NovaGo Therapeutics AG
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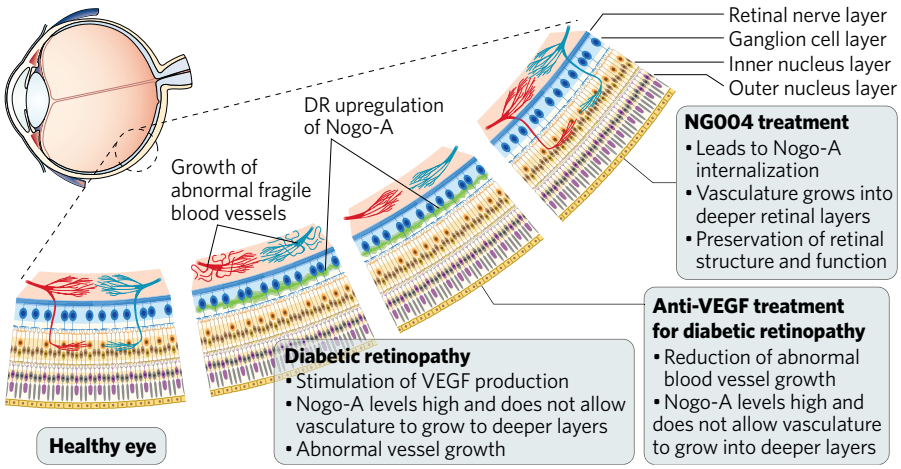
A new treatment for diabetic retinopathy

NovaGo Therapeutics is developing a first-in-class fully human antibody therapy to treat diabetic retinopathy. With its novel disease-modifying mode of action, it could save the sight of the many patients who respond poorly to current treatments.

Treating diabetic retinopathy (DR) is still a significant challenge for clinicians and remains a leading cause of blindness worldwide. NovaGo Therapeutics is developing a human antibody therapy that not only treats the symptoms of this condition, but has the potential to renew healthy vascular growth, reversing retinal degeneration and providing hope for the many who do not respond to current treatments. Pre-clinical results for its leading drug NG004, show a new mode of action and NovaGo plans to move into the clinic in 2021.

Based in Schlieren, Switzerland, NovaGo was founded in 2015 by ETH Zurich neuroscientist, Martin Schwab, to develop therapeutics that target the growth guidance protein, Nogo-A. The company is backed by Pureos Bioventures, and the biotech company, Neurimmune, whose proprietary human antibody platform has been instrumental in developing NovaGo's pipeline. In March 2019 NovaGo successfully closed a series A financing round of CHF 10 million ($10.9m) enabling rapid advancement of its ophthalmology clinical candidate. "Today NovaGo has a focused strategy in ophthalmology, and benefits from the globally recognised scientific expertise of our founders, " said chief executive officer, Ian Metcalfe, who recently joined the company, bringing more than 20 years of industry experience.



The hypothesized mechanism of action of NG004 in diabetic retinopathy. The increase of Nogo-A expression in retinal müller cells in DR contributes to restricting blood vessels growth in deeper layers of the the retina, causing them to deviate into the vitreous body of the eye. NG004 therapy leads to decreased Nogo-A levels in the retina, which allows vascular growth to return to the deeper layers of the ischemic retina, repairing the retinal blood supply and enhancing retinal cell survival. DR, diabetic retinopathy; VEGF, vascular endothelial growth factor.

Enter Nogo-A

The company has developed a best-in-class human monoclonal antibody that targets Nogo-A. "It's a fully human antibody which has the potential of having a much better safety profile than other humanized antibodies, " said NovaGo chief development officer, Eduardo Vianna. The antibody was developed using Neuroimmune's proprietary Reverse Translational Medicine (RTM) platform, which is based on high-throughput analyses of the immune response to disease-related proteins from human white blood cells.

Nogo-A is a strong inhibitor of blood vessel and nerve growth, and blocking its action has led to a new paradigm in central nervous system research. But with recent data on its role in the revascularization of damaged tissues, NovaGo is, for the first time, targeting this protein to treat DR, a complication of diabetes that damages the back of the retina. One third of the 285 million people with diabetes worldwide will have signs of DR and it will become vision-threatening in one in three of these cases[1]. Current anti-vascular endothelial growth factor (VEGF) therapies work by blocking the production of new blood vessels, but, according to Metcalfe, "a significant proportion of people treated for diabetic retinopathy are poor responders and a large percentage of patients continue to progress to blindness."

Evidence suggests that in patients with DR, an increase in Nogo-A expression in retinal nerve cells restricts normal retinal blood vessel growth. This leads the cells to secrete angiogenic factors which produces pathological new vascular growth. "By targeting Nogo-A with our antibody, we are able to return healthy growth of the vascular tissue, and stop the abnormal neovascularization that is characteristic of DR," explained Vianna. Novago's lead clinical molecule NG004 has been shown to restore blood supply in the retina and retinal functional activity in animal models.

Pre-clinical studies show that after treatment with NG004, the retinal vasculature of animals with retinopathy has a structure very similar to that of healthy animals. Recent results also show that Nogo-A is up-regulated in the retina of diabetic patients compared to healthy individuals, which further supports the role of Nogo-A in DR pathophysiology, and the rationale for targeting Nogo-A with NG004 .

Next steps and beyond

"The novelty of this mode of action is really exciting, and pre-clinical studies validate that targeting Nogo-A has a disease-modifying effect, rather than just treating the symptoms," said Metcalfe. The company is now getting ready to move to the clinic, with a well-established regulatory and development pathway to follow, based on the development of previous classes of retinopathy drugs. Its first-in-human study will assess safety, tolerability and collect efficacy evidence. "You can start seeing evidence of efficacy early on in clinical trials for this type of treatment, so we hope to offer early proof of principle in humans," said Vianna. The company is planning to initiate phase 1 trials by the third quarter of 2021 and move to phase 2 by the end of 2022.

NovaGo has started a series B raise of CHF 40 million ($44m) to support further development of NG004. "We have a novel, potentially disease-modifying agent, with a strong, growing company behind it, and we're looking for investors to work with us and help us deliver on the promise of our therapy for patients," said Metcalfe.

1. Lee, R. et al. *Eye Vis (Lond)* **2**, 17 (2015).

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