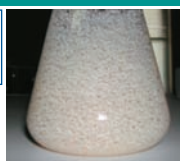


A faster, better, cheaper route to new drugs

This project aims to isolate new enzymes from bacteria and use them to make complex chemical compounds needed for pharmaceutical development.

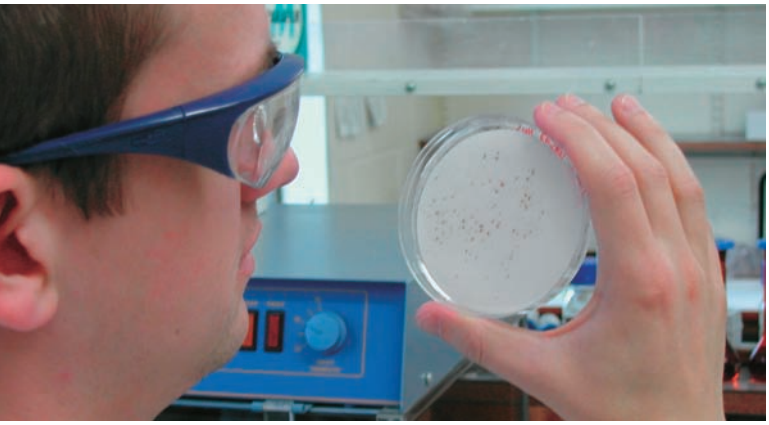
Key benefits

- a faster, better, cheaper route to new drugs
- new chemicals can be produced more efficiently
- new enzymes will be isolated and modified for use in industrial processes

The aim of the project is to develop new industrial processes which use enzymes (biocatalysts) from microbes (such as bacteria) to manufacture complex chemical compounds required for pharmaceutical development. In particular a class of enzyme known as lyases will be isolated, produced using engineered microbes and then used to manufacture amino acids and hydroxy acids for fine chemical and pharmaceutical applications.

The enzymes to be developed will be isolated from microbes found in soil but will then be improved or adapted using genetic methods applied in the laboratory to make them more suitable for industrial conditions.

Dr. Ian Fotheringham, project lead and president of Ingenza, says: "We are using a suite of enabling technologies, all our general skills and some new methods and tools, to isolate new enzymes from bacteria and use them to make chemicals. This gives the potential to produce new chemicals more efficiently than by using traditional chemical or industrial processes."



The project is led by Ingenza Ltd, in close partnership with Novacta Biosystems Ltd. Both Novacta, based in Hatfield, and Ingenza, based in Edinburgh, are renowned for their expertise in the application of enzyme catalysis (also known as white biotechnology) to solving industrial problems.

Research Director of Novacta, Dr Mike Dawson, said: "Working with Ingenza will bring complementary expertise and also exciting prospects for working together on future commercialisation."

Dr Fotheringham adds: "We are also pooling any results and successes that come from this research, so there's no way we are in competition with each other. We are sharing resources, success and knowledge.

"Success is likely to lead to business expansion, opening up new markets and could lead directly to job creation at the two companies."
The total cost of the project is £567,912, with the DTI through the Technology Programme, providing £227,165. The project started in December 2005 and runs for three years.

Objectives

Enzymes can carry out chemical reactions which are sometimes difficult to achieve using traditional chemical methods and can also be used under milder conditions than many chemical reagents.

Certain types of enzymes have been used for many years in industrial application. For example,

'hydrolases' such as proteases and lipases have been used in washing detergents to break down stains. Also 'amylase' and 'isomerase' enzymes have been used in the food industry to break down starch and to produce high fructose corn syrup respectively.

Dr Fotheringham says: "The development of new, rapid and versatile methods of gene isolation and manipulation over the past 10-15 years has meant that the genetic material (genes) which encodes many other enzymes can now be easily isolated and used to produce these enzymes in engineered bacteria.

"As a result we can identify, isolate and test many other enzymes from microbes as possible tools for the industrial applications such as the manufacture of valuable chemicals.

"By producing the enzymes through new processes, the cost can be reduced. This will create a faster, better, cheaper route to new drugs."

Solutions

The two most critical contributions to the new methods are PCR (polymerase chain reaction) and Bioinformatics. PCR is a method used to quickly obtain any gene from its natural source and transfer it to an engineered organism for enzyme production. Bioinformatics is the genome sequencing project which means that the entire DNA composition of more than 200 native micro-organisms is now freely available on the internet and can be used to find new enzymes encoded in the DNA.

Dr Fotheringham says: "We can use methods of gene mutation and efficient screening to identify specific changes in the structure and the properties of the enzymes we are studying, which adapts the enzymes for industrial use. For example certain mutations in the structure of the enzyme might make it more stable under the operating conditions of a chemical reactor. Other mutations might increase the rate or selectivity of the reactions which the enzyme carries out on the target compounds we are interested in producing. This is called 'directed evolution'."

Results

Both partners have identified the lyase enzymes they have chosen to work on and have cloned the necessary microbial genes which encode these enzymes. They have produced the enzymes in engineered microbes as 'micro-factories' and are now testing the enzymes on some model target compounds. They are also now developing the screening methods which will be used to identify mutations which improve the properties of these new biocatalysts for industrial use. In the coming year they will demonstrate small scale reactions to produce beta amino acid targets of commercial importance.

Dr Fotheringham adds: "We really got off to a flying start, largely because the partners know each other so well.

"We have isolated all the enzymes we are interested in working with. We are now working to produce them as efficiently as we can. We are also working to modify them so they are most appropriate for use in an industrial environment."

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Collaborative Research and Development

Collaborative Research and Development is one of two DTI business support solutions delivered through the Technology Programme, the other being Knowledge Transfer Networks (KTNs). Its primary objective is to enable the industry and research communities to work together in strategically important areas of science, engineering and technology in order to develop successful new products, processes and services. It also enables the latest thinking and understanding to flow between universities, other research centres and business.

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