# From artificial cellulosomes to cellulosic biofuels and chemicals production.

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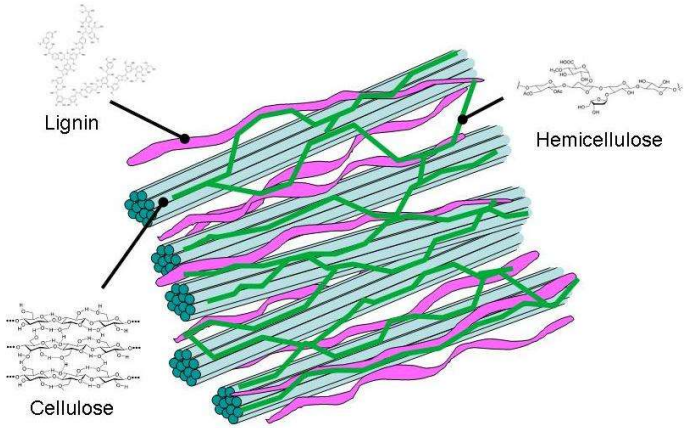
# Introduction

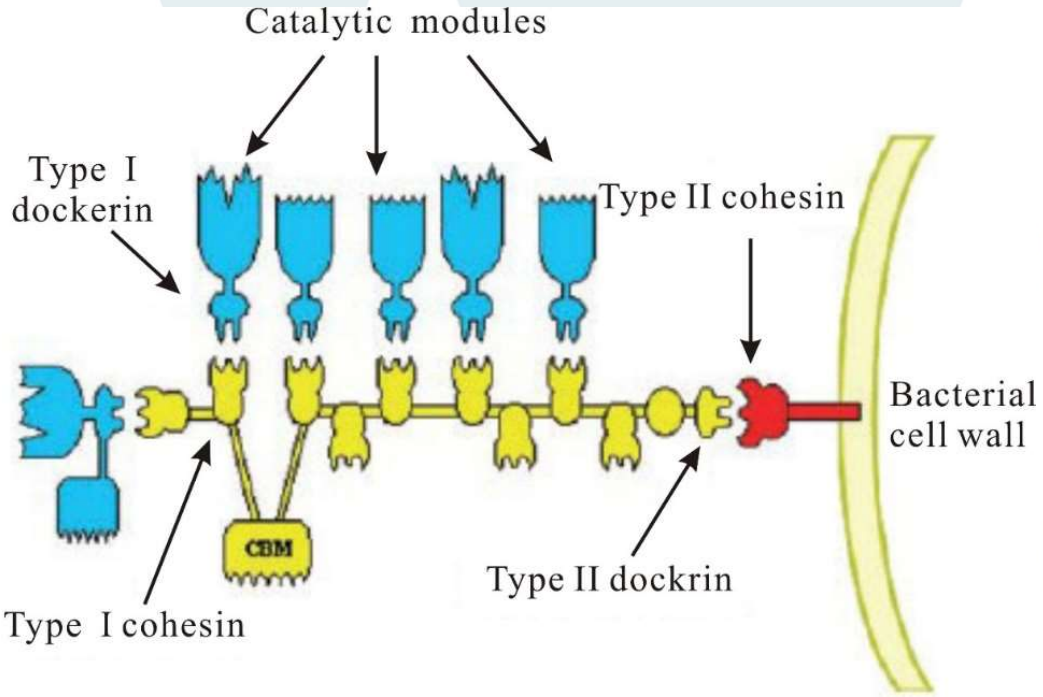
- Biofuels are increasingly used as alternatives to fossil fuels both for cars and **jets**.
- They are mainly produced from **crop-derived sugars**, making the process of biofuel production controversial
- The use of **lignocellulosic residues** is an attractive alternative
- Unfortunately, lignocelluloses are recalcitrant substrates requiring expensive **pre-treatments** to be hydrolyzed by **fungal enzymes** which are inefficient
- **Consolidated bioprocessing** (CBP) is when a single organism simultaneously hydrolyzes lignocellulose and ferments the released sugars into biofuels



# Introduction

## Bacterial cellulosomes versus fungal cellulases

- Some anaerobic bacteria assemble their cellulases into multi-protein complexes called cellulosomes
- **Cellulosomes** have been shown to be at least **10 times more efficient** that **fungal cellulases** and alos required **milder** pretreatments of lignocellulose
- **Cellulosomes** consist of a large protein called scaffoldin which contains several cohesin domains
- **Cellulases** with different catalytic modules bind to the cohesins via dockerin domains



# Introduction

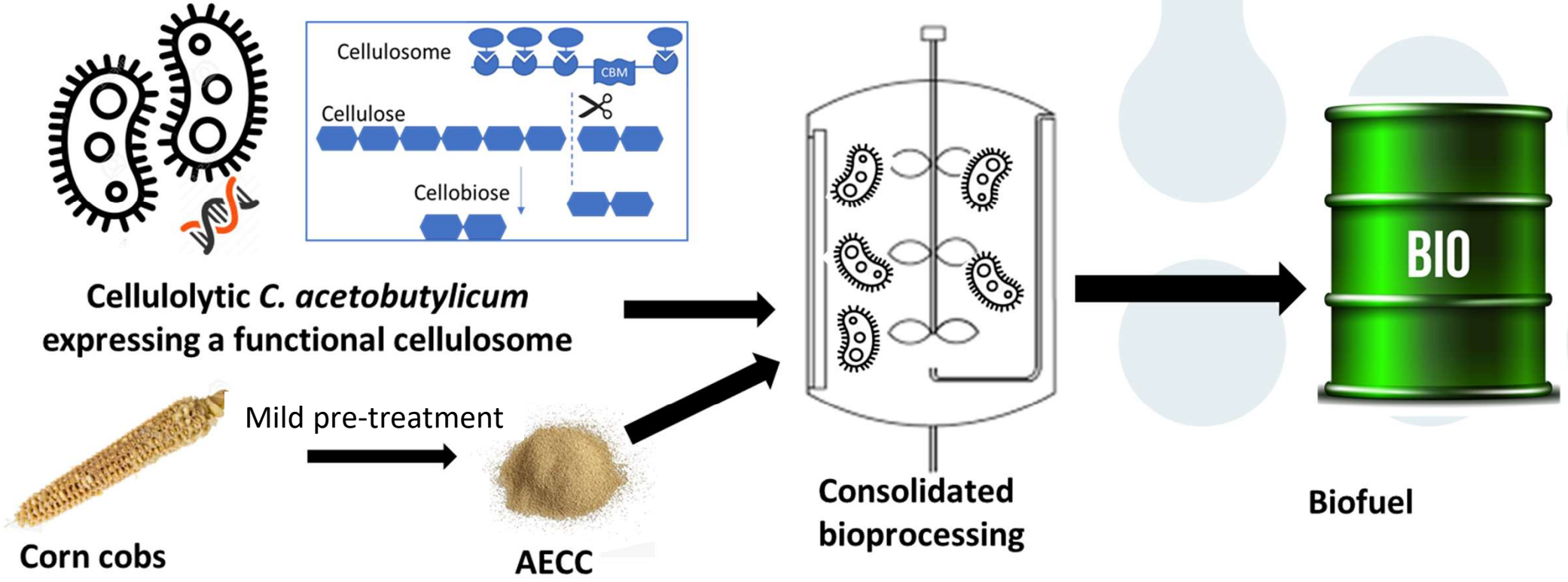
- *Clostridium acetobutylicum* is an attractive candidate for CBP as it has previously been used industrially to produce **acetone** and **butanol** from **corn** (***Weizmann Process***)
- **Systems** and **Synthetic** Biology tools are available
- But…….previous efforts to engineer *C. acetobutylicum* to grow on **cellulose** were **unsuccessful!**
- However, all the **genes** necessary to produce a **cellulosome** are present in its genome – but its cellulosome was reported to be **inactive**

Acetone production using *C. acetobutylicum* ***(Weizmann strain)*** during World War 1

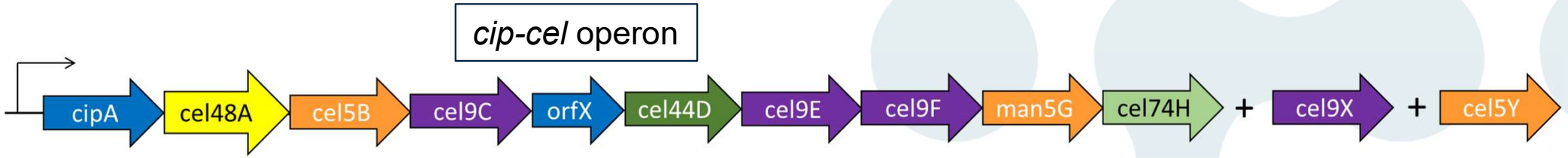
Yoo et al (2015). *mBio*, 6, e01808-15
Nguyen et al (2018). *Nature Com* 9:3682
Wilding-Steele et al .(2021) *Int. J. Mol. Sci.*. 22, 3704
Foulquier, et al, (2022) *Nature Com* 13:491

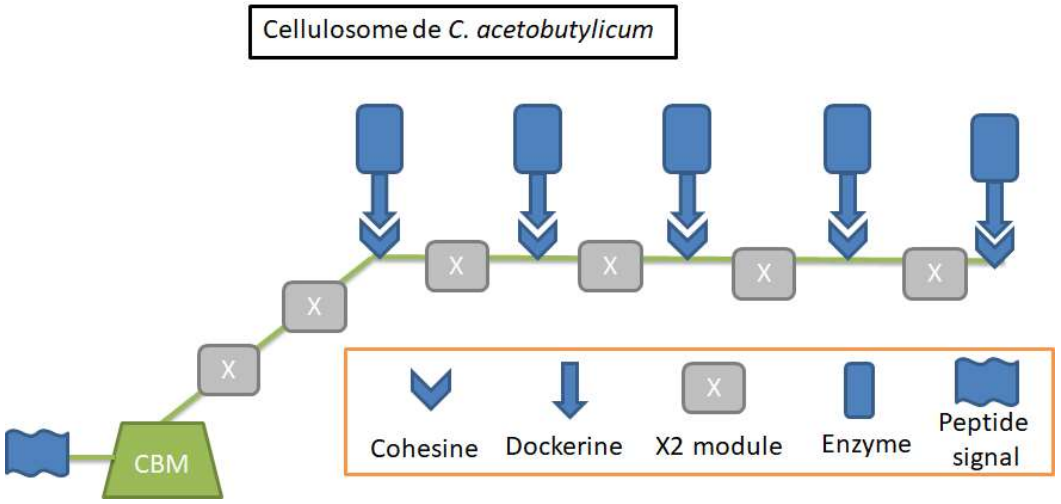
# Introduction

The purpose of this study is 1) **to characterize** the cellulosomal components and 2) **engineer synthetic cellulosomes** to allow *C. acetobutylicum* to grow on lignocellulosic feedstocks and produce biofuels



# *C. acetobutylicum's* cellulosome




| Cellulosomal components | Function | Molecular mass (kDa) | Modular structure | Homolog | | |
|---|---|---|---|---|---|---|
| | | | | in Ccel | in Ctm | in Ccl |
| CipA | Scaffolding | 154 | CBD3a-X-5(X-CohI) | CipC | CipA | CbpA |
| **Cel48A** | **Endocellulase** | **81** | **GH48-DD** | **Cel48F** | **Cel48S** | **Exg48S** |
| **Cel5B** | **Endocellulase** | **54** | **GH5-DD** | **Cel5N** | **Cel5G** | **Eng5N** |
| **Cel9C** | **Endocellulase** | 80 | **GH9-CBD3c-DD** | **Cel9G** | **Cel9F** | **Eng9H** |
| OrfXp | Anchoring protein | 18 | PTS-CohI | OrfXp | OlpA | HbpA |
| Cel44D | Endocellulase | 67 | GH5-DD | Cel44O | - | – |
| Cel9E | Endocellulase | 74 | GH9-CBD3c-DD | Cel9J | Cel9P | Eng9L |
| Cel9F | Endocellulase | 60 | GH9-DD | Cel9M | Cel9P | Eng9L |
| Man5G | Mannanase | 47 | GH5-DD | Man5K | Man5A | |
| Cel74H | Endocellulase | 91 | GH9-CBD3b-DD | – | XgH74A | – |
| | | | | | | |
| **Cel9X** | **Endocellulase** | **96** | **CBD4-Ig-GH9-DD** | **Cel9E** | **Cel9K** | **Eng9K** |
| **Cel5Y** | **Endocellulase** | **110** | **(SLH)3GH5-DD** | **–** | **Cel5E** | **Eng5E** |

Sabathe et al (2002) *FEMS Microbiol. Lett.* 217, 15-22

Sabathe et al (2003) *J. Bacteriol.* 185, 1092-1096.

# Characterisation of *C. acetobutylicum's* cellulases

- **Cel9C**, **Cel5Y** and **Cel5B** were successfully produced and purified from *E. coli* and were shown to be active

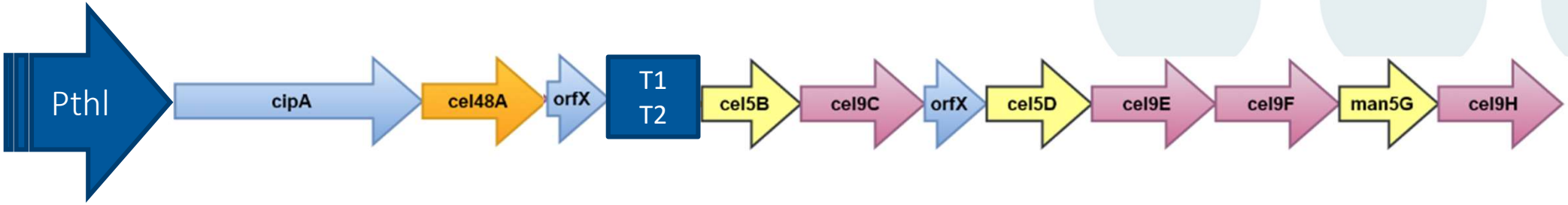
- We were **unable** to successfully produce and purify from *E. coli* **a soluble version** of the two processive endocellulases **Cel9X** and **Cel48A**

| | Activity (IU/µM) | | | | |
|---|---|---|---|---|---|
| | *C. acetobutylicum* | | | *R. cellulolyticum* | *R. thermocellum* |
| | **Cel9C** | **Cel5B** | **Cel5Y** | Cel9G | Cel5G |
| **CMC** | 1217 | 132 | 264,7 | 1170 | 180 |
| **PASC** | 25.8 | 47 | 36,6 | 38 | 127 |
| **Avicel** | 2.6 | 1.9 | 0,9 | 5 | 9 |

Wilding-Steele et al .(2022) Genetically Modified Lignocellulolytic *C. acetobutylicum. Int. Patent Application.*

# Characterisation of Cel48A produced in *C. acetobutylicum*

- A strain was constructed in which the native promoter of the ***cip-cel*** operon was changed to the strong **thiolase promoter**
- Secondly, the **T1T2 terminator** was inserted after *cel48A* along with a second copy of *orfXp,* this resulted in only *cipA, orfxp* and *cel48A* being expressed
- An additional strain was constructed in which the mutation E61Q was introduced into Cel48A
- E61 is the proposed proton donor and the equivalent mutation introduced in Cel48F (*E55Q*) resulted in only residual activity

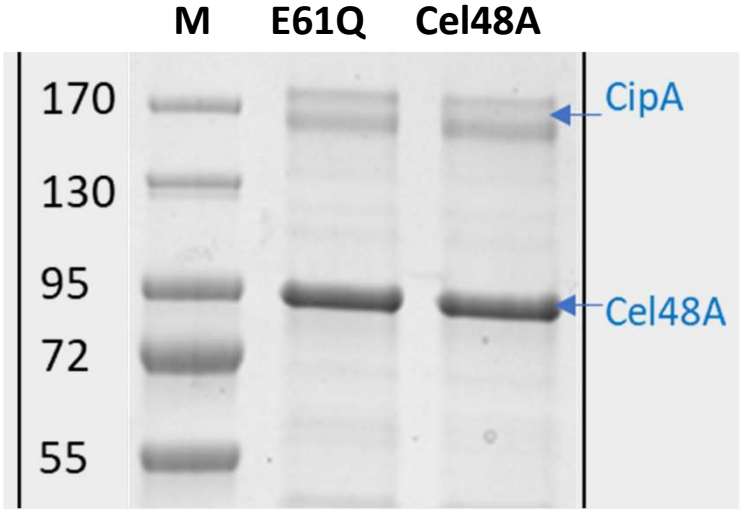



Wilding-Steele et al .(2022) Genetically Modified Lignocellulolytic *C. acetobutylicum*. *Int. Patent Application.*

Wilding Steele et al .(2021) *Int. J. Mol. Sci.*. 22, 3704

# Characterisation of Cel48A produced in *C. acetobutylicum*

- The mini-cellulosome was purified from the two strains and was shown to consist of mainly **CipA** and Cel48A
- **Cel48A** is **active** on Avicel and PASC, while significantly lower activity is observed for Cel48A-E61Q
- Cel48A has lower activity on PASC compared to Cel48F
- Slightly higher activity is observed on Avicel, although this is probably due to Cel48A being in a complex with CipA



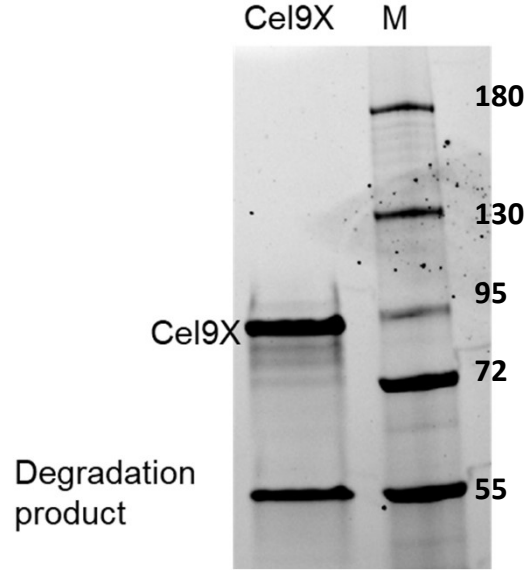

| Substrate | Activity (mUI/mg) | | |
|---|---|---|---|
| | **E61Q** | **Cel48A** | **Cel48F** |
| PASC | 2,7 | 25,7 | 130 |
| Avicel | 1,3 | 4,8 | 3,2 |

**Cel48A is active**

Wilding-Steele et al .(2022) Genetically Modified Lignocellulolytic *C. acetobutylicum*. *Int. Patent Application.*

# Characterisation of Cel9X produced in *C. acetobutylicum*

- The promoter of *cel9X* was changed to the strong thiolase promoter
- This resulted in a protein whose size corresponded to Cel9X being produced
- Cel9X was purified from the supernatant using cellulose affinity chromatography
- **Cel9X** was shown to be **active** on both PASC and Avicel




| Substrate | Activity in mU/mg |
|---|---|
| PASC | 262 |
| Avicel | 5.2 |

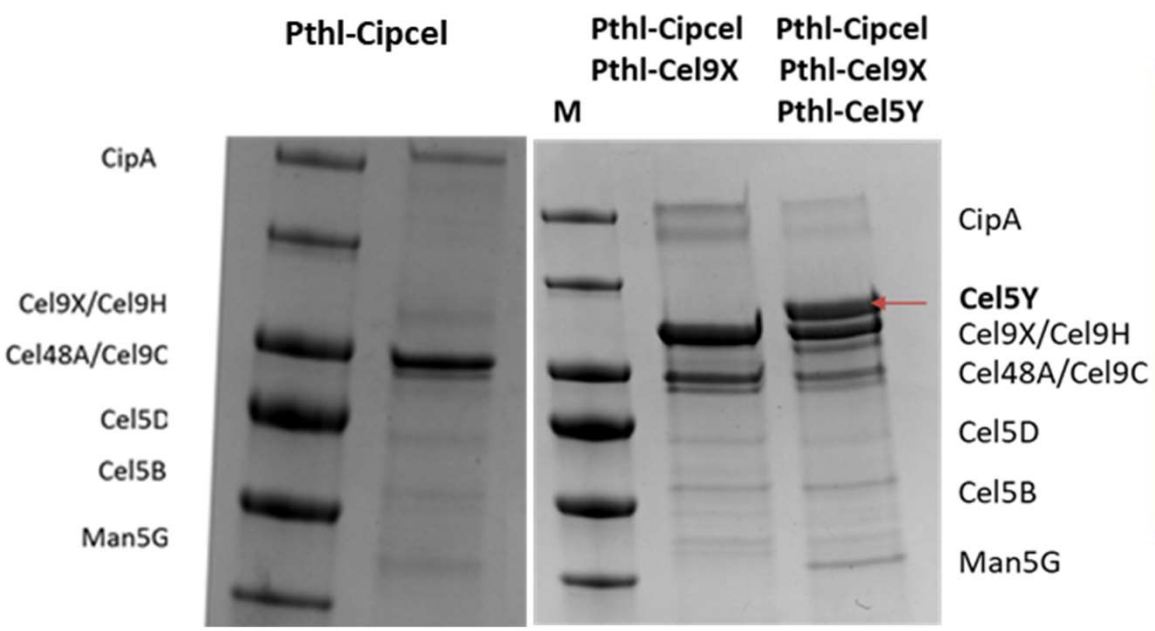
**Cel9X is active**

Wilding-Steele et al .(2022) Genetically Modified Lignocellulolytic *C. acetobutylicum*. *Int. Patent Application.*

# *C. acetobutylicum's* native cellulosome is active

- The *cip-cel* operon along with *cel9X* and *cel5Y* were overexpressed by changing their native promoters to the strong thiolase promoter

- High production of CipA the main scaffoldin protein and all of the main cellulosomal components was observed



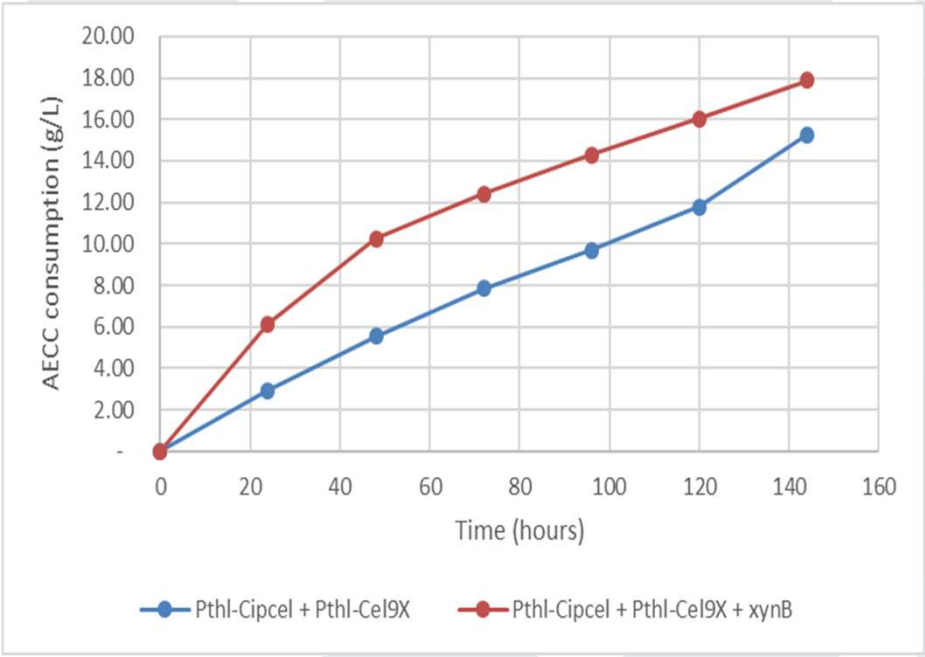

| Substrate | Activity (mUI/mg) | | | |
|---|---|---|---|---|
| | *R. Cellulo -lyticum* | *pthl-cip-cel* | *pthl-cipcel, pthl-Cel9X* | *pthl-cipcel, pthl-Cel9X pthl-Cel5Y* |
| PASC | 368 | 281 | 403 | 1333,3 |
| Avicel | 39 | 9,4 | 21 | 25,6 |

***C. acetobutylicum's* native cellulosome is active**

Wilding-Steele et al .(2022) Genetically Modified Lignocellulolytic *C. acetobutylicum. Int. Patent Application.*

# Role of xylanases in AECC degradation

- For growth on AECC, the expression of hemi-cellulases encoding genes is also important: preliminary experiments showed that addition of commercial xylanases resulted in faster growth on AECC
- The *xynB* gene from *C. acetobutylicum* was then overexpressed by cloning a second copy downstream of the thiolase gene, in *Pthl-cipcel*, *Pthl-cel9X*
- This resulted in significantly improved AECC degradation
- Importantly, there was **co-consumption** of both **hexose** and **pentose** sugars with no carbon catabolite repression observed




Fermentation performed in vials with 25 g/L AECC

Wilding-Steele et al .(2022) Genetically Modified Lignocellulolytic *C. acetobutylicum*. *Int. Patent Application.*

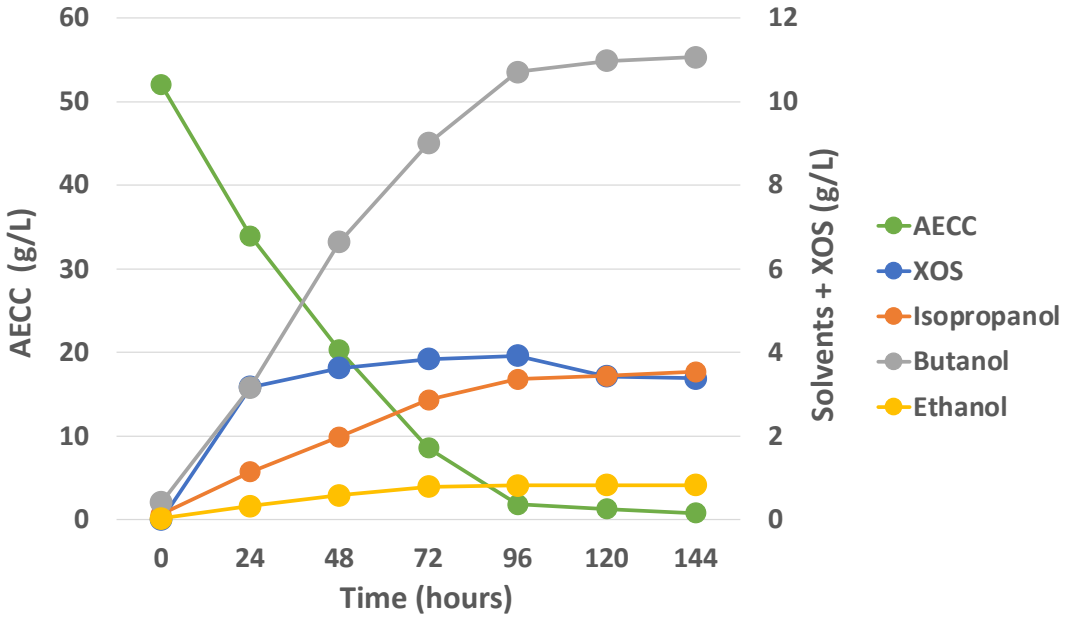
# Direct conversion of AECC to advanced biofuel mixtures

- Our basic cellulolytic strain was further improved by i) engineering the **cellulosome composition** as well as ii) its **efficiency of secretion**.

- The lignocellulolytic strain was then metabolically engineered to produce produce a mixture of **Isopranol-Butanol-Ethanol** by deleting the *ptb-buk* genes and overexpressing the *ctfAB-adc-sadH-hydG* genes from a plasmid.

- All AECC was solubilized in 96 hours and a titer of **15,4 g/L of advanced biofuel** was obtained

- The **average biofuel productivity** was **0.16 g/l.h** and the yield was **0.3 g/g.**




Fermentation performed in fermentor at pH5.5 with 50 g/L AECC

**To the best of our knowledge, these values are the highest ever obtained for a CBP process performed on "real" lignocellulosic feedstocks**

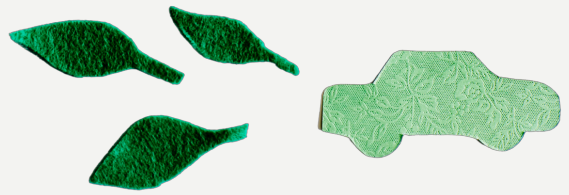
# Conclusion

- We demonstrate that the main components of the cellulosome of *C. acetobutylicum* are functional, including the key processive endocellulases Cel48A and Cel9X.
- By engineering synthetic cellulosomes and improving their efficiency of secretion we demonstrate that it possible to hydrolyze 50 g/l of AECC in less than 96 hours while co-metabolizing C6 and C5 sugars.
- This strain was further engineered to produce a mixture of advanced biofuels from lignocellulose in a CBP process at the highest titer, yield and productivities ever reported.
- This strain has now been further engineered to produce ethanol only from ligno-cellulose.

# LAUNCH OF CELLUOL

Celluol

Embracing Climate-Friendly Fuels and Chemicals
for a Sustainable Planet



**If you want to know more about our technology or business model**
**Please contact me!**

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# Metabolic engineering of *Cupriavidus necator* H16 for the bioproduction of chemicals

Katalin Kovács

Synthetic Biology Research Centre

BBNet Conference, Sheffield
10th of April 2024

# Vision for sustainable product synthesis

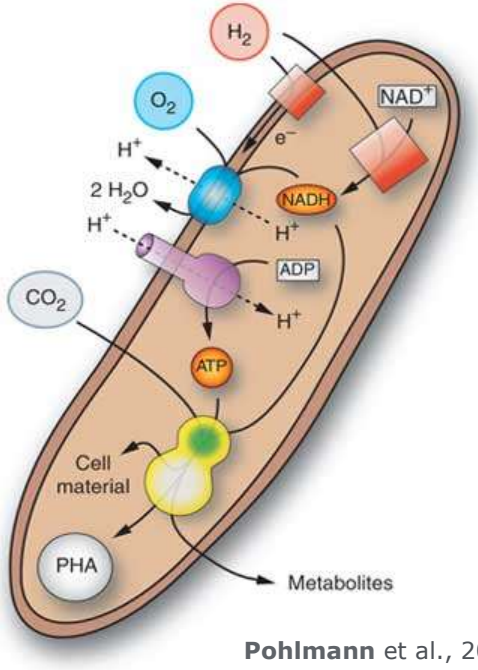


## Systems biology and engineering biology principles

**Overall strategy**

1. Choosing the appropriate biocatalyst - Why *Cupriavidus necator*?
2. Pathways and products – Engineering biology strategies and systems biology tool to prioritise
3. Examples of pathway engineering for biosynthesis from organic substrates and/or $CO_2$
4. Process engineering/optimisation, e.g. co-polymer production via mixotrophic feeding ( ie. AD-VFA and $CO_2$)

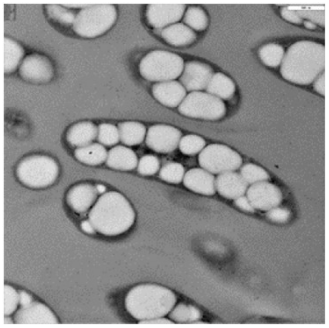
*Cupriavidus necator* H16



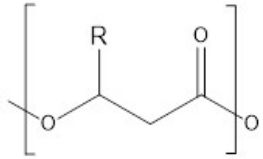

**Pohlmann** et al., 2006

# *Cupriavidus necator* H16

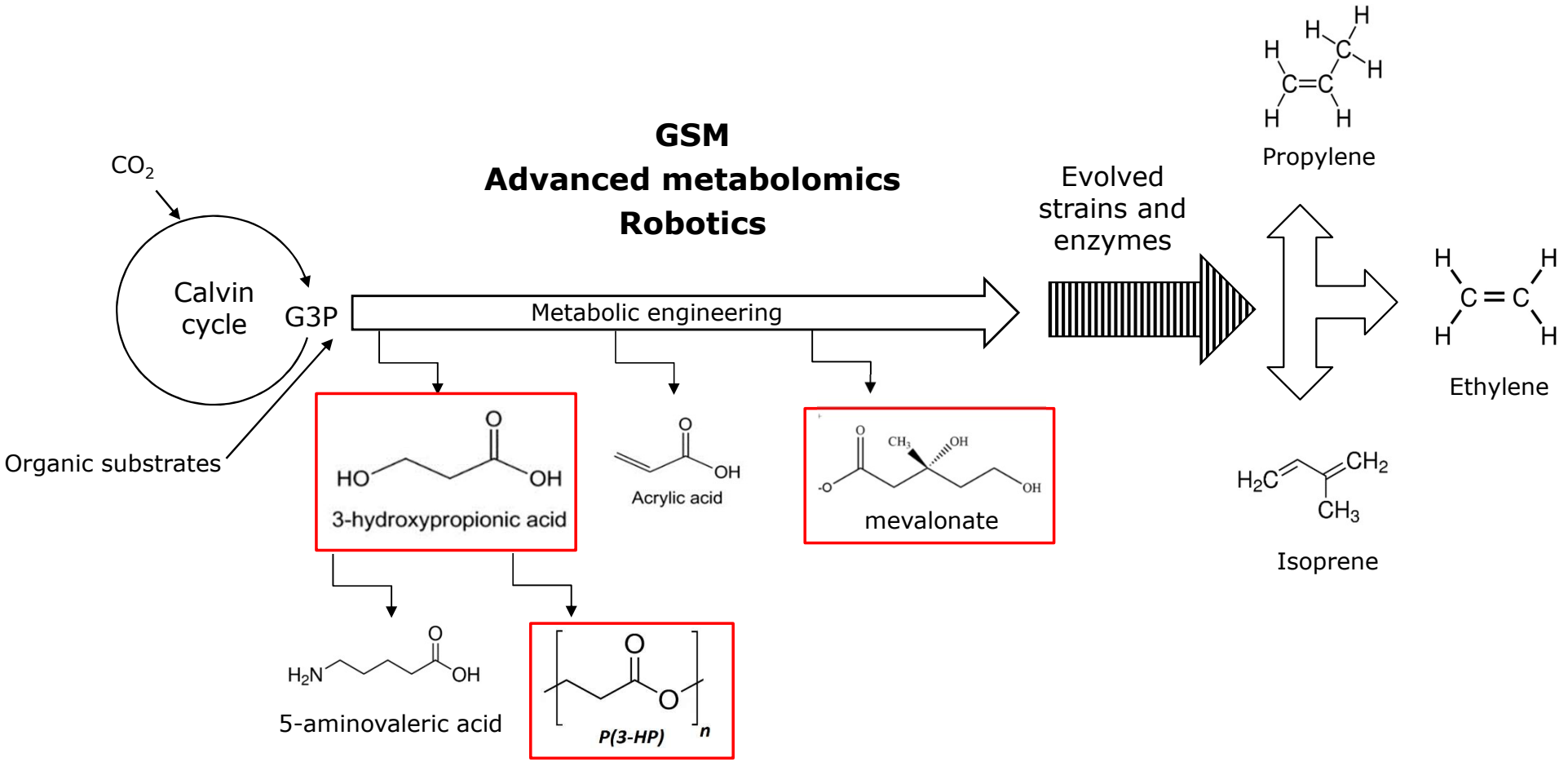
- Gram-negative betaproteobacteria
  - soil and freshwater
- Chemolithoautotroph
  - organic carbon sources, $CO_2$ and $H_2$ as sole carbon and energy sources
- Can reach high cell densities (~200 gDCW/L)
- Known for accumulation of polymer
  - Polyhydroxyalkanoates (PHAs)
- Industrially relevant organism
  - previously used to produce polymers, ethanol, ketones, isopropanol, fatty acids



*C. necator* harbouring PHB granules



# Targets via industrially relevant intermediates

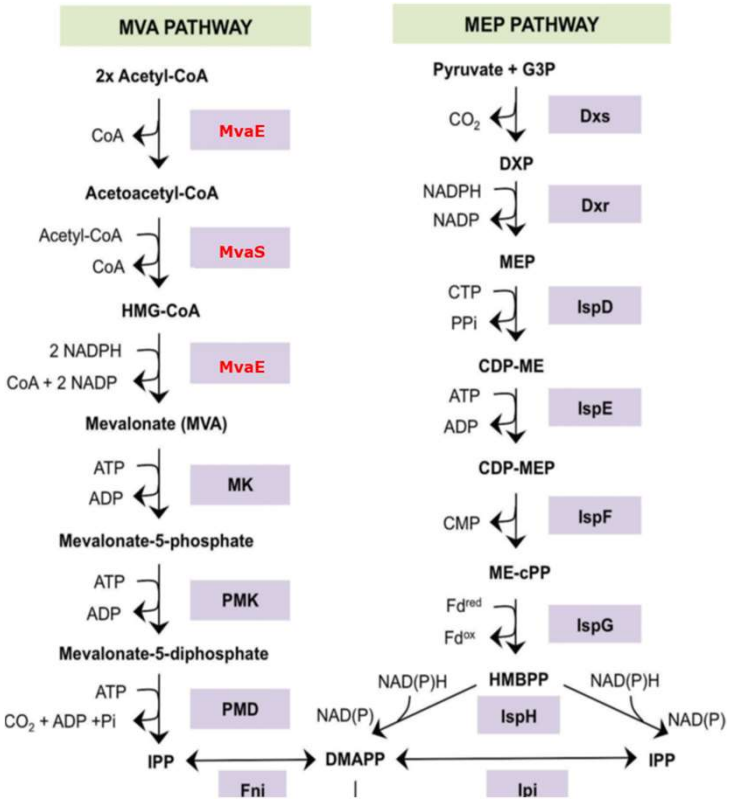


# 3-HP and Mevalonate

## 3-hydroxypropionic acid (3-HP)

- Important building block for **acrylic plastics** and **biodegradable polyesters**
- Can be converted into other high value chemicals
- Chemical synthesis - is **not commercially feasible** due to low yield and high production cost
- Biological synthesis - **thermodynamically favourable** pathways

## Mevalonate (MVA)

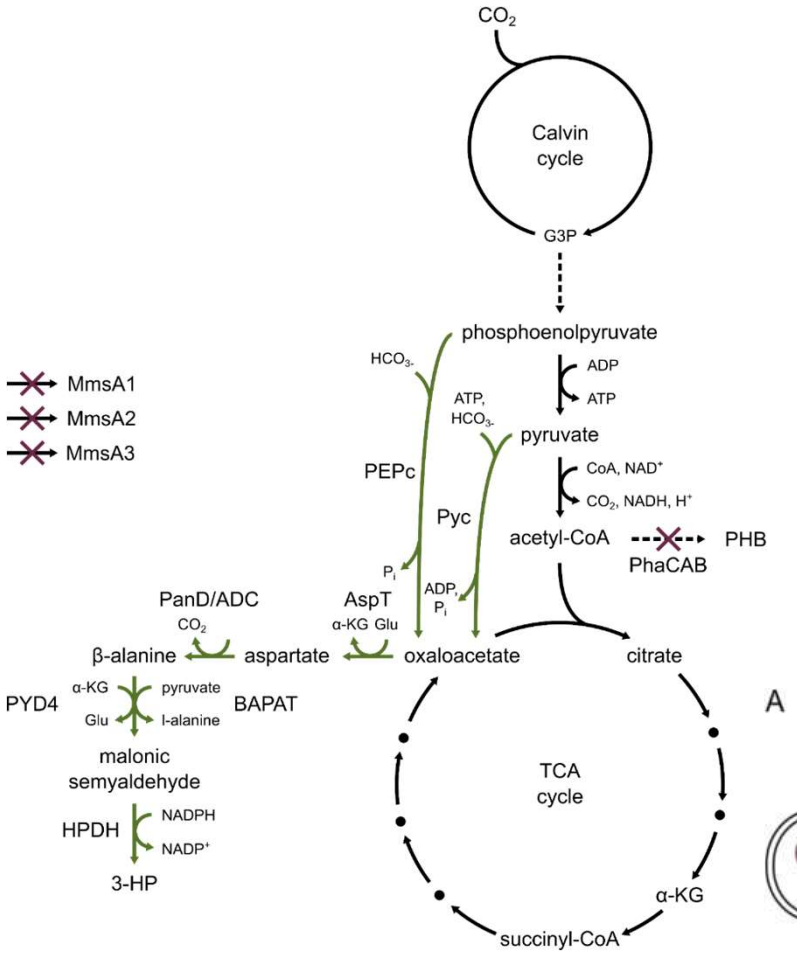


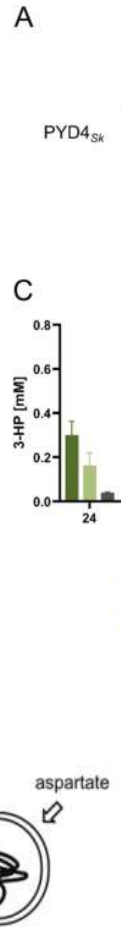

## Isoprenoid Backbone Biosynthesis

- MEP pathway is native in *C. necator*
- Heterologous MVA pathway to increase the flux towards production of IPP and DMAPP
- IPP and DMAPP are precursors of terpenes (e.g. isoprene, limonene)
- **Mevalonate** is used in cosmetics and as a building block to produce sustainable polymers

# 3-HP production in *C. necator* H16

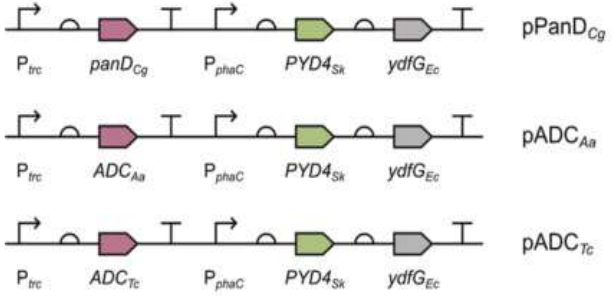


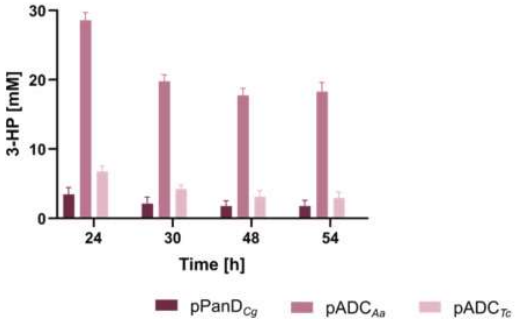









Arenas *et* al., 2019

Salinas *et* al., 2022

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# 3-HP production in *C. necator* H16

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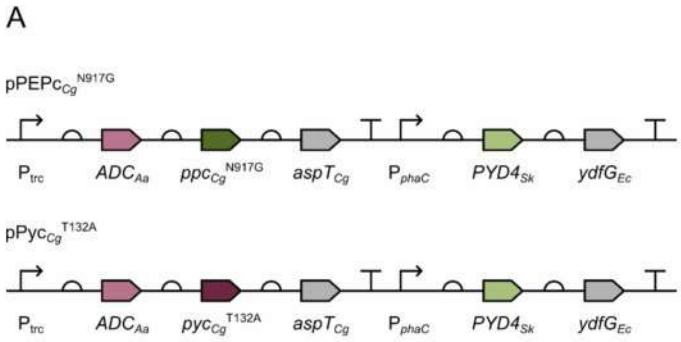
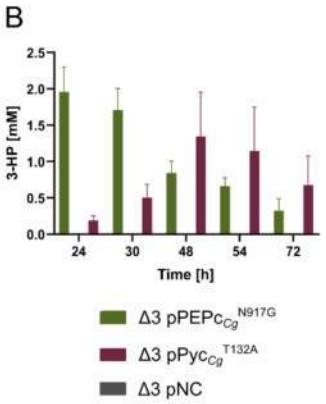
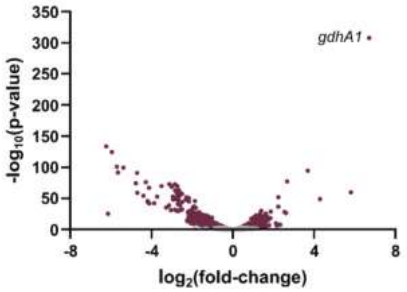
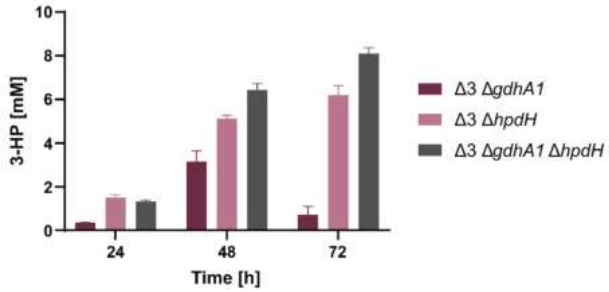
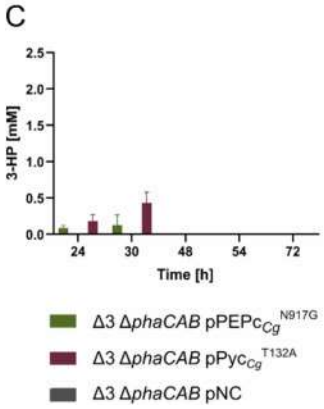
a BBSRC/EPSRC Synthetic Biology Research Centre

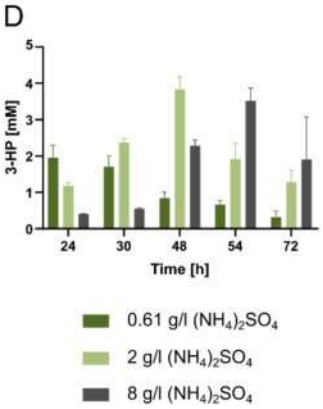


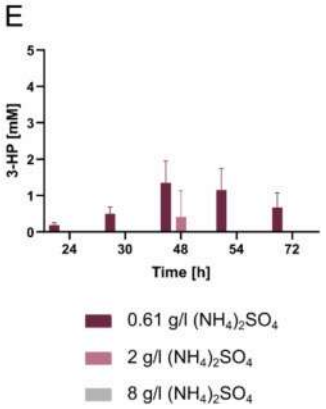



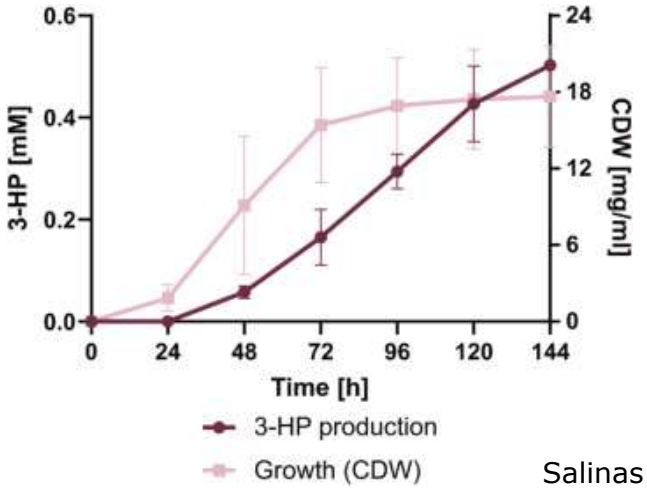



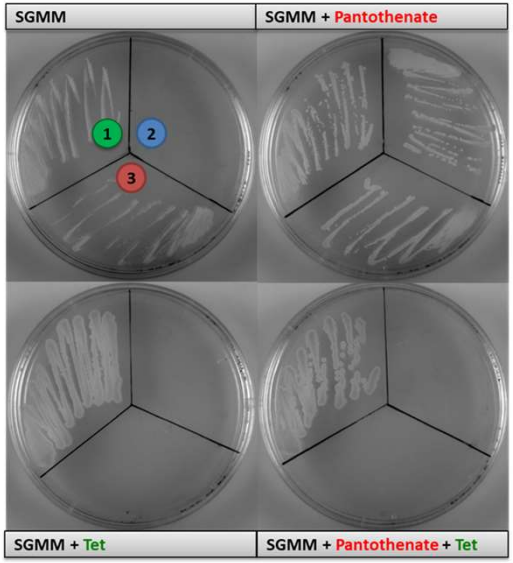




Salinas *et* al., 2022

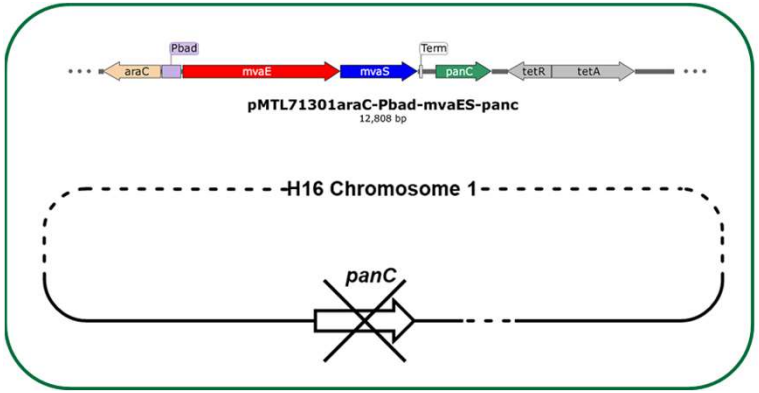
# MVA production in *C. necator* H16

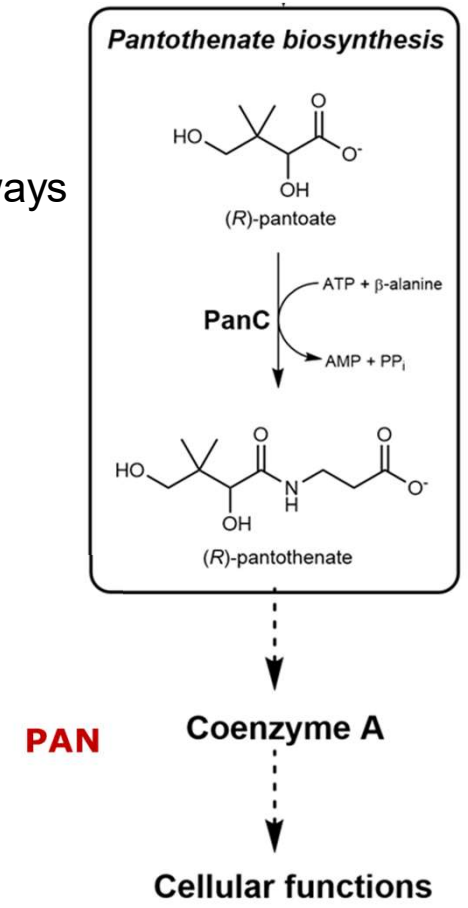
- Plasmid based expression of the *mvaE* and *mvaS* genes from *Enterococcus faecalis* – product (MVA) synthesis in shake flask – plasmid stability
- Pathway integrated into the genome – reduced product formation
- Develop a plasmid addiction systems allow stable overexpression of heterologous pathways without the use of antibiotics:
  - pantothenate synthetase (*panC*) in *C. necator* genome (single copy)
  - Sole pathway for pantothenate and Coenzyme A biosynthesis

  (required for essential cellular functions)

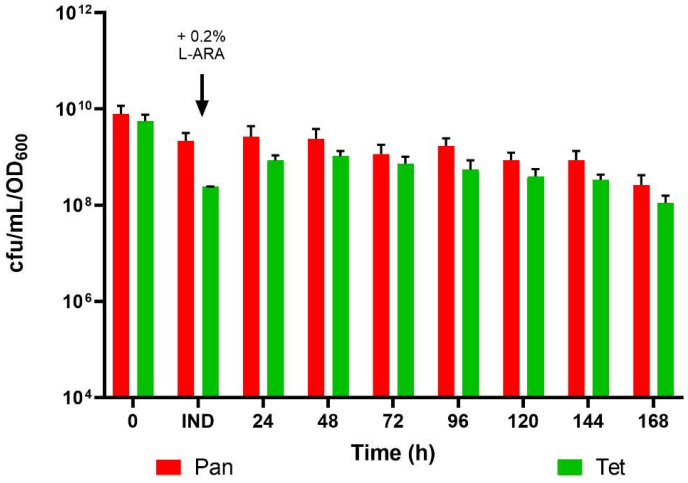


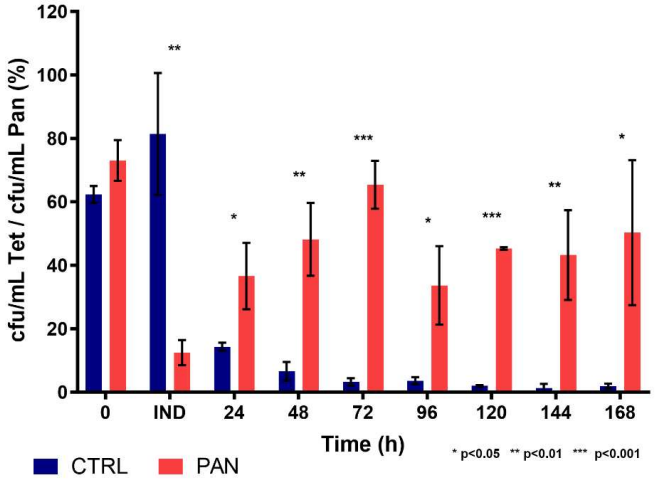

1 = H16 *ΔpanC* / pMTL71301::*panC*
2 = H16 *ΔpanC*
3 = H16 Wild type



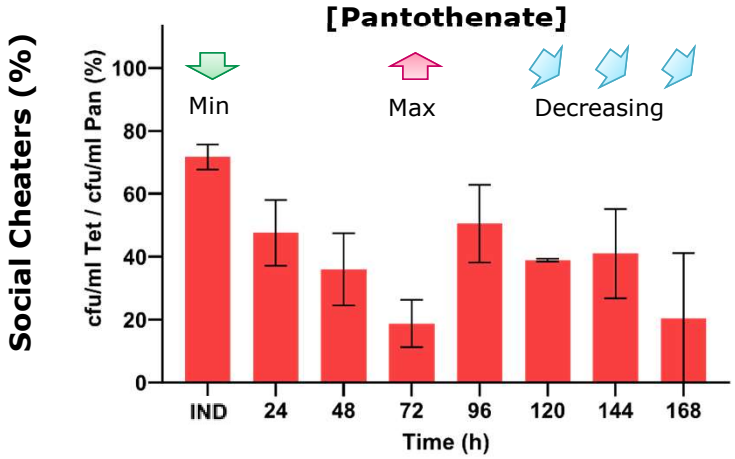



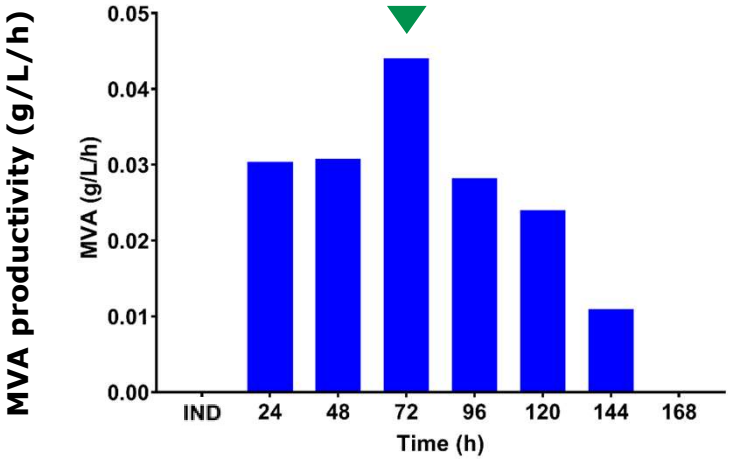
# MVA production and plasmid stability




## Emergence of "social cheaters" and MVA production in PAN

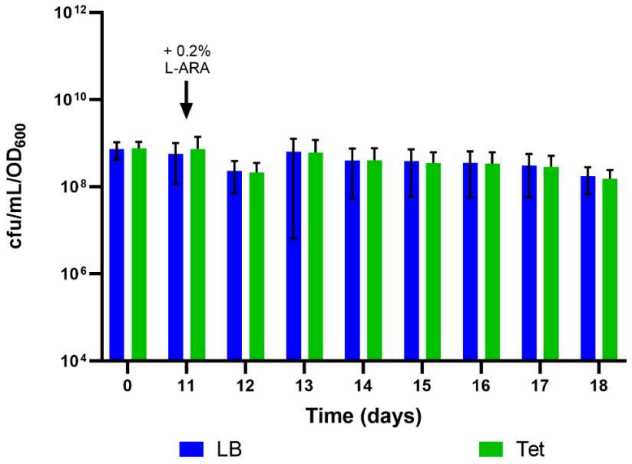


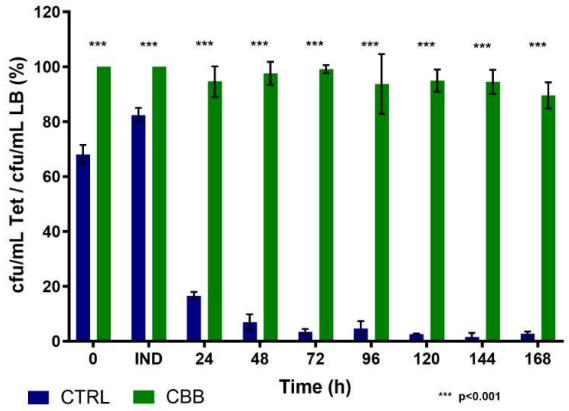



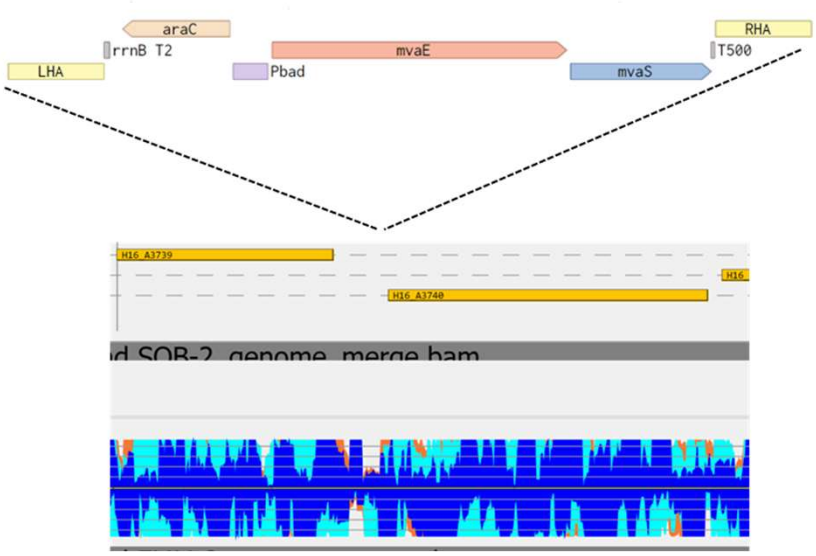

- correlation between MVA production rates and the levels of "cooperators"
- highest MVA productivity when the percentage of "social cheaters" in the population was the lowest.
- *panC*-based plasmid addiction system is not reliable enough to be used in fermentation processes at larger scales

# Alternative plasmid addiction system

- We have identified RuBisCO-encoding operons as targets (RuBisCO – “private good”)
- Generated H16 mutants (*ΔΔcbbLS*) lacking both copies of the RuBisCO-encoding operons (*cbbLS2* and *cbbLSp*) - unable to grow under autotrophic conditions
- Their ability to grow on $CO_2$ and $H_2$ was restored by a plasmid-borne copy of the *cbbLS2* operon (P*phaC*)



# MVA production from $CO_2$



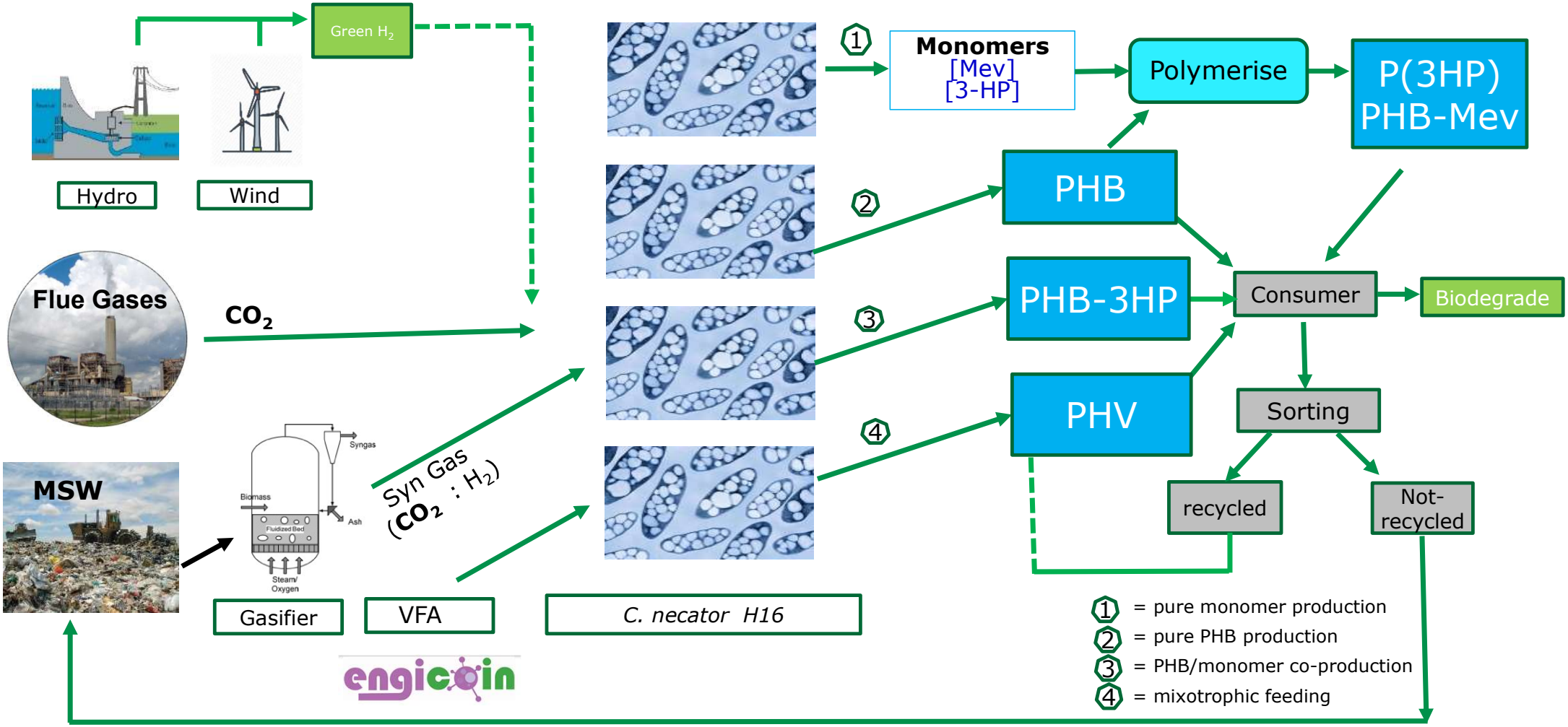
## Post-induction $CO_2$ consumption and MVA yields

| Strain | Post-induction $\Delta CO_2$ (mmol) | MVA (mmol) | MVA (Cmmol) | MVA yield (Cmol/Cmol) |
|---|---|---|---|---|
| CTRL | 693.677 | - | - | - |
| PAN | 1126.077 | 20.277 | 121.663 | **0.108** |
| CBB | 589.886 | 24.825 | 148.948 | **0.253** |
| KI | 588.089 | 2.591 | 15.547 | **0.026** |

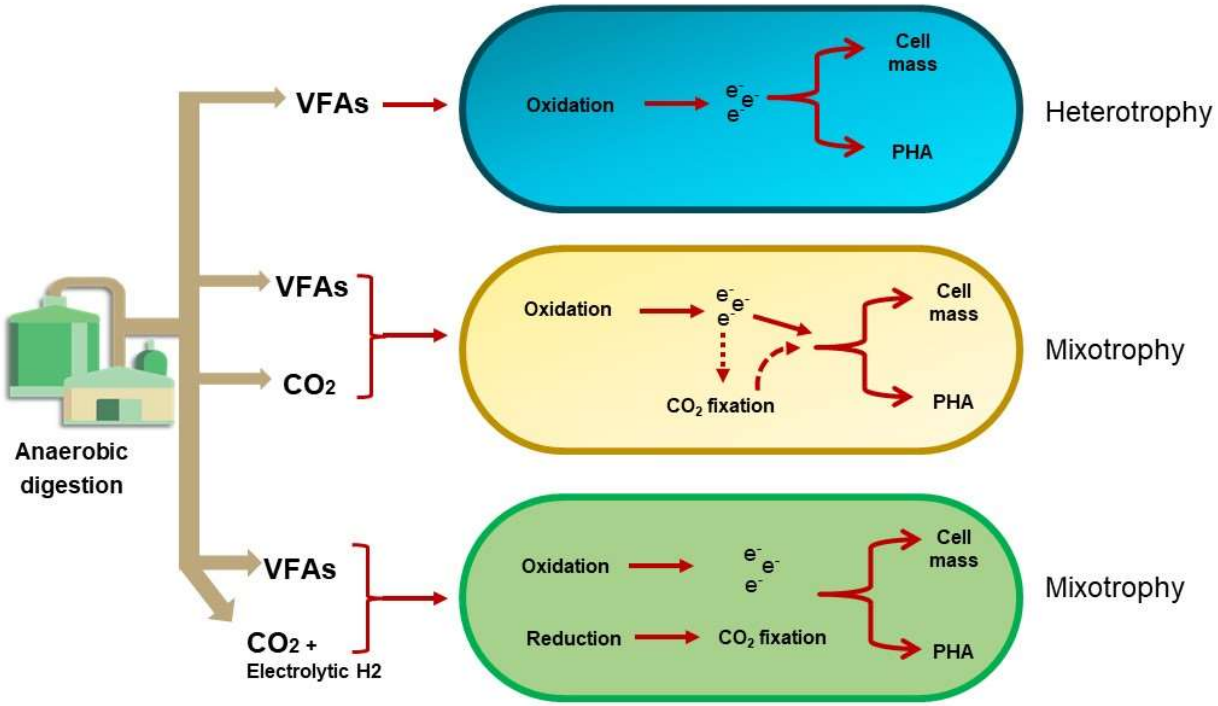
- The **H16 *ΔΔcbbLS*/pMTL71301::*araC*-Pbad-*mvaES*::*cbbLS*** (**CBB**) strain showed the **highest MVA yields** from $CO_2$ (~2.4-fold and ~9.7-fold higher than PAN and KI, respectively).

# *C. necator H16* - Circular economy context





## Establishing Mixotrophic Growth of *Cupriavidus necator* H16 on $CO_2$ and Volatile Fatty Acids (VFAs)




- VFAs available in significant amounts (40-60 g/L) in the AD digestate
- Customize PHA compositions by the inclusion of other monomers from VFAs
- Use of VFAs will also help to reduce the burden of the electrolytic $H_2$
- Mixotrophy with VFAs → increase in product yield

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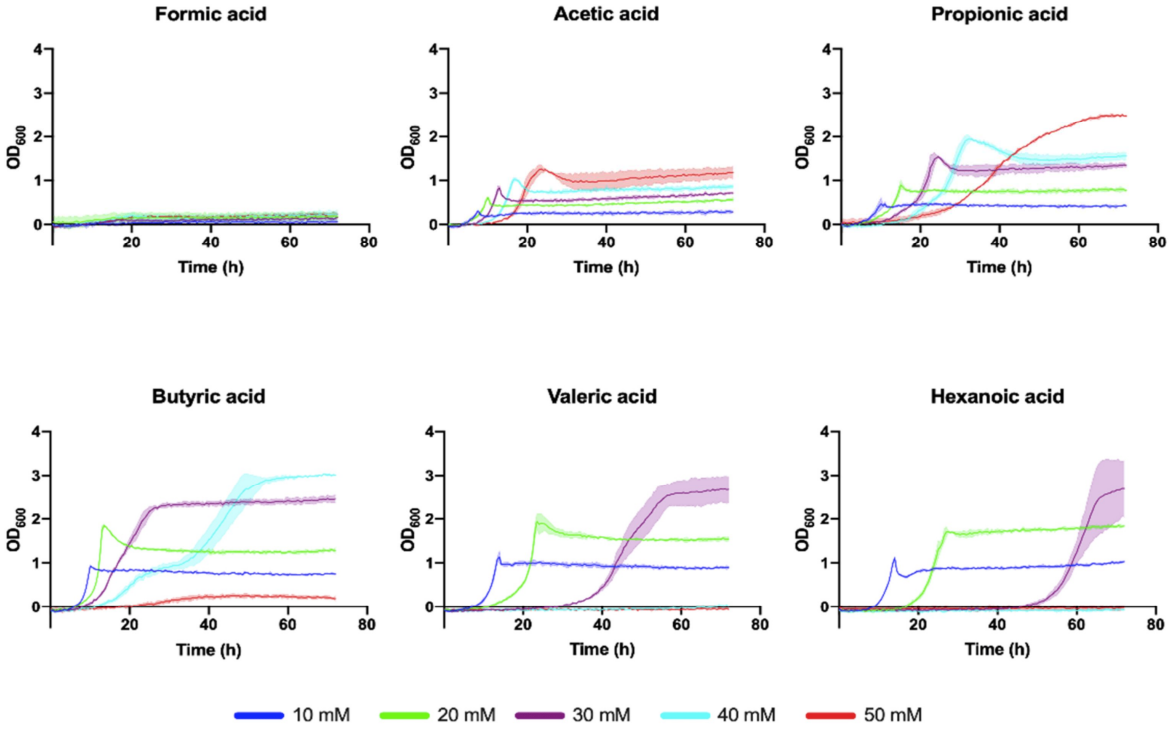
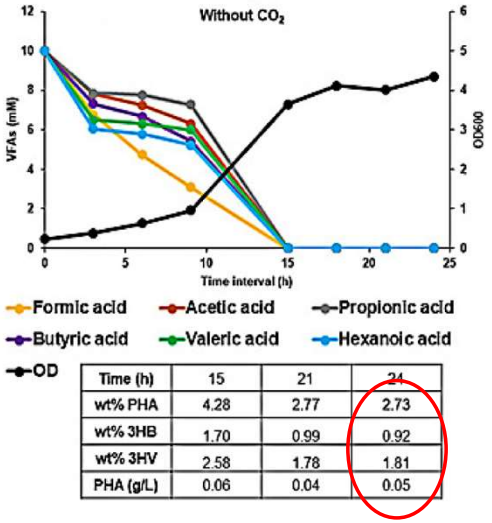
# Mixotrophic Growth of *C. necator* H16 on $CO_2$ and VFAs



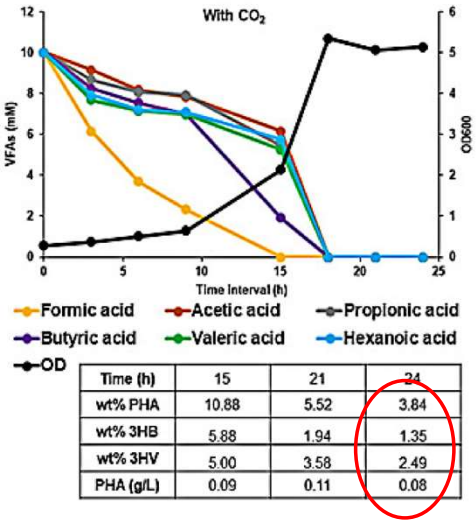
## Toxicity of VFAs




## Mixotrophic conditions




| Time (h) | 15 | 21 | 24 |
|---|---|---|---|
| wt% PHA | 4.28 | 2.77 | 2.73 |
| wt% 3HB | 1.70 | 0.99 | 0.92 |
| wt% 3HV | 2.58 | 1.78 | 1.81 |
| PHA (g/L) | 0.06 | 0.04 | 0.05 |




| Time (h) | 15 | 21 | 24 |
|---|---|---|---|
| wt% PHA | 10.88 | 5.52 | 3.84 |
| wt% 3HB | 5.88 | 1.94 | 1.35 |
| wt% 3HV | 5.00 | 3.58 | 2.49 |
| PHA (g/L) | 0.09 | 0.11 | 0.08 |

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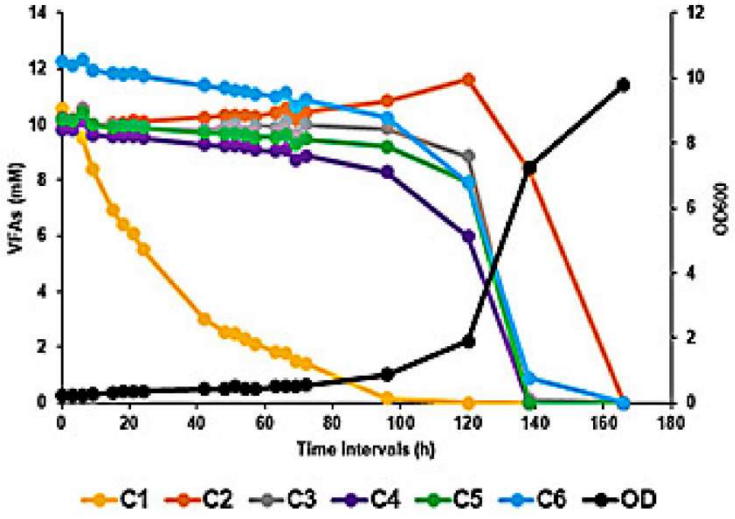
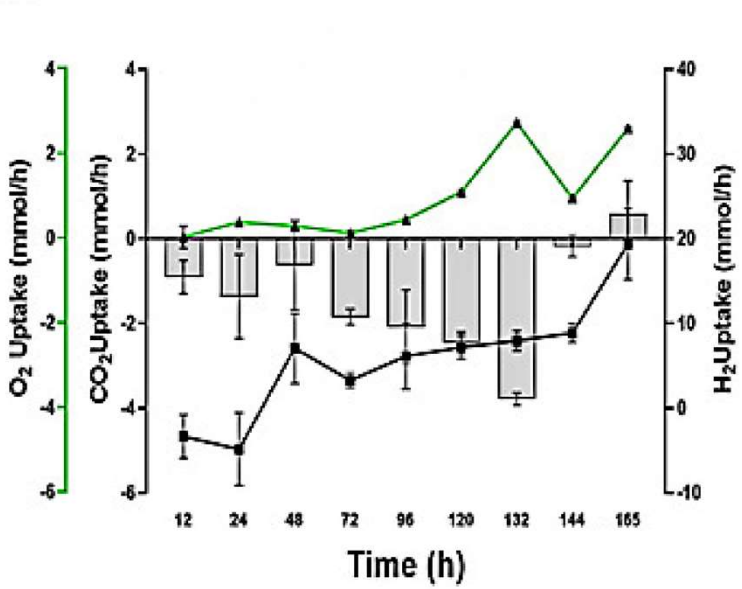
# Mixotrophic Growth of *C. necator* H16 on $CO_2$ and VFAs



## VFA+$CO_2$+$H_2$




| Time (h) | 144 | 166 |
|---|---|---|
| wt% PHA | 10.24 | 13.27 |
| wt% 3HB | 5.08 | 5.15 |
| wt% 3HV | 11.82 | 1.46 |
| PHA (g/L) | 0.19 | 0.37 |

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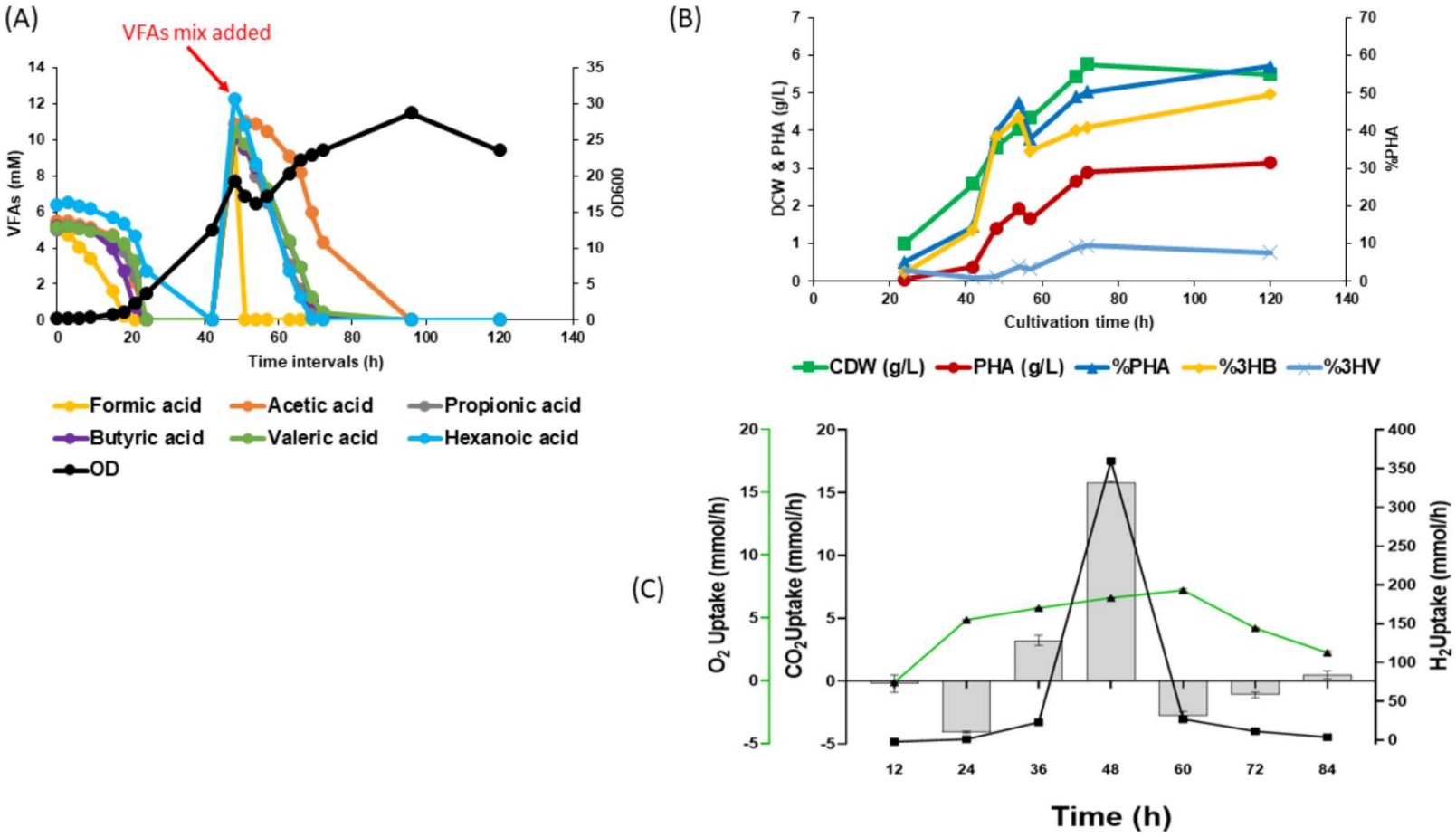
# Mixotrophic Growth of *C. necator* H16 on $CO_2$ and VFAs

$VFA+CO_2+H_2$

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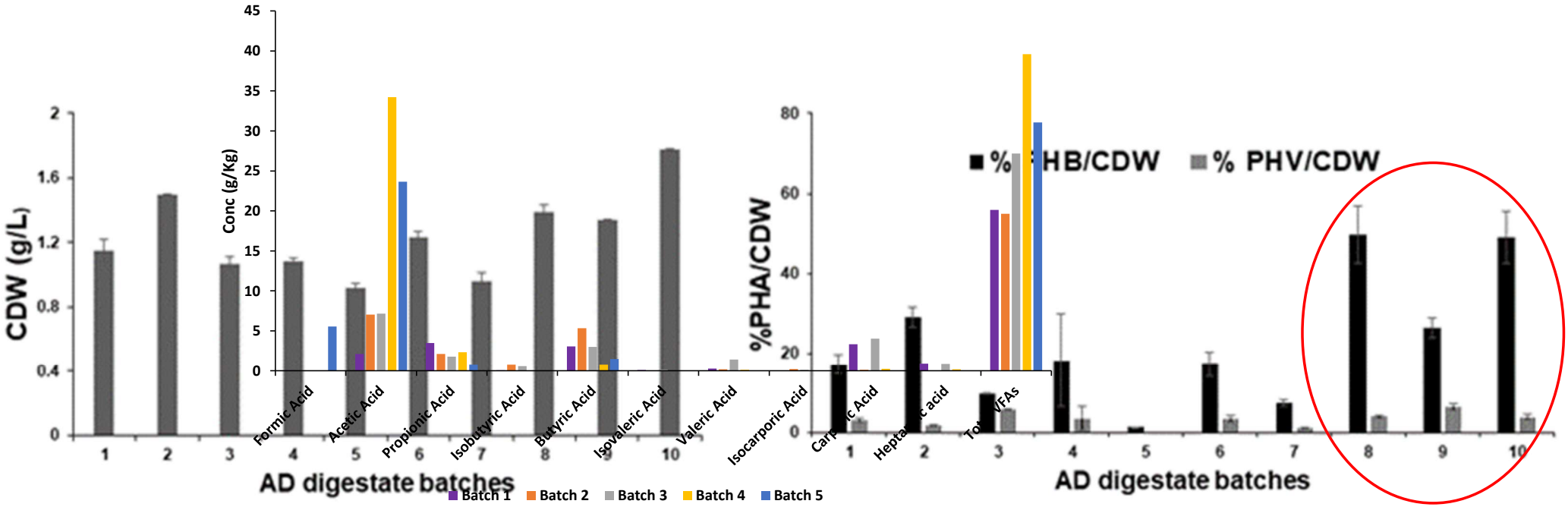
# Mixotrophic Growth of *C. necator* H16 on $CO_2$ and VFAs



## AD derived VFAs

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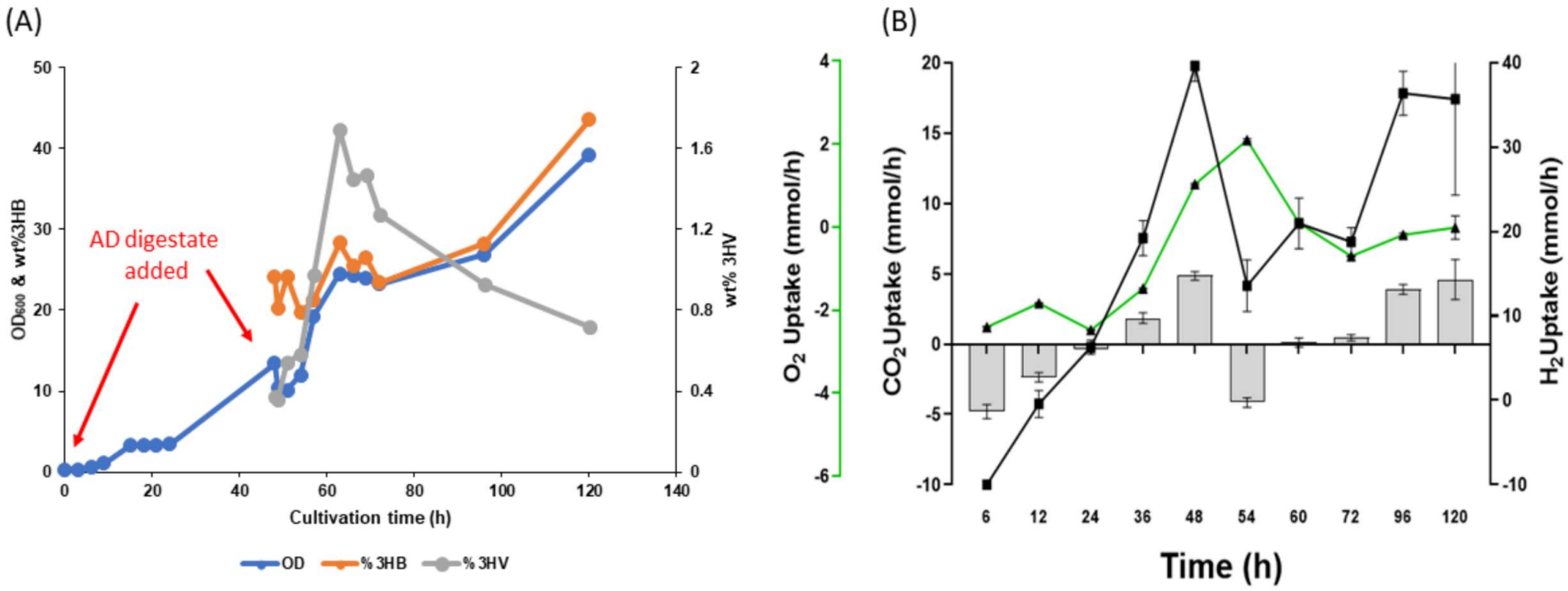
# Mixotrophic Growth of *C. necator* H16 on $CO_2$ and VFAs



## AD derived VFAs+$CO_2$+$H_2$

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University of Nottingham
UK | CHINA | MALAYSIA

SynBio
SBRC Nottingham
a BBSRC/EPSRC Synthetic Biology Research Centre

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- Klaus Winzer
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CCnet C1 CARBON RECYCLING

UKRI Engineering and Physical Sciences Research Council

UKRI Biotechnology and Biological Sciences Research Council

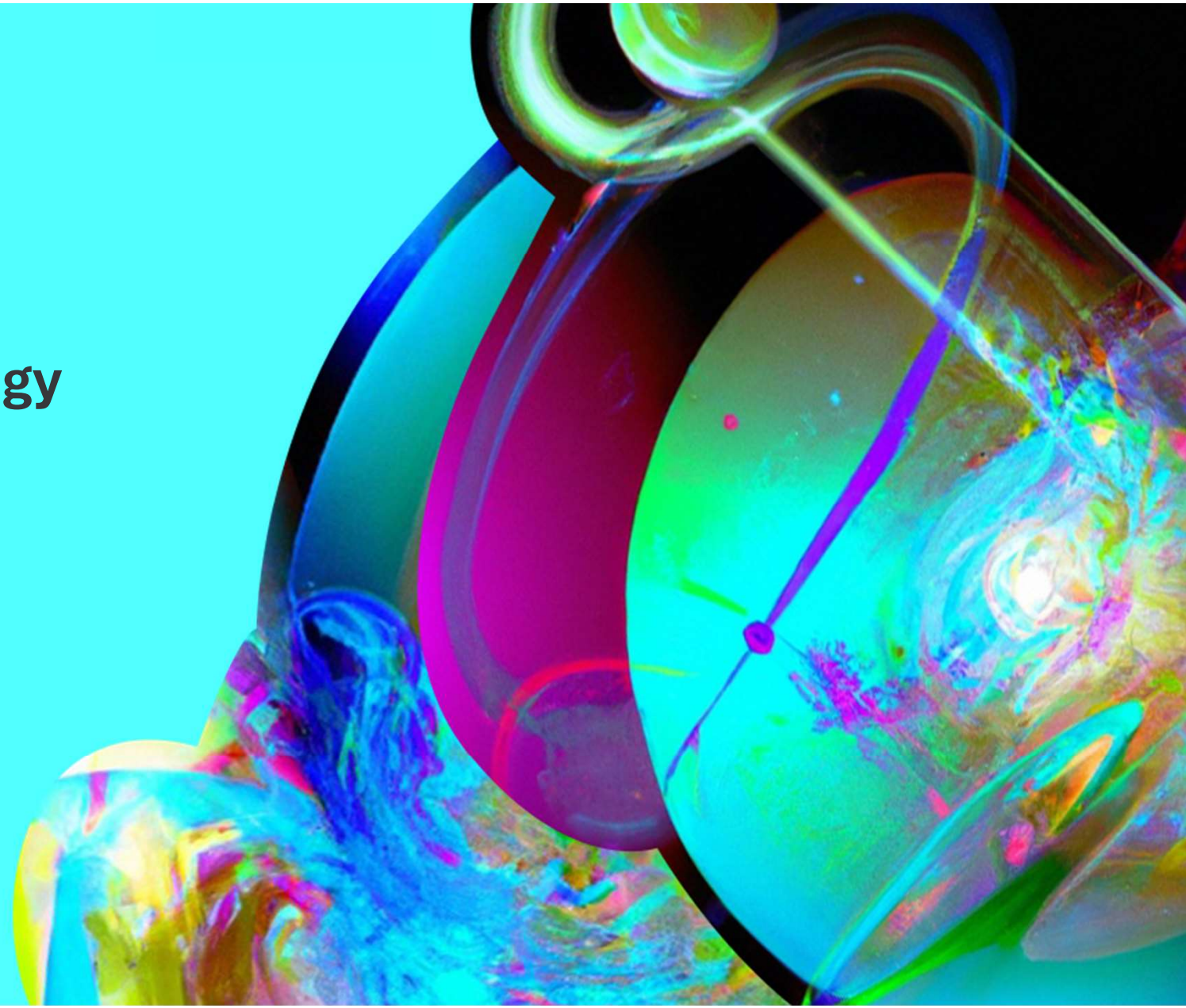
Horizon 2020 European Union Funding for Research & Innovation

Department for Science, Innovation & Technology

# National Vision for Engineering Biology

India Higgins

Policy Advisor, Engineering Biology



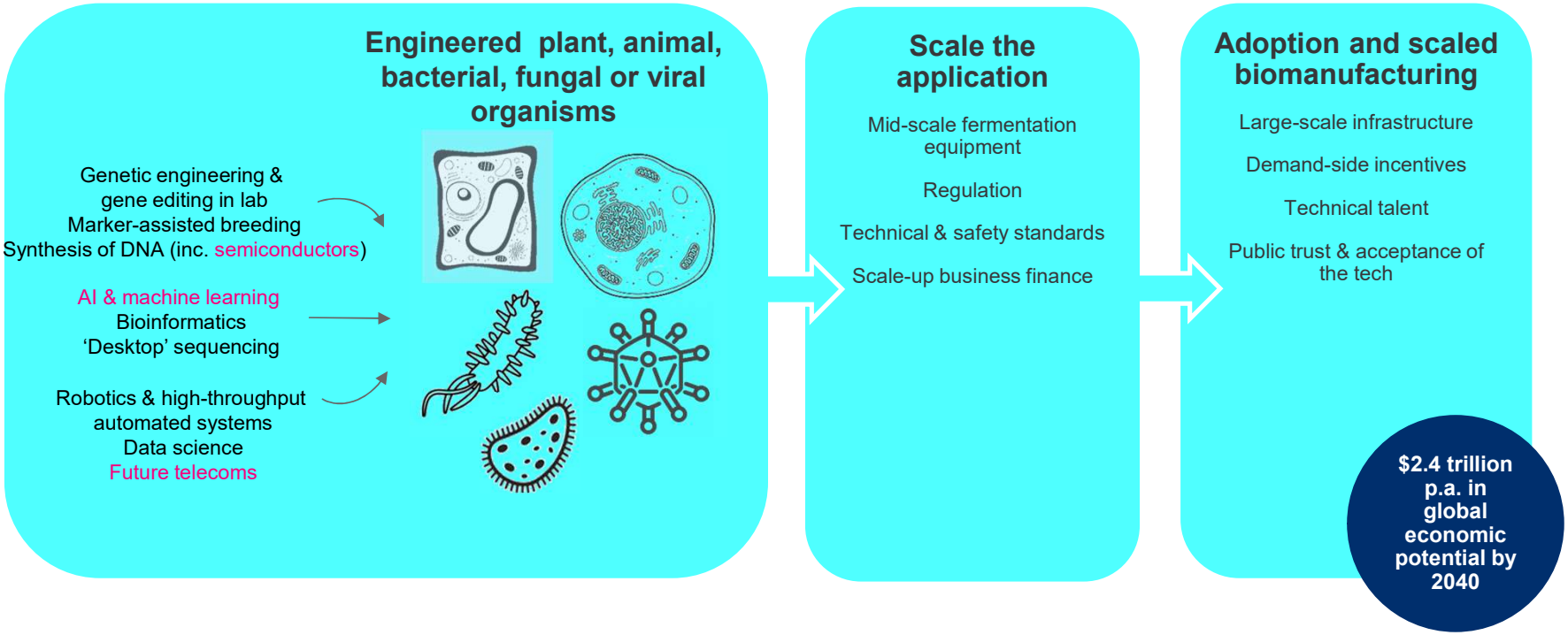
# Six key announcements and new policies

- The Vision is underpinned by public investment, supportive infrastructure, enabling regulation and standards, open markets, and a culture of responsible and trustworthy innovation.

1. Commitment to spend £2 billion on engineering biology over the next ten years.
2. A new Engineering Biology Steering Group to bring together both the current and the next generation of academic, start-up and industry leaders.
3. A plan for UK start-up and scale-up facilities.
4. £5m on new regulatory sandboxes for engineering biology, through the Engineering Biology Regulators' Network.
5. Fostering a cohort of investors and customers who are well-informed about engineering biology's potential, and a pipeline of firms who understand potential customers' priorities.
6. **Making the UK a world leader in responsible innovation by 2030**

# Engineering biology is the design, scaling & commercialisation of biology-derived products & services

- The term captures the full ecosystem of technical and business enablers of new products and services




- *Sources: Royal Academy of Engineering; McKinsey*

# EB applications are in five broad sectors: the ‘bioeconomy’

- UK firms demonstrate the opportunities of EB applications for growth, the environment and Net Zero

**Defra:** veterinary vaccines and diagnostic tools; animal and plant health policy & sector teams

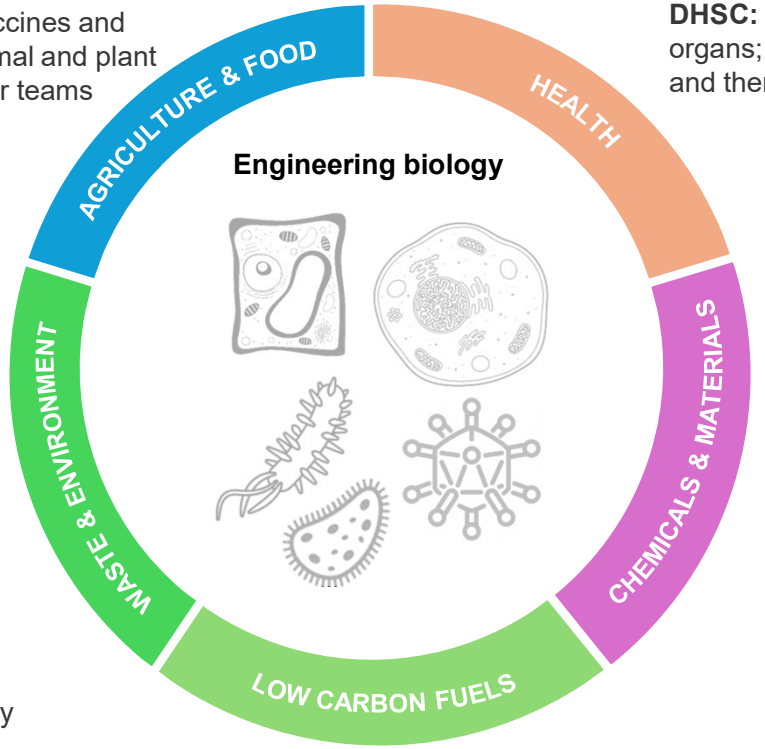
**DBT:** Food and agriculture sector team

**MOD:** trauma medicine, and future medicines

**DESNZ:** Biomass Strategy and CCS/CCU

**Wales:** South Wales MedTech sector

**CO:** Biological Security Strategy




**DHSC:** precision and personalised medicine; artificial organs; smart and responsive drugs; mRNA vaccines and therapies; CERSI and MHRA collaboration.

**HO & Police:** improving and expediating health response for national security; detection of materials, synthetic drugs

**DBT:** Life Sciences sector team

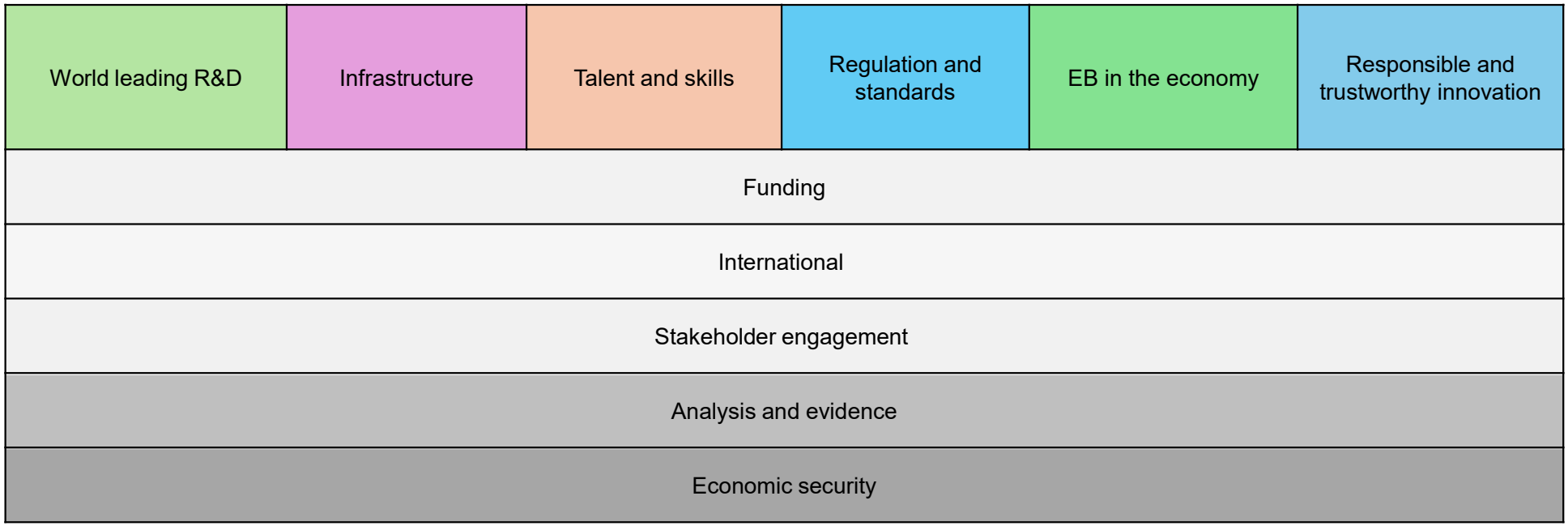
**Scotland:** CPI Medicines Manufacturing investment, and Life Sciences Programme; strengths in personalised medicine

**DBT:** Chemicals and Materials sector team

**DfT:** Sustainable Aviation Fuel Programme

## The Vision is of a broad, rich engineering biology ecosystem in the UK, that can safely develop and commercialise the many opportunities to come

- We aim to capture as much economic value, security, resilience and preparedness as possible from our hard-won strengths.



# Infrastructure

We will use UK infrastructure to reduce the costs of both the early stages of engineering biology innovation, and its scale-up.

**New policy:**

- Develop a plan for lab-scale and pilot-scale facilities
- Work with existing facilities to make them more accessible and discoverable
- FCDO will track international infrastructure development
- Support access to international capabilities and capacity

# Talent and skills

We will grow and retain a diverse talent pool within the UK to match demand from academia and industry, covering scientific, technical and entrepreneurial skills at all levels.

**New policy:**

- For scientific skills, implement the Discovery Fellowships
- For technical skills, draw on DfE's delivery plan under the S&T Framework: Institutes of Technology, increase uptake of apprenticeships by SMEs, establish occupational standards, develop degree apprenticeships.
- For entrepreneurial skills, celebrate the success of the UK's EB firms, and join-up successful leaders with emerging entrepreneurs

# Regulation and standards

We want the UK to have a regulatory landscape that allows EB-derived products to reach markets.

**New policy :**

- Regulations should be clear and support innovation, and a responsive regulatory environment is key for generating public trust in the technology.
- We have created the EB Regulators' Network for collaboration, knowledge sharing and horizon scanning
- £5 million for regulatory sandboxes to help the EBRN develop new regulatory frameworks for products derived from EB
- The Regulatory Horizons Council is undertaking a project on EB to deliver recommendations
- Defra will engage with stakeholders on implementation of the UN's Convention for Biological Diversity
- We will support adoption of technical standards where helpful, including internationally

# EB Sandbox Fund will accelerate regulatory reforms of EB-derived products

UK regulators can submit a bid for funding to run sandboxes focused on products derived from engineering biology

***Sandbox:*** *an environment that allows for research and development activities and facilitates extensive dialogue between industry and a regulator to inform regulatory thinking and actions*

**How will it work?**

- **Round 1 –** Closes 19 April. £1.8m available.
- **Round 2 –** Will open end of 2024. £3m available

Sandboxes should be **targeted**, **ambitious** and **collaborative.**

We are looking for proposals which address the regulatory challenges associated with market innovation, emerging technology or new business models – projects which embody "innovation friendly regulation" thereby encouraging investor conditions within the UK.

https://www.gov.uk/government/publications/engineering-biology-sandbox-fund

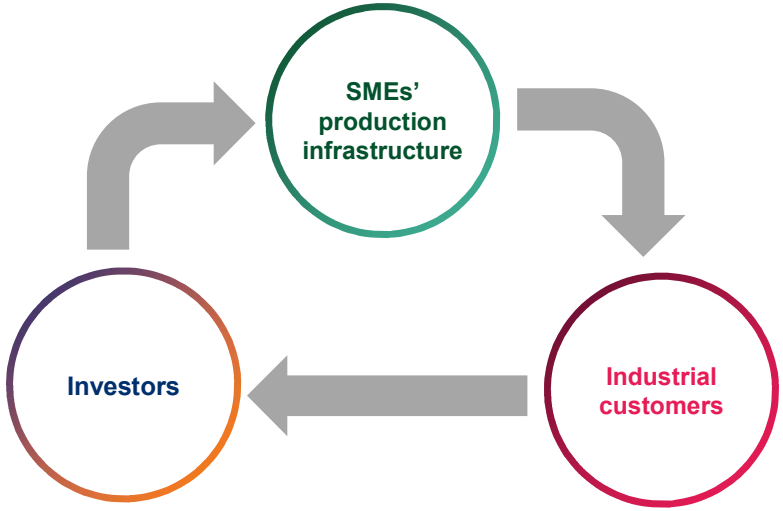
# EB in the economy

We will foster a cohort of UK investors and customers who are well-informed about the potential of engineering biology and the pipeline of UK firms and entrepreneurial talent that is emerging.

We will also help those firms to understand customers' priorities and requirements.

**New policy:**

- Structure interactions between firms and potential customers, while building investors' understanding and assurance.
- We will run a showcase of UK engineering biology for industrial customers and investors
- Consider technology milestones to give investors and customers greater assurance about tech readiness



# Responsible and trustworthy innovation

We will make the UK a world leader in responsible innovation by 2030, ensuring the UK secures the economic, health and societal value from advances in biosciences and biotechnologies while guarding against potential misuse.

**New policy:**

- Build public trust through a safe and responsible innovation ecosystem, and holding a positive, transparent and constructive public dialogue
- We've created the Biosecurity Leadership Council and given them some initial priorities for advice
- Further embed principles and standards for responsible research and innovation
- Work in multilateral forums to shape global norms and standards, particularly the OECD
- Build an evidence-backed analysis of the public's view of EB

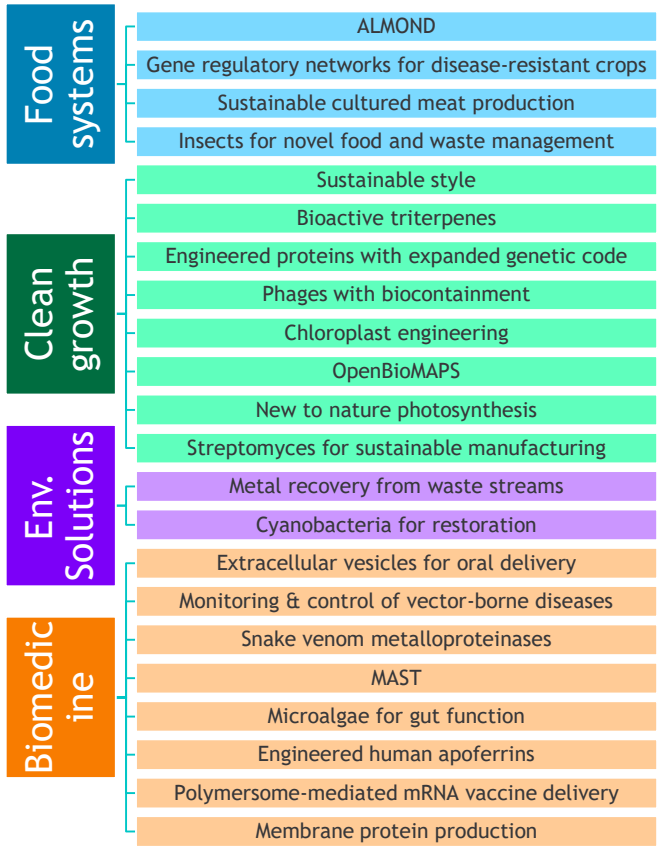
# UKRI has announced six new EB Mission Hubs and 22 Mission Awards

£100 million investment, themed around food systems, clean growth, environmental solutions & biomedicine

## Mission Hubs

1. Environmental Biotech Innovation Centre (Cranfield)
2. EB Hub for Microbial Foods (Imperial)
3. Engineering Genetic Control Systems for Advanced Therapeutics (Edinburgh)
4. Environmental processing and recovery of metals (Kent)
5. GlycoCell: glycan biomanufacturing for health (Nottingham)
6. Preventing Plastic Pollution with EB (Portsmouth)

## Mission Awards




*Source: UKRI*

# Next steps

1. Appointing the Co-Chair and members of the Engineering Biology Steering Group
2. Standing up cross-government work streams based around each chapter of the Vision
3. Developing a clear action plan for each work stream, using the principles set out in the Vision
4. Delivering the engineering biology regulatory sandboxes