Developing locally applicable biotechnology value chains

Petri-Jaan Lahtvee
Assoc. Prof. in Food Tech and Bioengineering
13.10.2022

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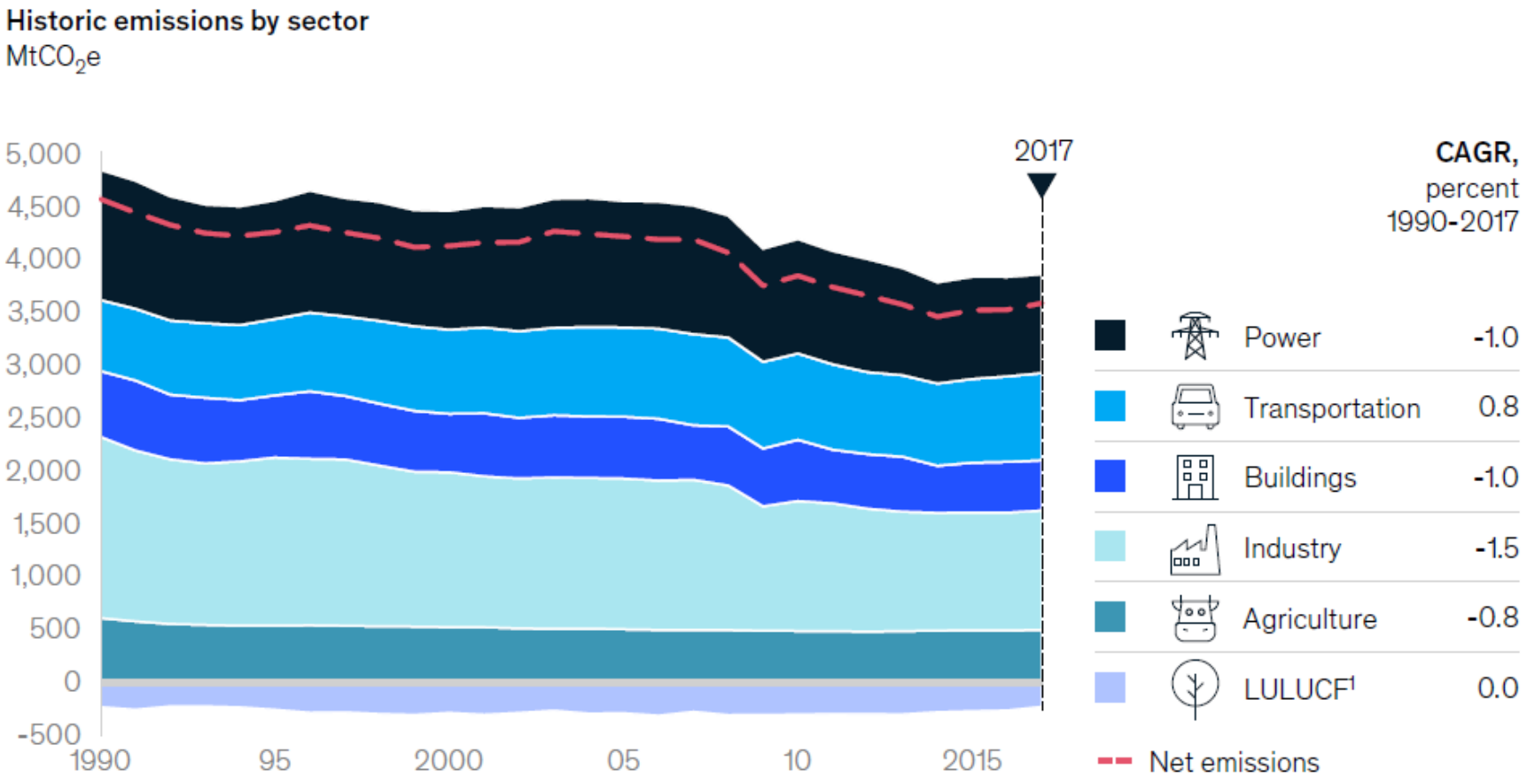
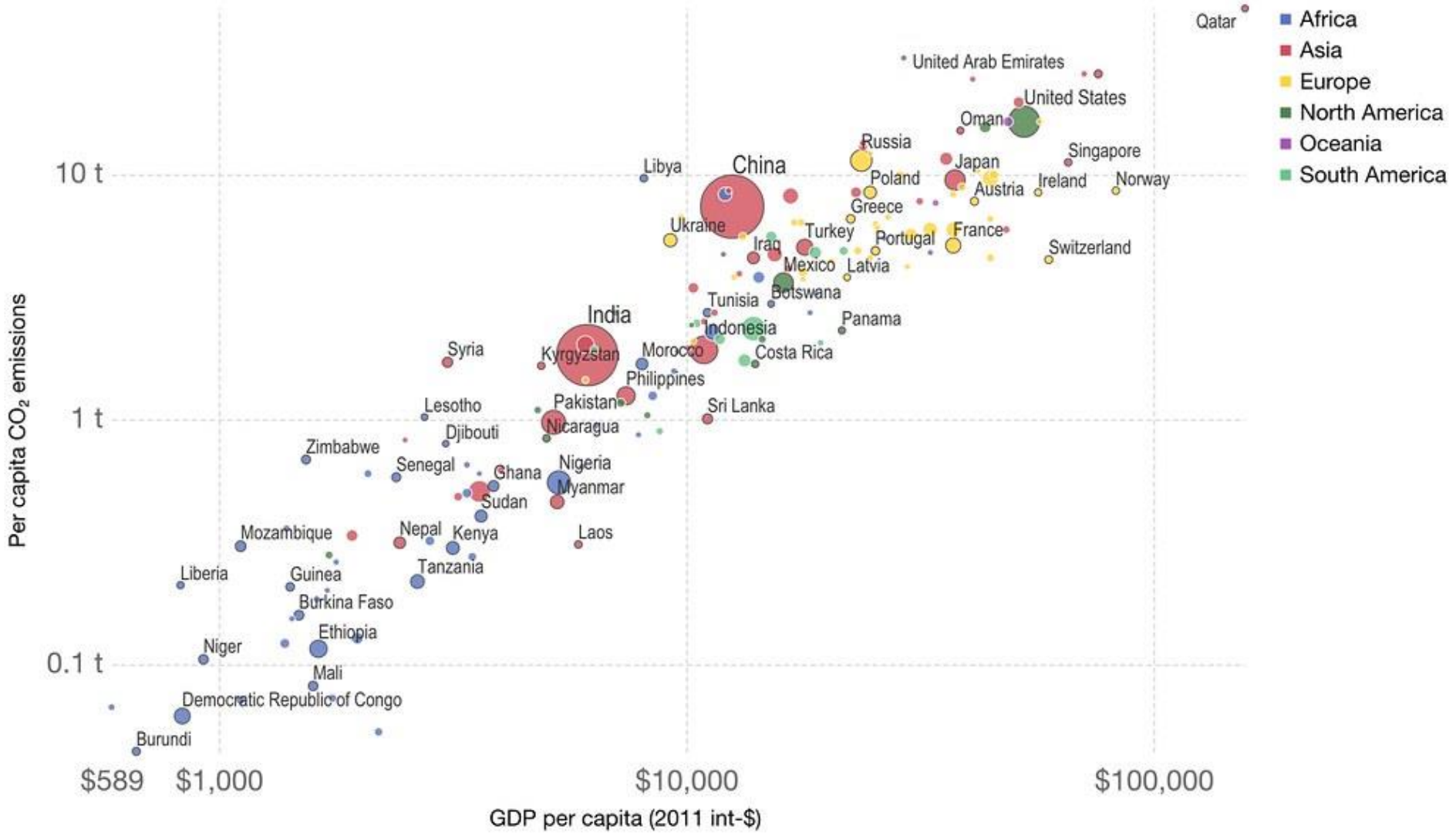
CO_2 emissions



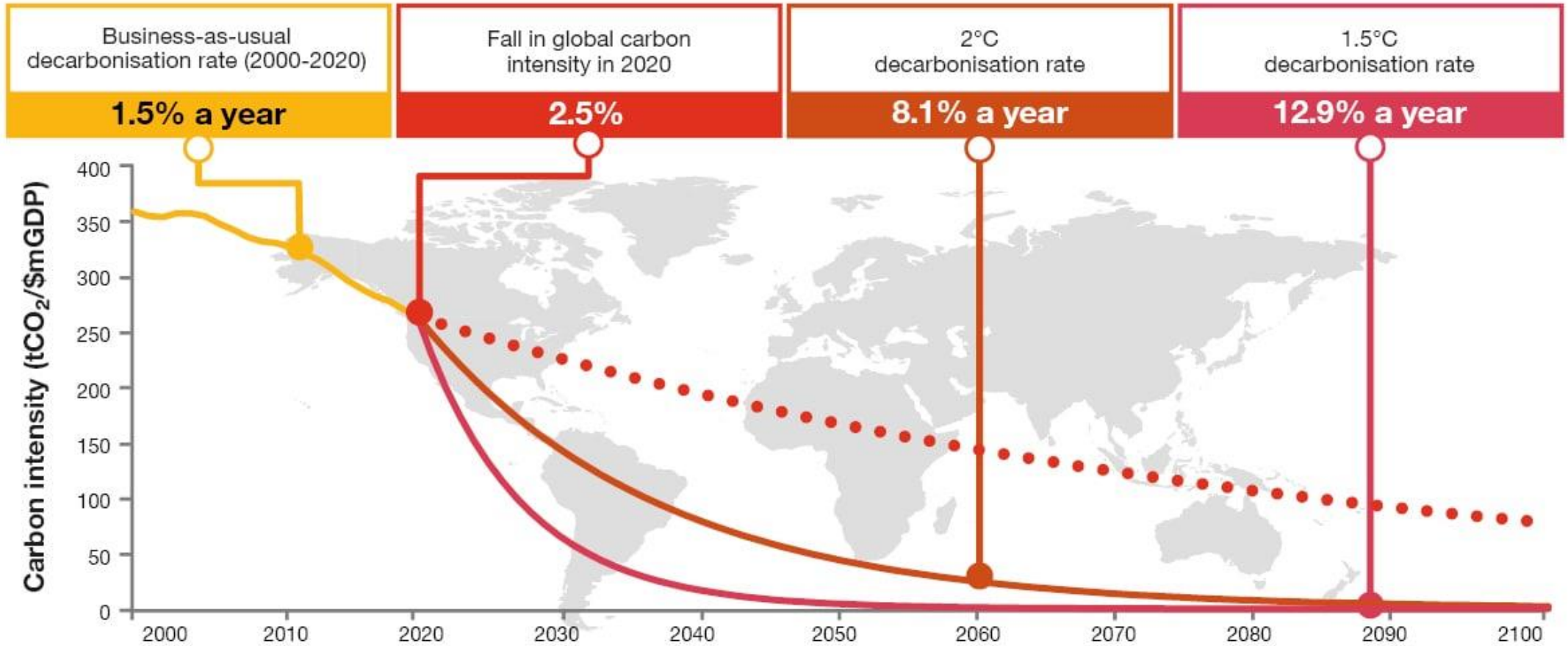
McKinsey Report, 2020

CO_2 emissions per capita vs GDP per capita, 2016

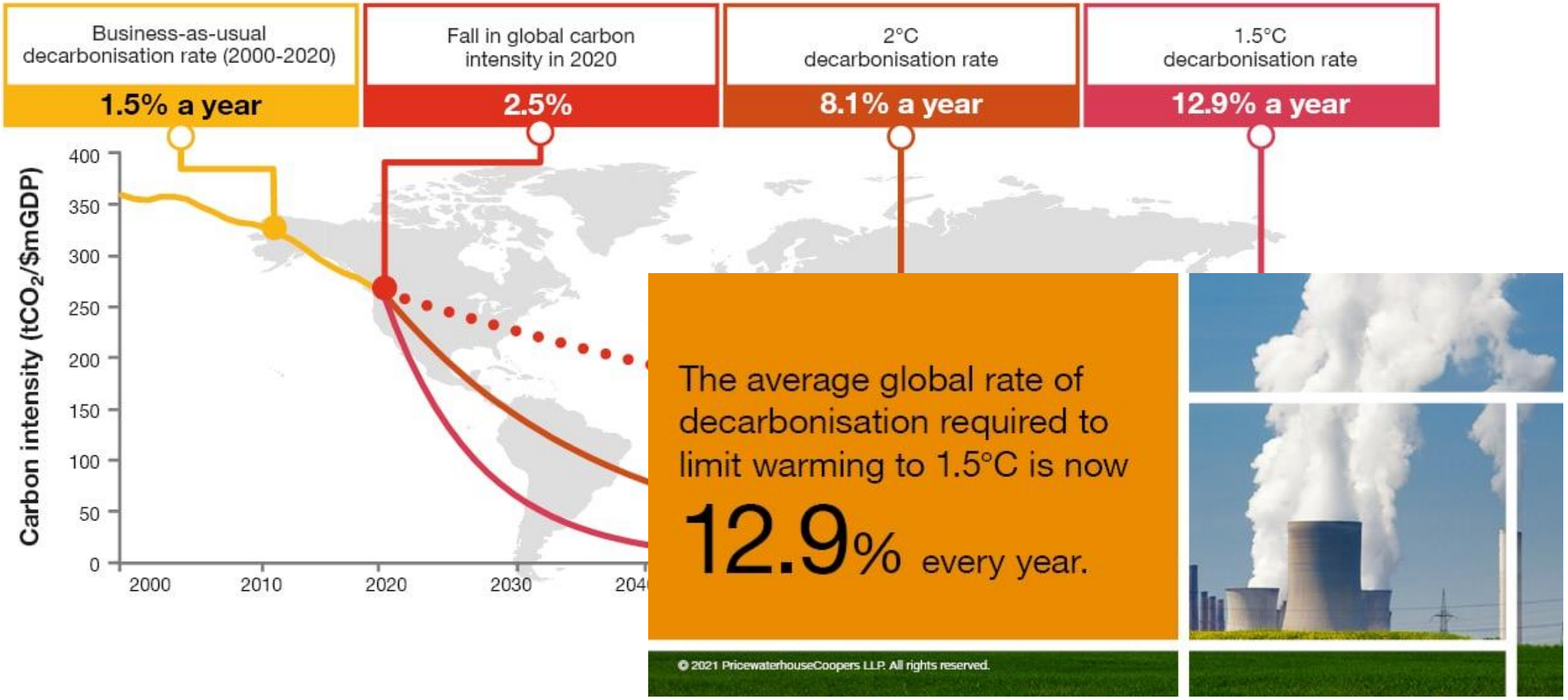
Carbon dioxide (CO_2) emissions per capita, measured in tonnes per person per year, versus gross domestic product (GDP) per capita, measured in 2011 international-$.



10/10 Source: Global Carbon Project, Maddison (2017) OurWorldInData.org/co2-and-other-greenhouse-gas-emissions/ • CC BY-SA 4


Business-as-usual decarbonisation rate (2000-2020)
1.5% a year
Fall in global carbon intensity in 2020
2.5%
2°C decarbonisation rate
8.1% a year
1.5°C decarbonisation rate
12.9% a year
Carbon intensity (tCO2/$mGDP)
400
350
300
250
200
150
100
50
0
2000
2010
2020
2030
2040
2050
2060
2070
2080
2090
2100

TAL TECH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Carbon intensity (tCO2/$mGDP)
400
350
300
250
200
150
100
50
0
2000
2010
2020
2030
The average global rate of decarbonisation required to limit warming to 1.5°C is now
12.9% every year.
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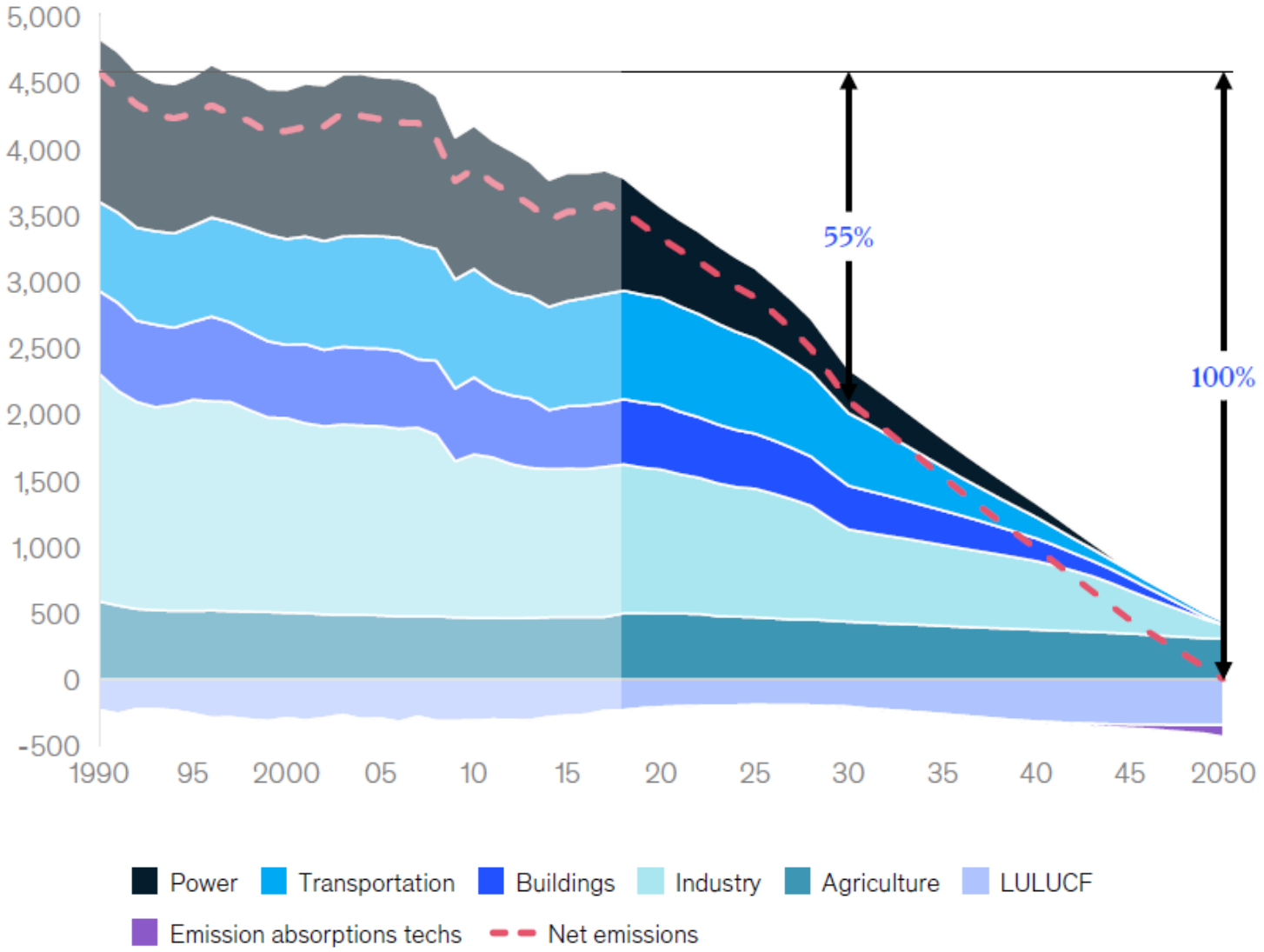
CO_2 emissions



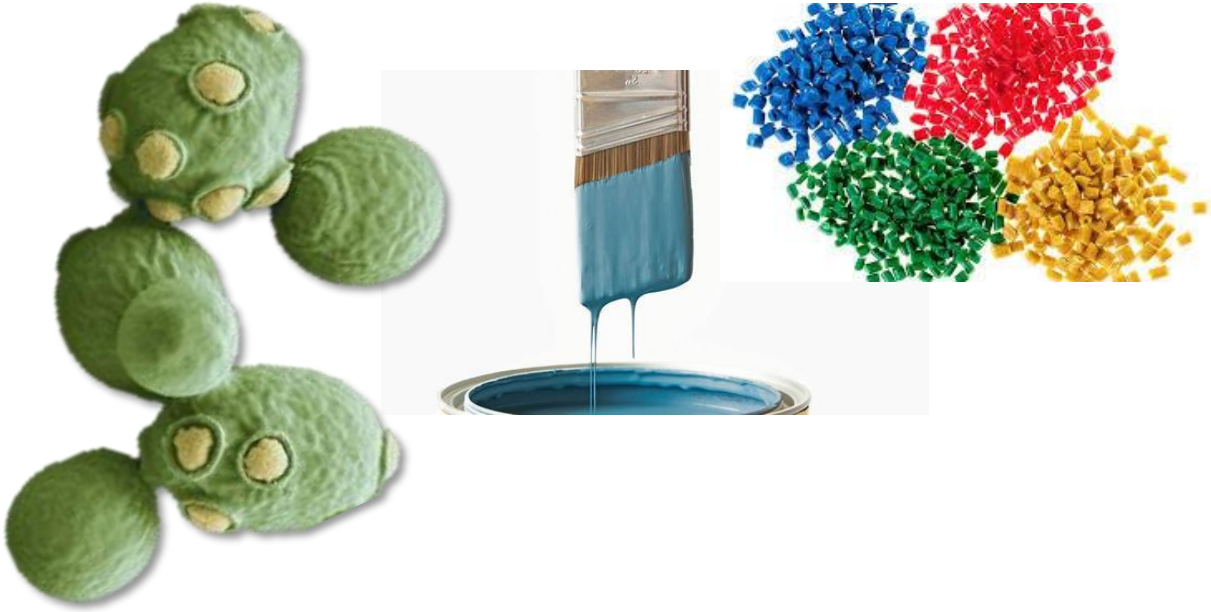
McKinsey Report, 2020

Designing life

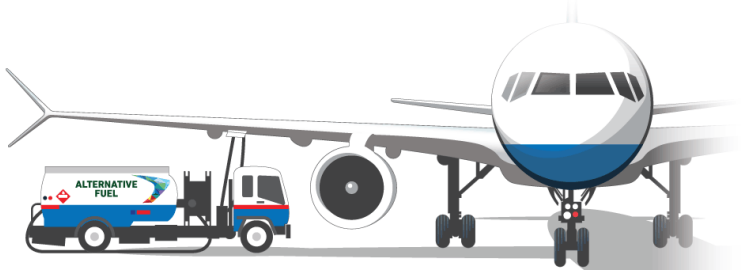
Locally available substrates

Industrial biotechnology value chain

Industrial biotechnology value chain



Industrial biotechnology value chain



Industrial biotechnology value chain

Fibenol

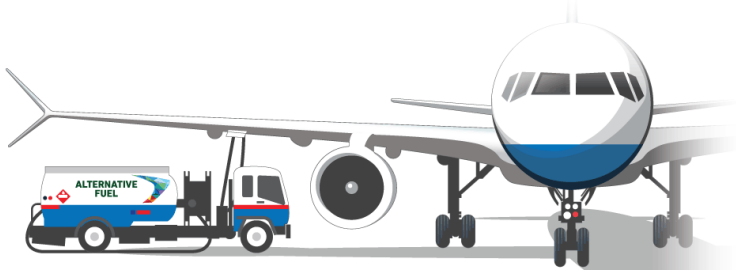
Borregaard

Eesti Maaülikool
Estonian University of Life Sciences

C6 sugars

C5 sugars

VFA



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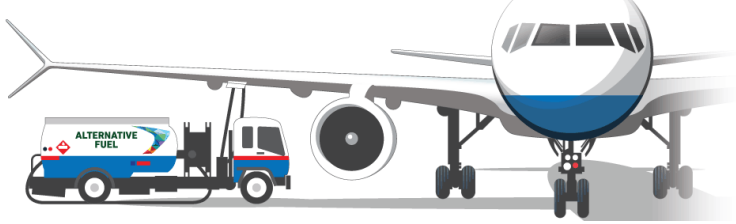

Industrial biotechnology value chain

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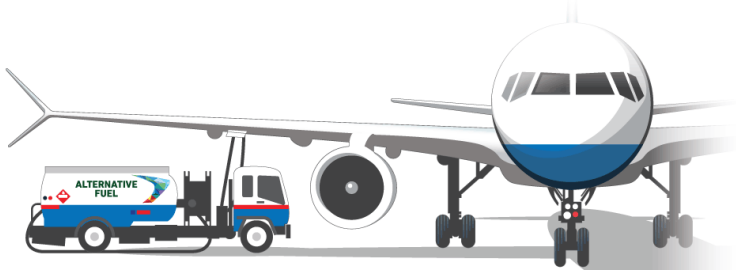

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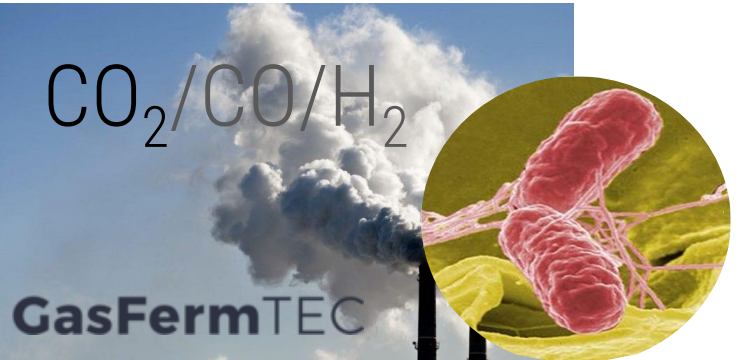
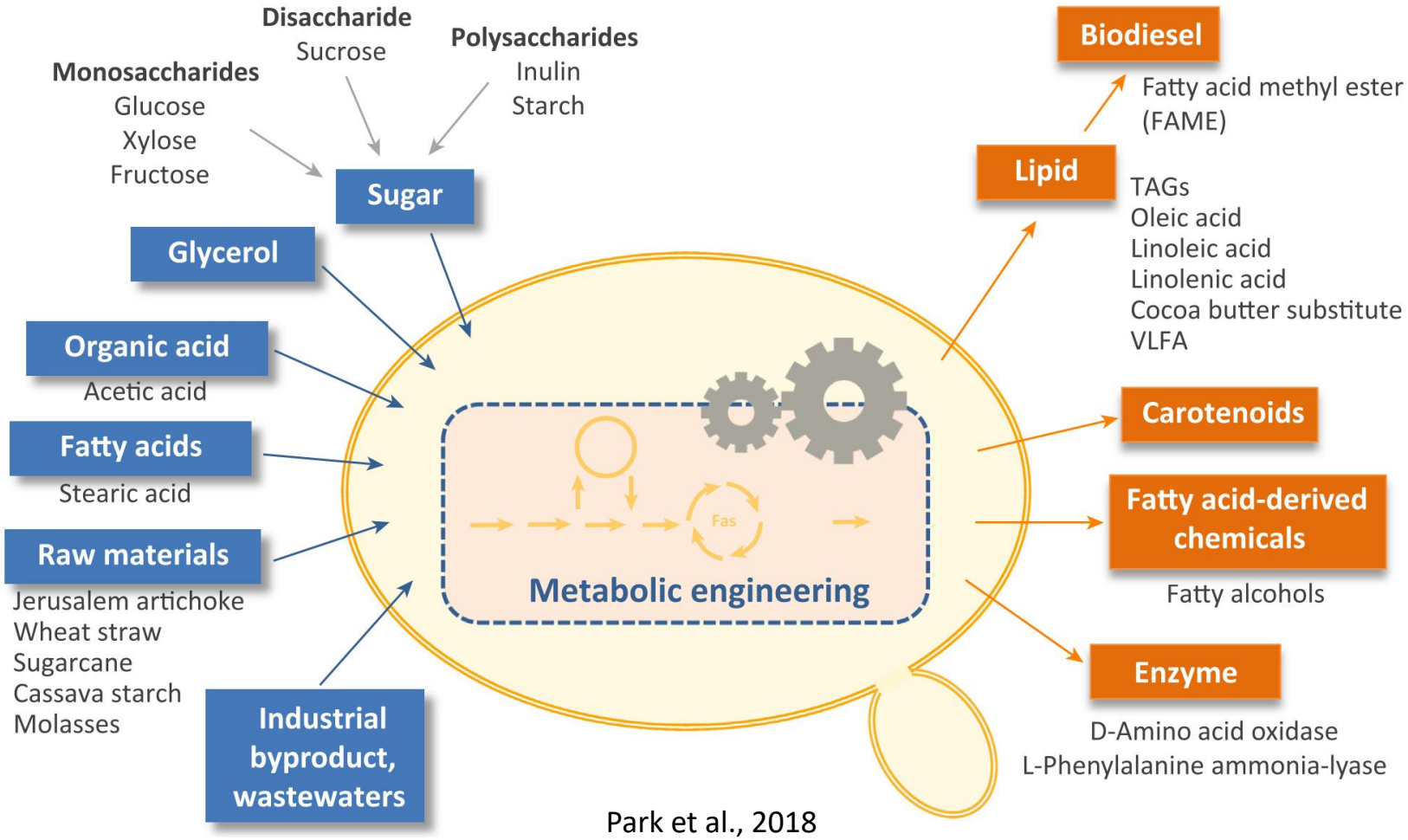


Oleaginous yeast *Rhodotorula toruloides*

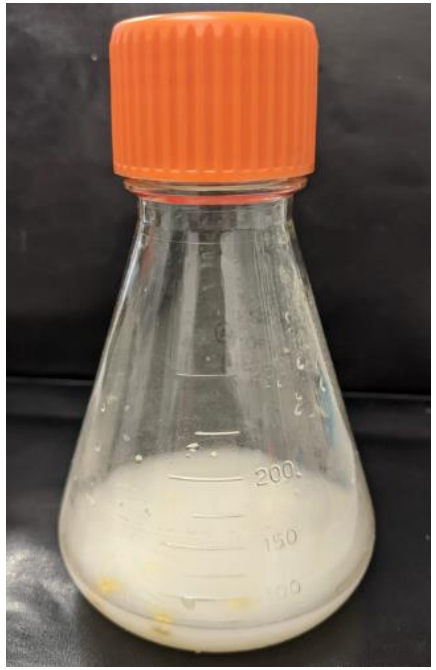


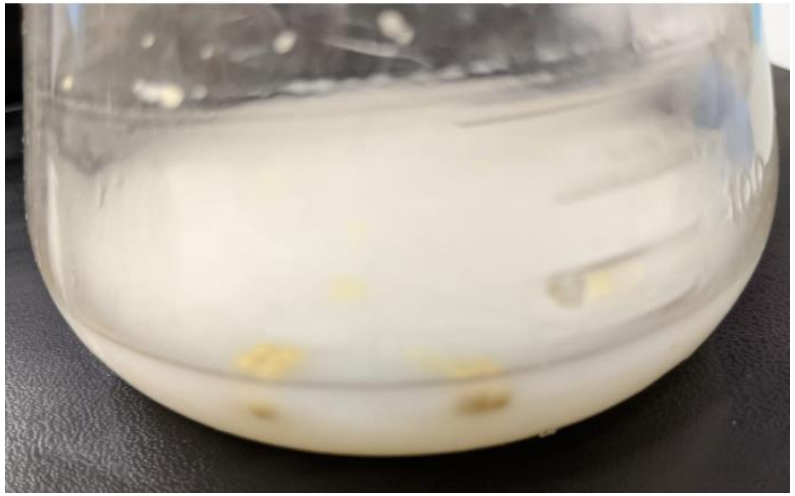
Park et al., 2018

Monteiro De Oliveira, 2021 Front. Bioeng. Biotech

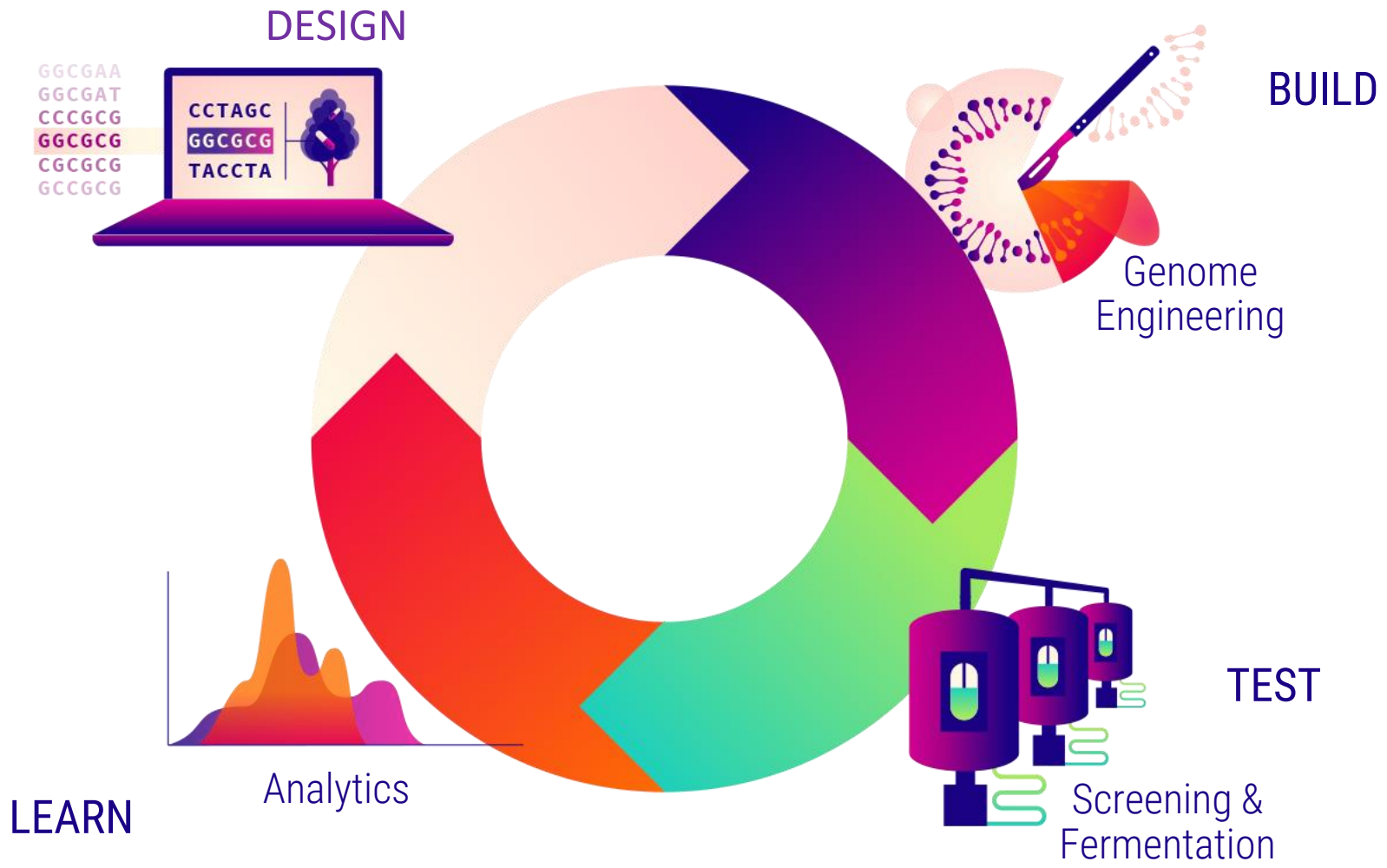
Lipid production platform

Lipid production platform

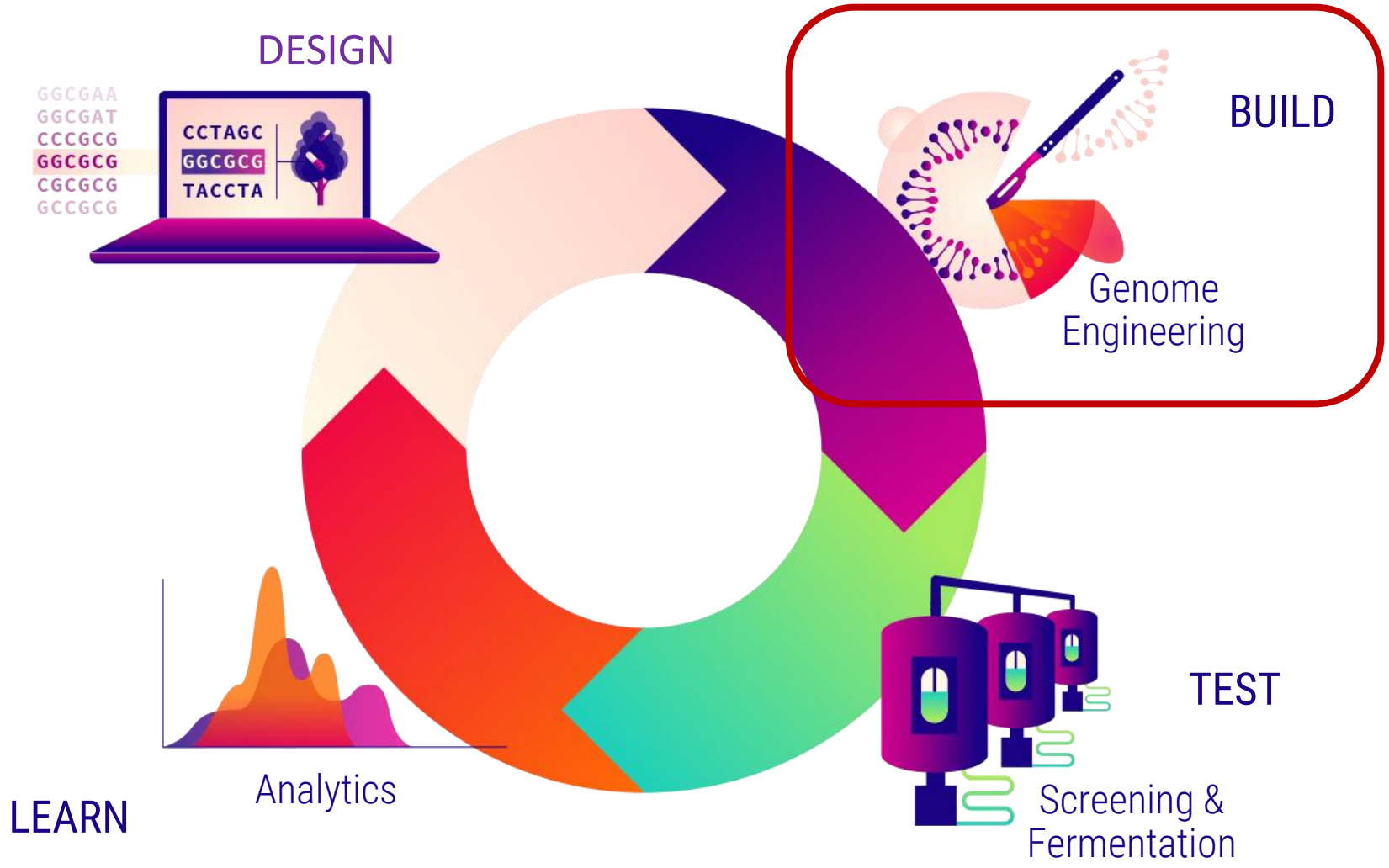




Design-Build-Test-Learn cycle

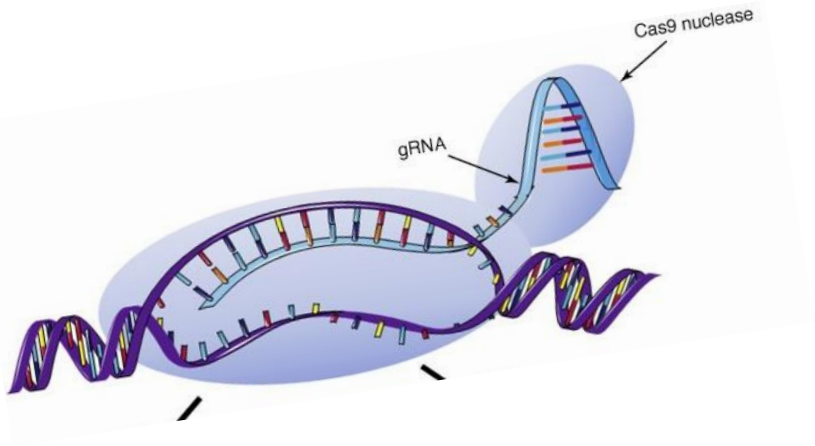


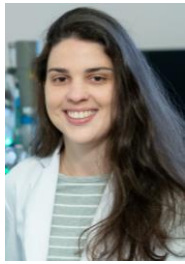
Design-Build-Test-Learn cycle



Synthetic Biology platform: Development of genetic engineering tools

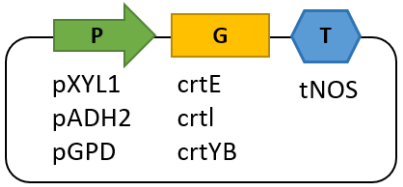
CRISPR-Cas9, Golden gate assembly, metabolic switches, biosensors, etc.



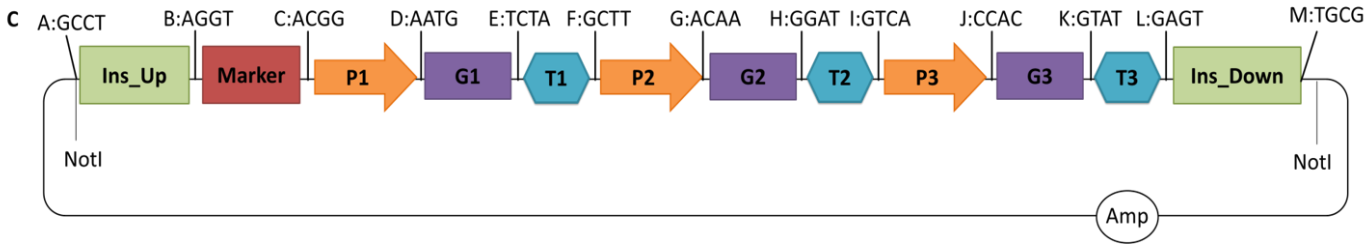


Level 1 (Library)

Level 2

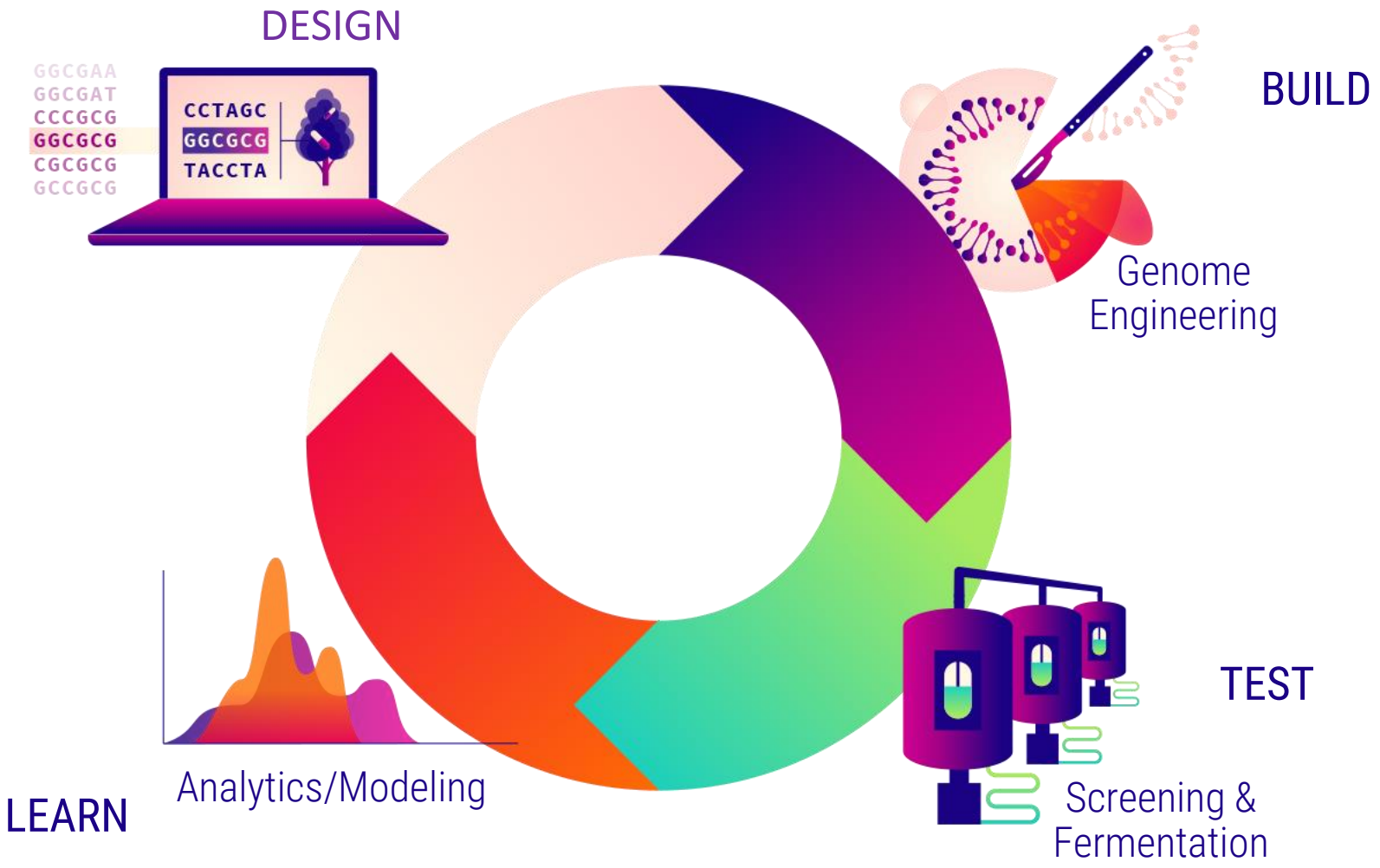


Level 3

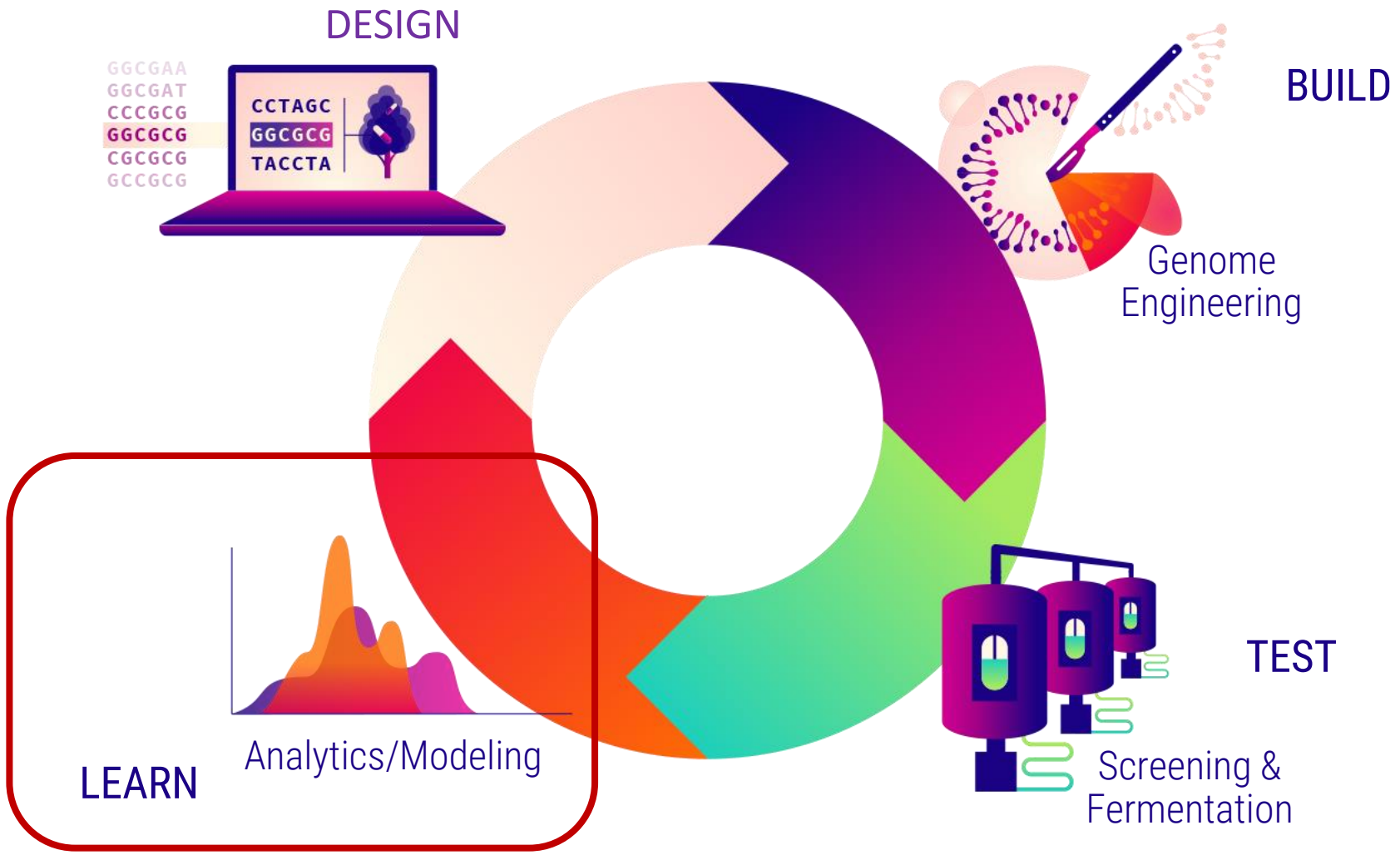


Bonturi et al., 2022, Met Eng Comm

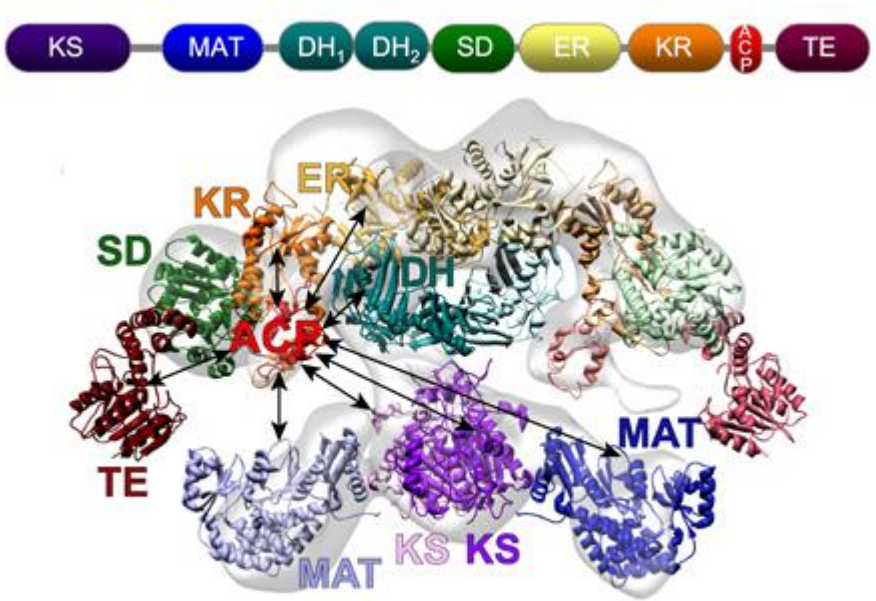
Design-Build-Test-Learn cycle



Design-Build-Test-Learn cycle



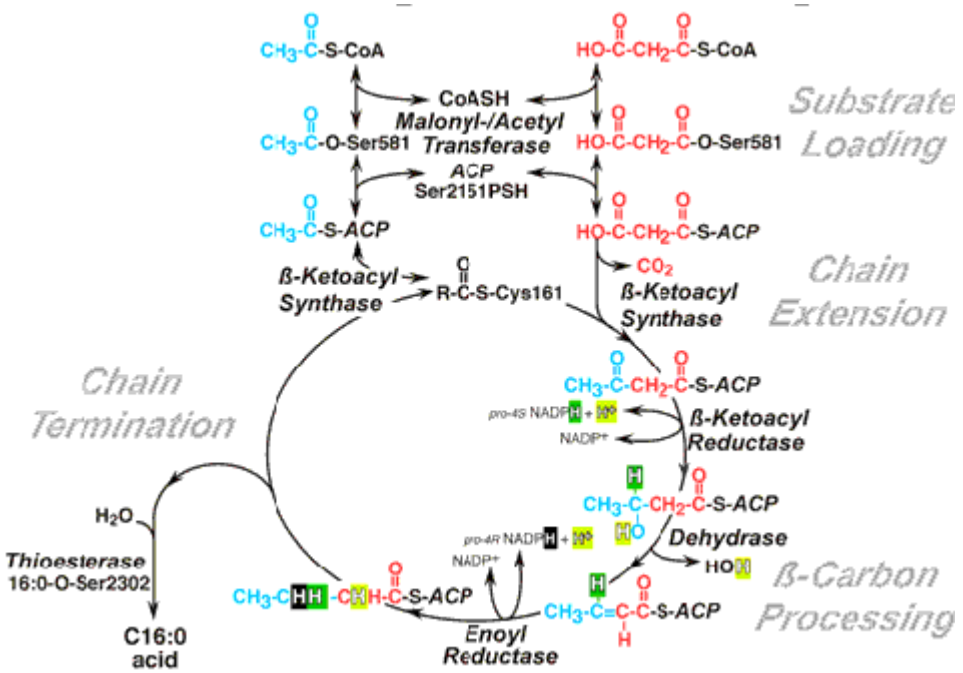
Fungal type I fatty acid synthases (FAS1)



Acetyl-CoA + 7 Malonyl-CoA + 14 NADPH + 14 H^+

↓

Palmitic acid + 7 CO_2 + 8 CoA + 14 $NADP^+$ + 6 H_2O

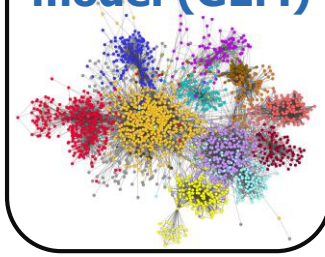


TAL TECH

Gecko

enhancing **G**enome-scale models with **E**nzyme **C**onstraints, using **K**inetics and **O**mics

Metabolic model (GEM)



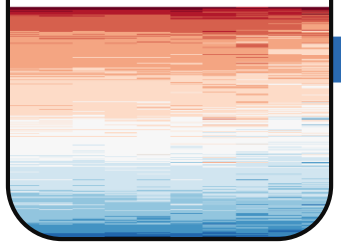
Enzyme data

BRENDA

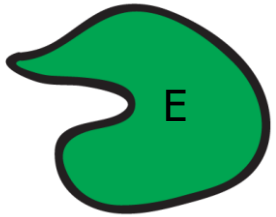
swissprot KEGG

paxdb 3.0

Proteomics (optional)



Enzyme usage: e [mmol/gDW]
e ≤ [E]



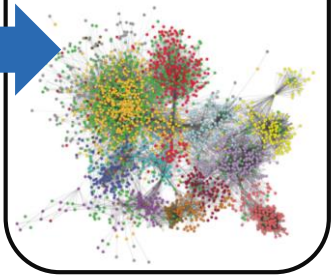
A → B

Flux: v [mmol/gDWh]

New stoichiometry: $A + 1/k_{cat}\ E \rightarrow B$

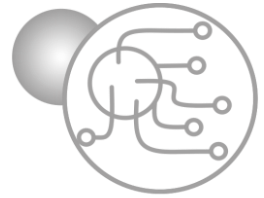
New constraint: $v \leq k_{cat} \cdot [E]$

Enzyme-constrained model



TAL TECH

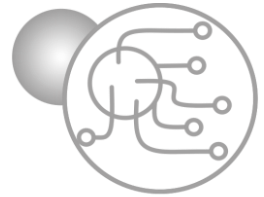
Insights into *R. toruloides* metabolism



- Majority of glucose is broken down in pentose phosphate pathway
- NADPH regeneration directly competes with ATP production
- Xylose catabolism is carried out using an alternative pathway

TAL TECH

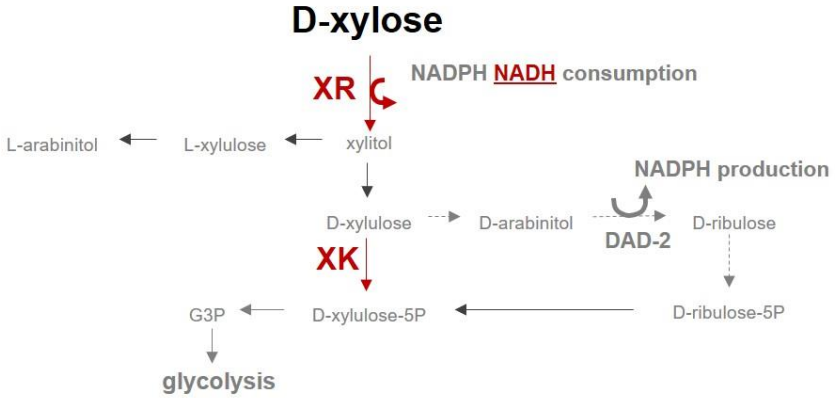
Insights into *R. toruloides* metabolism



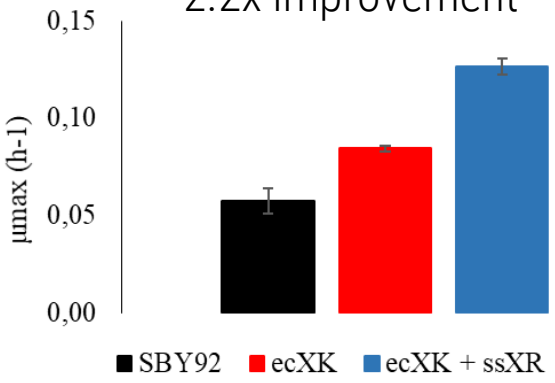
- Majority of glucose is broken down in pentose phosphate pathway
- NADPH regeneration directly competes with ATP production
- **Xylose catabolism is carried out using an alternative pathway**

Metabolic engineering of *R. toruloides* for improving xylose consumption

Xylulokinase + Xylose reductase

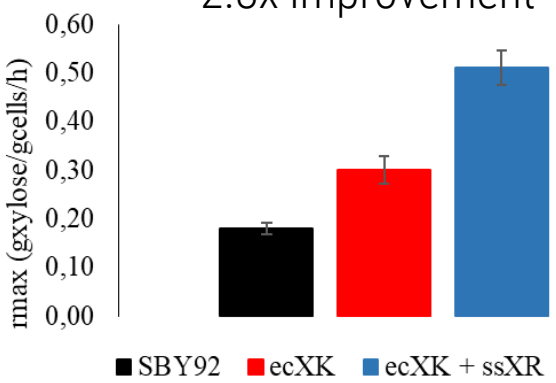


2.2x improvement

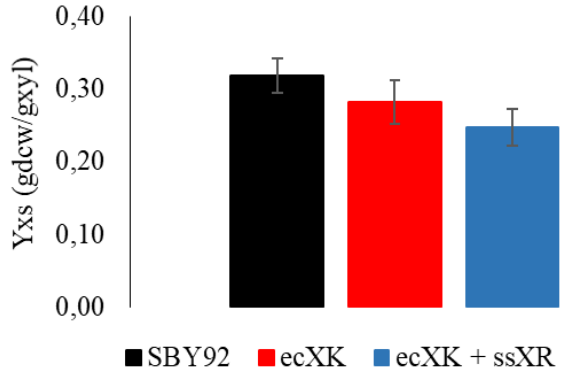


Growth rate

2.8x improvement



Xylose uptake



Biomass yield

Process scale-up

Applications:

- Coating materials
- Plastic
- Food
- Feed

Summary

- Non-conventional yeasts are efficient in converting locally available substrates into value added metbolites
- Efficient Design-Build-Test-Learn cycle will speed up the strain engineering pipeline
  - Automatization required for higher throughput
- Metabolic models provide a good understanding on metabolic peculiarities of the cells and help guiding metabolic engineering

Acknowledgements:

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Chalmers (Sweden)
Prof. Jens Nielsen
Eduard Kerkhoven, PhD

Imperial College London
A. Prof. Rodrigo Ledesma-Amaro

University of Washington
A. Prof. Alshakim Nelson

UniCamp, Brazil
Prof. Everson Alves Miranda

Swedish Agricultural Uni.
Prof. Volkmar Passoth
Dr. Bettina Müller

Funding: