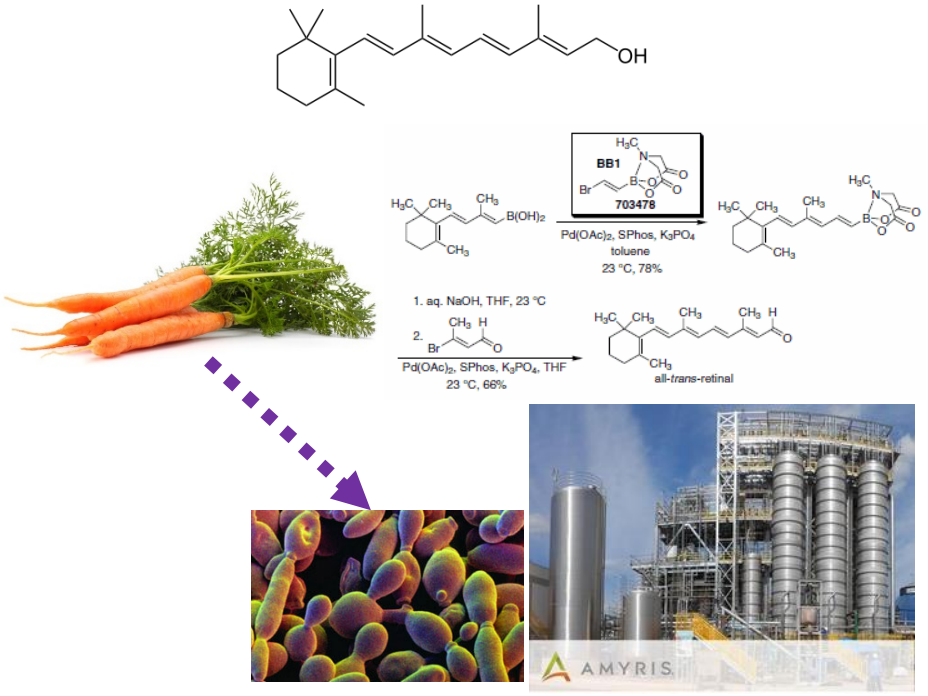
BioIndustry 4.0

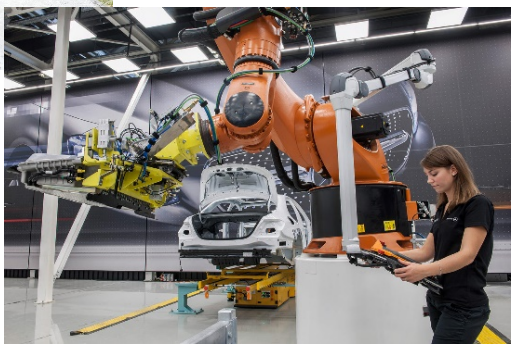
Lars Keld Nielsen

DTU Biosustain
The Novo Nordisk Foundation Center for Biosustainability

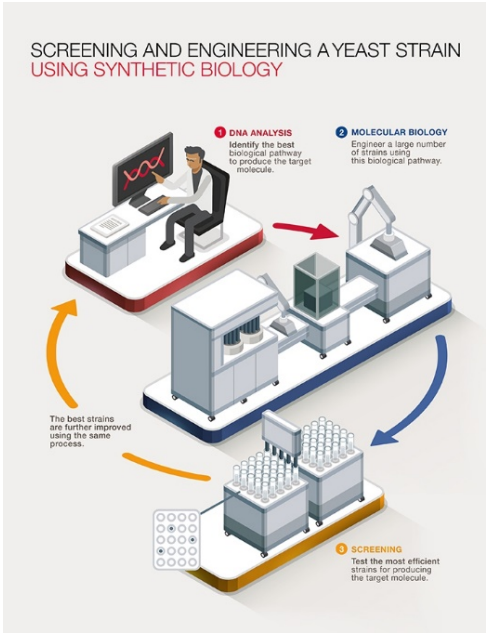
AIBN Australian Institute for Bioengineering and Nanotechnology



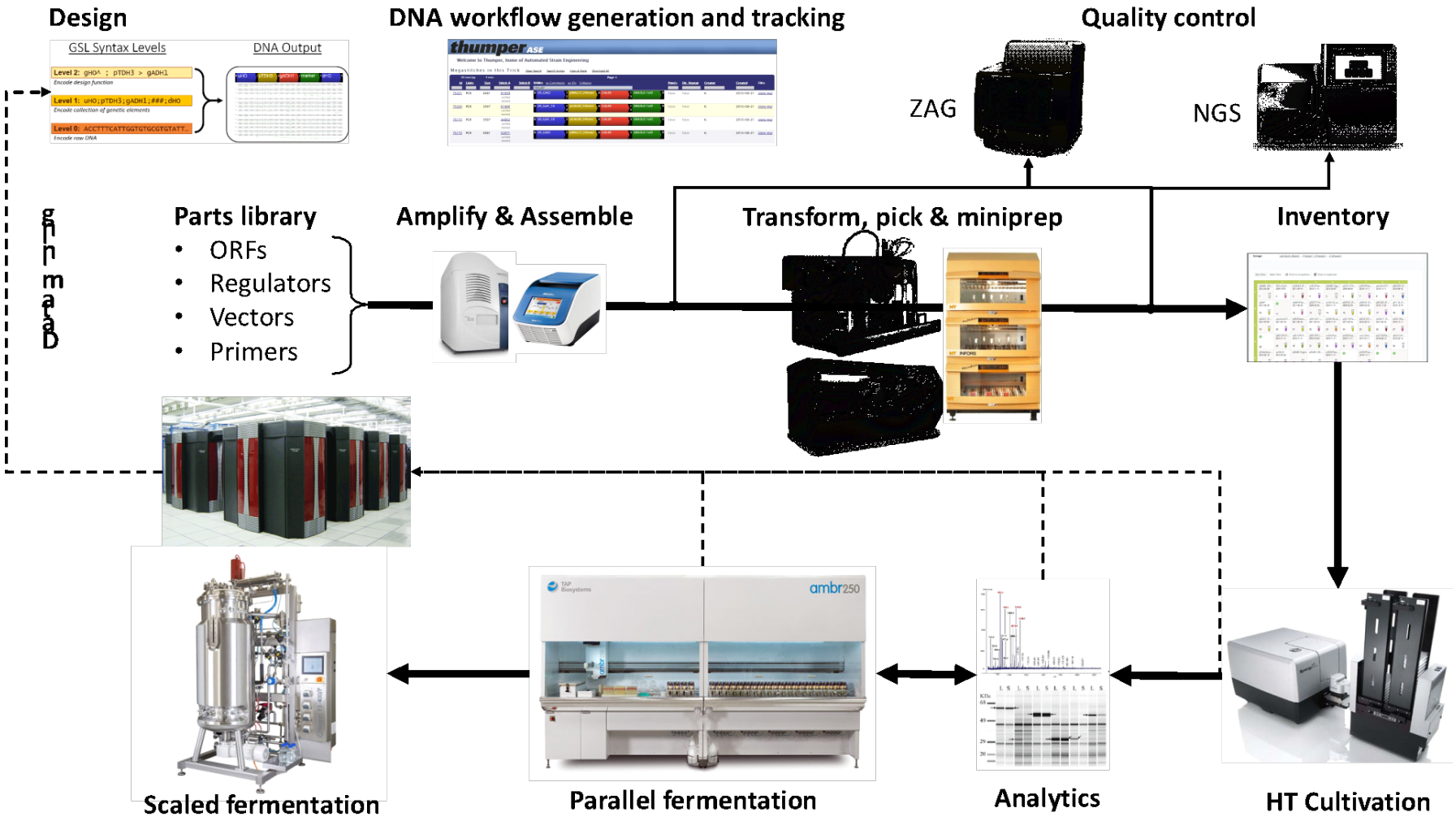
BioIndustry 4.0



Automated
Strain
Engineering



Queensland Strain Factory



DARPA Living Foundries

1000 molecules

Amyris: 450 molecules

Zymergen: 450 molecules

MIT Broad: 100 molecules

Year 1: 450 @ mg quant

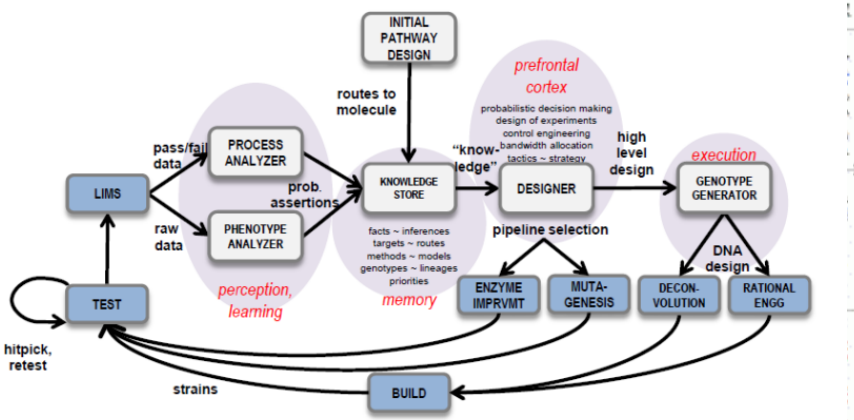
Year 2: 150 @ g quant

Year 3: 50 @ g/L/h

Year 4: 10 @ 1 kg

M2K

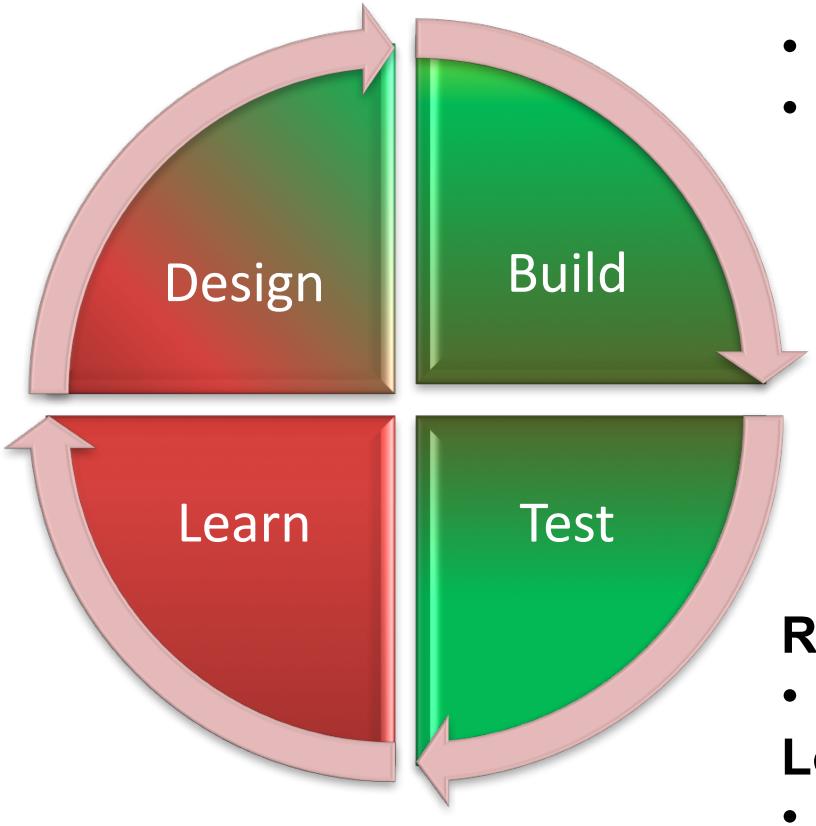
Do we need humans?



The automated scientist

Strain engineering

First generation
- BNICE
- OptKnock
- M → ME



Rational
- 10 promoter strengths
- 20 genes
- 1000 strains/month

Robotics
- Accurate growth & titre

Low cost HT Chemistry
- **Transcriptomics (RNAseq)**
- **Proteomics (SRM/PRM)**
- Metabolomics

Strain engineering

Possible designs

20 genes, 10 levels:

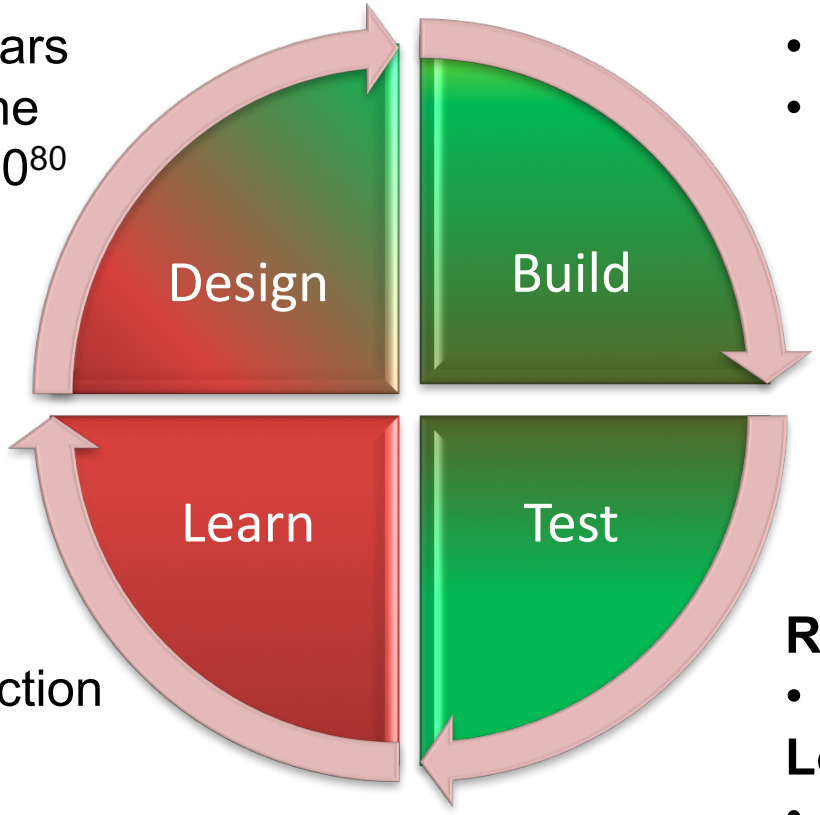
- 10^{20} = 2 x 10^{15} years

1000 candidates/gene

- $(10)^{20}(1000)^{20} = 10^{80}$

Enzyme engineering

- 20^{400} sequences



Rational

- 10 promoter strengths
- 20 genes
- 1000 strains/month

Naïve statistical design

- Complex response function
- Poor performance

Naïve "Big Data" mining

- Extrapolation essential
- Poor performance

Robotics

- Accurate growth & titre

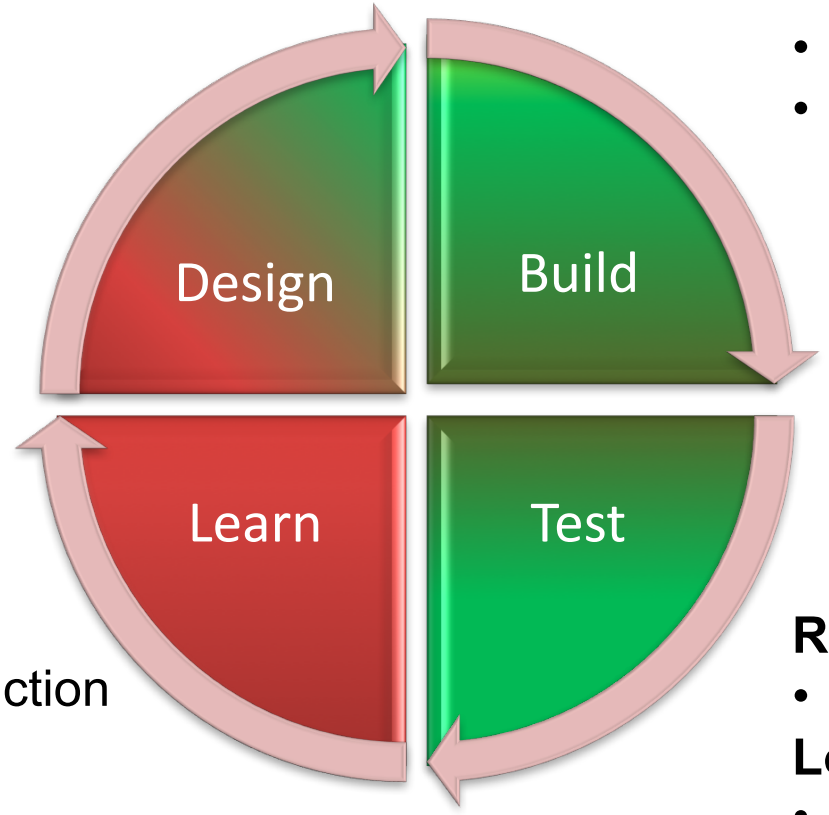
Low cost HT Chemistry

- **Transcriptomics (RNAseq)**
- **Proteomics (SRM/PRM)**
- Metabolomics

Strain engineering

First generation
- BNICE
- OptKnock
- M → ME

Second generation
- Slow progress



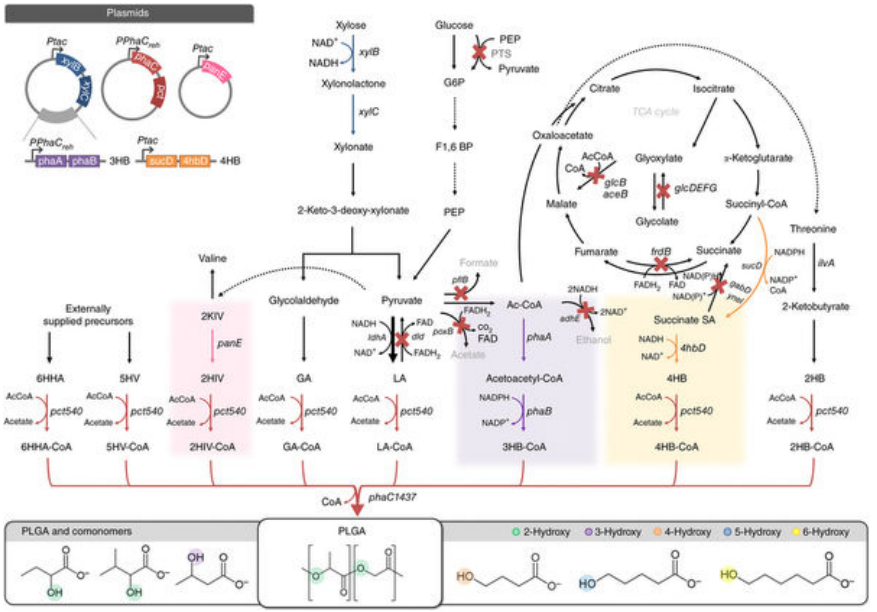
Rational
- 10 promoter strengths
- 20 genes
- 1000 strains/month

Naïve statistical design
- Complex response function
- Poor performance

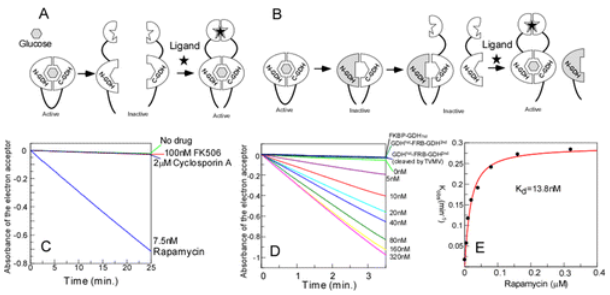
Naïve "Big Data" mining
- Extrapolation essential
- Poor performance

Robotics
- Accurate growth & titre

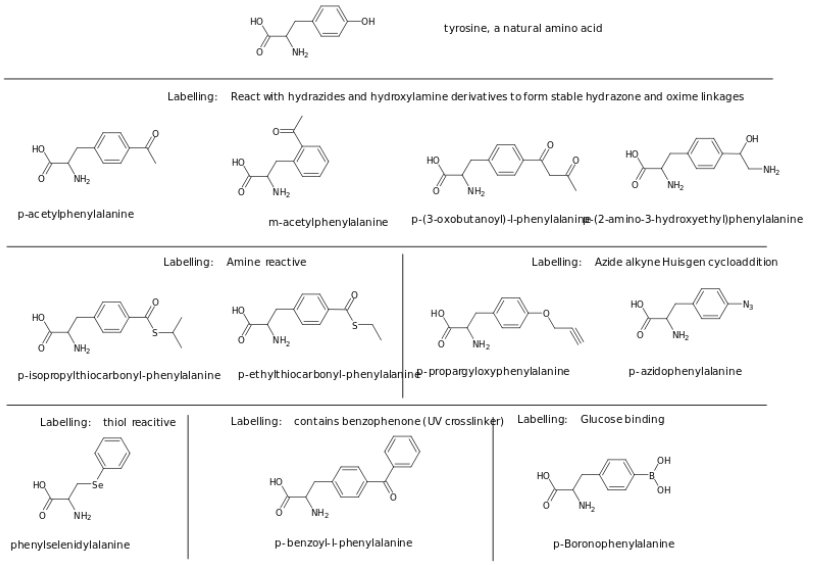
Low cost HT Chemistry
- **Transcriptomics (RNAseq)**
- **Proteomics (SRM/PRM)**
- Metabolomics



Biopolymers

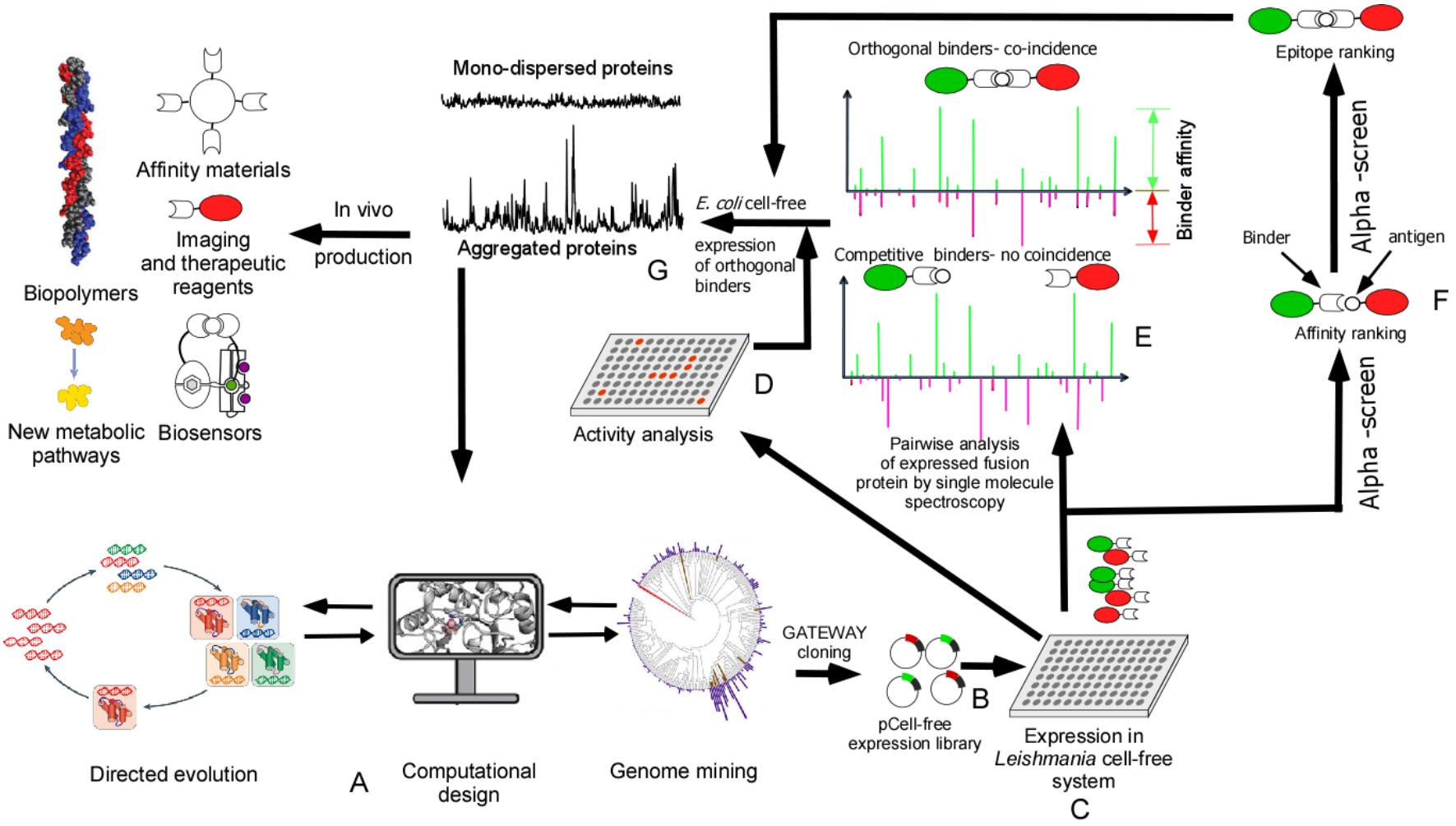


MOLECULAR WAREHOUSE

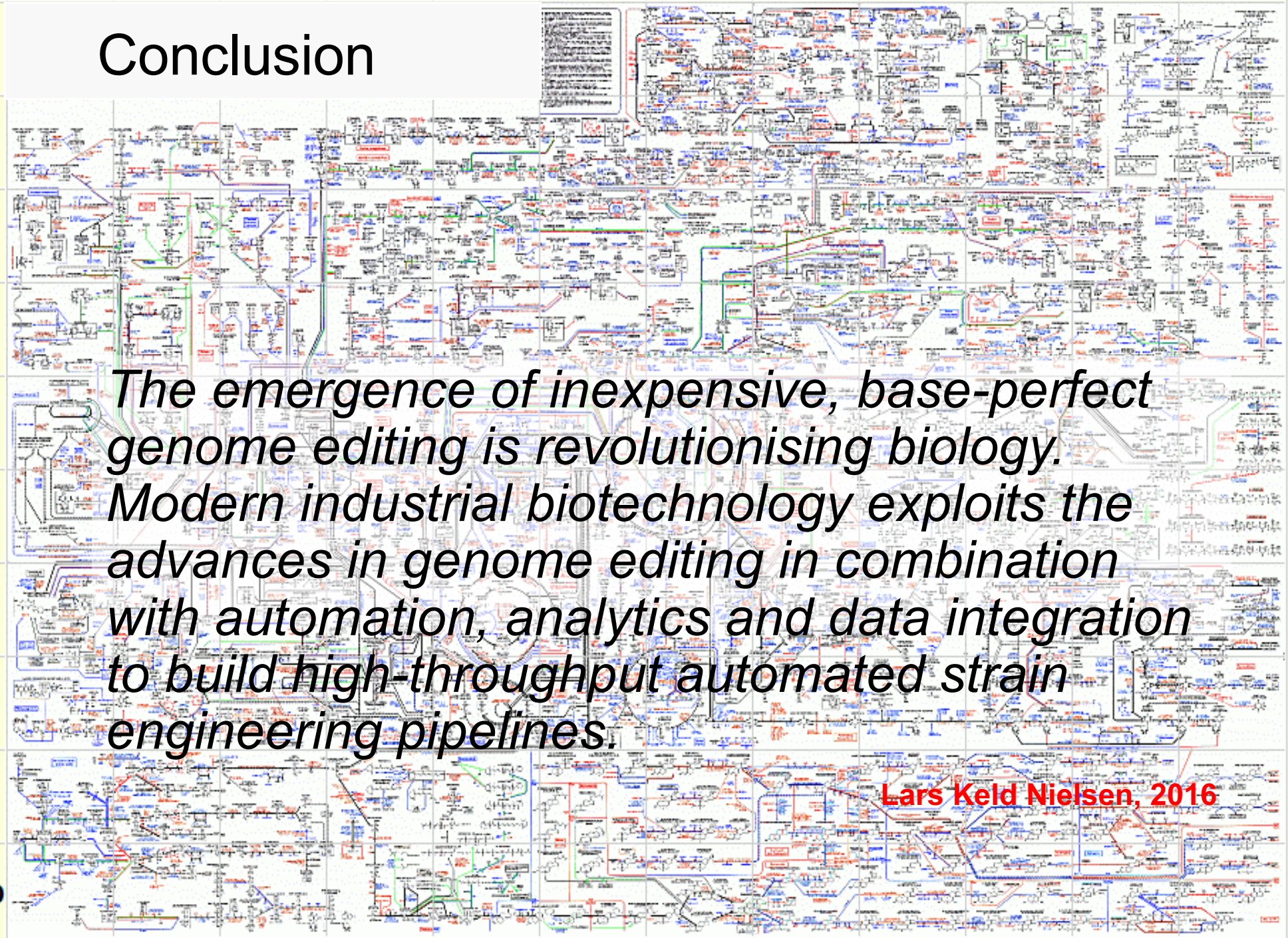


Expanded genetic code

Queensland Protein Foundry



Conclusion



The emergence of inexpensive, base-perfect genome editing is revolutionising biology. Modern industrial biotechnology exploits the advances in genome editing in combination with automation, analytics and data integration to build high-throughput automated strain engineering pipelines.

Lars Keld Nielsen, 2016