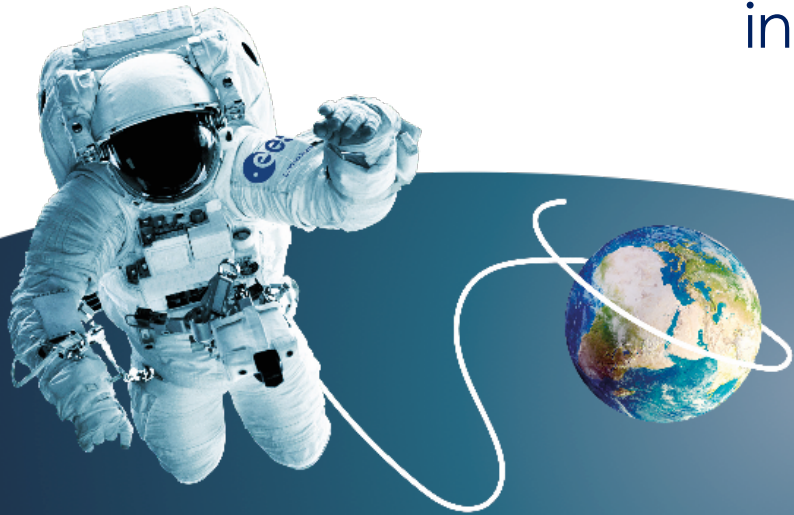




CREATING  
A CIRCULAR  
**FUTURE**

**PARAGEN 1.0:** a synthetic bacteriocin gene collection for rapid *in vitro* antimicrobial peptide selection for the microbial control of industrial fermentation



**Jason Bland, PhD.**  
R&D Project Manager  
Syngulon  
[mjbland@syngulon.com](mailto:mjbland@syngulon.com)





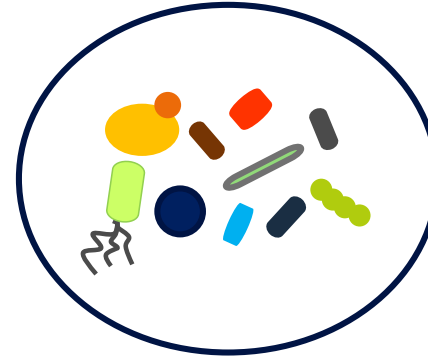
## Presentation Structure



1. Importance of microbes for our ecosystem
2. Need of microbial control
3. Bacteriocins
4. PARAGEN
5. Bacteriocins in the age of synthetic biology



# The importance of microbes for life on Earth



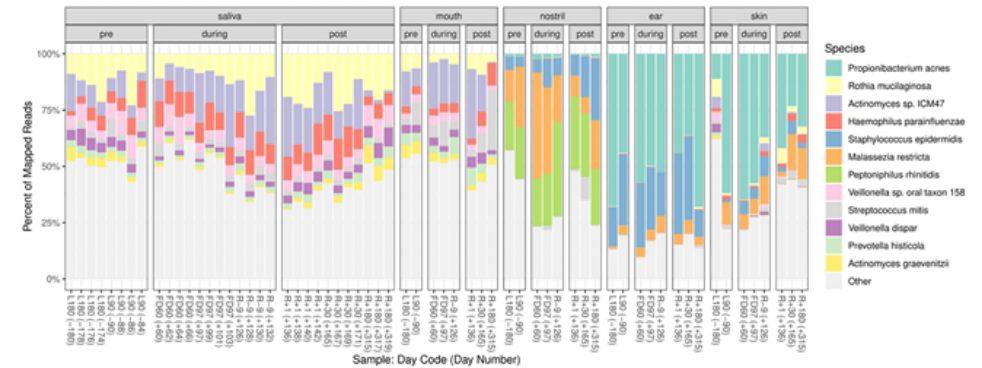
- Microbes are found in every environment on Earth (and beyond!)
- Ubiquitous microbial presence has beneficial and detrimental impacts for human health and the economy
- Microbes are collaborating and fighting with each other to reach certain equilibrium to form communities: “microbiota”
- These microbiota have evolved to generate unique chemical reactions via species synergies



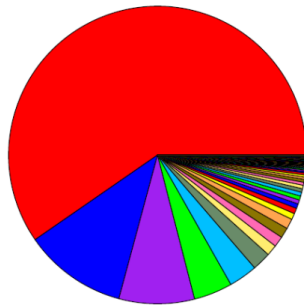
## Microbial analysis of the International Space Station



## Most abundant species from crewmember samples, pre- and post-flight



No PMA treatment  
(total bacterial community)



Top 11 family level taxa

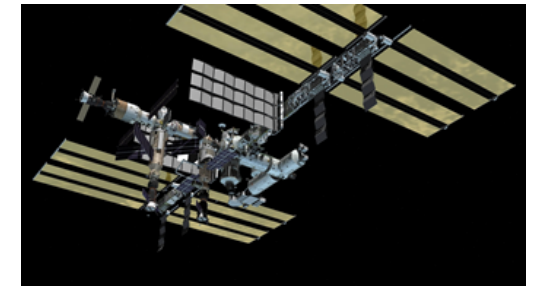
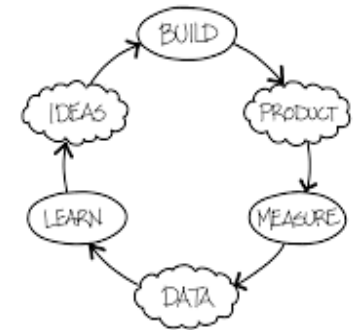
- Enterobacteriaceae
- Methylobacteriaceae
- Staphylococcaceae
- c\_Bacilli
- Paenibacillaceae
- Corynebacteriaceae
- Streptococcaceae
- o\_Bacillales
- o\_Clostridiales\_Family\_XI
- unidentified sequence
- Moraxellaceae

Avila-Herrera *et al.* PLoS ONE (2020)

- Metagenomic analysis to sample bacterial diversity
- Bacterial composition in space is of great interest!



# Application of microorganisms in industry



Microbial communities are the biocatalysts of our planet and industries

**How can we control microbial communities?**



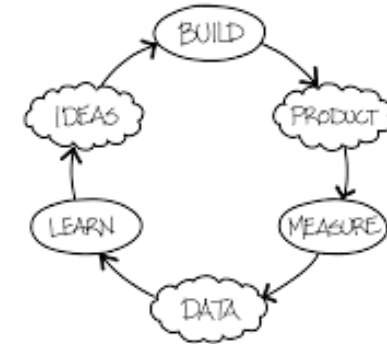
# Synthetic Biology approaches to Microbial Control



Understand



**“Evolutionary” based chassis**  
**Constructed by modules (parts)**  
**Behavior code based**  
**Self coding and self replicative**



« Bio » Control



## Intensification of microbial activity in industrial processes in the age of synthetic biology

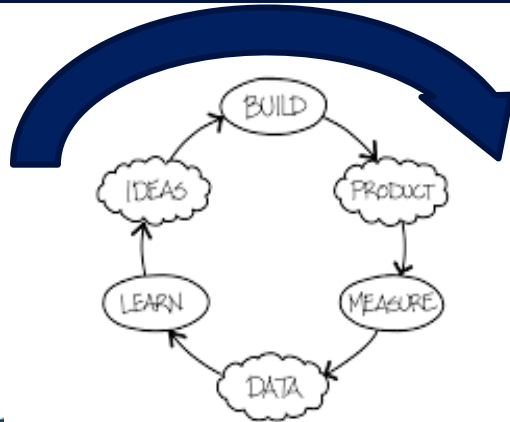
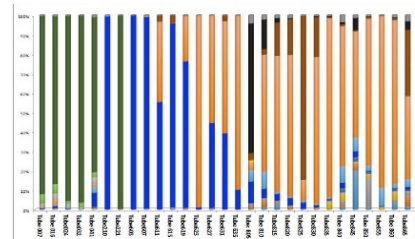


Understand



« Omics sciences » allow to make the link between microbial physiology and the genetic code.

Proportion of bacterial species (%) in the different samples



Microbe identification based on genomic barre-codes (metagenomic)

Basic research is very active



What genes can we use to control microbiota?

(R) Explore the world of bacteriocins

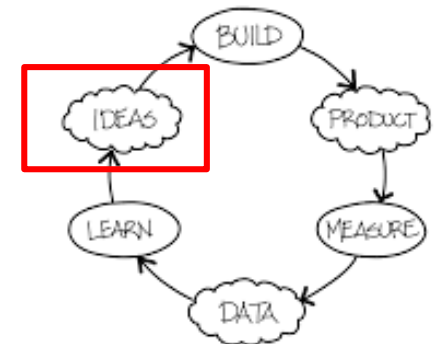
- Discovered in 1925 by Belgian scientist: “**André Gratia** (1893–1950): Forgotten Pioneer of Research into Antimicrobial Agents”
- Heterogenous group of **antimicrobial peptides** produced **ribosomally** by **bacteria**
- Used to **kill related species** to **reduce competition** for resources and space
- **Present species-specific toxicity**



André Gratia



Apply synthetic biology



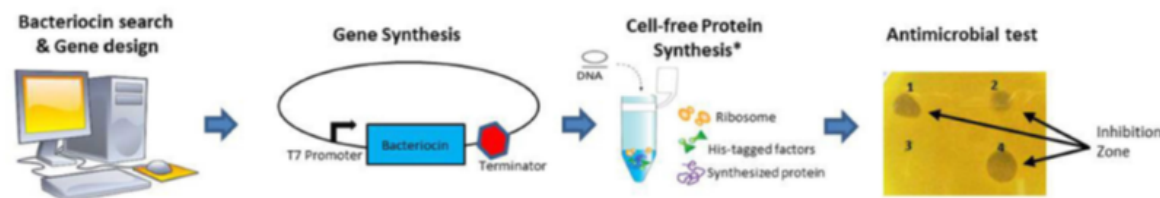




# The PARAGEN 1.0 Collection

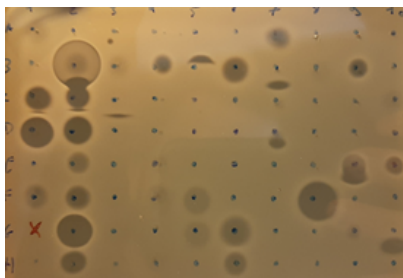
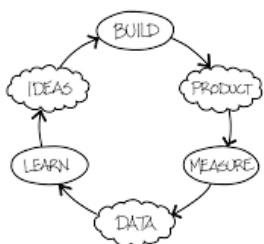


To explore the diversity of bacteriocins we have built a collection of synthetic genes in a standardized format allowing rapid activity measurements of bacteriocins.



## Physical Collection of Bacteriocin Genes and Peptides

3 publications in the last year



BRIEF RESEARCH REPORT ARTICLE  
Front. Bioeng. Biotechnol., 06 September 2019 | <https://doi.org/10.3389/fbioe.2019.00213>



## PARAGEN 1.0: A Standardized Synthetic Gene Library for Fast Cell-Free Bacteriocin Synthesis

Philippe Gabant\* and Juan Borrero\*  
Syngulon, Seraing, Belgium

~400 bacteriocin genes

> 100 “wild type” bacteriocins chemically synthesized

Home / *Chimica Oggi-Chemistry Today* / Vol. 38(4) / Antimicrobial peptides to...

MICHAEL J. BLAND, PHILIPPE GABANT\*  
\*Corresponding author  
Syngulon, Seraing, Belgium

BIOTECHNOLOGY

### ANTIMICROBIAL PEPTIDES TO SHAPE BIOBASED CHEMICAL PRODUCTION

Keywords: anti-microbial peptides, antibiotics, bacteriocins, biotechnology, industrial fermentation, microbiome, one health

Open Access | Perspective

### In the Age of Synthetic Biology, Will Antimicrobial Peptides be the Next Generation of Antibiotics?

by Félix Jaumaux, Luz P. Gómez de Cadiñanos and Philippe Gabant\*

Syngulon, Rue du Bois Saint-Jean 15/1, 4102 Seraing, Belgium  
\* Author to whom correspondence should be addressed.

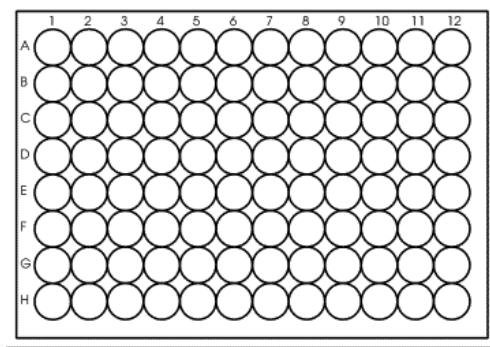
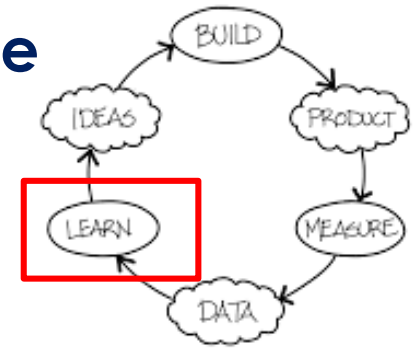
*Antibiotics* 2020, 9(8), 484; <https://doi.org/10.3390/antibiotics9080484>

Received: 14 July 2020 / Revised: 1 August 2020 / Accepted: 4 August 2020 / Published: 6 August 2020

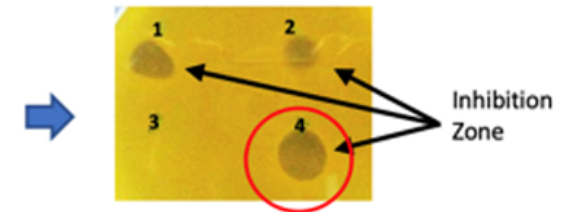




# Mutant Library generation to determine structure/function relationships



### Antimicrobial test



### Type of mutations

- Alanine scan
- Deletion
- Single or multiple amino acid mutation
- (Charge variation)
- (Disulfide bonds)



Prof Cédric Govaerts and Prof Abel Garcia-Pino



Professor Pascal Hols

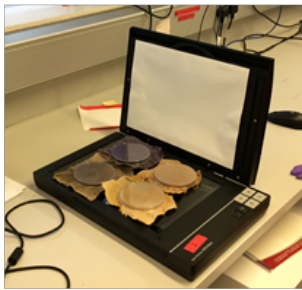
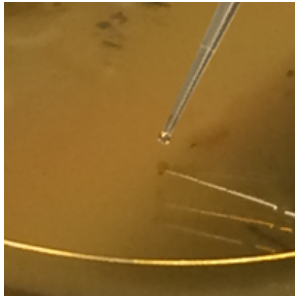


Félix Jaumaux

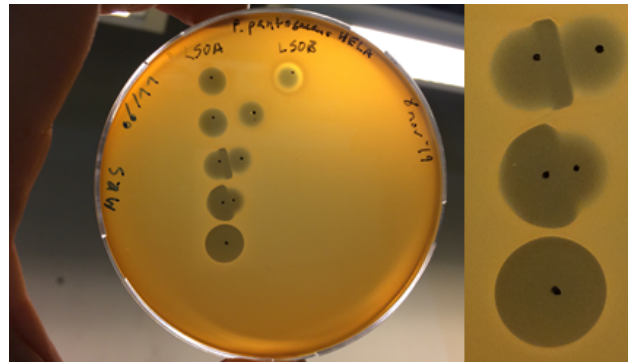




# Analysis of bacteriocin interactions



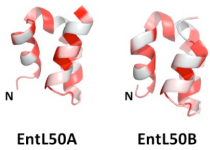
Experiments carried out at Imperial College London



Can observe bacteriocin interactions using plate spot assay



ScanLag Time-lapse 20 h of growth at 30°C

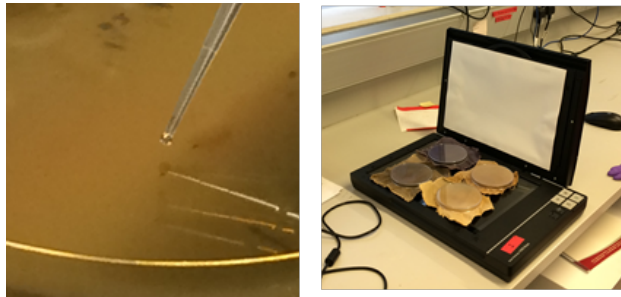
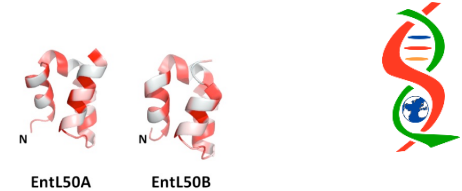


Prof. Ramesh Wigneshweraraj  
Imperial College London

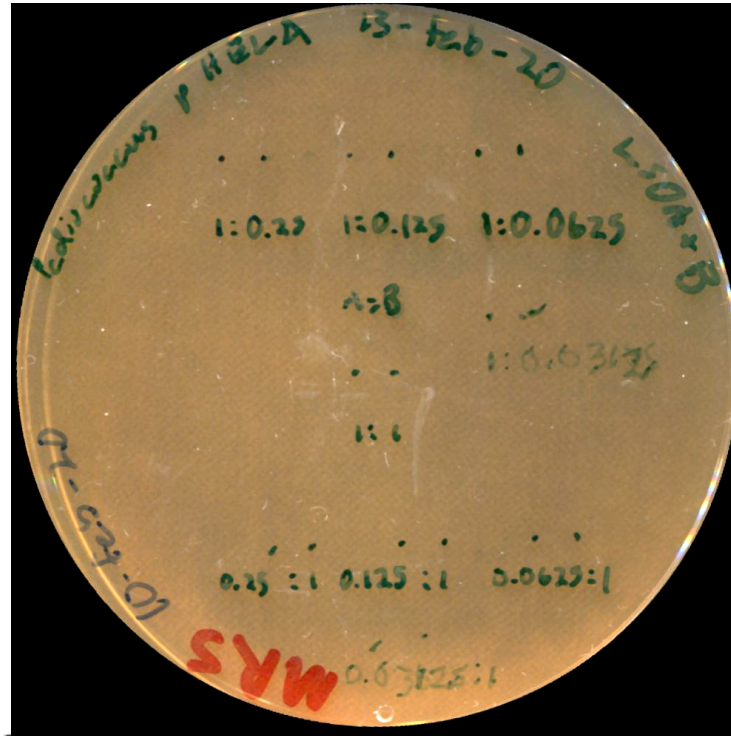




# Analysis of bacteriocin interactions



Diffusion of bacteriocins into the medium inhibits growth of bacteria



ScanLag Time-lapse 20 h of growth at 30°C

Experiments carried out at Imperial College London

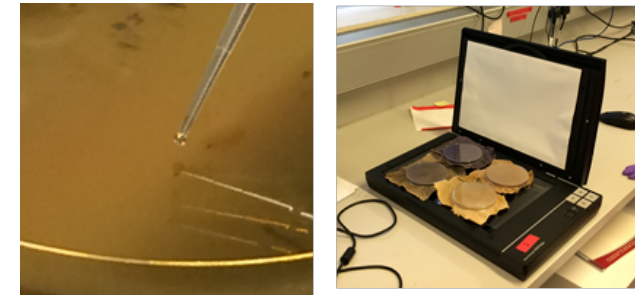
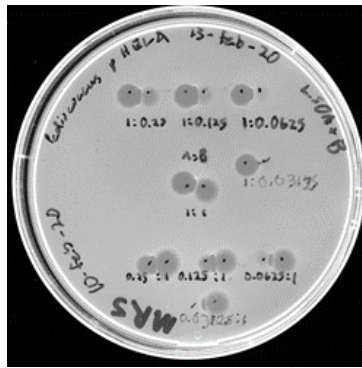


Prof. Ramesh Wigneshweraraj  
Imperial College London

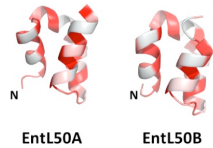


# Analysis of bacteriocin interactions

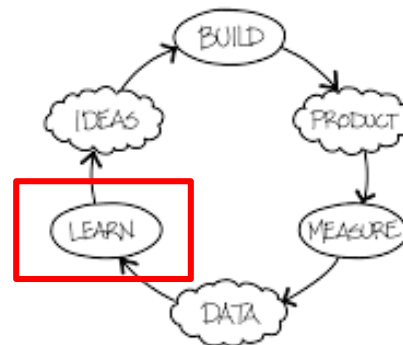
Other studies: concentration dependence, resistant mutant dynamics



Experiments carried out at Imperial College London



ScanLag Time-lapse  
20 h of growth at 30°C



Prof. Ramesh Wigneshweraraj  
Imperial College London

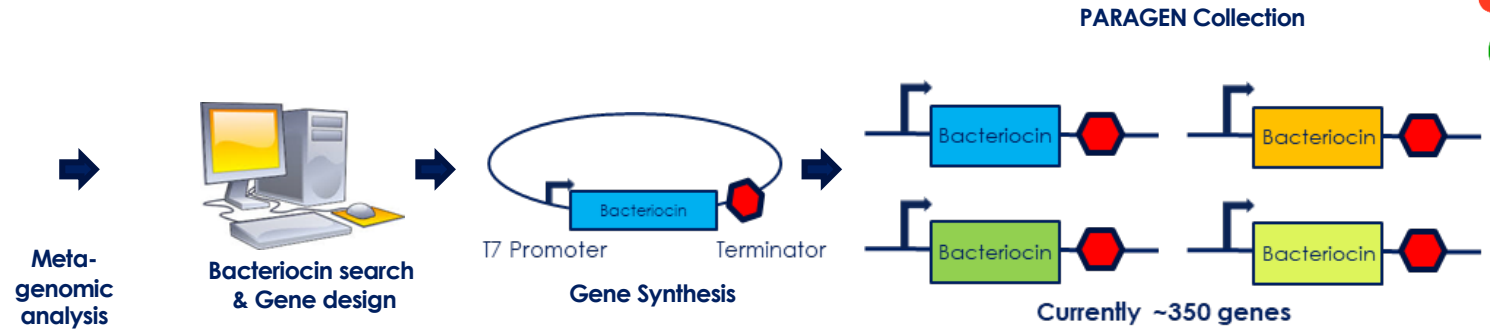


# MELISSA



Natural microbiome diversity

## A. PARAGEN Bacteriocin Collection



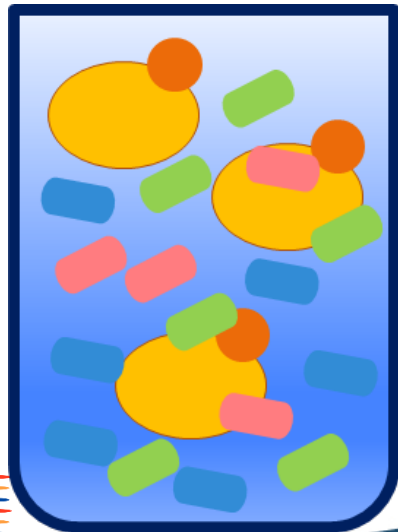
## B. PARAGEN in Industrial Context

Industrial bio-production environment microbiomes

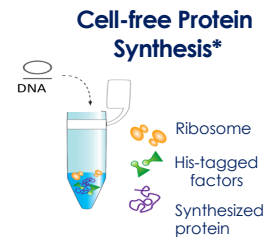
Genomic data of microbiome to identify community members

Standard Functional Bacteriocin Screen Against Microbes of Interest

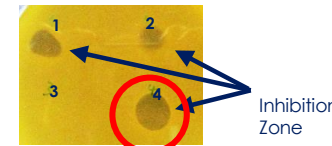
Application of bacteriocins to shape microbial community



C C G A T G C G  
G G A T C A G C  
T A C G A G C T

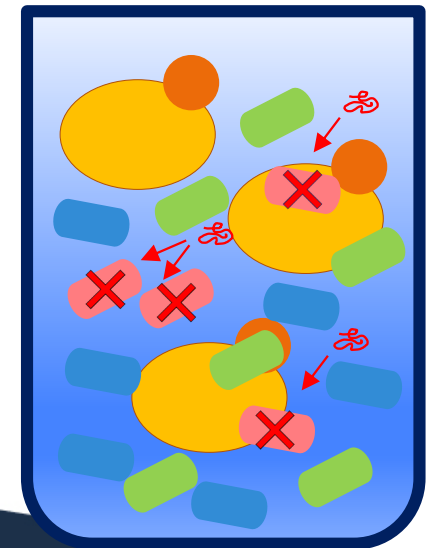
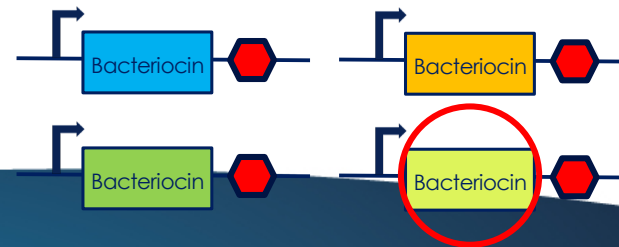


Antimicrobial test



Inhibition Zone

Selection of Appropriate Bacteriocin







# Where could biocontrol by bacteriocins be applied?

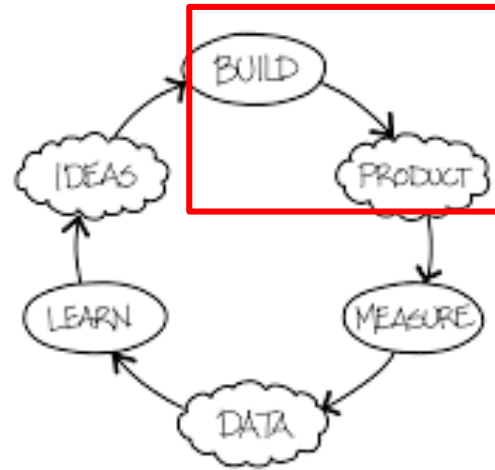


Clean tech

Food  
E234 Nisin

Human health

Biobased  
production



Animal health/feed

Cosmetics

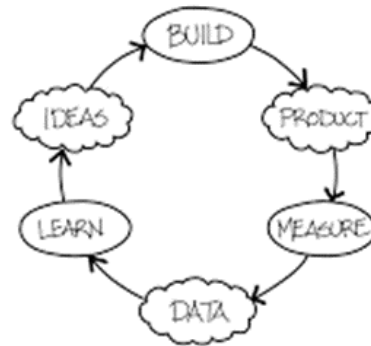
Space



# Take-home message



1. Search for new ways to control microbial flora (microbiota)
2. Synthetic biology allows reprogramming of biological functions
3. Bacteriocins are natural antimicrobial peptides (AMP) used by bacteria to protect their ecological niche
4. Syngulon has built PARAGEN, a unique collection of synthetic bacteriocin genes
5. Via academic collaborations Syngulon is studying the mode of action of bacteriocins
6. Via different industrial partnerships Syngulon is testing applications of bacteriocins





### Team



Guy Hélin, Co-founder, CEO  
Dr. Philippe Gabant, Co-Founder, CSO



Dr. Mohamed El Bakkoury, CTO Yeast  
Dr. Jason Bland, R&D Project Manager  
Dr. Luz Perez, R&D Project Manager  
Félix Jaumaux, PhD Student  
Dr. Baptiste Dumont, R&D Project Manager  
Anais Pagès, R&D Scientist  
Dr. Anandi Martin, Senior Project Manager - Infectious Disease  
Hajar Amraoui, PhD Student  
Loïc Mues, R&D Scientist

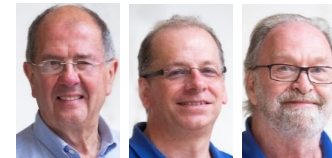


Collaboration with:  
Universidad Complutense Madrid (UCM)  
Dr. Juan Borrero



### Scientific Advisory Board

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Pr Laurence Van Melderen, ULB, Charleroi (BE)  
Pr Ruddy Wattiez, UMONS, Mons (BE)



IN MEMORIAM  
Dr Régis Sodoyer, ex-Sanofi Pasteur, Lyon (FR)



### R&D Partners



# MELISSA



MICRO-ECOLOGICAL  
LIFE SUPPORT SYSTEM  
ALTERNATIVE



## Q & A

**THANK YOU.**

Dr. Jason Bland

*Syngulon*

[mjbland@syngulon.com](mailto:mjbland@syngulon.com)

[www.melissafoundation.org](http://www.melissafoundation.org)

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