

Treating hair loss and diabetes

Follicum is developing an anti-diabetic treatment while simultaneously providing treatment for hair loss. At first glance this may seem like an odd combination in a development portfolio, but in fact the two indications are like two beads on a string of pearls.

The two endogenously derived peptides FOL-005 and FOL-014 are currently being developed by Follicum for the treatment of hair loss and diabetes, respectively. What is the nexus between these two seemingly distinct indications?

Logical explanation

"There is in fact a clear and established biological connection that explains this relationship in a quite logical manner", says Jan Alenfall, CEO at Follicum and continues,

"Studies have demonstrated an association between hair loss and diabetes as well as an association between hair loss and cardiovascular events such as myocardial infarction and ischemic heart disease.¹ Even at early stages of diabetes - the metabolic syndrome - males with insulin resistance often have hair loss, leading researchers to suggest that hair loss may be an early phenotypic marker of type 2 diabetes.² Some evidence also suggests that there is a similar connection in women.³"

Jan Alenfall further explains how hair loss on the lower limbs appears as a clinical manifestation of long-term peripheral arterial disease among diabetics.² Further, excessive amounts of insulin (hyperinsulinism) is associated with excessive hair growth, indicating that insulin receptors on the hair follicle are susceptible to the level of insulin in the body.^{4,5}

"These are the phenotypic features of the biological connection between hair loss and diabetes. On a cellular level, insulin seems to play a role when the hair follicles transfer from the resting phase into the growth phase", Jan Alenfall explains.

Minoxidil (the most widely used topically applied hair growth promoter), and a diabetes drug, diazoxide, can reduce blood pressure by opening specific ion channels in the vascular smooth muscle, causing the musculature to relax resulting in vasodilation. Both minoxidil and diazoxide trigger hair growth. Recent research has yielded more information about the structure and function of these ion channels that control the flow of potassium ions across cell membranes in many tissues, e.g., in the hair follicle, the vascular smooth muscle cells, the heart and the pancreas. The activity of these ion channels also controls diverse cellular functions such as pancreatic insulin secretion, protection against heart ischemia, and also affects hair growth, all together giving support to the connection of Follicum's two seemingly diverse projects.⁶

Endogenous peptides involved in repair mechanisms

Furthermore, normal hair growth alternates between activity and inactivity. The duration of the inactive resting phase of the hair follicle is critical for hair growth, and experimental studies have demonstrated that the inflammatory response seen in diabetes has an impact on the normal cycle of the hair follicle, by elongating the resting phase, whereby the normal hair growth from the follicle is postponed.² The hair cycle process can in a sense be compared to tissue repair mechanisms when the hair follicle circulates between the different phases of the hair cycle. Similarly, many of the diabetic complications occur due to a deficient or impaired tissue repair processes. Given that Follicum's peptides prove to be beneficial for the tissue repair mechanisms, the goal is to improve diabetic complications.

Follicum has identified receptors that bind the peptides in the hair follicles and in the beta cells of the pancreas, the latter being the production site for endogenous insulin. The two lead compounds, FOL-005 and FOL-014, are both endogenously derived peptides that appear to be involved in the repair mechanisms of the target organs, the hair follicles and the beta cells of the pancreas, respectively.

Stimulating hair growth

FOL-005 has been investigated in early clinical trials where intradermal injections of FOL-005 resulted in increased hair growth of healthy humans. Further clinical development is currently ongoing in a phase IIa study together with key opinion leaders at pre-eminent specialised sites in Germany with extensive experience and expertise in hair growth and clinical studies. Moreover, a topical formulation has been developed and will be investigated in upcoming clinical trials. The formulation development has been a challenge as it is far from trivial to develop a peptide drug for topical delivery, however Follicum recently completed the development phase with good results. A topical formulation will make the administration procedure simpler and contributes to a high compliance.

With knowledge about targets and the underlying mechanisms of hair growth, it is possible that Follicum can pursue other indications in the future where poor treatment options currently are available and where a high medical need exists.

Stimulating own insulin production

The second lead peptide by Follicum, FOL-014, has been shown to stimulate endogenous insulin release in different models both *in vitro*, *ex vivo*, and *in vivo*.

"In several experimental models FOL-014 shows the same potential as current GLP-1 analogues. We are currently looking into further pre-clinical trials that will explore the scientific and medical potential of FOL-014", Jan Alenfall says, pointing to the partnership between Follicum and academia.

Follicum is a partner of a large public-private research collaboration on diabetes along with Lund University. The project is funded to the value of 100 MSEK by the Swedish Foundation of Strategic Research.

(Link: <https://strategiska.se/en/research/ongoing-research/industrial-research-centres/project/8343/>)

"Within this large project we are exploring the potential beneficial effects of our peptides on diabetic complications which will be an important differentiating factor for the project", he says.

The focus of Follicum

Albeit the biological connection between diabetes and hair regulation is scientifically established, the current main focus of Follicum is to carry on the clinical development of a compound for hair stimulation.

"At the moment our main focus is the continued development of safe and efficient treatment of hair loss for both men and women, for which there is a large unmet need globally. In addition, our new diabetes project is very exciting, but still in an early stage", Jan Alenfall ends.

Reference List

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