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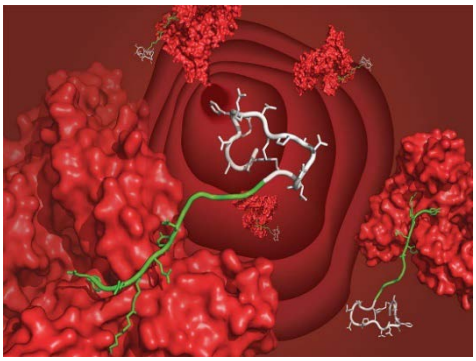
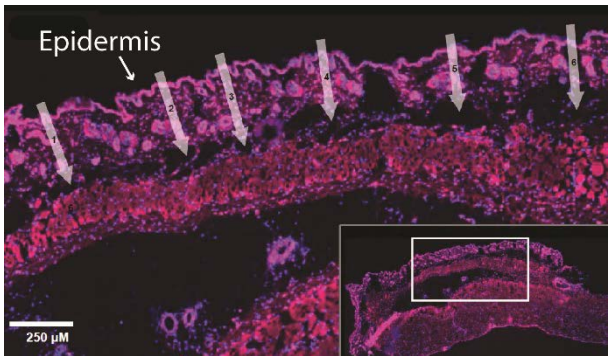
Licensing Opportunity

TTO – Technology Transfer Office

Potent tissue kallikrein inhibitors towards the first therapy for the rare disease Netherton Syndrome





Cyclic peptide-based KLK5 and KLK7 inhibitors. The peptides are highly potent and selective. They are stable in human plasma and present a favourable PK profile, with half-lives in mice of around 4 hrs (IV) and 6 hrs (SC). IV administration of the peptide-based KLK5 inhibitor (MW ≈ 3 kDa) to mice was enriched in the epidermis, where the disease targets are located. This property could represent a competitive advantage compared with larger molecules, such as monoclonal antibodies (mAbs).

Ref. Nr

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Keywords

Netherton syndrome, orphan diseases, inflammation, chronic diseases, cyclic peptides, orphan drugs.

Intellectual Property

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Publications

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Description

The Netherton syndrome (NS) is a genetic skin disorder that affects around 1 in 200,000 newborns. It manifests with symptoms like chronic inflammation of the skin and severe dehydration, as it causes the disruption of the skin barrier. Although the molecular mechanism (validated in mouse models) is known to be the dysregulation of the two tissue kallikrein-related peptidases 5 and 7 (KLK5 and KLK7), no specific therapy exists.

In our lab we have developed cyclic peptide-based inhibitors of KLK5 ($K_i \approx 1$ nM) and KLK7 ($K_i \approx 30$ nM). We have engineered them to improve their PK properties, achieving a half-life of around 6 hours in mice upon SC administration. In addition, we have demonstrated that the KLK5 inhibitor is enriched in the epidermis, where the disease targets are located. The efficient biodistribution to the skin is probably achieved thanks to the relatively low molecular weight of the molecules (≈ 3 kDa), thus providing an advantage over drugs based on larger molecular formats (e.g. mAbs).

Advantages

In the setting of NS, a therapeutic based on a cyclic peptide format can present several advantages over other molecular formats.

Advantages over small molecules:

- High target specificity
- Low risk of toxicity derived from metabolic products
- Less frequent administration

Advantages over larger proteins and mAbs:

- Efficient diffusion into the epidermis
- Cost-effective manufacturing
- Low risk of immunogenic responses

Applications

Further development as the first therapeutic specifically designed for the rare disease NS.

Offering

We are looking for a licensing partner with experience in the field that is interested to further develop the molecules into a NS therapy.