Newcastle disease. Newcastle disease virus (NDV) is highly infectious among avian species, most notably chickens. This can result in the euthanasia of an entire flock to prevent further spread of the disease (Spickler, 2016). The IDPs we use may contribute to survival under extreme conditions such as temperatures of up to 150°C and desiccation (Horikawa, 2012). We hypothesize our method will protect the vaccine by preventing the aggregation³ of viral proteins after exposure to heat.



¹The cold chain: is the series of actions and equipment to maintain a product within a specific low temperature range from production to usage.

²Intrinsically disordered proteins: these proteins lack a fixed 3D-structure, but remain functional.

³Aggregation: the local accumulation of molecules by binding to each other; in other words, the formation of assemblages. Proteins will not be accessible anymore to our cells and antibodies rendering the vaccine useless.

References:

A. R. Spickler.
Newcastle Disease. Avian Paramyxovirus-1 Infection, Goose Paramyxovirus Infection, Ranikhet disease
. Jan. 2016. 9 pp.

Daiki D. Horikawa. "Survival of Tardigrades in Extreme Environments: A model for Astro-
biology". In: Cellular Origin, Life in Extreme Habitats and Astrobiology.21

Team UCSC

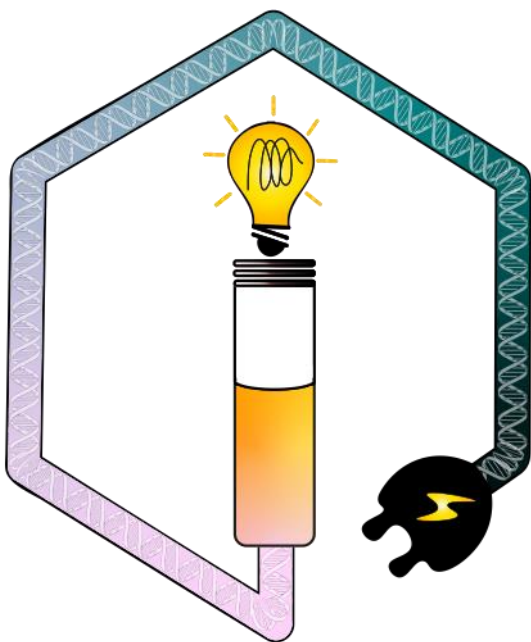


Team members

Andrew Zarzar, Aren Pageler, Ikenna Anigbogu, James Hahn, Jiasui Xu, Jonah Pierce, Liana Beld, Manpreet Kaur, Marcella Mirabelli, Marcus-Charles Strauss, Martina Pedersen, Melody Azimi, Nicolasa Cardenas, Rita Ousterhout, Shayan Vahdani, Varuna Dharasker

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facebook.com/ucscigem/
Instagram: @igemucsc

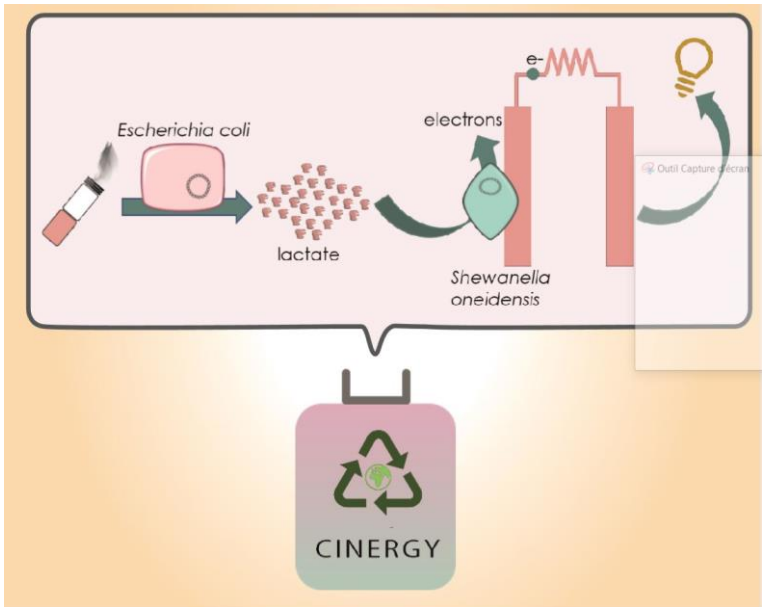
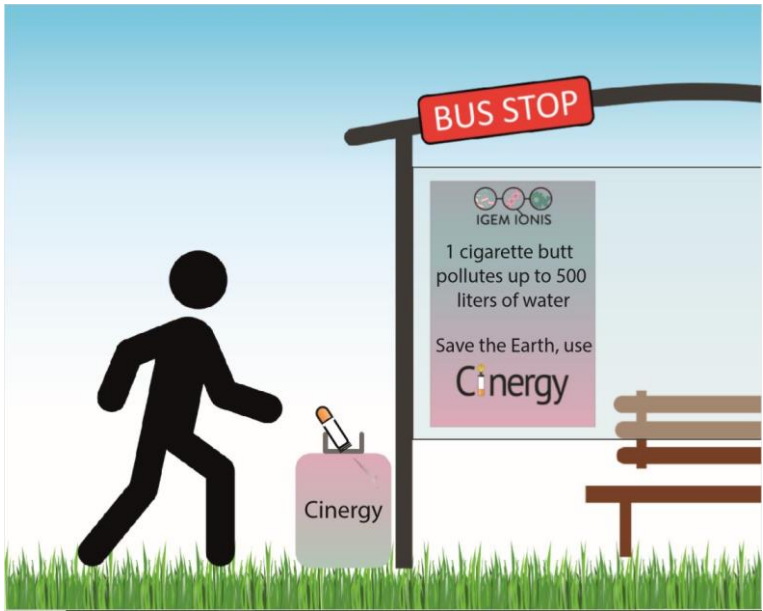


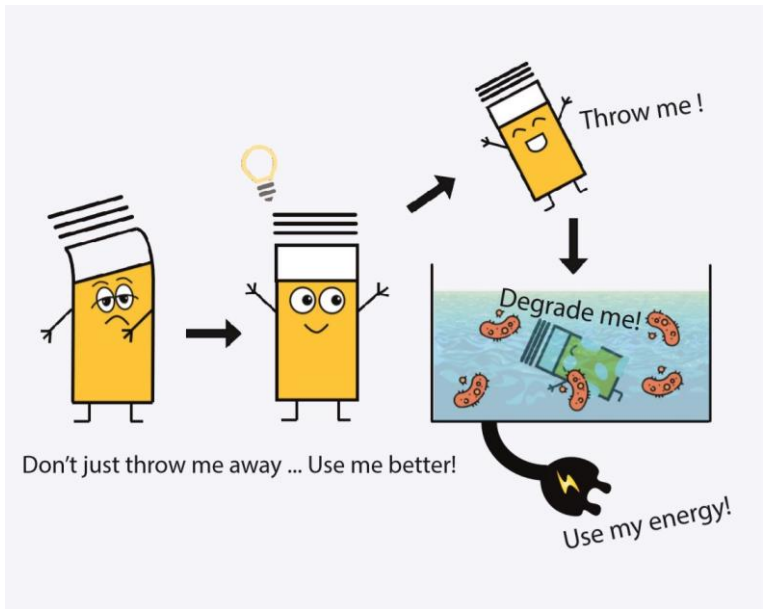


CINERGY

Recycle to preserve







Abstract

Cigarette butts represent a major danger to our environment, with one cigarette butt polluting up to 500 liters of water. Part of the international synthetic biology competition iGEM, our project Cinergy aims to add value to cigarette butts' filters, made of cellulose acetate (CA), by producing electricity. The microbial fuel cell used will include genetically modified bacteria, *Escherichia coli*¹ and *Shewanella oneidensis*², and be linked to a battery device. This system will contain two *E. coli* populations: the first one degrading the CA into substrate molecules to produce lactate and the second one producing flavins. These will be used by *Shewanella oneidensis* to produce a more efficient electrical current.



¹*Escherichia coli*: bacterium, that normally inhabits intestines of e.g. humans; often used for scientific research because its genome is well known, and lab protocols are very advanced.

²*Shewanella oneidensis*: bacterium, named after its first isolation from Lake Oneida, NY in 1988.

Team Ionis Paris



Team members

Research (biology) : Lucas Bourmancé, Julie Breiner,
Caroline Suant, Ambre Leleu

Research (electronics) : Hermann Cieur and Joachim Vu

Communication : Mathilde Barbier, Chloé Doizelet

Funding : Marina Firpion, Sarah Duquesne, Baptiste Rubino

IT : Anis Ladram, Augustin Chabrilac

Human practices : Mélissa Chagnaud and Eva Zanditenas

igemionis.com/en/
2019.igem.org/Team:ionis_Paris
Twitter: @IGEM_IONIS
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POP CULTURE

We will blow up your yeast!



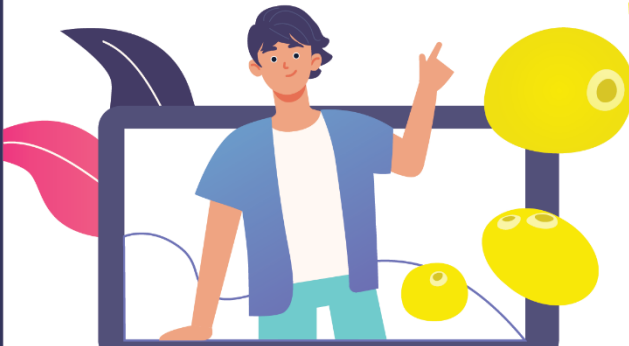
Do you know what
**BREAD, BEER AND
BIOFUEL** share in
common?



You might
think of a letter
in the beginning

B

ut the try similarity
lies in **YEAST**



Yeast can produce a lot of valuable compounds



however, this little factory has a rigid cell wall

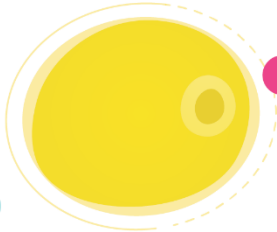
That's why the extraction of the compounds is **TIME AND COST CONSUMING**



IDEA

Introduce into yeast extra copies of

Repress activity of **enzymes** involved in cell wall biosynthesis



glucanases that are able to destroy the wall



yeast cell

POP CULTURE

will decrease time and costs associated with bioproduction

YOU will get stuff for cheaper



Abstract

Our goal is to develop the autolytic¹ yeast strain. The use of this strain as a basis for yeast cell factories will ease the extraction of valuable compounds from the cells and decrease the production cost. Usually, a chemical cell lysis² method is used, and it is quite expensive and time-consuming for large scale production.

We introduce extra copies of yeast genes³ encoding for cell wall⁴ degrading enzymes⁵ (glucanases) and modify some enzymes involved in the cell wall biosynthesis⁶. Firstly, we induce the production of glucanases and downregulate cell-wall synthesizing enzymes to make the cell wall weaker and to promote releasing of the cellular content into the media⁷. Then, we hope to develop a fully automated system to control lysis of the cells. The lysis will be activated automatically at a certain point of the cell lifespan (e.g. if the cell is old or has produced enough amount of final compound).



¹Autolytic: autolytic cells open up on their own without the need of adding chemicals or mechanical forces.

²Cell lysis: to open up cells.

³Genes: parts of DNA that encode information for components of the cell.

⁴Cell wall: a coat surrounding the cell; occurring in bacteria, plants and fungi.

⁵Enzyme: molecule which accelerates chemical reactions.

⁶Biosynthesis: production of substances by biological organisms.

⁷Media: substance containing nutrients for microorganism; can be liquidous or solid; microorganisms are either plated on solid media or put into liquid media for cultivation.

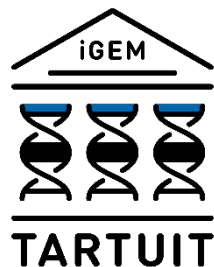
Team Tartu TUIT

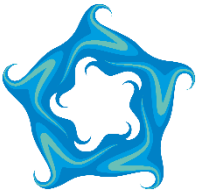


Team members

Valeria Leoshko, Nihat Aliyev, Huynh Ngoc Chau Phan,
Frida Matiyevskaya, Nadezhda Chulkova Irina Borovko
Aleksandra Panfilova, Turan Badalli, Kate Ponamareva,
Turgay Hasanov Dags Macs, Zafer Ahmad, Ruslan Sokolov,
Mark Merzlikin, Nikita Nesterenko, Jhalak Sethi, Gleb Kovalev,
Nargiz Kazimova

2019.igem.org/Team:Tartu_TUIT
www.facebook.com/iGEMEST/
www.instagram.com/igemestonia/
tartutuit@gmail.com



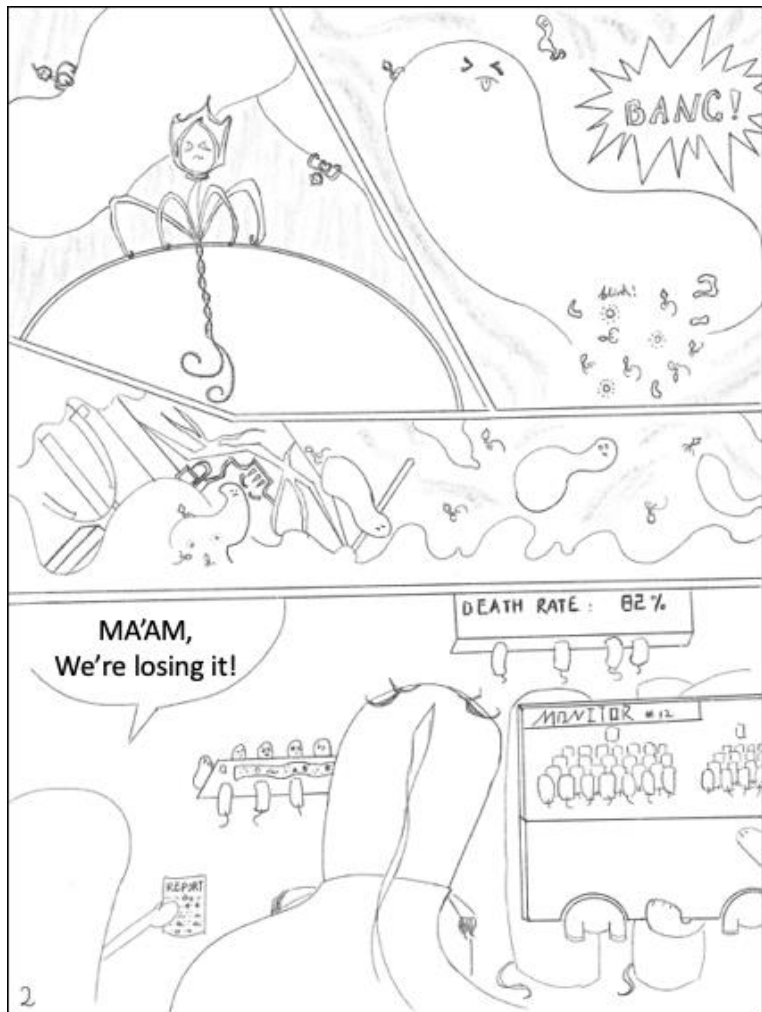


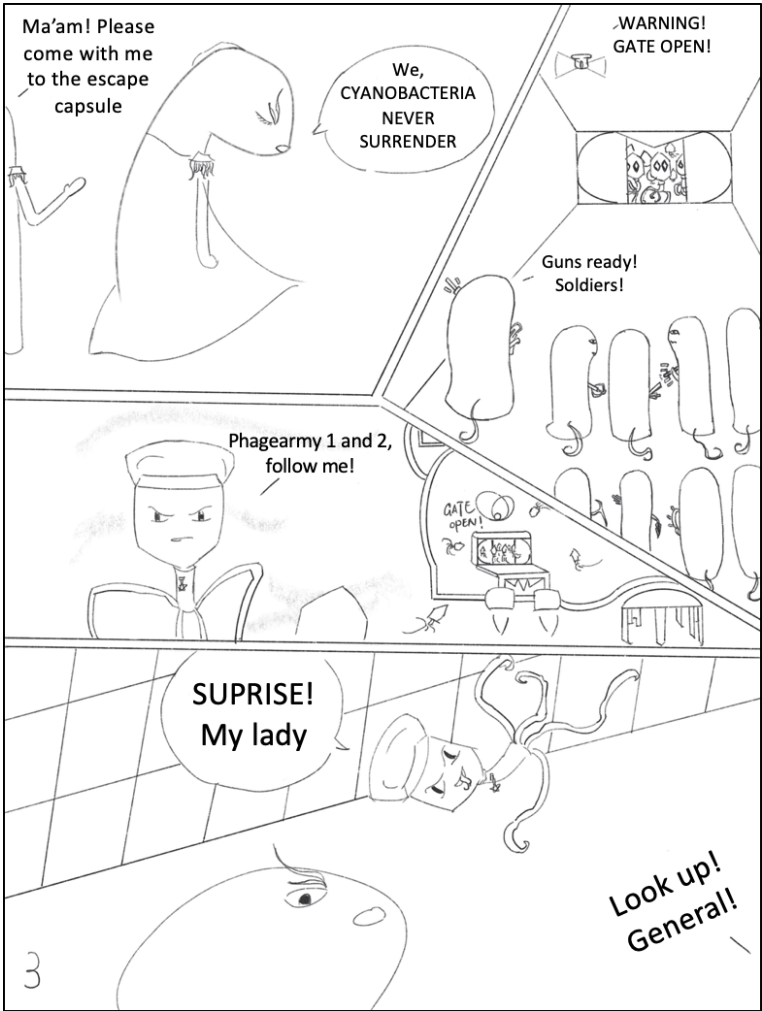
OCYANO

a new wave of sustainable solutions

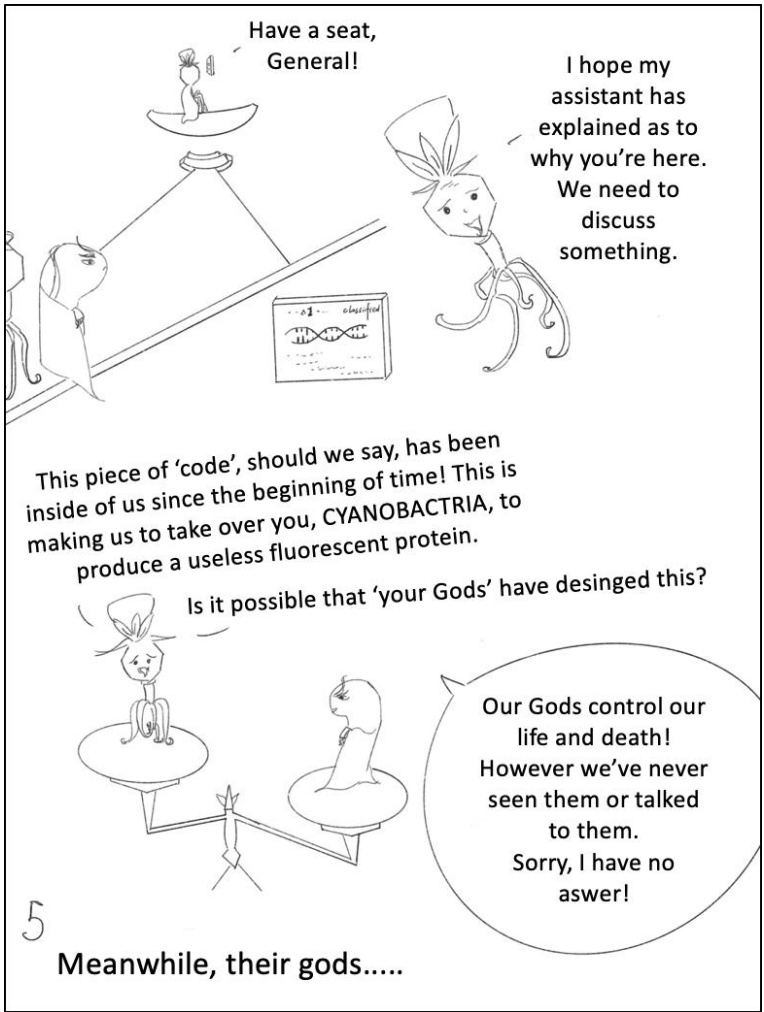
We're under
phage
attack!











Have a seat,
General!

I hope my
assistant has
explained as to
why you're here.
We need to
discuss
something.

This piece of 'code', should we say, has been
inside of us since the beginning of time! This is
making us to take over you, CYANOBACTERIA, to
produce a useless fluorescent protein.

Is it possible that 'your Gods' have desinged this?

Our Gods control our
life and death!
However we've never
seen them or talked
to them.
Sorry, I have no
answer!

5
Meanwhile, their gods.....

Abstract

In a world of increased urgency for durable sustainable solutions, the iGEM team of KU Leuven decided to focus on the development of alternative and more sustainable ways of enzyme¹ production. Our team project, Ocyano, explores using cyanobacteria as means of photosynthetic biomanufacturing², mitigating the need for large amounts of growth media³ required by classic heterotrophic⁴ expression systems. Two systems are investigated. Firstly, a recently discovered ultra-fast-growing cyanobacterial strain will be engineered for protein expression and secretion. The growth rates of this strain are comparable to fungi and *e. coli*⁵, and its competitiveness with these traditional systems will be investigated from an economical point of view. In a second system, phages⁶ are used to open up cyanobacteria to harvest its enzymes, that are needed in the industry. This last system introduces a new cheap production method, as it allows to harvest the ocean as a biomass resource.



¹Enzyme: molecule which accelerates chemical reactions.

²Biomanufacturing: a type of manufacturing that uses biological systems to produce commercially important molecules like drugs and vitamins.

³Media: substance containing nutrients for microorganism; can be liquidous or solid.

⁴Heterotrophic: mode of nutrition in which organisms depend on other organisms (organic compounds e.g. plants, meat).

⁵*E. coli*: *Escherichia coli*, bacterium, that normally inhabits intestines of e.g. humans; often used for scientific research because its genome is well known, and lab protocols are very advanced.

⁶Phage: a virus that infects and replicates within bacteria and archaea.

Team KU LEUVEN



Team members

Senne van den Broeck, Bas Moonen, Francheska Cadacio,
Yuansheng Lu, Konrad Joseph Migacz, Bert Karine Karel
Callens, Nikoleta Boron, Anke Nauryzgaliyeva, Amber Lesage,
Lore De Valck, Lucas Coppens, Federica Mare, Erik Tedre

2019.igem.org/Team:KU_LEUVEN
www.igemleuven.be/
[instagram.com/kuleuvenigem/](https://www.instagram.com/kuleuvenigem/)
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KU LEUVEN



MEDEA

Machine-Enhanced Directed Evolution of Aptamers

AGGTCCATGATTCTGT

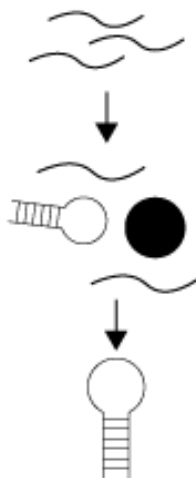
UUAGCAACGAUC



AGGTCCATGATTCTGT

Aptamers
are *short*
DNA or RNA molecules
that bind targets with
high affinity and specificity

Currently,
SELEX is used to
identify new aptamers.
An initial pool of sequences is
incubated with the target
and,
through
multiple rounds
of selection,
aptamers that bind the target
are identified



SELEX has **drawbacks**



Up to **6 months** to identify new aptamers



Expert knowledge is **required**.

SELEX uses non-physiological conditions,
aptamers not fully functional *in vivo*



Cost of materials and experts required
do not allow its application
in many labs



Aptamer sequence
AGGUCCAUGAUUCGU

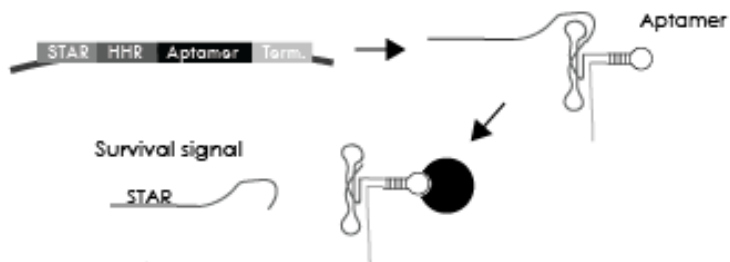


ACGUCCGUGAUCCAU



MEDEA revolutionises

this process by combining
a computational pipeline,
generating aptamer sequences
against a target, which
are further **refined** through
in vivo directed evolution.



Our design allows for selection during the aptamer evolution.

When the aptamer **successfully binds** the target in vivo, the cell **survives**.
If *no binding* occurs, the cell *dies*.
This way, there is **selection pressure** to evolve better aptamers.

Why it is important?



Simple



Lower costs

Accessible
medicine



Abstract

This year, our team is working on developing an innovative, but also effective and affordable way to synthesize aptamers¹ in vivo². More specifically, we suggest a system based on **the directed evolution³ of aptamers guided by in silico design⁴**. Our project aims at the creation of a genetic⁵ system, which will introduce random mutations^[1] in a known aptamer and select the ones with the highest binding affinity⁶ to the chosen target molecule. The initial sequence of the aptamer will be designed using bioinformatic systems and subsequently, the project will be realized through the experiments we will carry out in the lab (wet lab) and with the help of computer design (dry lab).



¹Aptamer: RNA – sequence that can bind a specific molecule. Once this molecule binds to the aptamer the product can be synthesized by the cell. If this molecule isn't bound to the aptamer, the aptamer prevents the synthesis of the product.

²In vivo: in living organisms.

³directed evolution: mimics the process of natural selection to generate a user-defined molecule.

⁴In silico design: performed on computer or via a computer simulation.

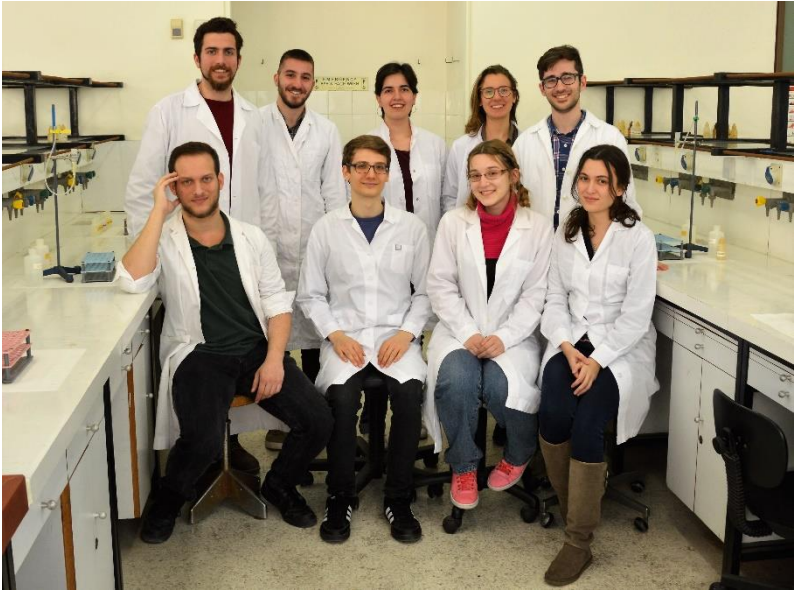
⁵Genetic: based on genes; a gene is a DNA-sequence encoding compounds for the living cell.

⁶Binding affinity: indicates how strong something (e.g. a specific molecule) binds to something else (e.g. aptamer).

Reference:

[1] [Shakked O., Halperin, Connor J. Tou, Eric B. Wong, Cyrus Modavi, David V. Schaffer & John E. Dueber](#) **CRISPR-guided DNA polymerases enable diversification of all nucleotides in a tunable window**, *Nature* volume 560, 248-252 (2018)

Team Athens



Team members

Anastasios Galanis, Maria Eleni Depian, Theofano Zoumpou,
Nikolaos Karvelas, Alexandra Karvela, Nikolaos Kalavros,
Iason Milionis, Iason Papadopoulos, Anna Maria Tsiatsiani

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DNA 
 **FREE** 
POETENTIAL

WHAT CAN POSSIBLY BE DONE
WITH A DNA FREE CELL ?



HEA
UN
HE
E



A POET BACTERIUM
WHOSE
EMPTINESS
REVEALS
UNEXPECTED
POEMS?



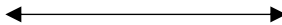
A PREHISTORICAL
DNA-FREE
BACTERIUM
THAT TELLS
US MORE
ABOUT OUR
ORIGINS?

THIS DNA-FREE BACTERIUM
IS AT THE SAME TIME
A LIVING POET,
A LEAP TO THE FUTURE
AND...



Abstract

To reinforce the link between synthetic biology and society, we act on two main axes: at the scientific level, we propose to increase chassis¹ safety by removing its genomic DNA thanks to newly described BioBricks² such as an original phage³ nuclease⁴. And at the artistic level, we have developed a new concept based on an artistic performance emphasizing the potential of DNA-free cells. Each experiment (about security, depollution, return to RNA primitive world, modelling of DNA-free-cell fate) is associated with a synthetic poem. The concept of a DNA-free cell is suitable to explain many fundamental and applied aspects of synthetic biology. We intend to use art as a universal way of communication to stimulate the dialogue between scientists and society about synthetic biology.



¹Chassis: the organism you change (genetically).

²BioBrick: a DNA sequence conforming to certain design rules to make them usable for every synthetic biology scientist; e.g. insertion of restriction enzyme sites. BioBricks are building blocks to design and assemble larger synthetic biological circuits from combining them to produce a certain function e.g. CO₂-fixation.

³Phage: a virus that infects and replicates within bacteria and archaea.

⁴Nuclease: enzyme⁵, which breaks down nucleic acids e.g. DNA.

⁵Enzyme: molecule which accelerates chemical reactions.



Team GO Paris-Saclay



Team members

Julien Herbelot, Hugues Herrmann, Lucas Larquet, Brahim Essadki,
Lucas Fucher, Clara Diaz, Colombe Maréchal, Marie Hautbois,
Natacha Mone, Laura Venezia, Arnaud Boudigou, Yacine Lyaoui,
Sarah Hammou, Guillaume Garnier

igem.parissaclay@gmail.com

twitter: @iGEMParisSaclay

Instagram: @igemgoparissaclay

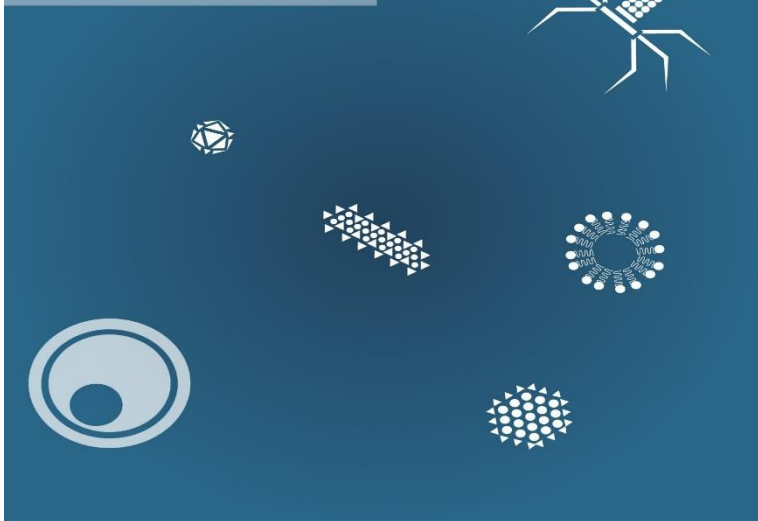


GO PARIS SACLAY
IGEM

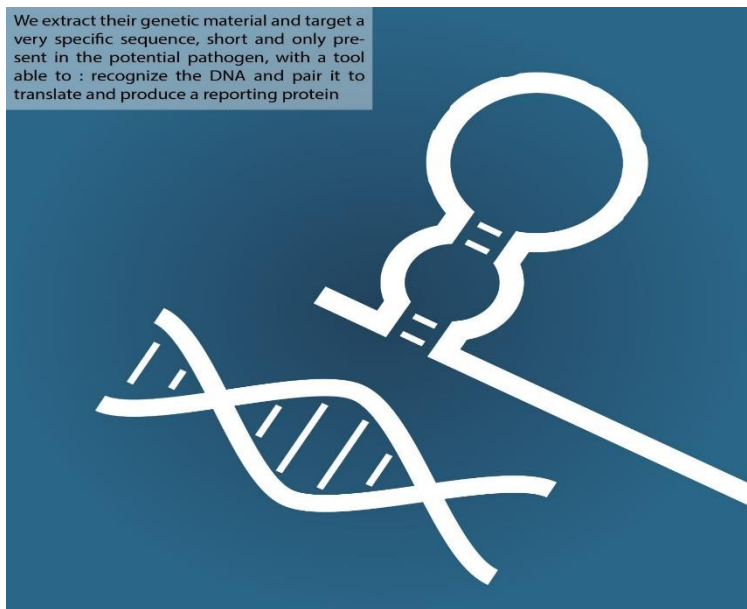


**TEAM IGEM
ULaval**

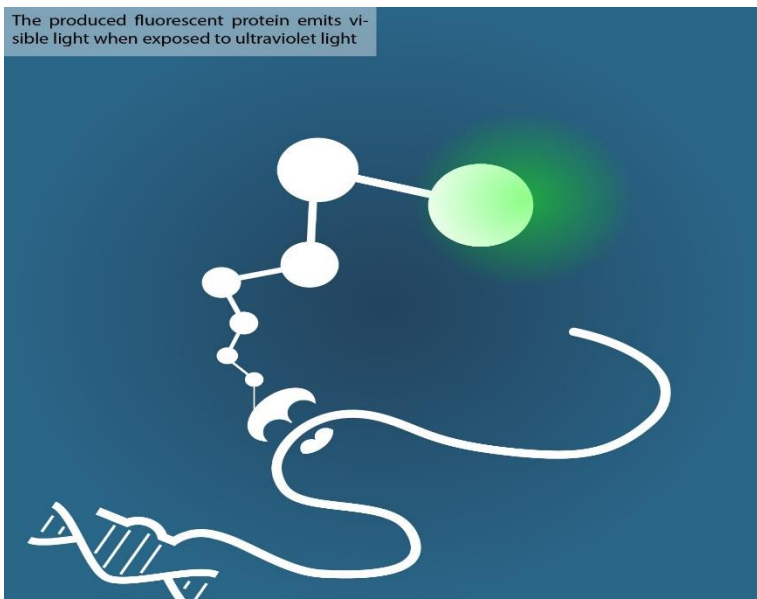
Some infections can be acquired through air. Our goal is to detect the presence of specific contaminants and pathogens by sampling and analyzing the air content



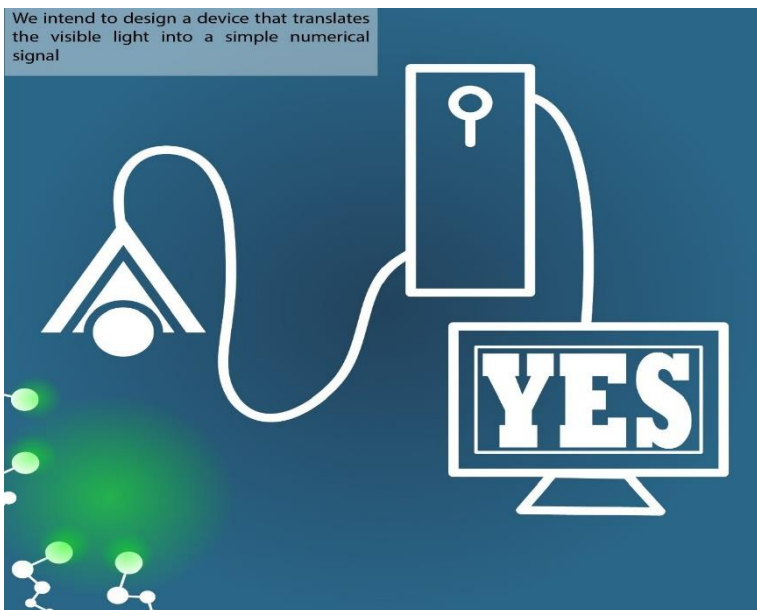
We extract their genetic material and target a very specific sequence, short and only present in the potential pathogen, with a tool able to : recognize the DNA and pair it to translate and produce a reporting protein



The produced fluorescent protein emits visible light when exposed to ultraviolet light



We intend to design a device that translates the visible light into a simple numerical signal



We are working on a software too. It designs the specific sequences for you depending on the target organism



Our system could be of use in the food, medical and transportation industries, as well as for any epidemiological application



Abstract

A.D.N., or Airborne Detector for Nucleic Acids, aims at improving air quality control in environments such as hospitals and nursing homes by creating an all-in-one and easy-to-use device to collect and detect human viral pathogens in the air. Using riboregulatory¹ elements called Toehold switches² as a detection method, our instrument is designed to recognize specifically the poxvirus (chickenpox), the norovirus (gastroenteritis) and the measles virus. Our project will help further the knowledge on aerial viral transmission in epidemic context and will be a cornerstone in implementing air quality control procedures to prevent these potentially deadly nosocomial³ infections.



¹Riboregulatory: a riboregulator is an RNA that regulates the expression of itself or another nucleic acid in response to a specific signal.

²Toehold switch: is an RNA that encodes the sequence of a protein (any protein you are interested in synthesizing). The synthesis of this protein (translation) is turned off by the structure of the toehold switch (it hides the binding site from the ribosome, which is the synthesizing machinery, as well as the starting sequence of the protein sequence. However, when a target RNA is present, it binds to the Toehold switch and thus changes the structure of the toehold switch. Now the protein can be synthesized, because the ribosome binding site and the starting sequence are no longer hidden. The ribosome now can bind to its binding site on the Toehold switch and synthesize (translate) your protein of interest.

³nosocomial: (of a disease) originating in a hospital.

Team ULaval



Team members

Catherine Marois, Elodie Gillard, Florian Echelard,
Francois Rouleau, Lucas Germain, Marianne Côté,
Nathan Dumont-Leblond, Pascale Lemieux, Martine Voisine,
Angel Cisneros, Jean-Michel Proulx, Karine Bouchard,
Carla Bautista Rodriguez, Guillaume Fournier, Julien Roy

2019.igem.org/Team:ULaval





iGEM
ERLANGEN

The logo for iGEM Erlangen features the text "iGEM" in a dark blue, sans-serif font. The lowercase "i" has a small green circle above it. Below "iGEM" is a horizontal line composed of several colored segments: a purple pentagon on the left, a blue segment, a green segment, a blue segment, and a yellow triangle on the right. Below this line, the word "ERLANGEN" is written in a multi-colored, sans-serif font, with each letter having a different color: E (orange), R (orange), L (orange), A (orange), N (orange), G (pink), E (pink), N (pink).



Abstract

We are the iGEM Team Erlangen 2019 and we create a bispecific antibody¹ (in the comic it is called bite) to recruit the T-cells² of our immune system to the colorectal³ cancer cells, whereby the T-cells kill the cancer cells. The bispecific antibodies help the T-cells to find the cancer cells by accurately binding to the surface molecules GPA33, which are on colorectal cancer cells, and to CD3, which are on the T-cells. Our treatment is an additional method to chemo- and radiotherapy to fight cancer.



¹Bispecific antibody: an antibody that does not only bind one specific molecule but two specific molecules.

²T-cells: are cells of the human immune system, they recognize exogenous molecules on the surface of our cells (exogenous molecules from viruses and bacteria are presented on infected cells). After T-cells recognize these molecules on the surface of infected cells, they can develop into cytotoxic T-cells that kill the infected cell, T-helper cells that alarm the immune system or regulatory T-cells that prevent an overreaction of the immune system e.g. killing healthy cells.

³Colorectal: relating to or affecting the colon⁴ and the rectum.

⁴Colon: the large intestine.

Team FAU Erlangen



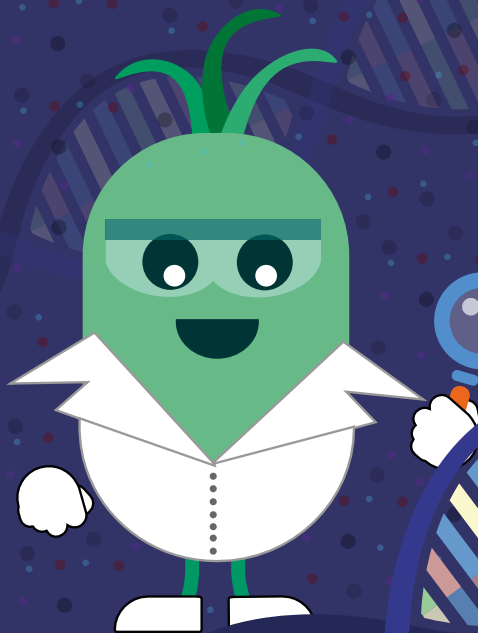
Team members

Leon Altmann, Selina Beck, Manuel Blank, Martin Borgmann,
Jule Brenningmeyer, Franziska Brodewolf, Ruben Caspary,
Verena Dietrich, Steffen Docter, Sirka Dormeyer,
Franziska Eidloth, Florian Fischer, Lea Grabmann,
Oliver Hirschmann, Markus Ingold, Alexander Kaier,
Antonio Maccataio, Valentin Müller, Eva Neugebauer,
Nadja Nolte, Felix Pfister, David Rüscher, Evelyn Schläfke,
Mortiz Schmidt, Lena Schorr, Marie Steffensen,
Anna Vandebosch, Lisa Vogg, Jannik Wagner,
Sven Waldmannstetter, Marie Wiedemann, Florian Wolz,
Linkai Zhang, Andreas Zink

2019.igem.org/Team:FAU_Erlangen

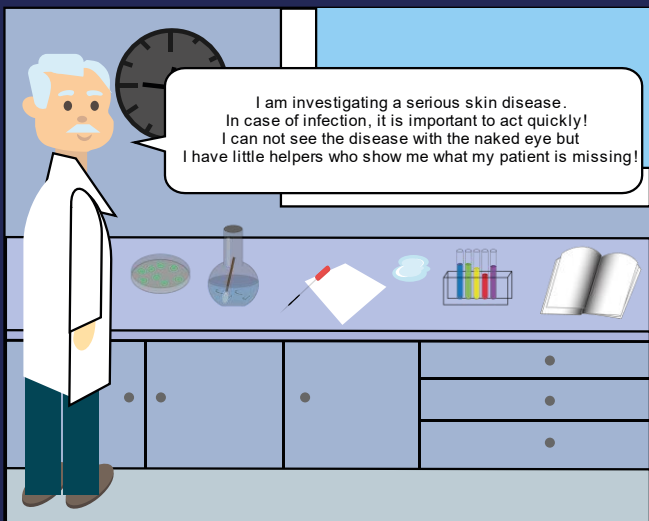


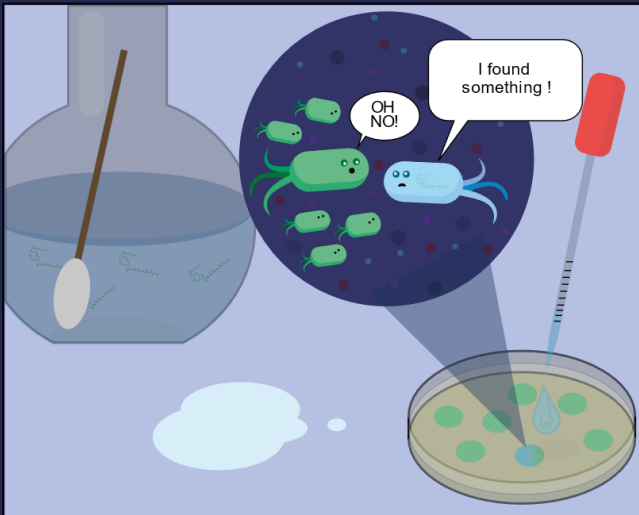
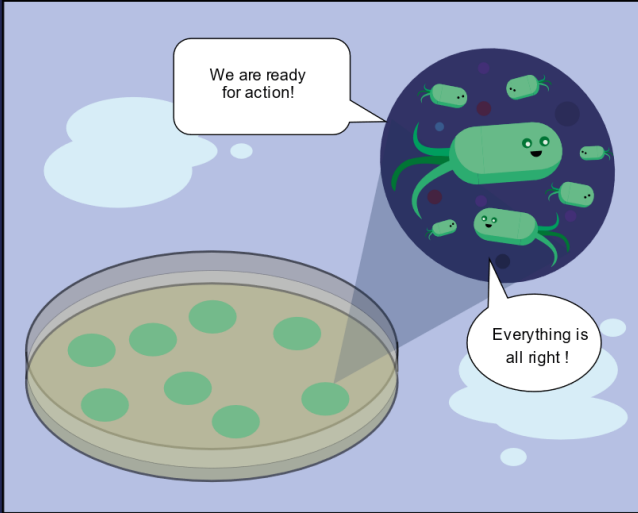
Dr. Coli's Adventures

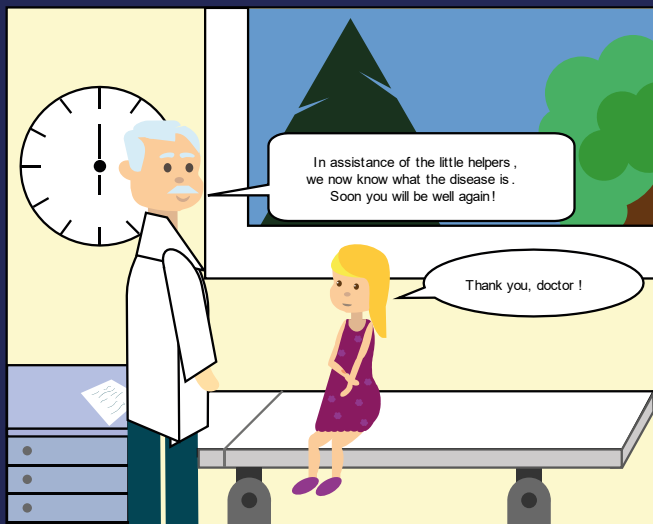
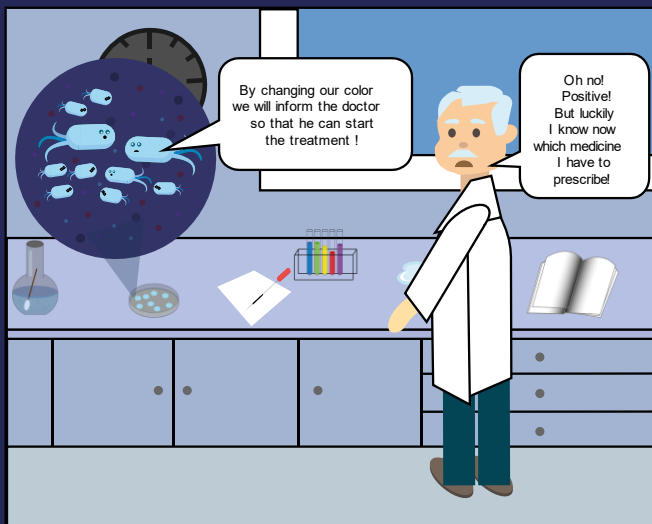


Mycolactone
Diagnostics







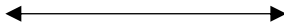


Abstract

Buruli Ulcer, an infectious disease caused by *Mycobacterium ulcerans*¹, is affecting thousands of people particularly in poor rural areas in Africa, Australia and Asia.

An early diagnosis of the disease is crucial for a proper treatment with antimycobacterial drugs. Established diagnosis methods are either too expensive, too insensitive or take too long.

Therefore, the aim of our 2019 iGEM project is to develop a fast, cheap and specific diagnostic test. Our approach includes the genetic modification of *Escherichia coli*² to generate a blue color in the presence of *M. ulcerans*. The diagnostic tool is based on an aptamer³ to which mycolactone, a toxin excreted by *M. ulcerans*, can bind. Upon presence and binding of mycolactone to the aptamer, a blue color (amilCP) will be produced to give a swift and clear response. A signal enhancer allows cell-cell communication and increases sensitivity of this diagnosis method. A default signal for cell viability control is realized with green fluorescent protein⁴ (GFP).



¹*Mycobacterium ulcerans*: bacterium that occurs in humid regions of tropical and subtropical latitudes from Africa to Latin America and Asia to Australia. It causes a skin disease by producing mycolactone, a toxin, that kills skin cells and suppresses the immune system.

²*Escherichia coli*: bacterium, that normally inhabits intestines of e.g. humans.

³Aptamer: RNA – sequence that can bind a specific molecule. Once this molecule binds to the aptamer the product can be synthesized by the cell. If this molecule isn't bound to the aptamer, the aptamer prevents the synthesis of the product.

⁴Fluorescent proteins: are proteins that emit light when exposed to light in the blue to ultraviolet range. They exist in different colors and are applied in science for detection and visualization of events in cells and tissues.

Team BOKU-Vienna



Team members

Martina Helmlinger, Stefan Karl Kaufmann, Andreas Luntzer, Katharina Lunzer, Michaela Mechura, Vanessa Przybyłowicz, Tobias Redl, Isabella Rybar, Melanie Salek, Theodor Simak, Zuzana Simovic, Marta Śtadczyk, Valentina Stuchlik, Eugen Wilk

2019.igem.org/Team:BOKU-Vienna
Instagram: @igemvienna
Twitter: @igemvienna



The End