

Ralph Ammann, Hannoversch Münden, Germany

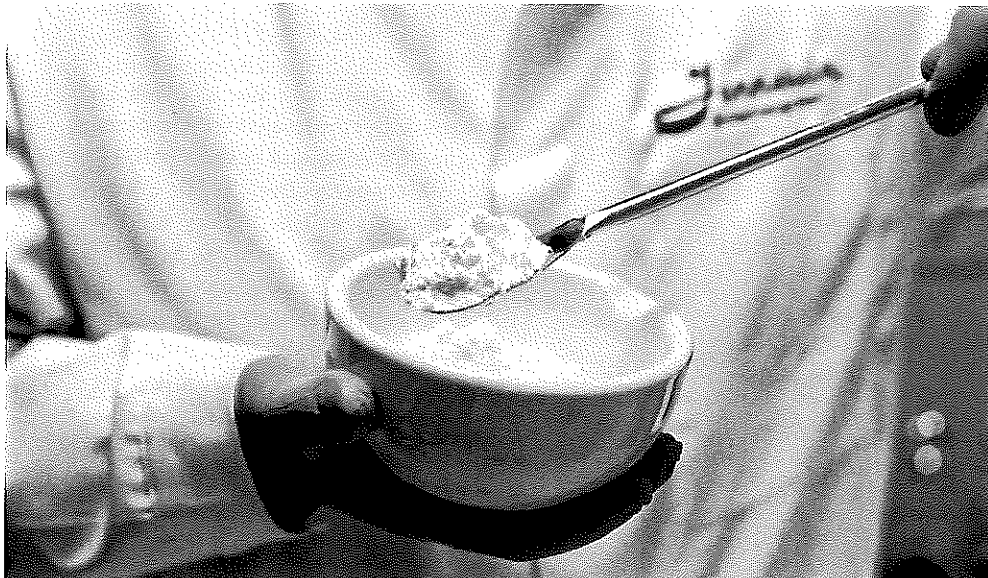
Achieving the impossible

Jennewein Biotechnologie is dedicated to the production of human milk oligosaccharides

Some time ago there was a rule in science: It is impossible to produce human milk oligosaccharides (HMOs), which occur naturally only in breastmilk, on an industrial scale. Nevertheless, the German company Jennewein Biotechnologie GmbH tried and succeeded. Since 2015, they have produced HMOs by bacterial fermentation. These HMOs have already been approved in the US, and more recently in the EU. This is the story of a hidden champion...

Sometimes you just have to believe in your ideas and keep trying until you succeed. A good example is Jennewein Biotechnologie GmbH, a company based in Rheinbreitbach, Germany. When it was founded by Dr Stefan Jennewein and his brother in 2005, they had only one goal in mind: the commercial production of human milk oligosaccharides (HMOs). These rare oligosaccharides are found only in human breastmilk, and they have well-known health benefits. Oligosaccharides are the fourth most abundant component of human milk, after lactose, fats and proteins. One litre human milk contains 5 to 10 g of HMOs, which are structurally very diverse – more than 200 different HMOs have been described.

Powdered and liquid products containing HMOs are the main business segment of Jennewein Biotechnologie GmbH.



The prebiotic effect of HMOs

HMOs can be defined as unconjugated complex glycans composed of various monosaccharide building blocks, specifically glucose, galactose, L-Fucose, N acetylneuraminic acid and N-acetylglucosamine. The German bacteriologist and paediatrician Theodor Escherich first reported the prebiotic effect of these molecules in the early 1900s. They promote the development of a healthy intestinal microbiome and thus have a positive impact on infant health.

Another reason for Dr Jennewein's interest in HMOs was that baby food producers faced a difficult challenge: the German public were very suspicious of new biotechnology products, resulting in strong resistance, but there was still

a need to develop manufacturing processes for HMOs at a reasonable cost. "Therefore, we decided to focus on HMOs", explains Dr. Jennewein. "Baby food is arguably the most strictly regulated foodstuff in the marketplace, and we were able to present scientific data to support the high quality and safety of our



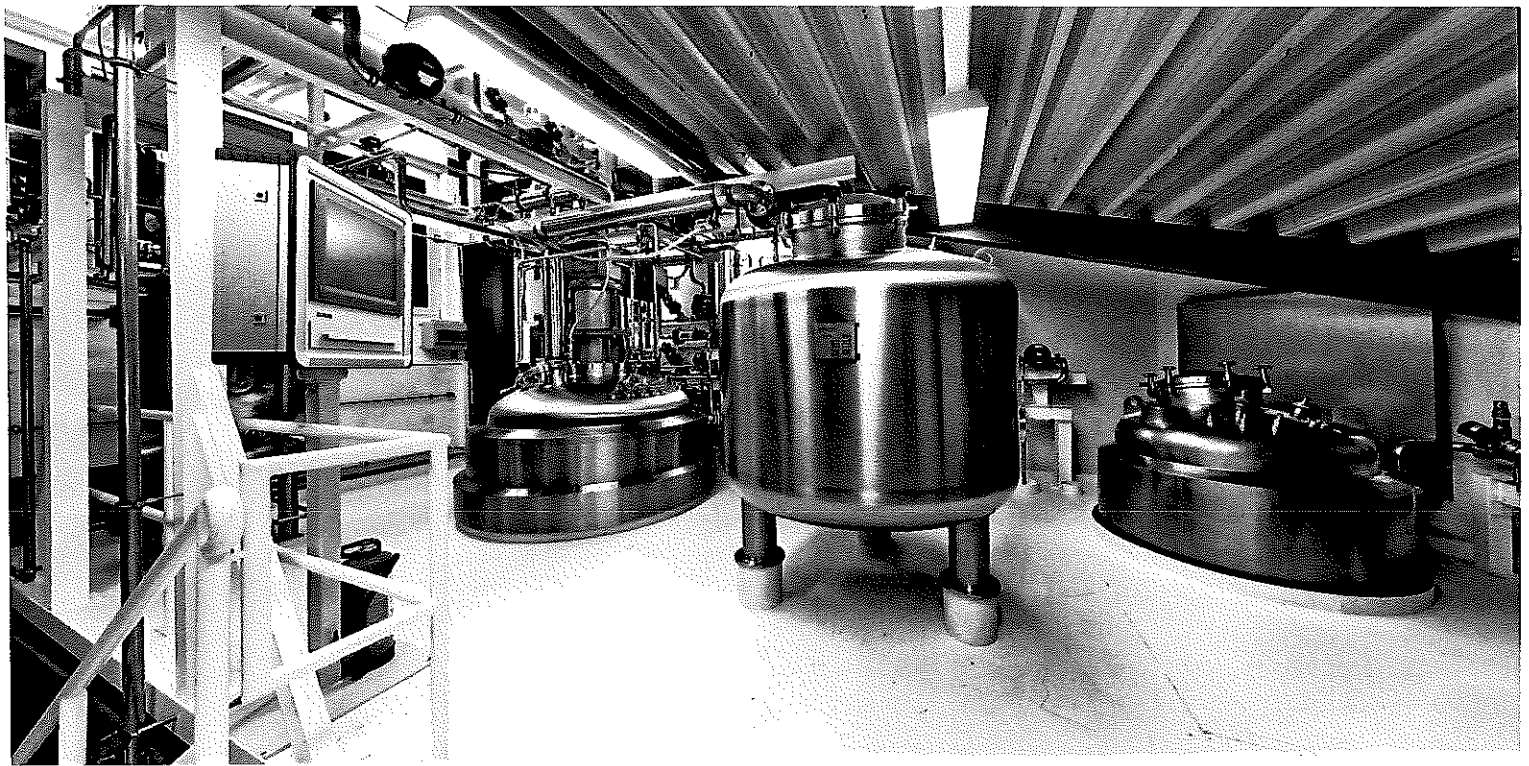
As far as I know, we are the only successful biotechnology company in the world which is based on one key idea.

Dr Stefan Jennewein,
Managing Director and Founder of
Jennewein Biotechnologie GmbH

products, particularly in the context of medical supplements." A key example is an ongoing cooperation with the German Centre for Cancer Research and the Children's Hospital in Heidelberg. These collaborations reduced the likelihood that Jennewein HMOs would be targeted by food activists.

First industrial-scale HMO production

The industrial production of HMOs was very challenging. Until the start of the Jennewein project, all attempts to produce HMOs by chemical synthesis were unsuccessful. "The main problems were producing the necessary



The fermenter is the core element of the production process for HMOs manufactured by Jennewein Biotechnologie GmbH.

quantities, and the need to use dangerous solvents like chloroform during the production process”, explains Dr Jennewein. A different approach was needed but was hard to find. It took a few years to develop an industrial production process, but eventually the company succeeded by establishing a process based on bacterial fermentation. The first Jennewein production process for HMOs was launched in 2013, and produces the most abundant HMO in breast milk: 2'-Fucosyllactose (2'-FL). For this purpose, Jennewein Biotechnologie built a specialized fermenter that can produce 180 grams of 2'-FL per litre. “The 2'-FL produced using our process is structurally and functionally identical to the natural molecule”, states Dr Jennewein. The main benefit for manufacturers is that the process is very efficient and economical, making it possible, for the first time, to produce HMOs in sufficient quantities to be used as a supplement in baby food. But before Jennewein HMOs could be added to baby food, the product and the manufacturing process had to be approved by the regulatory authorities according to strict quality and safety criteria. This hugely important goal was achieved in 2015 when the US Food and Drug Administration (FDA) awarded GRAS status (generally recognized as safe) for the production process, allowing Jennewein 2'-FL to be included in commercial baby food products. For Jennewein Biotechnologie, this was an important milestone on the way to the commercial rollout of their 2'-FL product on a worldwide scale. “As far as I know, we are the only successful biotechnology company in the world which is based on one key idea”, Dr Jennewein states, summarizing the impact of his work over the last ten years.

Approval in the EU

FDA approval was a major milestone, but in 2016 Jennewein 2'-FL was also approved by the EU under the European Novel Foods Regulation for use in liquid and powdered food products (including medical supplements). “This was very important for us because our HMO was the first to be approved as a Novel Food ingredient”, says Dr Jennewein. “Before EU approval, we mainly focused on the US and Asia. But now we can market this product in Europe too.” Other approvals are imminent in China and other parts of Asia. Today, Jennewein Biotechnologie markets its self-produced HMO under the brand Mum's Sweet Secret in the US, Asia and Europe. The main market sector is infant foods, but one of the approvals also covers medical foods so Jennewein Biotechnologie has now started to include 2'-FL in such products. “The probiotic effect of HMOs makes this a really interesting business segment for us,” Dr Jennewein reports. A successful example is the medical food Ultra GI

Replenish marketed by the US company Metagenics. It is no surprise that many of the leading baby food producers worldwide, as well as some dairies, have already become customers of Jennewein Biotechnologie. To meet the demand, Jennewein Biotechnologie now produces HMOs not only at their own facilities in Rheinbreitbach, but also at partner sites. The production of 2'-FL is only the starting point. The next step is the production of other HMOs, and mixtures of them. “Our aim is it to combine the qualities and benefits of different HMOs in one product”, says Dr Jennewein. This expansion to new products will also help the company to grow. “Today we have 70 employees, but we hope to increase our workforce to 100 by the end of the current business year.” The company has already demonstrated the will and the ability to overcome hurdles, as recognized by the innovation award Pionier-Geist from the German federal state Rheinland-Pfalz Ministry of Economics in 2007. So there is no reason why Dr Jennewein's prediction should not be fulfilled, come next March. ▲

Work in progress: 70 employees in the production area at the Jennewein Biotechnologie facility in Rheinbreitbach, Germany. (photographs: Jennewein Biotechnologie GmbH)

