iGEM TEAM
MANCHESTER - GRAZ
Parkinson’s Disease

“Over years their life just gets smaller and smaller” Professor Tod, University of Manchester

- Depletion of dopaminergic neurons
- Symptoms: muscle spasms, slow movement, resting tremor
- Other non-motor effects

Maurice Williams, Earth, Wind and Fire
Michael J Fox
Muhammed Ali
Current Parkinson’s Treatment

**Oral levodopa**
- up to 12 doses/day
- ON/OFF

**Duodopa**
- invasive
- aftercare
- ~$100,000 per treatment
'The idea of actually having [L-DOPA] gently fizzing away in the gut to feed the brain seems to me rather splendid'. Julia, Parkinson’s sufferer, 63.
L-DOPA

Tyrosinase
BBa_K1670008

Chaperone
BBa_K1670009

L-Tyrosine

L-DOPA

Gut Lumen

E. Coli
Nissle 1917
L-DOPA

Tyrosinase
BBa_K1670008

Chaperone
BBa_K1670009

AADC
BBa_K1670006

L-Tyrosine

AADC
BBa_K1670006

Gut Lumen

E. Coli
Nissle 1917
Gut Lumen

L-DOPA -> Tyrosinase BBa_K1670008 -> L-Tyrosine

Chaperone BBa_K1670009

AADC BBa_K1670006

L-DOPA -> Tyrosine -> Tyramine

CYP2D6

E. Coli
Nissle 1917
Gut Lumen

E. Coli
Nissle 1917
Pathway Analysis via HPLC

- To separate the standard compounds

- 95% water & 5% methanol, without acid

(C18-column)
Regulatory system
We designed a plasmid from scratch.
Plasmid assembly

- 10x Sequence verification
- 3x Overlap Extension PCR
- Gibson assembly
Kinetic modelling of DOPA DOSER
L-DOPA synthesis can replace Duodopa

- Duodopa: 20-200 mg/h
- DopaDoser: 80 mg/h
pCERI characterisation in *E. coli* BL21 and Nissle 1917
Our Biobricks work

- BBa_K1670005
- BBa_K1670001
- BBa_K1670002
- BBa_K1670003
Synthase characterisation via *Chromobacterium violaceum* CV026
Homoserine lactone synthesis works partially

- pCERI
- BBa_K1670000
- BBa_K1670004
Summary

- Assembled plasmid from scratch
- Modelled a complex enzyme network
- Characterised and submitted 8 BioBricks
- Improved 2 existing BioBricks
Impact on Patients

- Patients come first
- Sociology and opinion

“You need to hurry up and get this done so I can give it to my clients!”

- Global perspective
  - Diets
Does DopaDoser work well using different diets?
Modelled effects of probiotics growth rate on DopaDoser

L-DOPA biosynthesis as a function of increasing *E. coli* BL21(DE3) growth rate

Carbon source: glucose
Industrial application

- **Levodopa vs. DopaDoser**
- Replacing chemical synthesis?
  - Environment, safety and efficiency

- Probiotic Treatment
The future of **DOPA DOSE**

“I can choose to be governed by the illness or I can choose not to be” (Julia, Parkinson‘s sufferer)

- Integrating pathway and regulation system
- Fewer doses required
- No fluctuations in plasma levels
- Industry support as use as a probiotic
- Regulatory system widely applicable
Modelled pathways for other iGEM teams

1. Butyrate pathway for NRP-UEA-Norwich iGEM

2. Neurotransmitter pathways for UCL
Attributions

Instructors
Prof Dr. Eriko Takano
Prof Dr. Rainer Breitling
Prof Dr. Sabine Flitsch
Prof Dr. Anton Glieder

Advisors
Lorna Hepworth
Nicholas Weise
Alexander Wood
Robert Harrison
Dr. Martina Gaier
Dr. Neil Swainston

Sponsors

The University of Manchester
Graz University of Technology