PROJECT PARTNERS: Tobias von der Haar and Anastasios Tsaousis, University of Kent; Hans Genee and Luisa Gronenberg, Biosyntia

Enhancing iron-sulfur cluster functionality in synthetic biology applications

"The findings are very relevant to our work on sustainably producing vitamins and we see a lot of potential for industrial applications. The results are encouraging and we look forward to continuing our collaboration," Biosyntia

PROJECT AIMS: Engineering host cells to express recombinant enzymes is used to produce high-value biochemicals such as flavours, fragrances and vitamins. The activity of some enzymes is dependent on cofactors that contain iron–sulfur clusters. Yet when enzymes containing iron-sulfur clusters are expressed in yeast cells — a popular expression system in industrial biotechnology — they are often less active than in their native organisms. This project will build on the recent discovery of an unusual iron–sulfur protein (called SufCB) from an anaerobic microbe that enhances the activity of other iron-sulfur enzymes. The aim is to test the usefulness of SufCB as a general tool for enhancing the activity of enzymes containing iron-sulfur clusters.

OUTCOMES & NEXT STEPS:

- A funding application to the Leverhulme Trust is planned for Sept 2021
- A manuscript related to SufCB, including work from this project, is in preparation
- Work is continuing on the use of SufCB expression as a promising avenue for improving the functionality of industrially relevant iron–sulfur cluster enzymes

RESULTS: The collaborators successfully made strains of yeast that express genomic SufCB integration. However, these yeast strains were unstable and all integrants that were tested lost the SufCB integration construct upon sub-culturing.

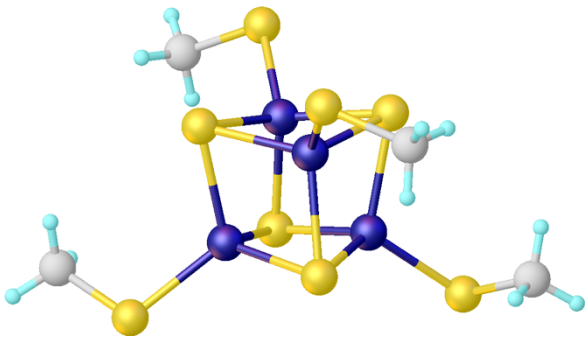
Despite this issue, plasmid-born copies of SufCB were used to show that SufCB expression stabilised the expression of an iron-sulfur cluster enzyme called CobG, which is important in the production of vitamin B12.

They showed that SufCB expression can be used to stabilise the expression of the Leu1 enzyme, which is used in biobutanol production. Moreover, SufCB expression was better than a published strategy that uses Nfs1 expression.

The collaborators are discussing alternative cloning strategies for continuing the work with the plasmid-born SufCB constructs.

KEY MESSAGE: SufCB stabilises the expression of iron–sulfur enzymes in yeast.

Change in technology readiness level: 1 to 2



Iron–sulfur clusters are critical co-factors in enzymes that catalyse diverse biochemical reactions of industrial interest.