Pharma | Technology Offer

Innovative, non-invasive treatment concept for atherosclerotic plaques / arteriosclerosis

Application area

The aftereffects of atherosclerosis, i.e. cardiovascular disease, are the leading cause of death in Western industrialized countries.
Atherosclerosis, a system disease of the arteries marked by the deposition of blood fats, thrombi, connective tissue and calcium hydroxyapatite into the walls of blood vessels ("vascular calcification"), increases with advancing age. However, nowadays younger people also suffer from this disease, which is mainly due to an unhealthy diet and lack of physical exercise. The deposits ("atherosclerotic plaques") cause a constriction and hardening of the arteries, with the result of a reduced or completely interrupted blood flow, culminating in a myocardial infarction or stroke.
Development of a non-invasive treatment concept that allows atherosclerotic plaques to be dissolved has been made possible, so that prevention as well as direct treatment of atherosclerosis might be a reality in future.

State of the art

At an early stage of atherosclerosis, the disease is treated conservatively with drugs that are meant to inhibit blood clotting and thus the emergence of thrombi. Drugs against fat metabolism disorders, so-called lipid or cholesterol-lowering drugs, might also be prescribed. In cases of advanced, i.e. life-threatening arteriosclerosis, generally only surgical interventions, such as performing a balloon angioplasty, the setting of a stent or laying a bypass promise good results.
Overall, the therapeutic possibilities are unsatisfactory, as they are either not very effective or invasive and have side effects. Prevention is best supported by life style changes.

Innovation

Scientists at the University of Konstanz have developed different systems of multi-functional block copolymers based on amino acids and polyoxazoline components, respectively. The latter self-assemble as micelles, i.e. they form polymeric nanoparticles. The block copolymers can remove cholesterol and calcium ions from the atherosclerotic plaques and thus dissolve them. Cholesterol and calcium ions migrate into the interior of the micelles and are excreted via urine. By changing their mixing ratio, block copolymers can also be adjusted to the plaque composition of the individual patient in order to optimize their effect.
Block copolymers could be used as a kind of blood filter ("rheopheresis") and ideally be taken as oral medication.

Technology transfer

TLB GmbH manages inventions until they are marketable and offers companies opportunities for license and collaboration agreements.

Your benefits at a glance

- ✓ Dissolving of atherosclerotic plaques
- ✓ Block copolymers are pharmacologically and toxicologically inert
- ✓ Block copolymers can be varied to optimize the treatment of individual patients
- ✓ Block copolymers can be used via rheopheresis or taken orally as medicine
- ✓ For therapy and prevention

Further Information / Status of development

Introduction of the idea and the system of PEG-peptide based polymers:
Keckeis, P., et al.: Multifunctional Block Copolymers for Simultaneous Solubilization of Poorly Water-Soluble Cholesterol and Hydroxyapatite Crystals. *Adv. Funct. Mater.* 2019, 29, 1808331.
https://doi.org/10.1002/adfm.201808331

Doll, F., et al.: Visualizing Cholesterol Uptake by Self-Assembling Rhodamine B-Labeled Polymer Inside Living Cells via FLIM-FRET Microscopy. Macromol. Biosci. 2019, 1900081.
https://doi.org/10.1002/mabi.201900081

Publications on polyoxazolines to follow soon.
In a mouse experiment carried out in cooperation with the DKFZ Heidelberg, it was shown that the injected polyoxazoline-based block copolymers are distributed throughout the entire body (blood and organs) and then leave the mouse via the bladder. Mice did not show any symptoms during or after the experiment.
Running experiments focus on verifying the promising results of this study in another *in vivo* test system with optimized polymers.

Patent portfolio

DE 102017007671 A1 and WO 2019/034429 A1 patent application pending.

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