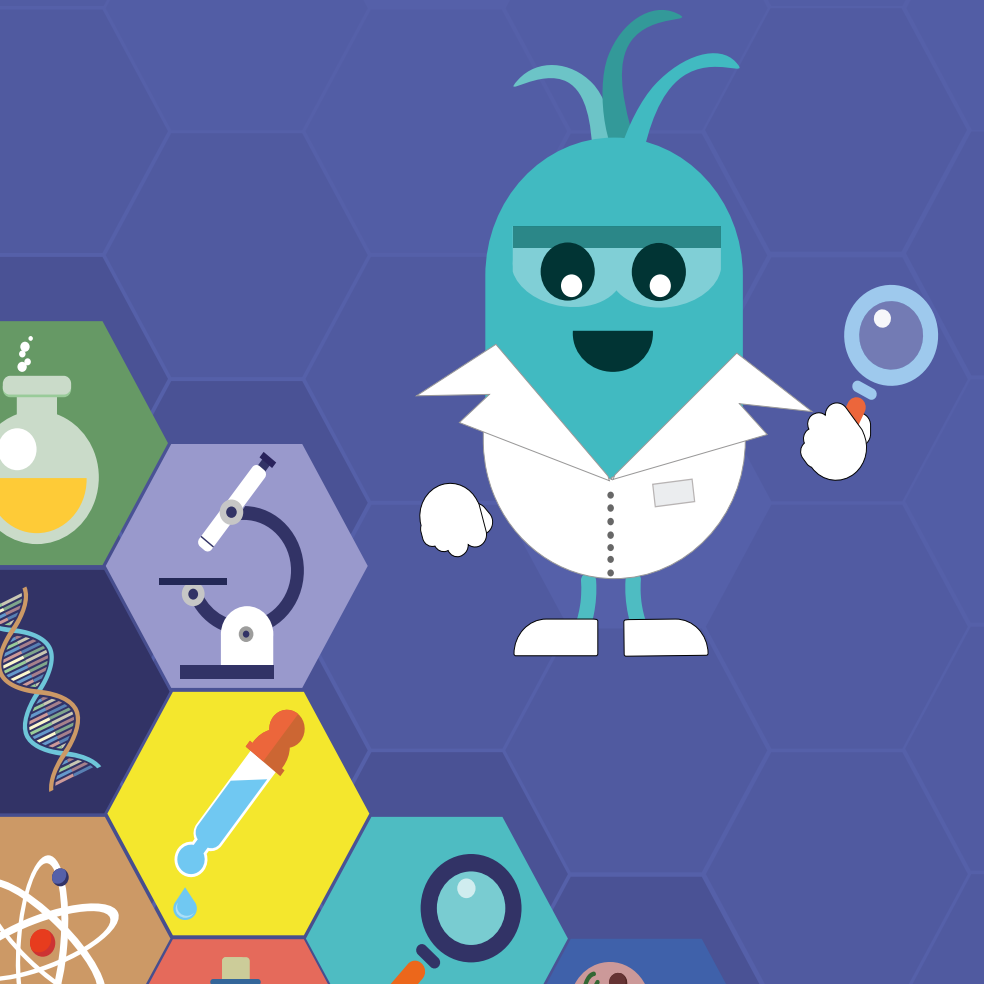
The wonderful world
of synthetic biology



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.

The Wonderful World of Synthetic Biology

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!

Table of contents

DIANE

Diagnosis is Now Easier

iGEM
PASTEUR
PARIS
2019

université PARIS-SACLAY

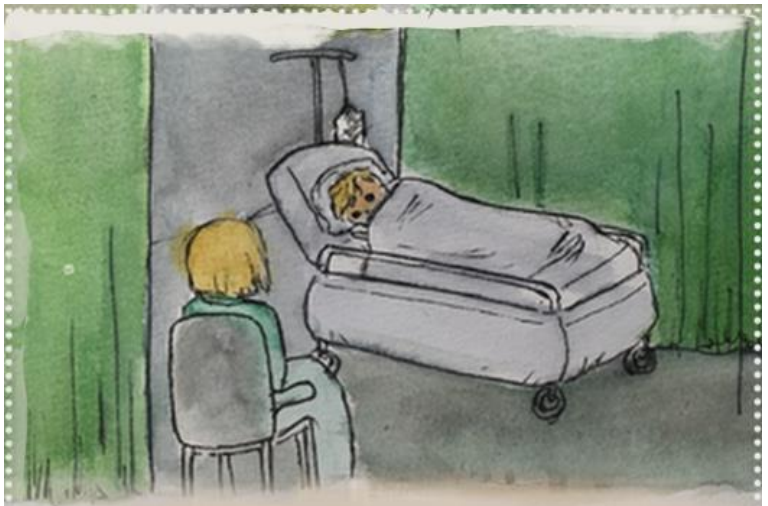
AgroParisTech

Chimie Paris ParisTech | PSL

SUP biotech

UNIVERSITÉ PARIS SUD
FACULTÉ JEAN HONNET
université PARIS-SACLAY

ESPCI PARIS | PSL



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

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

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 choose 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 culture[1], 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 aptamer[2]-based sensing electrode[3].

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

[2]Aptamer: 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.

[3]Electrode: 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

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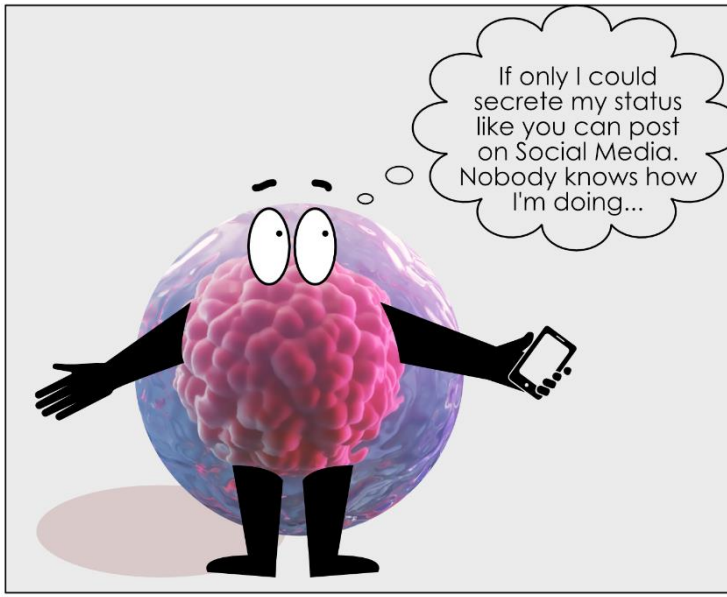
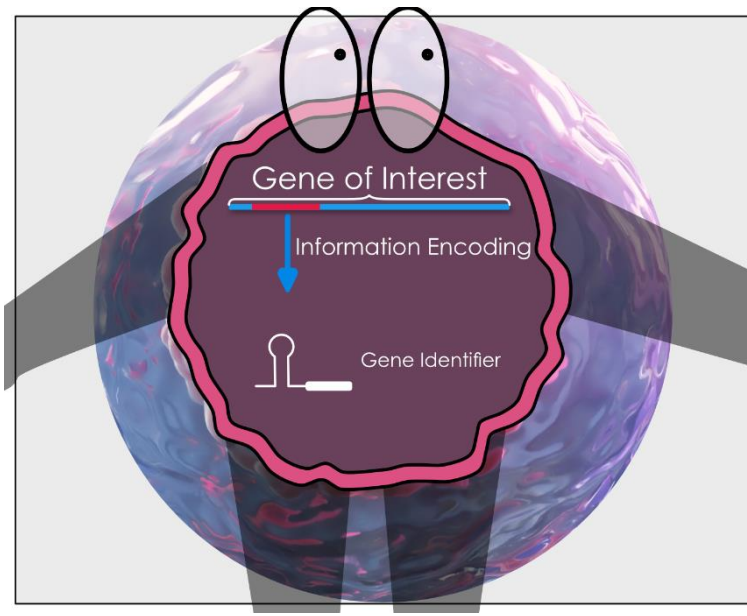
instagram.com/igem.pasteurparis/?hl=fr

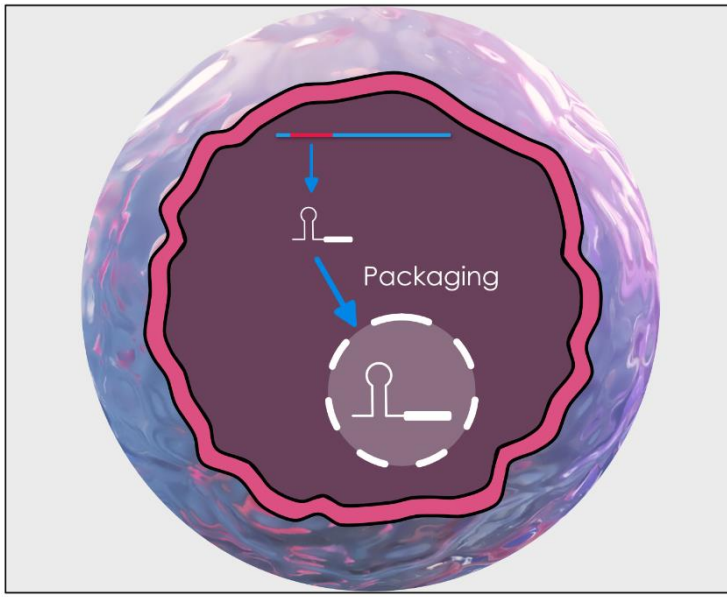
iGEM
PASTEUR
PARIS
2019

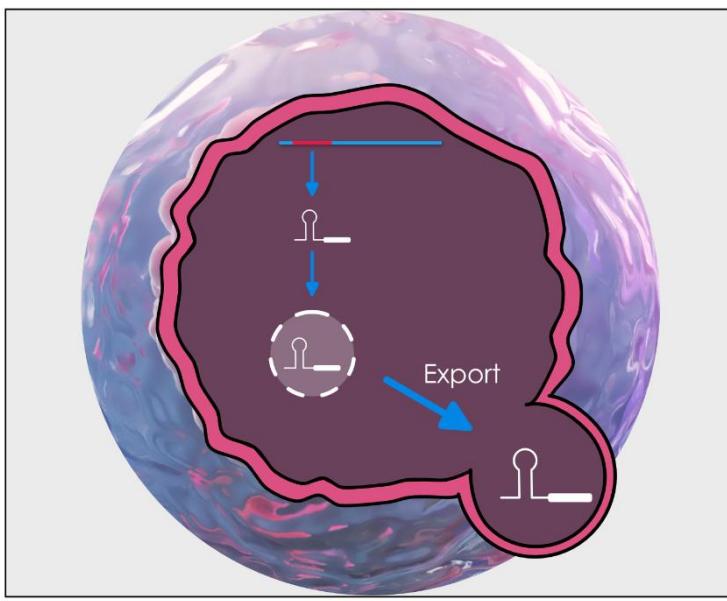
ALiVE

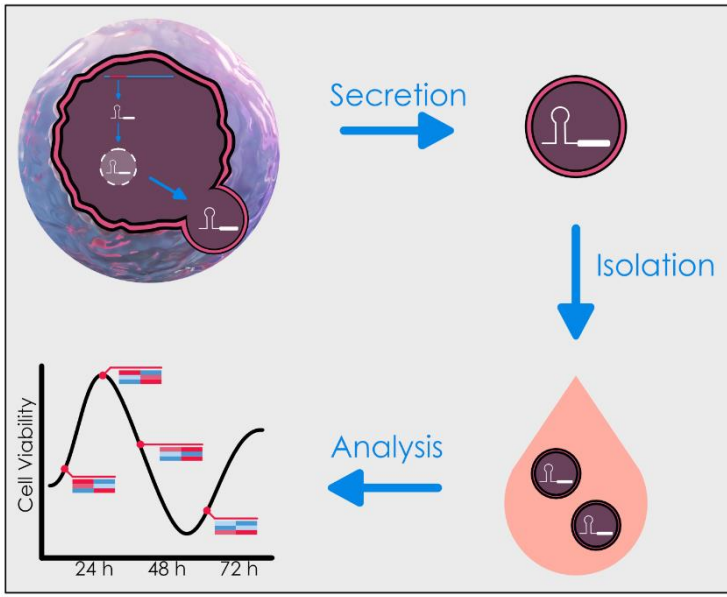
Analysis of Living cells by Vesicular Export

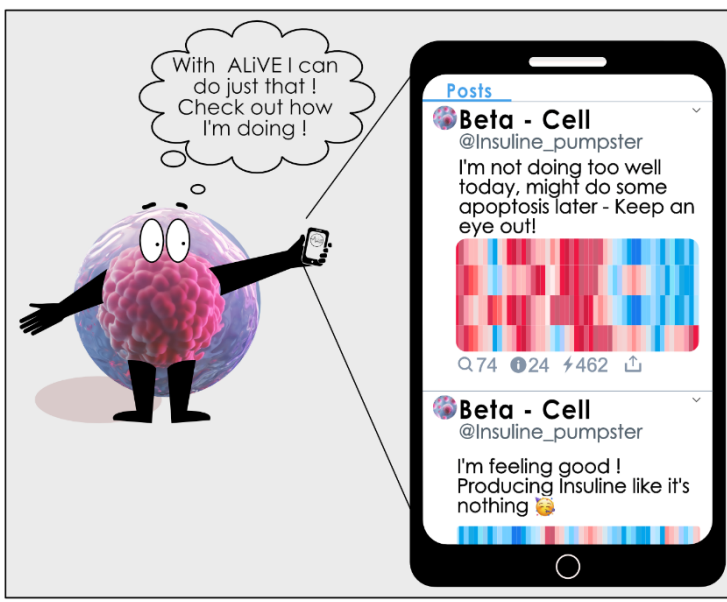

If only I could secrete my status like you can post on Social Media. Nobody knows how I'm doing...


Gene of Interest
Information Encoding
Gene Identifier


Packaging


Export


Secretion
Isolation
Analysis
Cell Viability
24 h
48 h
72 h


With ALiVE I can do just that ! Check out how I'm doing !
Posts
Beta - Cell
@Insuline_pumpster
I'm not doing too well today, might do some apoptosis later - Keep an eye out!
74
24
462
Beta - Cell
@Insuline_pumpster
I'm feeling good ! Producing Insuline like it's nothing

Abstract

New therapeutic methods like CAR-T cell therapy[1] have great potential for treating patients, who have cancer, but also brings new problems to research. Transplanting engineered cells[2] 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 mRNA[3] into vesicles[4]. The vesicles are then secreted and purified from the extracellular fluids, allowing continuous long-term monitoring of the cells´ status over transcriptome[5] analysis.

[1]CAR-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.

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

[3]mRNA: 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.

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

[5]Transcriptome: 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

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igemmunich.mwn.de/index.php/1-welcome-to-igem-munich.html
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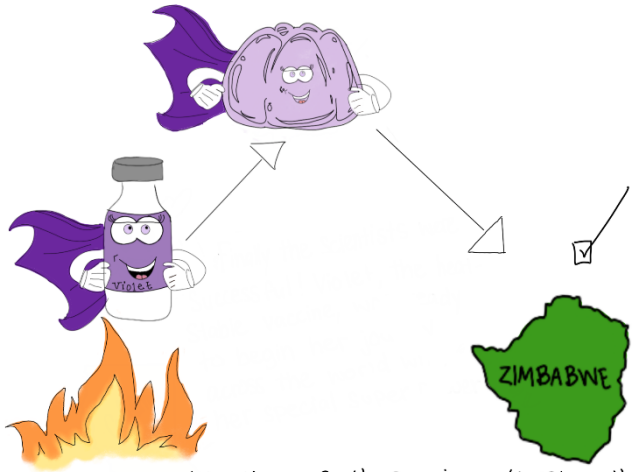
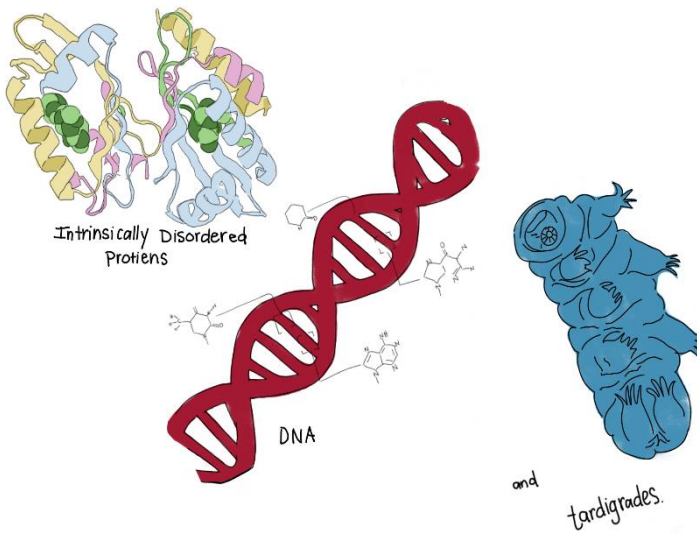
UCSC iGEM 2019

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



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

The scientists used:



Abstract

Around the world, many people lack access to vaccines as a result of the cold chain[1]. 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 proteins[2] (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 aggregation[3] of viral proteins after exposure to heat.

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

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

[3]Aggregation: 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

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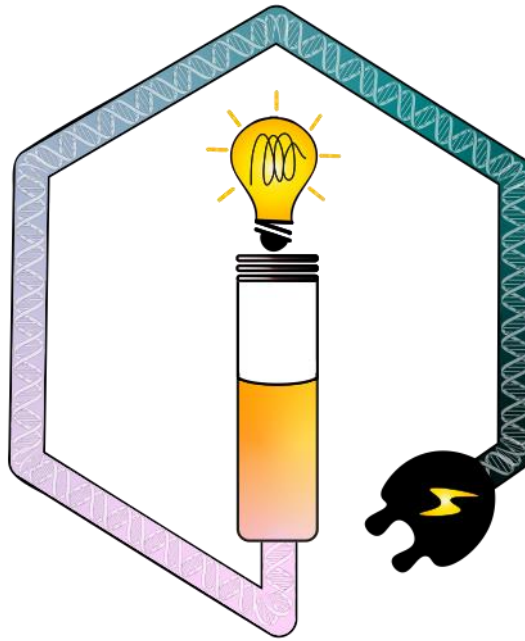
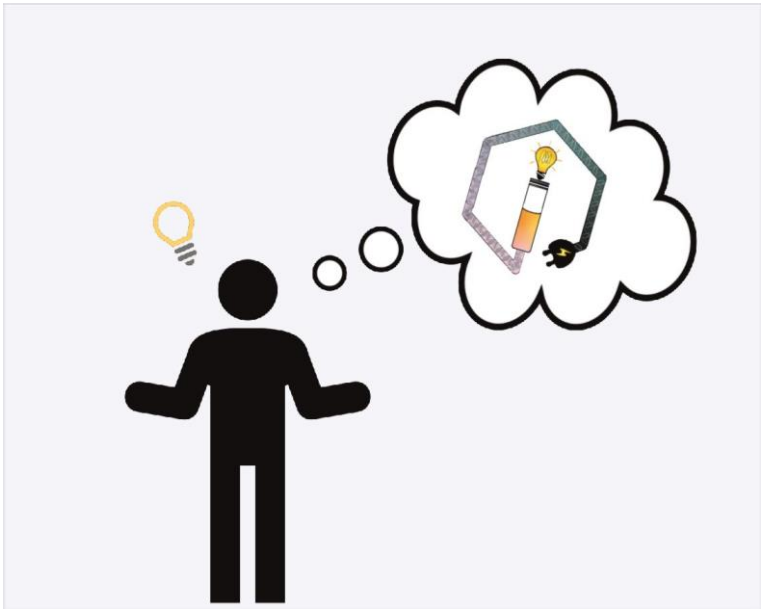
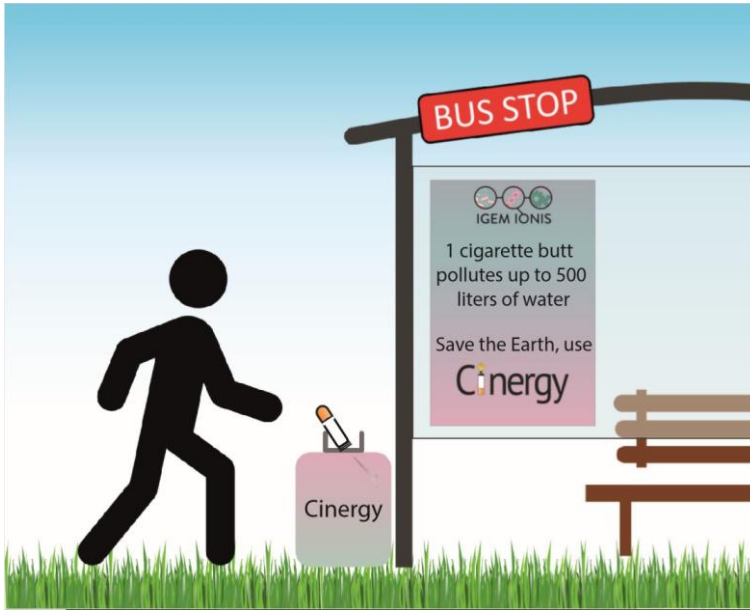
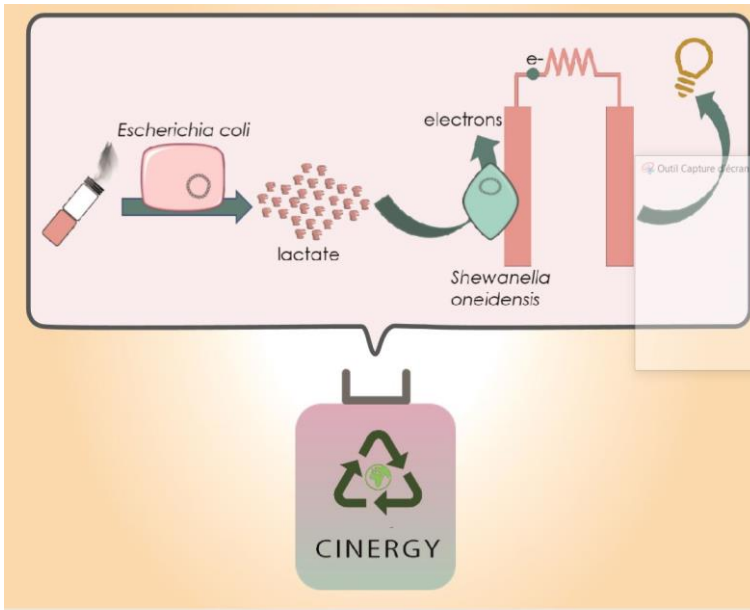


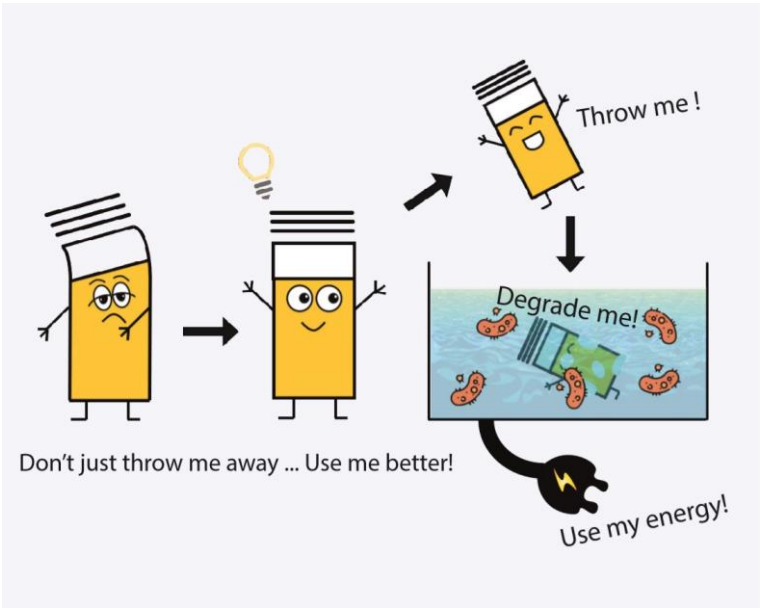
CINERGY

Recycle to preserve




BUS STOP
IGEM IONIS
1 cigarette butt pollutes up to 500 liters of water
Save the Earth, use
Cinergy
Cinergy


e-
electrons
Escherichia coli
lactate
Shewanella oneidensis
CINERGY


Throw me !
Degrade me!
Don't just throw me away ... Use me better!
Use my energy!

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

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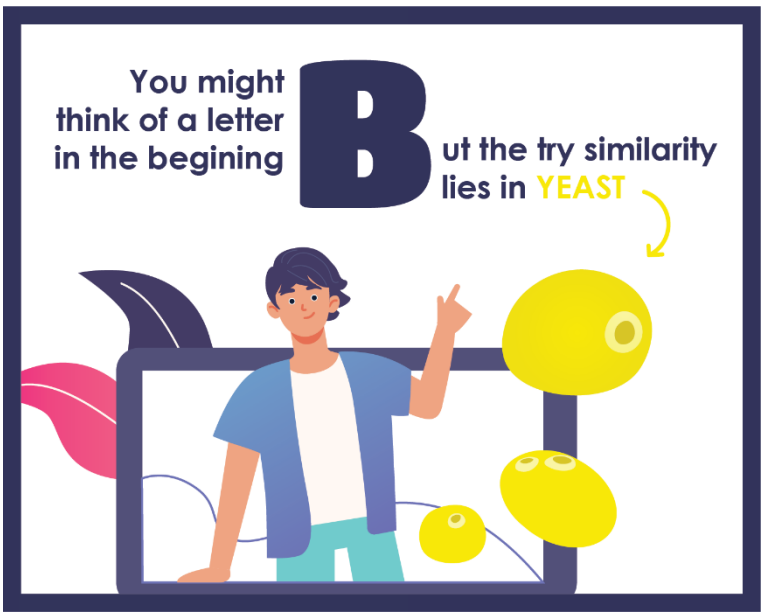
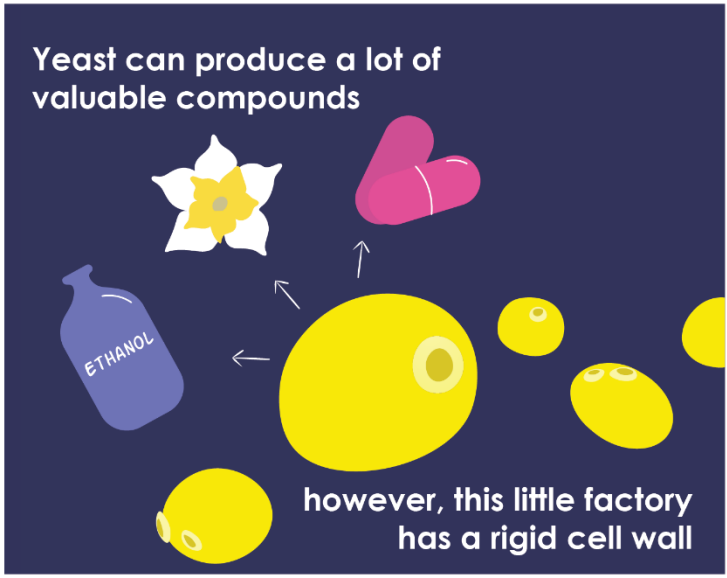
IGEM IONIS

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 begining
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

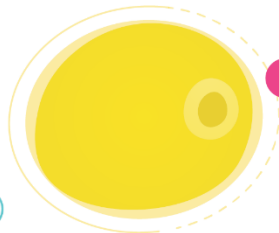
That's why the extraction of the compounds is TIME AND COST CONSUMING

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 autolytic[1] 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 lysis[2] method is used, and it is quite expensive and time-consuming for large scale production.

We introduce extra copies of yeast genes[3] encoding for cell wall[4] degrading enzymes[5] (glucanases) and modify some enzymes involved in the cell wall biosynthesis[6]. 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 media[7]. 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).

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

[2]Cell lysis: to open up cells.

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

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

[5]Enzyme: molecule which accelerates chemical reactions.

[6]Biosynthesis: production of substances by biological organisms.

[7]Media: 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

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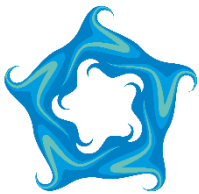
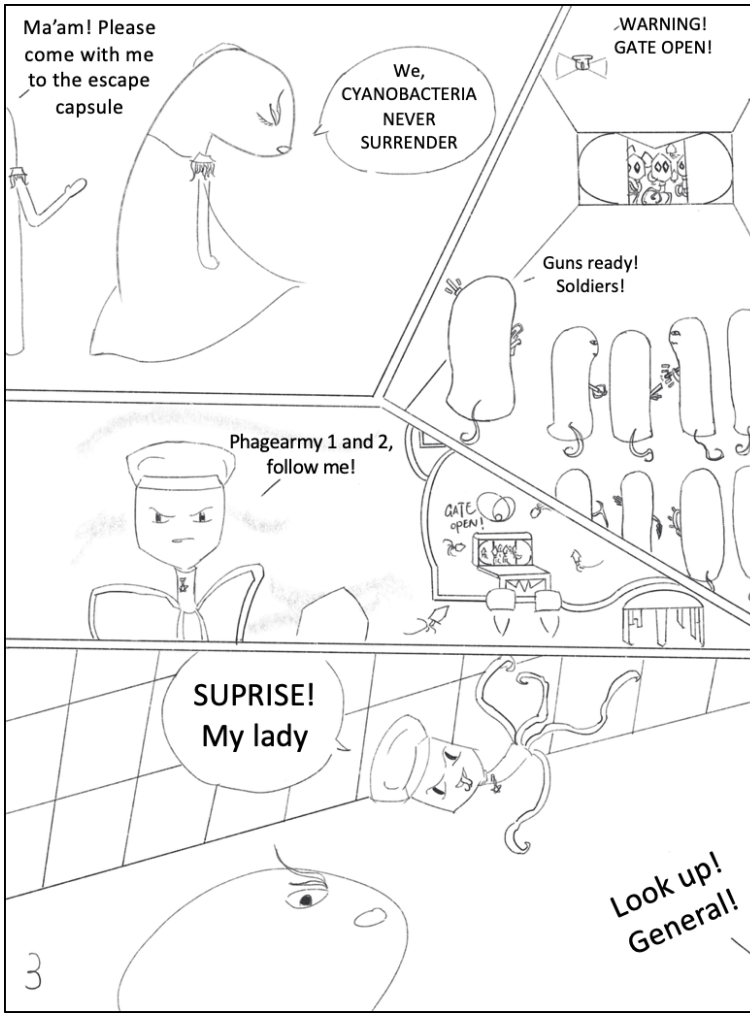


OCYANO

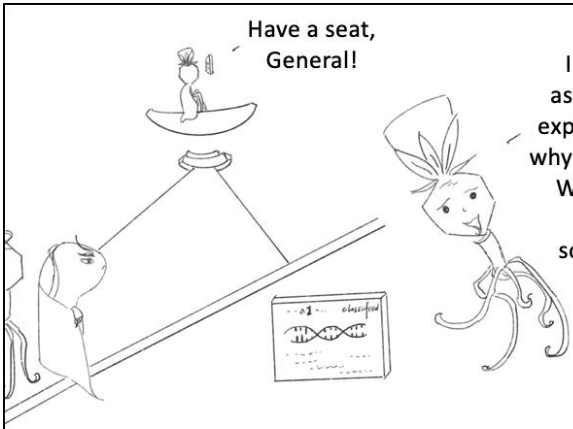
a new wave of sustainable solutions


We're under phage attack!
SIDE BLACK
Tough up! Soldiers!
OCYANO

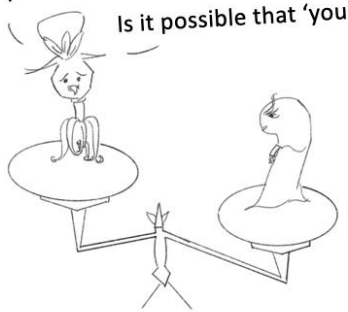

BANG!
DEATH RATE : 82 %
MA'AM,
We're losing it!
MONITOR #12
REPORT
2


Ma'am! Please come with me to the escape capsule
We, CYANOBACTERIA NEVER SURRENDER
WARNING! GATE OPEN!
Guns ready! Soldiers!
Phagearmy 1 and 2, follow me!
GATE OPEN!
SUPRISE! My lady
Look up! General!
3


BANG!
See you!
4



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, CYANOBACTRIA, to produce a useless fluorescent protein.



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 enzyme[1] production. Our team project, Ocyano, explores using cyanobacteria as means of photosynthetic biomanufacturing[2], mitigating the need for large amounts of growth media[3] required by classic heterotrophic[4] 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, phages[6] 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.

[1]Enzyme: molecule which accelerates chemical reactions.

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

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

[4]Heterotrophic: 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.

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

Team KU LEUVEN

Team members

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KU LEUVEN

MEDEA

Machine-Enhanced Directed Evolution of Aptamers

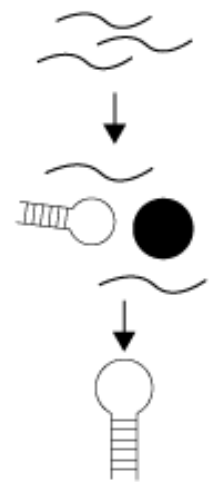
AGGTCCATGATTCGT

UUAGCAACGAUC

AGGTCCATGATTCGT

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

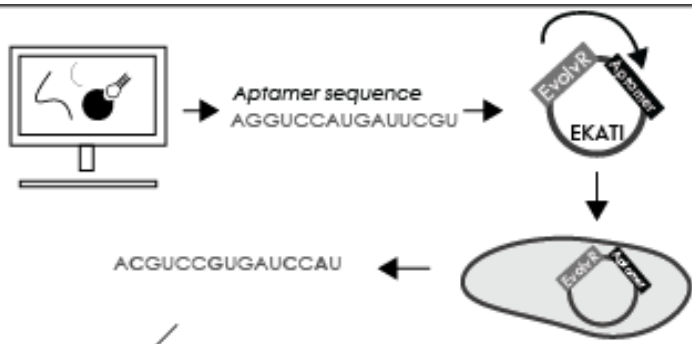


SELEX has drawbacks

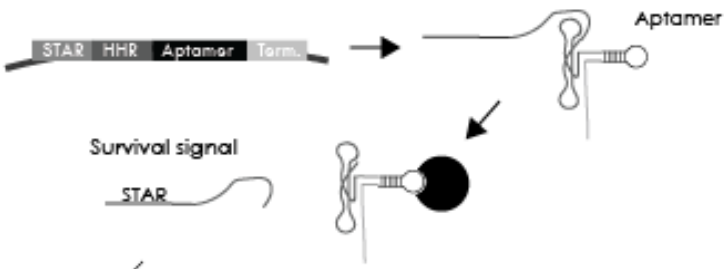
Up to **6 months** to identify new aptamers

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



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 aptamers[1] in vivo[2]. More specifically, we suggest a system based on **the directed evolution[3] of aptamers guided by in silico design[4].** Our project aims at the creation of a genetic[5] system, which will introduce random mutations[1] in a known aptamer and select the ones with the highest binding affinity[6] 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).

[1]Aptamer: 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.

[2]In vivo: in living organisms.

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

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

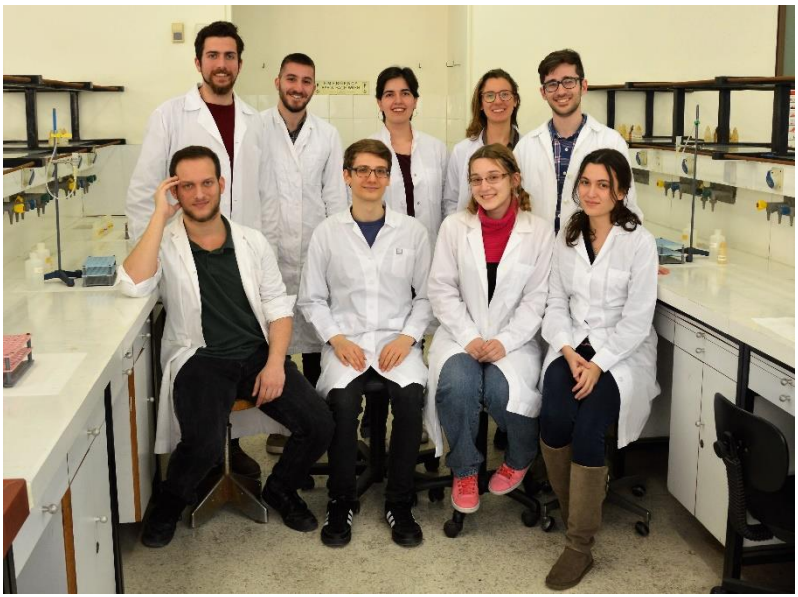
[5]Genetic: based on genes; a gene is a DNA-sequence encoding compounds for the living cell.

[6]Binding 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



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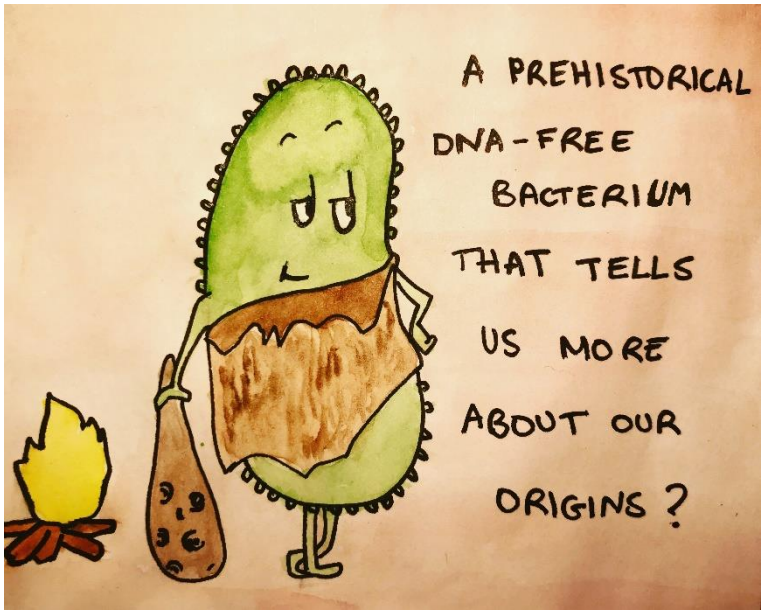
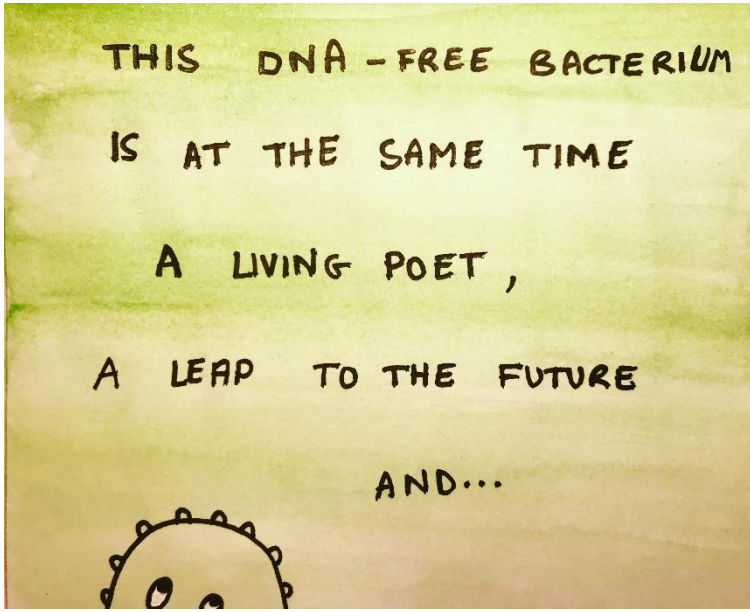
DNA
FREE
POETENTIAL


WHAT CAN POSSIBLY BE DONE WITH A DNA FREE CELL ?


A SUPER BACTERIUM ABLE TO FIGHT CONTAMINATION !
WITHOUT CONTAINMENT ISSUES ?


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...


...
INTO
THE PAST!

Abstract

To reinforce the link between synthetic biology and society, we act on two main axes: at the scientific level, we propose to increase chassis[1] safety by removing its genomic DNA thanks to newly described BioBricks[2] such as an original phage[3] nuclease[4]. 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.

[1]Chassis: the organism you change (genetically).

[2]BioBrick: 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.

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

[4]Nuclease: enzyme[5], which breaks down nucleic acids e.g. DNA.

[5]Enzyme: molecule which accelerates chemical reactions.

Team GO Paris-Saclay

Team members

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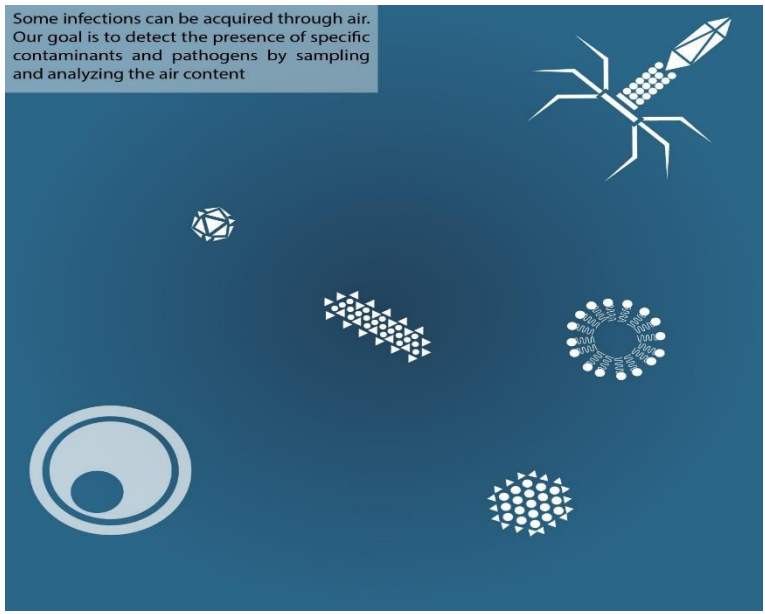
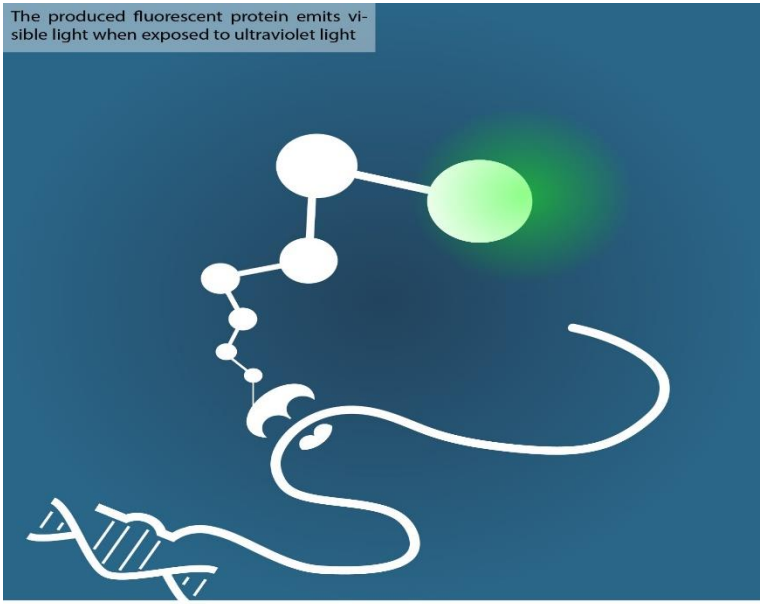
GO PARIS SACLAY
IGEM

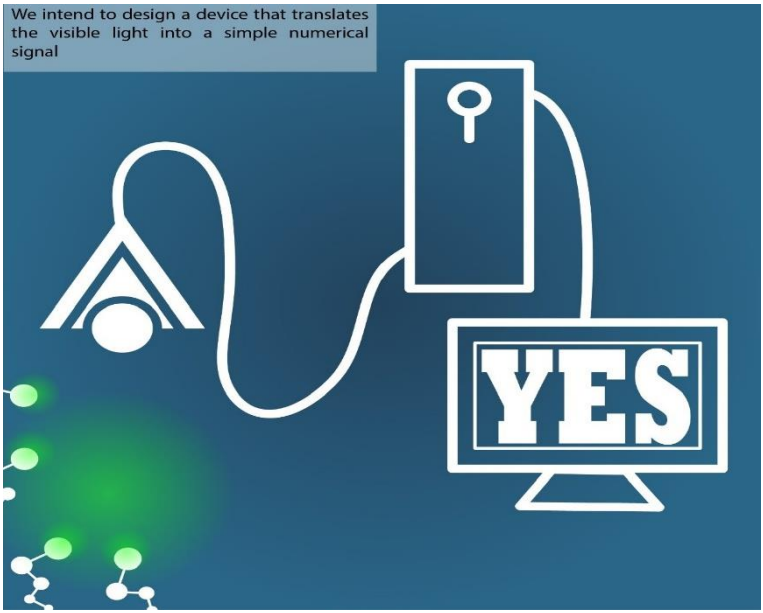

TEAM IGEM
ULAVAL

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

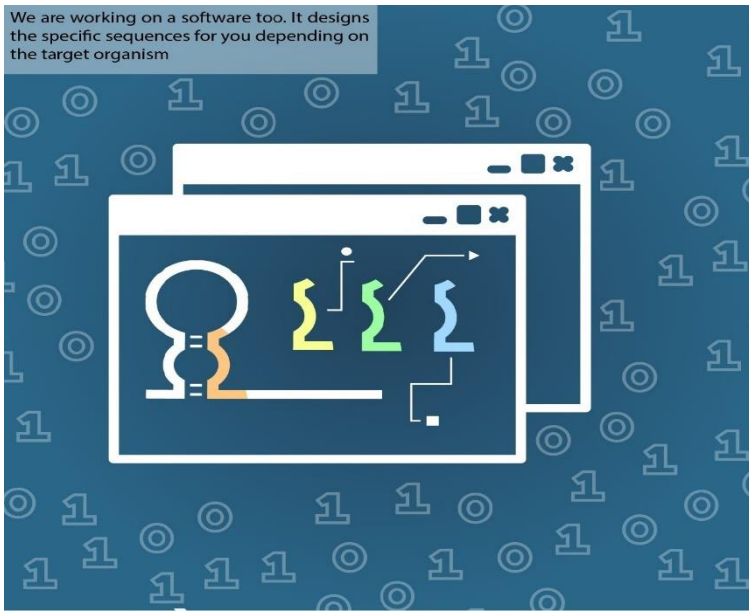


We extract their genetic material and target a very specific sequence, short and only present in the potential pathogen, with a tool able to : recognize the DNA and pair it to translate and produce a reporting protein

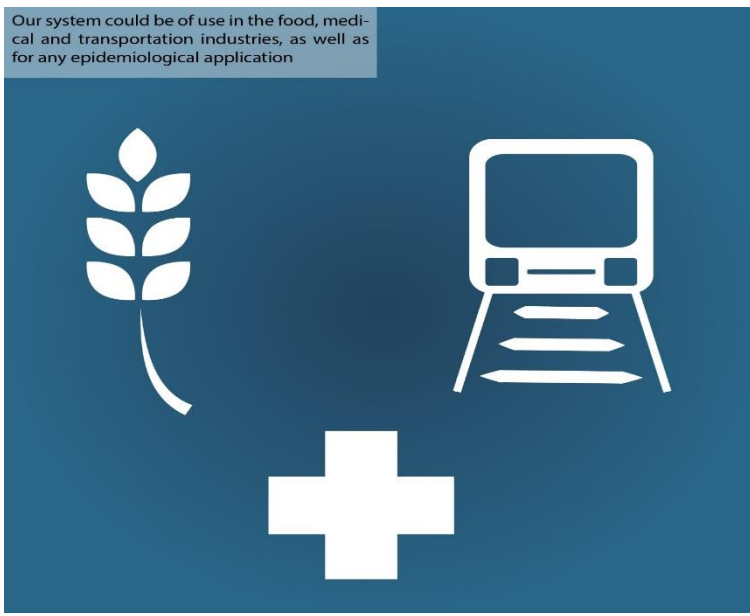

The produced fluorescent protein emits visible light when exposed to ultraviolet light


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

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

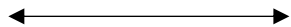


Our system could be of use in the food, medical and transportation industries, as well as for any epidemiological application



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 riboregulatory[1] elements called Toehold switches[2] 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 nosocomial[3] infections.



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

[2]Toehold 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.

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

Team ULaval

Team members

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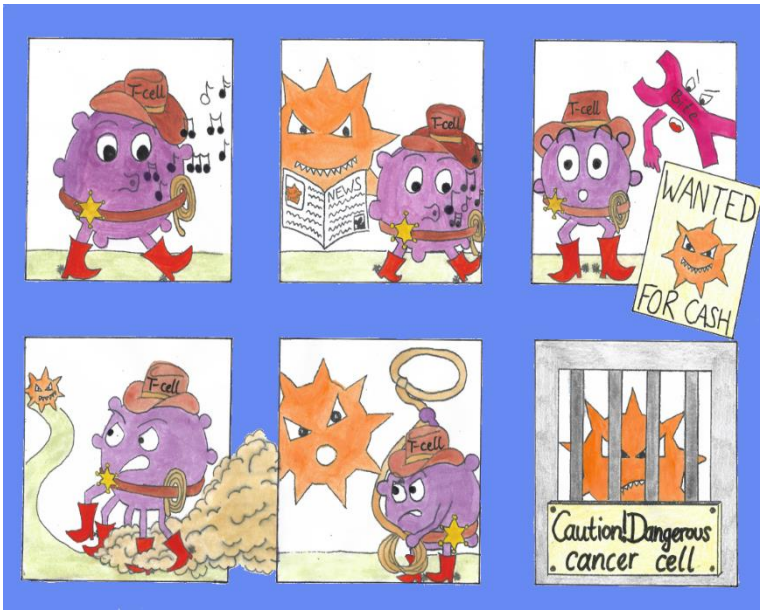
2019.igem.org/Team:ULaval

TEAM IGEM ULAVAL


iGEM
ERLANGEN


T-cell
T-cell
NEWS
T-cell
Bacte
WANTED
FOR CASH
T-cell
T-cell
Caution! Dangerous
cancer cell

Abstract

We are the iGEM Team Erlangen 2019 and we create a bispecific antibody[1] (in the comic it is called bite) to recruit the T-cells[2] of our immune system to the colorectal[3] 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.

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

[2]T-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.

[3]Colorectal: relating to or affecting the colon[4] and the rectum.

[4]Colon: the large intestine.

Team FAU Erlangen

Team members

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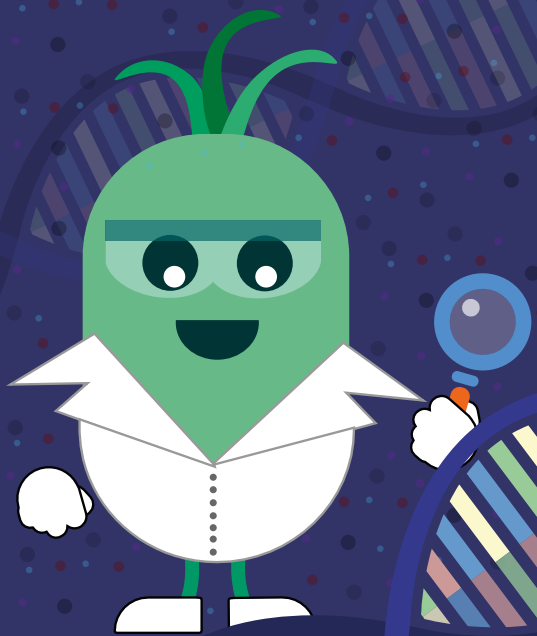
2019.igem.org/Team:FAU_Erlangen

iGEM ERLANGEN

Dr. Coli´s Adventures

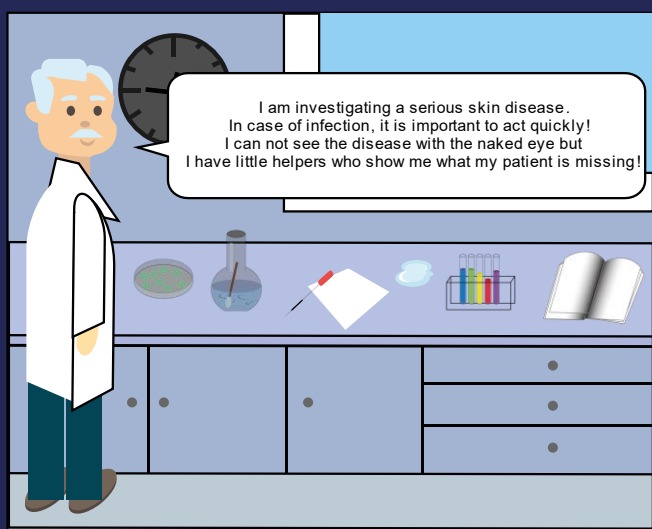


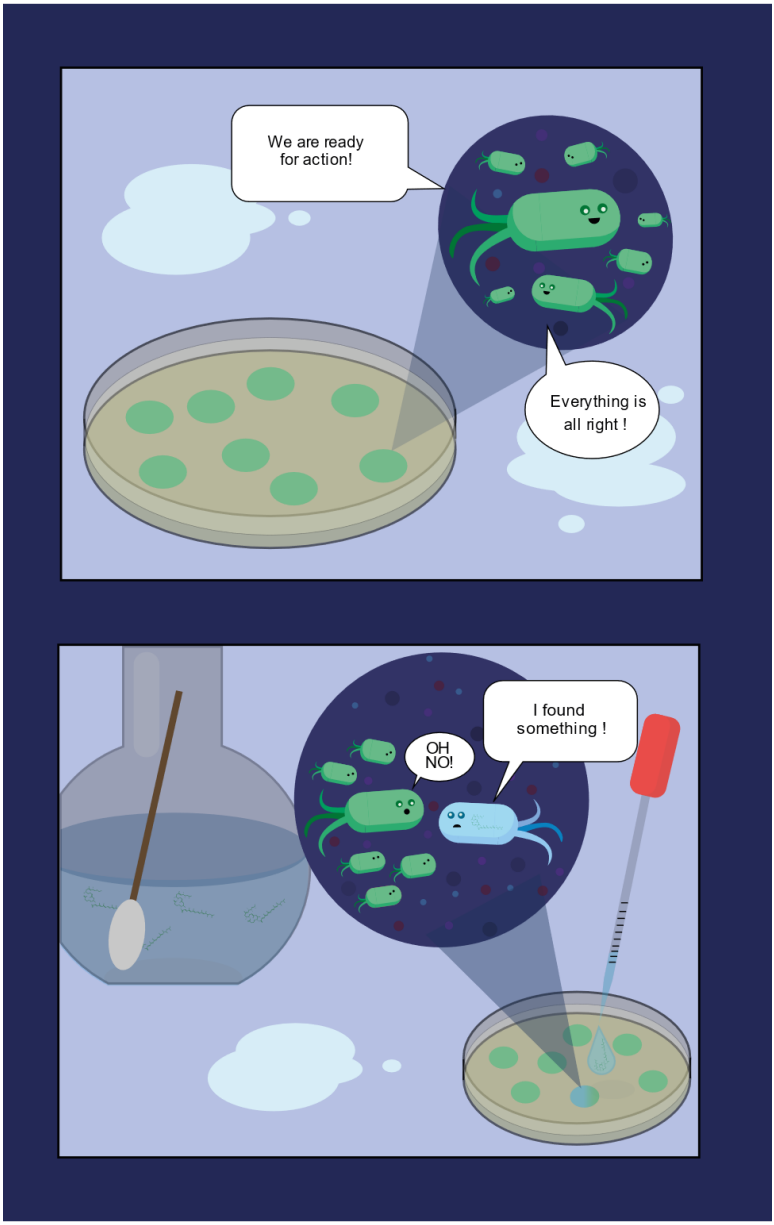
Mycolactone Diagnostics

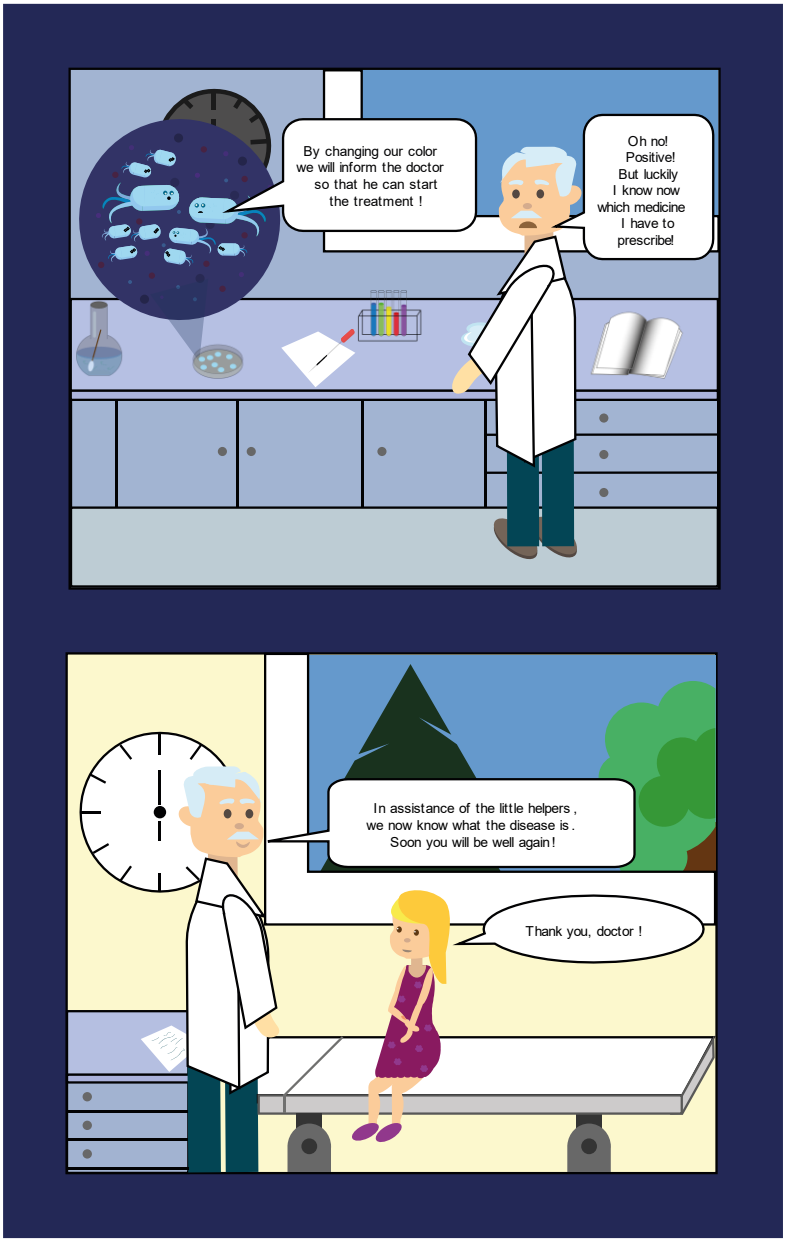
BOKU

universität wien


We will make a swab to find out
what medicine will help you.


I am investigating a serious skin disease.
In case of infection, it is important to act quickly!
I can not see the disease with the naked eye but
I have little helpers who show me what my patient is missing!


We are ready for action!
Everything is all right !
I found something !
OH NO!


By changing our color we will inform the doctor so that he can start the treatment !
Oh no! Positive! But luckily I know now which medicine I have to prescribe!
In assistance of the little helpers , we now know what the disease is . Soon you will be well again !
Thank you, doctor !

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 aptamer[3] 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 protein[4] (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.

[3]Aptamer: 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.

[4]Fluorescent 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

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iGEM VIENNA

The End