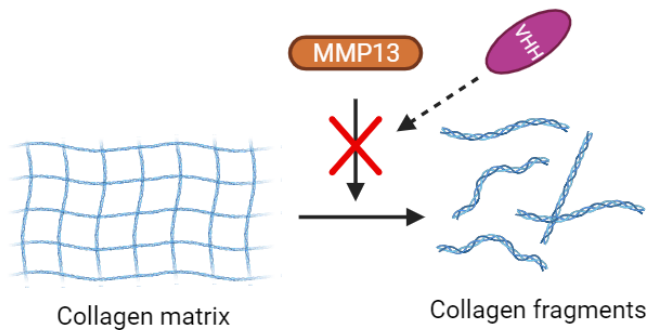


MMP-13 targeting VHHs as potential therapeutics in osteoarthritis

Project description

Osteoarthritis is mainly characterized by progressive degradation of cartilage due to amongst others proinflammatory factors secreted into the joint. These proinflammatory factors are leading to increased levels of matrix metalloproteinase 13 (MMP13), which in turn breaks down the collagens of the cartilage matrix. Inhibiting the activity of MMP13 could serve as a potential treatment for osteoarthritis.

We have developed llama-derived small antibodies (VHHs) that target MMP13 and show signs of inhibiting MMP13 activity. So far, we have performed the first successful tests on recombinant MMP13, but these tests should be elaborated in vitro and in combination with cells. As a next step, the VHHs should be incorporated into a slow-release drug delivery system based on hydrogels that can be injected into the joint.



Assignment

In this master assignment you will investigate the MMP13-inhibiting capacity of the VHHs by using multiple assays with recombinant MMP13. The next step will involve cell culture experiments in which chondrocyte pellets will be treated with the VHHs. Read-outs on these pellets involve qPCR analysis, immunohistochemical stainings and western blots. Furthermore, the VHHs have to be conjugated to tyramine-functionalized dextran or hyaluronic acid polymers for creating hydrogels as drug delivery system. Coupling efficiency, affinity after coupling and drug release profiles will have to be analysed in order to characterize our end-product.

Laboratory techniques involved

- Peptide cleavage assays and collagen degradation studies to study recombinant MMP13 affinity and inhibition
- Chondrocyte pellet culture, qPCR, immunohistochemical stainings, western blots for in vitro analysis
- VHH-polymer conjugation, SDS-PAGE, SPR and ELISA for characterizing polymer coupling
- VHH release study and ELISA to determine release profile.

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