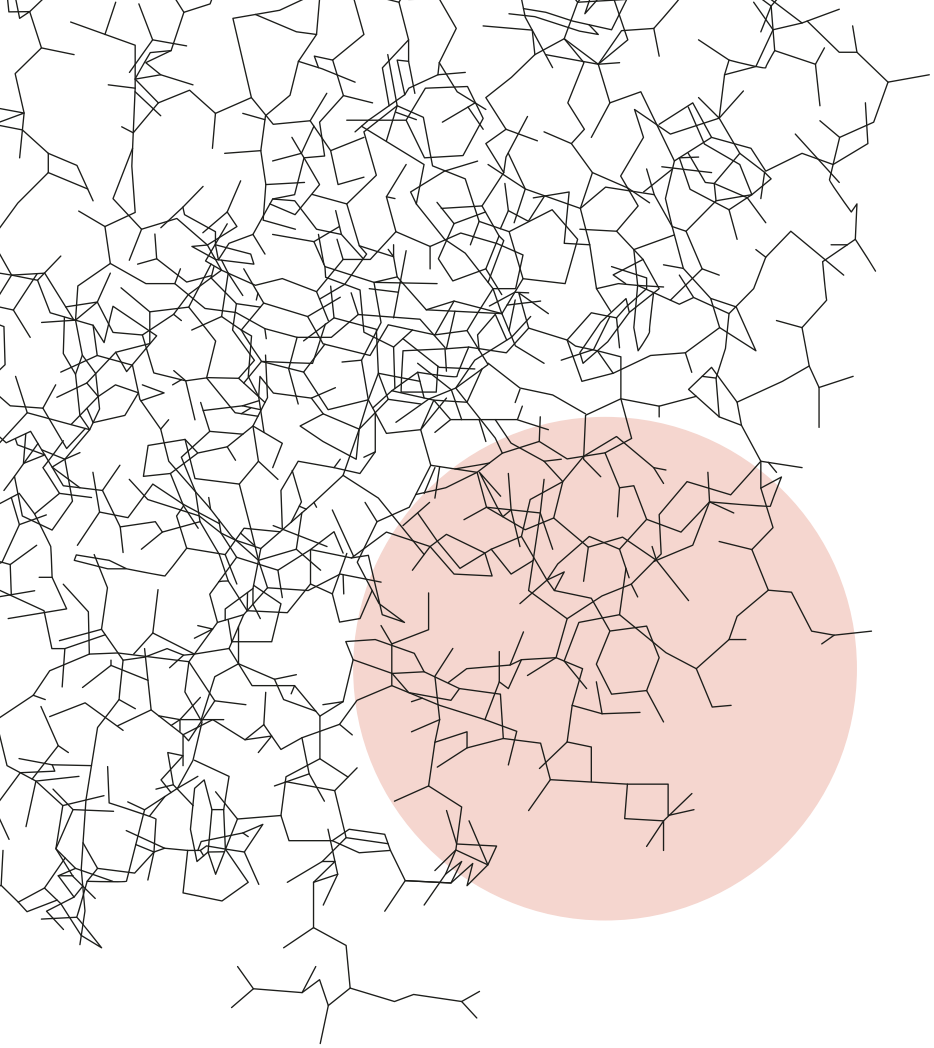
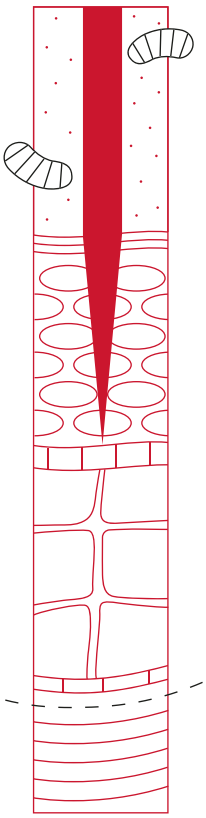
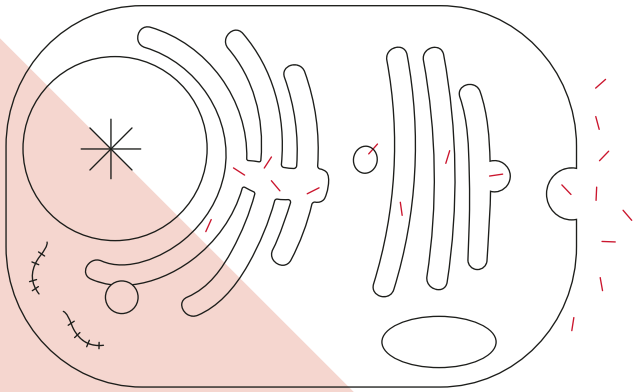




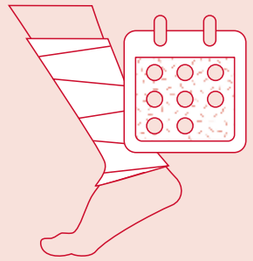


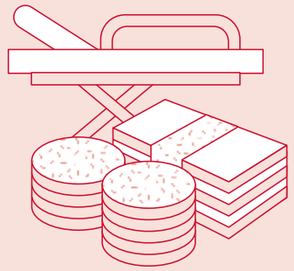
Biological care for wound patients

The combination of natural biodiversity and biotechnology opens up new prospects in wound treatment. This benefits patients, nursing staff and the health system in equal measure. Special enzymes point the way.

There are a growing number of patients with chronic wounds in Europe and other parts of the world. The number of cases in Germany alone is estimated at three million, but there are surely a large number of unreported cases. Since this mainly concerns elderly people, demographic change is pushing up patient figures. Other factors include diet-related conditions such as obesity, diabetes or malnutrition.

BRAIN's researchers have developed a new treatment to improve the situation of wound patients. The active principle is an enzyme with the product name Aurase®, which is modelled on the maggots of the common green bottle fly *(Lucilia sericata*). It has been known for centuries that open wounds infected with these maggots heal better.





40 m

There are more than **40 million patients with chronic wounds** worldwide. Doctors speak of chronic cases when treatment takes longer than eight weeks. In Germany, the wounds of about one third of patients become chronic.

EUR 10,000

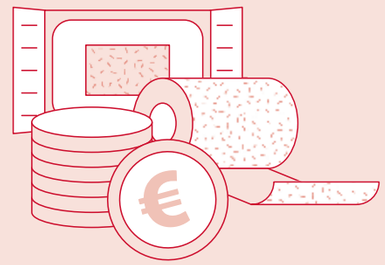
The costs of treating patients with chronic wounds amount to EUR 2 – 4 billion each year in EU member states. **Individual treatment costs are around EUR 10,000 per patient**. Wound dressings and bandages account for about a fifth of these costs.

50 %

About **half of all patients with decubitus ulcers** (also known as bed sores) and diabetic foot syndrome **become chronic wound patients**. Treatment may take many months or even years.

USD 20 bn

Experts presume that the **global market for wound treatment products and bandages** will reach an annual volume of **more than USD 20 billion by 2020**. The average annual growth rate of this market between 2014 and 2020 is estimated at eight per cent.



BRAIN's researchers have developed a new treatment to improve the situation of wound patients. The active principle is an enzyme with the product name Aurase®, which is modelled on the maggots of the common green bottle fly (*Lucilia sericata*).

BRAIN has translated this gift from nature's treasure trove into new wound care products.

The starting point was the identification of an enzyme that promotes wound healing in maggot therapies. The high-purity Aurase® enzyme is produced by means of biotechnological processes. The product name was based on the Latin for gold (aurum) and refers to the German name of the fly (literally "golden bottle fly") that served as the natural model.

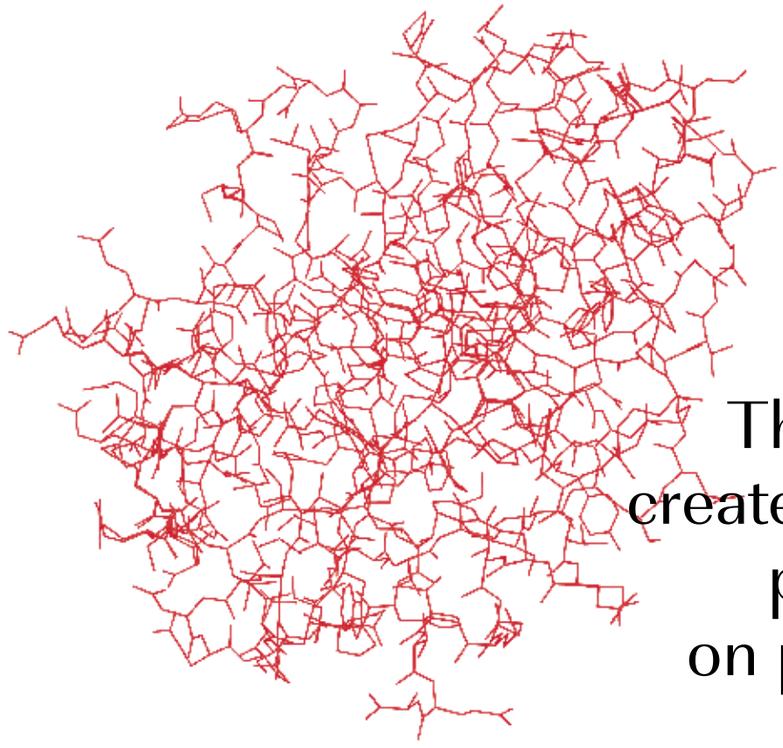
BRAIN extended its patent coverage for commercial use of Aurase® in the 2016/17 business year. We are currently exploring specific applications and various marketing options.

Aurase® ...

... is a new enzymatic active ingredient developed by BRAIN for the **biological treatment of open wounds**.

... illustrates the **enormous and still largely untapped potential of biodiversity**, here based on the common green bottle fly as a natural model. BRAIN's BioArchive contains a sliver of this biodiversity.

... is a new enzyme product for which BRAIN has already received **patent coverage in some 20 countries** of Europe, Asia, North America, Oceania and Africa for the fast growing market for the treatment of chronic wounds.



... is a **gentle option** for the growing number of chronic wound patients, and an **effective addition** to other sometimes painful and unpleasant procedures such as surgical debridement or maggot therapy.

The objective is to create a range of Aurase® products based on proven processes.

Our Aurase® enzyme unites bio-tech with nature

An interview with Dr Bela Kelety, Unit Head New Business Development at BRAIN AG, and Dr Alexander Pelzer, Project Manager and Platform Coordinator Tailor-made Biocatalysts

What is the special challenge involved in the treatment of open wounds?

BELA KELETY

Our skin acts as a barrier that protects us from pathogens. If this barrier is destroyed, there is a risk of contamination and infection that adds to the task of wound healing. Open wounds therefore require regular cleaning. To allow new tissue to grow, dead tissue has to be continually removed. This procedure is called debridement, and can be performed surgically under anaesthetic or by applying enzymatic substances. A third option is maggot therapy, in which fly maggots feed on the dead tissue. The choice of suitable debridement procedure depends on the type and size of the wound.

What was the starting point of your research into the Aurase® enzyme?

ALEXANDER PELZER

We worked on the assumption that therapies using the maggots of the common green bottle fly rely on the action of specific enzymes. Enzymes are proteins (biocatalysts) that speed up biochemical reactions. Nature offers a rich collection of these biomolecules that are essential to life.

How do enzymes act in maggot therapy?

ALEXANDER PELZER

Maggots use the wound debris as a source of nutrients and export enzymes that break down the protein fibrin, among others. That is one of the main constituents of the wound debris that impedes wound healing. Before we carried out our work, it was not known which enzyme plays a key role in this biological process. We knew that maggot therapies are either very unpleasant or completely unacceptable for many patients. That spurred us on to decode the process involved.

What were the essential steps in this research?

ALEXANDER PELZER

We have managed to develop a gentle biological option for wound treatment that unites nature and biotechnology. First of all, we succeeded in identifying exactly which maggot enzyme breaks down fibrin without attacking the surrounding healthy tissue. We characterised this enzyme, which we later baptised Aurase®, and then developed a biotechnological process to produce it in large volumes with a high degree of purity. The microorganism Pichia Pastoris is the production organism here. This involves a safe biotechnological expression system that is already being widely used.

How did people discover that the maggots of the common green bottle fly have medical properties?

BELA KELETY

It has been known since the Middle Ages that open wounds infected with maggots often heal better. Some even say that the Maya, the indigenous people of America, and the aborigines in Australia used maggots to heal wounds. The first scientific foundations were laid in the 1920s. This form of treatment fell into oblivion due to the development of antibiotics, and only regained popularity in the 1990s. Its current applications in hospitals are based on this ancient knowledge, and make use of specially bred sterile maggots.

What advantages does the Aurase® enzyme offer as compared with other enzymatic active substances?

ALEXANDER PELZER

The Aurase® developed by BRAIN is an enzyme derived from the serin protease family that can break down proteins or peptides. Aurase® acts very specifically on the protein fibrin. This is not always the case with other enzymes. Some wound treatment enzymes are obtained from pineapple plants or pathogens. Such enzymes act unspecifically and not only break down fibrin, but may also damage healthy tissue. They are therefore used in low concentrations or only applied for short periods of time. That makes nursing more time-consuming and lengthens the wound cleaning process.

What positive effects do you expect from the Aurase® products?

BELA KELETY

Our interest focuses on wound patients whom we would like to offer a well-tolerated, effective alternative to the sometimes very painful and unpleasant

“Aurase® will be easy to use and fit smoothly into existing processes.”

Dr Bela Kelety

forms of therapy available at present. While both surgical debridement and maggot therapy are effective, they are also time-consuming and cost-intensive forms of treatment, which call for a specialised infrastructure and detailed medical knowledge. We hope the Aurase® products will reduce the need to train nursing staff and the overall healing outlay. Aurase® will be easy to use and fit smoothly into existing wound management processes at hospitals, nursing homes or nursing care at home.

What form will the final Aurase® products take?

ALEXANDER PELZER

Various forms are conceivable in theory. A wound gel containing the active ingredient Aurase® has proved to be favourable, and has been shown to be effective and well-tolerated in pre-clinical trials.

Can we expect BRAIN to focus on pharmaceutical biotechnology as well in future?

BELA KELETY

Our focus is and remains industrial biotechnology. In this context, we concentrate on developing new enzymes, natural active ingredients and high-performance microorganisms. However, our expertise in these three areas also enables us to address a variety of tasks. Aurase® is a medical product, and this is admittedly an unusual market segment for BRAIN. But when we realised the benefits we could harness with our know-how for patients and nursing staff, we couldn’t just ignore it. Apart from that, this offers attractive market opportunities.

What are the next steps in realising Aurase® products?

BELA KELETY

On the one hand, we are presently working to optimise the yield of the biotechnological production system for the Aurase® enzyme. Parallel to this, we are taking steps to extend patent coverage. We are also in touch with experts to prepare clinical studies for our first Aurase® products and to obtain marketing authorisation.

When do you intend to launch Aurase® products on the market, and what business model will you use?

BELA KELETY

We will continue to drive development forward until we receive marketing authorisation and make the products available on the market. We intend to show that Aurase® products work under real-life nursing conditions and offer clear advantages for patients, nursing staff and doctors. We expect our first sales at the end of the decade, and are currently examining various options for business models to grow this business in future.
Experts estimate the annual sales volume of the market that BRAIN can address for Aurase®-based products at more than EUR 100 million in Europe alone. We intend to take part in this development.

The next steps include expanding patent coverage and preparing for a clinical study in order to obtain market authorisation.

We succeeded in identifying exactly which maggot enzyme breaks down fibrin without attacking the surrounding healthy tissue. We are presently working to optimise the yield of the biotechnological production system for the Aurase® enzyme.