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Mosses for pharmaceutical production

Factor H as a therapeutic option for viral diseases - including COVID-19

The search for drug candidates for COVID-19 diseases is well underway. Factor H, which is part of the innate immune system, might also be a future therapeutic option. The Freiburg-based biotech company eleva has developed a technology for producing this human protein in moss cells. The active ingredient, which might also have a regulatory effect in other diseases, is currently undergoing preclinical testing.

The innate immune system is one of our body's important weapons against harmful invaders such as viruses or bacteria. It recognises and eliminates pathogens very swiftly with the help of various cell types and biomolecules, thus fending off a large number of infections without us even being aware of the danger.

The so-called complement system, a group of plasma proteins that act as an initial barrier against attacks on the human organism, for example when you cut yourself, is part of this vital protective mechanism. These biomolecules are always active in healthy people, destroy foreign cells in a complex cascade and regulate inflammatory processes. Factor H, a soluble glycoprotein that the body uses as a control protein and negative regulator, thus protecting the body's cells, plays a key role in the complement cascade. A lack of factor H leads to excessive inflammation and risk of tissue damage.

Human factor H from moss cells has already undergone preclinical testing



Human factor H can be produced as a recombinant protein in moss cells.
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According to recent findings, the destruction of a patient's lung tissue observed in severe cases of COVID-19 could also be due to this type of unregulated inflammatory reaction. Therefore, one current therapy is to block this inflammatory reaction with artificial antibodies, which, however, simultaneously prevents the immune system from attacking pathogens, thus creating a considerable risk of infection. An alternative option could therefore be to administer factor H in order to reestablish complement balance, thereby protecting the body's own lung cells without completely halting the immune reaction.

However, producing factor H is not easy: it is a complex, glycosylated molecule that is very difficult to produce in established systems, such as the CHO cells used for producing biotechnological drugs. For this reason, the Freiburg-based biotech company eleva GmbH (formerly Greenovation) started to develop recombinant factor H several years ago: eleva's factor H is a recombinant protein produced bryotechnologically - i.e. in moss cells: "The moss cells are only our production vehicles," explains Dr. Andreas Schaaf, CEO/CSO of eleva. "They contain the entire gene sequence of human factor H and produce the recombinant glycoprotein. We cultivate the organisms in reactors, factor H is secreted into the culture medium, and we harvest, filter and purify the product." Eleva's biomolecule was originally intended for the therapy of glomerulopathy in the kidney, amongst other things, and has already successfully passed the preclinical phase in this context.

Factor H could protect lung cells in COVID-19 patients

"In the meantime, however, studies[1] have shown that factor H has a general anti-inflammatory effect and that its administration can significantly reduce tissue damage caused by complement," reports the biotechnologist. "Put simply, the task of the complement system is to make holes in attacker cells and thereby destroy them. However, as the system reacts so quickly, there is a risk that it will also attack the body's own cells in the process. In order to prevent such damage, nature brings factor H into play: a negatively regulating component that protects the body's own cells."



Human factor H can be produced as a recombinant protein in moss cells.
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A connection between the complement system and acute respiratory distress syndrome (ARDS)[2] has also recently been established for infections caused by the novel coronavirus: even with the viral load already under control, it has been observed that an inflammatory situation triggered by the complement system contributed to continued damage to the alveoli. "There is certainly no end to research in this area," says Schaaf. "But it is already safe to assume that an excessive complement reaction leads in any case to organ damage. By the way, this is not only true for COVID-19, but also for many other virus-related diseases, which often attack the heart or kidneys. And we believe that factor H, due to its regulatory function, might be a promising therapeutic option."

Factor H can be considered as a general therapy option for viral diseases

The eleva experts are currently looking for cooperation partners so that they can use the biomolecule therapeutically as quickly as possible. "We already have a recombinant factor H glycoprotein as a result of our previous development work, and which we also produced in mosses. It is already available for other indications, even before clinical testing," says the scientist. "With regard to coronavirus SARS-CoV-2, this will of course not be a short-term affair - we are anticipating many years of development until possible approval. But we believe that, whatever happens, the effort will be worth it, as the therapy will also be open for consideration for many other viral diseases. This is obviously a general principle. Factor H would be a case of regulating rather than blocking, which would mean that we could benefit from the therapy in a broad range of infectious diseases."

However, eleva, whose central focus these days is on the further development of a factor H therapy, does not want to be an integrated pharmaceutical company that markets its products itself one day. Schaaf calls the company an "early-stage developer" that supplies the biopharmaceutical market with new, innovative therapy options. "We develop drug candidates on the basis of our technology up to the GMP process or up to an early clinical phase - that is our business. After that, we look for partners for further development."

This is also the case with factor H: the company is specifically looking for clinical and pharmaceutical research partners that specialise in viral diseases in order to jointly investigate the preclinical context in cell and animal models and accelerate COVID-19-specific evaluation. As far as other indications (C3-glomerulopathy (C3G)) are concerned, the development of factor H is very advanced and discussions with potential partners are already underway.

References:

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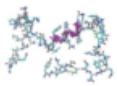
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