The National Food Institute develops bacterial cell factories that can produce food ingredients from sustainable resources such as residual products from the food industry. Fermentor. Mikal Schlosser

# Cell factories produce milk protein without the use of a cow

Take a residual product from the food industry and instead of discarding it, look at it as a side stream and use it to develop a new food. The National Food Institute can e.g. make milk protein without the use of a single cow. Rather, a cell factory does all the work.

At the National Food Institute, the researchers can make a bacterium produce milk proteins in a so-called cell factory. This is a smart idea – because if you can make bacteria convert side streams into milk proteins efficiently and profitably, you can produce foods that are high in protein without having access to animal products.

As the world population keeps growing, there is an increased demand for healthy and tasty foods that are rich in proteins. Finding efficient and environmentally friendly methods to produce and grow foods that are able to feed billions of people is proving to be quite a challenge.

"At the National Food Institute we can produce milk proteins without the use of a cow. For example, we modify the bacterium Bacillus subtilis slightly so that it starts producing large quantities of milk proteins with good functional and nutritional properties. For this process, it is possible to use residual products from the industry as feedstock for the bacteria - that is the food the bacterium gets so it can grow," Professor Peter Ruhdal Jensen says.

A cell factory is not a building or an instrument. The factory consists of the bacterium itself as well as the processes that take place inside this bacterium.

### Previously the pigs could have it - at best

An important part of working with cell factories is to utilize the side streams - residual products - which are created during the production of foods and thus produce another product from the side stream. Whey from milk processing contains large quantities of sugar, which may have previously been thrown out or used as pig feed, at best. Instead, dairies will in the future be able to convert the sugar into a substance which will be very valuable to the food industry in the future. This will offer a more efficient resource utilization and thus a more sustainable food production.

5 7

"Some of the food ingredients which can be developed by cell factories may be of interest worldwide as a means to feeding the constantly growing population. If we look 30 years ahead, we will be almost 10 billion people on Earth. We might be able to provide food for all these people if we utilized all land areas, cut down the rainforest and so forth. However, we would rather do this in a sustainable way to ensure that the impact on the environment is as small as possible. A sustainable solution is that we learn to use our resources in a suitable and efficient way. In the future, we do not want any unutilized side streams. Everything must be used – and preferably to produce food for humans," Peter Ruhdal Jensen says.

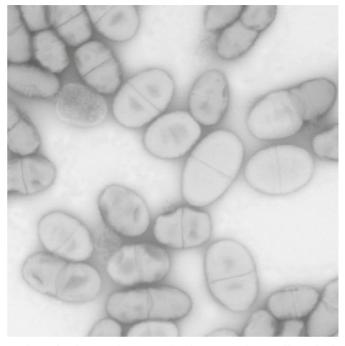
#### A cell factory turns one substance into something else

The cell factory can turn a side stream such as lactose into butter aroma by feeding a bacterium with the milk sugar which then spits out butter aroma – a food ingredient that food companies can use as flavouring in different products, from cookies to sauces. To produce the butter aroma, the researchers have slightly modified certain processes, which naturally take place inside the bacterium. The bacterium has been genetically modified: Some genes have been removed whereby routes in the metabolism have been redirected and the enzymatic reactions have been changed.

The Institute can make cell factories in two different ways: One is the natural way, another is by means of genetic modification. In the natural way, the researchers screen for suitable bacterium. They are looking for a needle in a haystack so to speak, and they may find a lactic acid bacterium suitable for producing butter aroma. The good thing about this method is that the researchers can produce an ingredient, which does not require a GMO - genetically modified organism. Therefore, the industry is free to use it to produce food and without labelling. However, the disadvantage of this process is that it is very time-consuming to identify which bacteria have the desired properties.

The genetic modification method, on the other hand, is much faster, but the disadvantage is that the food ingredient must undergo an authorization process and will subsequently be subject to labelling requirements because it is a GMO. According to the Professor, this is a paradox:

"In the butter aroma example, genes from other organisms have not been added, and the genetically modified version has fewer and more accurate genetic changes. Based on a rational assessment, the genetically modified version should thus be preferred to the 'naturally' produced one. Therefore, it would be nice to have a more nuanced debate as we really need to be able to use these techniques in the future race to secure a sustainable food production," Peter Ruhdal Jensen says.



By using cell factories, the National Food Institute is able to get slightly modified lactic acid bacteria to produce milk protein by feeding the bacteria with residual products from the production of food.

Lactococcus lactis, lactic acid bacteria. National Food Institute

**The ambition is** to learn how to make the most of all side streams. This will have a positive impact on our emission of greenhouse gases, and when all comes to all: The greater utilization of the foods we produce, the smaller impact on our agricultural land. Thus, we can avoid using all of nature and preserve e.g. the rainforest. We should not just do this because nature is beautiful, but also because it is important to maintain biodiversity. Moreover, the forests also keep the CO<sub>2</sub> level low.

In the future scenario, we will not only use the side streams from dairies, breweries, and other food production. We will also utilize all resources from the agricultural sector. Today, we burn straw from wheat production in straw-fired boilers and make heat from it. In the future, we have hopefully found even more alternative ways to produce heat, making it possible to use straw as a feed for the microbiological production of foods, chemicals, and jet fuels. 5 9

Peter Ruhdal Jensen Professor

#### Alcowhey turns lactose into alcohol

Alcowhey is the name of a spinout company from the National Food Institute, which is based on patented technology in the form of a cell factory developed at the Institute. By means of lactic acid bacteria, the cell factory turns residual lactose from dairies into ethanol - the alcohol contained in spirits.

In the production of cheese, nine-tenths of the milk ends up as whey. As previously mentioned, whey contains sugar and protein. Large dairies such as Arla have the technology and know-how to further process these side streams themselves. However, small dairies do not necessarily have the resources to process the whey. In addition, it is a low-value product and is usually either sold as animal feed or it ends up as waste. Alcowhey offers the dairies a solution which enables them to use the whey in a more profitable way. Alcowhey can help small dairies to convert whey to ethanol. Subsequently, the dairy can sell the ethanol to distilleries, who in turn use it in the production of alcohol. Alcohol is usually made from e.g. maize, cane sugar, or wheat - that is foods which could feed people. Therefore, it is also an advantage from a sustainability perspective that a residual product can be used to produce the alcohol.

In brief, the cell factory creates value in many ways: It turns a residual product into a new high-value product instead of drawing on foods that we could eat instead. In addition, it helps the dairies to develop a new business area.

#### Something is brewing - new ways to more foods

The National Food Institute has invested in new fermenters. They can convert side streams to new food ingredients by using these as growth media for growing bacteria. This is a sustainable utilization of resources and part of the solution to the problem with feeding the growing population.

Fermentation converts a side stream – such as lactose from whey – to butter aroma by feeding the bacteria with lactose.

The bacteria used may be genetically modified so that they produce a substance which they would not produce naturally. In order to make the bacterium convert e.g. lactose to butter aroma, the researchers have removed some genes from the bacterium.

In other cases, the researchers can compare different bacteria which had their different genes 'turned up' or 'turned down'.

This allows the researchers to examine which bacterium would be the right candidate for the ingredient someone is wanting to produce.

To compare different bacterial strains, the Institute has invested in several BIOSTAT® A-fermenters: Ten of them have a volume of one litre and two of them have a volume of five litres. Here the researchers can control the conditions in the fermenters such as oxygen, temperature, and pH.

The purpose of the work is to compare the bacterial growth and metabolism, under controlled circumstances, and thus to gain valid knowledge of the process and the result so that the new substances can be used in innovative industrial collaborations over time.



## WIDE SPAN IN RELEVANT RESEARCH AREAS FOR THE INDUSTRY

"As representatives from the industry, we really appreciate the cooperation with the National Food Institute. The Institute has a wide span in relevant business areas for the industry, and it is thus easy to access qualified knowledge and know-how.

We in the industry are favourably disposed to the fact that the Institute wants to be among the leading national food institutes in Europe, and that this is done through research cooperation with recognized universities.

It is a great strength that the National Food Institute works very closely with the industry and serves the authorities at the same time. It offers more substance to the cases on which we in the industry collaborate with the Institute.

Finally, the focus on life-long learning really makes sense. The industry demands opportunities to keep their employees up-to-date with the recent research-related development," says Vice President Esben Laulund from Chr. Hansen A/S, who is also a member of the Advisory Board at the National Food Institute. Esben Laulund Chr. Hansen A/S