Nose2Brain – Active substances without detour through the nose into the brain

Effective drugs for the treatment of diseases of the central nervous system, such as multiple sclerosis, do exist. However, the blood-brain barrier, which protects the brain as the body's control center, makes it especially difficult for therapeutic biomolecules to pass through. Thus, researchers from an international consortium coordinated by the Fraunhofer Institute for Interfacial Engineering and Biotechnology IGB have spent the last four and a half years developing a novel system in the EU project "N2B-patch" that can be used to bypass this barrier. The new approaches will be presented at a virtual international final symposium on June 17, 2021.

lacing medications as close as possible to the site of the disease: This sounds completely believable in theory, but is unfortunately not so simple in practice. While this works well for many drugs via the bloodstream or the digestive tract, it does not apply to the brain. In this case, special protective mechanisms such as the blood-brain barrier do protect the brain and ensure that foreign substances including therapeutic agents can only reach the brain with great difficulty and to a significantly reduced extent. However, for pathomechanisms within the central nervous system (CNS, brain and spinal cord) in particular, it is crucial that the drugs reach this organ as efficiently as possible. One example is the treatment of multiple sclerosis, a major driver of neurological disability already in young age with high socioeconomic impact.

Gentle form of administration for biopharmaceuticals through the nose

For this reason, the EU-funded joint project "N2B-patch" was launched in January 2017, in which an international consortium of eleven partners coordinated by Fraunhofer IGB set itself the task of proving a more efficient, alternative option for the therapy of multiple sclerosis. Also with the expectation that other CNS diseases may also benefit from the platform technology.

With success: the international consortium has demonstrated the proof of concept and has therefore shown that a nasal delivery system for biopharmaceuticals in the upper region of the nasal cavity via the olfactory mucosa, the regio olfactoria, is possible.

In contrast to treatment by nasal spray, which acts via the respiratory epithelium, or intravenous injection directly into the bloodstream, this innovative "nose-to-brain" approach may enable an active ingredient to bypass the path through the bloodstream and reach the brain directly. This is because the brain is separated from the nasal cavity only by the perforated ethmoid bone and a few additional cell layers, so that drugs are able to penetrate this barrier and reach the CNS directly over a short distance. Now the project ends after four and a half years.

"During our project, there were great successes to report, but also some challenges to overcome," reports Dr. Carmen Gruber-Traub, project manager of N2B-patch at IGB. "Not least due to the Corona pandemic, which ultimately even necessitated a project extension of six months. However, all partners worked with great commitment to fulfill the work plan and achieve the project goals. At the same time, we have grown close in the consortium, and long-term partnerships have emerged that will certainly last long beyond this project – not something to be taken for granted."

Future platform technology for a wide range of indications

The novel delivery system is so promising that a patent application is to be filed shortly. It was shown, among other things, that the formulation is stable and can thus even be stored for days and weeks at room temperature.

Since the novel system is designed to be flexible, the method may also be used in the future as a potential platform technology for other CNS diseases – for example, for the therapy of strokes and Alzheimer's disease – or even for specific cancers.

Preclinical studies convincing

"The system developed in cooperation with Beiter GmbH & Co. KG and tested by in vivo models is so gentle in its application that smelling may not be impaired in any way and no germs may enter the nose. In addition, generally no effects on the nasal microbiome were observed. Preclinical and microbiome studies have shown this," says Gruber-Traub. With the new system, it may be possible that the active ingredient could be continuously and reliably administered to the brain over a period of up to two weeks. After that, another application must be made.

However, surveys conducted by the consortium have shown that patients perceive this fact not as a burden. If repeated use also shows good tolerability by the patients, the system may also be suitable for long-term or even lifelong treatment. The system cannot be self-administered, but must be applied by a physician or trained personnel who have appropriate skill and experience. The European Multiple Sclerosis Platform (EMSP) closely accompanied the project as a partner throughout the entire duration and thus regularly involved those affected through events, campaigns or interviews.

End with symposium, but research continues

Although the new platform technology is still some time away from approval, everything is being prepared accordingly: "Work is already underway on marketing, on production in accordance with GMP (Good Manufacturing Practice) guidelines anyway, and of course the patent applications are being pushed ahead," says Gruber-Traub. "In addition, the basic research work continues even beyond this specific project, as part of the Marie Sklodowska-Curie Bio2Brain network for young scientists from around the world."

On June 17, 2021, the project will officially end with a virtual final symposium (10 a.m. to 3:30 p.m.). The event is open not only for experts from science and industry, but also patients and the interested public. During the symposium various scientific publications and short films about the novel drug delivery method that have been produced in recent years will be presented.

The program is available on the project website www.n2b-patch.eu/symposium. Interested parties can register for the free symposium via the link provided there.

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Further information

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