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Cofactor optimization for production of commodity chemical in *Acetobacterium woodii*

Many industrial processes, such as refining, steel milling, and chemical plants discharge significant amounts of waste gases containing mainly CO and H2 into the atmosphere either directly or through combustion. Certain microbes can be exploited to convert these waste gases to chemicals and fuels as, for example, ethanol. This microbial process is a recognized Green Technology, reflecting the application of environmental science to curb the negative impacts of industrialisation. However, this technology has known limitations including low growth rates and productivity. This application addresses this point by helping to develop methods to enhance metabolic processes within specific bacteria that are able to grow on simple, cheap substrate such as Acetobacterium woodii.

In fact, A. woodii is one the better characterized acetogens and previous work has led to an improved understanding of its underlying biochemistry. It major reducing cofactor would appear to be NADH and it appears to lack a system to convert NADH into NADPH. Therefore, when trying to engineer new pathways into A. woodii it is important that they are adapted to use NADH rather than NADPH. In this application we aim to clone in a pathway that normally contains an NADPH-dependent enzyme, so initially we wish to redesign this enzyme so that it become NADH-dependent. The whole pathway, with the redesigned NADH-dependent enzyme, will then be transferred to A. woodii. Our aim is to develop A. woodii so that it can make a compound called 1,3-butanediol and on so doing we hope to demonstrate how metabolic engineering can be used to advance production methodologies for important commodities from very cheap substrate.

In order to achieve this ambitious goal we have assembled a highly interdisciplinary team of researchers covering such diverse areas as microbiology, biotechnology and engineering. Only via such an integrated approach will it be possible to design the desired functioning bacterial factories. Through the exchange of concepts, ideas, and technologies between the industrialists and academics will we be able to advance our ideas at a rapid pace. Overall, we are confident that we will be able to contribute to the development of new sustainable approaches to the generation of chemicals and fine chemical and for their rapid incorporation into manufacturing with leading companies