CBMNet

CROSSING BIOLOGICAL MEMBRANES NETWORK, A BBSRC NIBB

The University Of Sheffield.

UNIVERSITY of York

BBSRC

Membrane Transporters as Critical Components for Bioprocessing

The Challenge

Bioprocessing – especially biotransformation's, but also fermentation, is critically dependent on getting substrate into, and product out of, a cell. Efficiency of process may rely upon normal biochemical functionality of the cell – where membrane integrity and robust energy supply are vital.

The tools and techniques required to identify, understand, and manipulate transporters specific for a unique process under development are not commonly accessible by industry.

Croda has a variety of processes – one in production, the others in development - where transporter functionality may be important. The current production process presents a complicated dataset involving uptake of a precursor and export of the product in a yeast system. The system is relatively poorly understood – having been empirically derived over a number of years and 'owners'.

The processes in development are more traditional IB – microbial production of natural products which are normally either secreted or intracellular and where improvements might involve synthetic biology (transfer to another host

The Meeting

A confidential meeting involving Croda (as industrial lead) and the CBMNet research community was set up to identify collaborative opportunities centred on the understanding and potential optimisation of transport phenomena for the existing and future Croda processes.

There was much valuable opinion expressed and some concrete suggestions for route to an improved process (without using Synthetic Biology which is not a current option for this product). Some of the constraints imposed by market size, customer conservatism, and production plant scheduling were also profitably discussed.

Overall, the expectation for the meeting is to provide Croda with:

- a clear view of the current status of research on transporters;
- the potential for development of understanding on the actual role of membrane trafficking in Croda IB processes (current and future);
- a route map to realisation of the capability to include transporters as a normal component of process design.

Biotechnology

Sustainable by Design

CBMNet Open Innovation Meeting

The Outcome

A number of approaches were developed for each process, including:

- Understanding of the 'natural' system – via *in silico* approaches - identification of genetic elements crucial for synthesis of product, survey for orthologs to create a 'components' toolkit.
- Development of metabolic/systems models, critically including components of substrate uptake and product secretion.
- Synthetic Biology approaches to integrate biosynthetic pathway with chassis organism metabolism.

Several ideas were also expressed for Croda to acquire more data from a production process.

Overall, there were options which could be addressed with relatively short projects which would lead into larger collaborative programmes as funding and business opportunities presented themselves.

The potential for alternative approaches should not be neglected and might form part of a parallel-track approach. There are quite well established platforms which could be used as 'chassis' for the products of interest in these studies.

The Future

The meeting provided Croda with an excellent overview of the available expertise which could be applied to resolution of several present and future challenges.

The participation of experienced scientists across a broad range of core speciality, especially including scientists from Europe, provided a clear indication of the potential routes to both improving current processes as well as achieving commercially viable yield of products in evaluation.

There are possibilities for very short term grounding work on each of the processes, which would naturally feed into larger programmes as funding opportunities come available.

In the short term, Croda will take the suggestions of the participants and synthesise a prioritised set of proposals for presentation to senior management. This will direct the programme of collaborative efforts which will be presented to appropriate members of the academic community to develop specific work packages leading to high quality responses to future funding calls.

Ultimately, the meeting and the potential concrete outcomes will enhance the ability of Croda to fully exploit IB – developing products which are price competitive and of highest quality for global markets.

"The open innovation meeting provided an excellent opportunity for Croda to engage with a panel of UK and EU scientists covering a broad range of expertise. The nature of the event permitted Croda to present a more detailed account of issues with commercial relevance. Such a situation could not occur outside of this type of event. We are very pleased with the outcomes of the event and fully expect to develop further collaborative projects in the coming months."

Dr Doug Cossar, Croda

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