CaSR nanobodies

Novel therapeutics for treating secondary hyperparathyroidism in patients with chronic kidney disease
Background

Chronic kidney disease (ckd) is a disorder that leads to the gradual loss of kidney function, impairing the ability to maintain ion homeostasis and regulate urinary secretion. Ckd is the 12th leading cause of death worldwide.

The invention

We have developed a novel class of biologics (nanobodies) that target the calcium-sensing receptor (CaSR) as treatment paradigm for chronic kidney disease (CKD) with secondary parathyroidism. Currently, secondary hyperparathyroidism (SHPT) is treated with a small molecule drug class ‘calcimimetics’ that target CaSR. However, the use of these drugs is limited due to severe side effects in patients.

Our solution to overcoming these side effects is CaSR-targeting nanobodies. Nanobodies are small variable domain fragments of single-domain antibodies derived from llamas offering several advantages compared to conventional antibodies. Thus, nanobodies are excellent tools to therapeutically modulate receptors.

Key features

• high target affinity
• high selectivity
• tissue- and disease-specific modulation
• reduced side-effects

Development status

We have identified and characterized monovalent nanobodies in vitro to determine mode-of-action at target, and delineated nanobody-binding epitopes. We have developed humanized nanobody-FC conjugates to improve circulatory half-life and target coverage, and bivalent nanobodies to improve pharmacology for the target. Moreover, we have explored the potential of combination therapy using nanobodies and calcimimetics.

Our next step is to test nanobodies and nanobody conjugates in pre-clinical in vivo models and further improve their pharmacokinetic and pharmacodynamic properties.

Intellectual property rights

CaSR nanobodies are patented under patent application EP19211709.1