Opportunity 2021051

Combination therapy (QM107 and QM111) for treating neovascular eye diseases

An alternative to VEGF therapy

QM107 and QM111 are novel anti-angiogenic therapeutics, the peptides target an endogenous signalling pathway on blood vessels which acts to stop angiogenesis, which has demonstrated efficacy in models of wet Age related Macular Degeneration (AMD), diabetic retinopathy and cancer models.

Background

Angiogenesis plays a pivotal role in a wide range of diseases and is particularly prominent for its role in some neovascular ocular diseases, including wet AMD, as well as in other disease setting such as cancer. Anti-angiogenic therapies have shown clinical response during studies in macular degeneration, either alone or in combination with existing first-line therapies.

The Problem

There are a number of serious side effects commonly associated with the use of anti-angiogenic compounds for example haemorrhage, hypertension, lymphopenia and diarrhoea. In addition, in the case of VEGF targeting therapies, there is also a significantly large number of patient non-responders (15-45%). Thus, there remains a need for alternative therapies and methods for treating diseases associated with angiogenesis. Macular degeneration diseases are the leading cause of blindness in the over 50s, the global macular degeneration treatment market size was valued at USD 7.45 Billion in 2020 and is projected to reach USD 11.98 Billion by 2028, growing at a CAGR of 6.01% from 2021 to 2028.

Invention: Benefits & Application

Syndecans are a family of transmembrane receptors that have been extensively investigated in-house for their key role in promoting angiogenesis and for their potential as promising therapeutic targets. Small peptide regions have been found to activate powerful anti-angiogenic pathways in various ocular disease models, while having no effect on cell proliferation. QM107 and QM111, based on fragments from syndecan-2 and syndecan-3 respectively, show exciting results when used alone. However, less variability and greater efficacy has been observed when the drugs are used as a combination therapy.

Patents

A patent claiming the combination therapy of QM107 and QM111 for the treatment of diseases relating to angiogenesis has been filed (WO 2023/007136).

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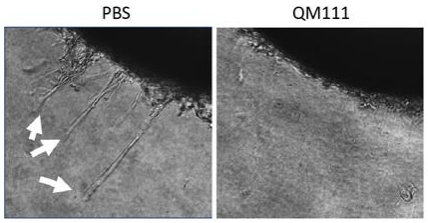
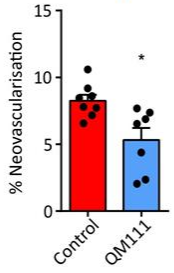
Project Development

The combination of QM107 and QM111 has been tested for its effects on:

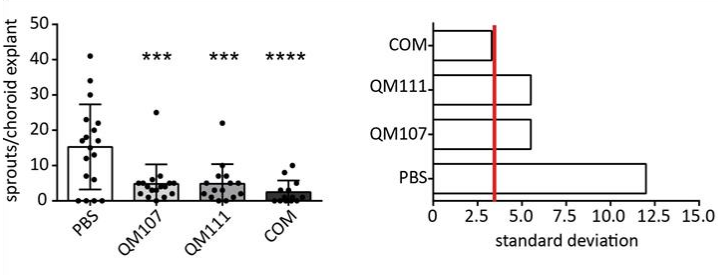
Rat Aortic Ring assay



Oxygen induced Retinopathy



Choroid Explant Assay



- **QM111** is a 9 amino acid anti-angiogenic peptide derived from Syndecan-3.
- **Rat Aortic ring Assay:** QM111 inhibits sprout formation by 85%.
- **Oxygen induced retinopathy mouse model**: QM111 achieves ca 50% reduction in neovascularisation.
- **Choroid explant model**: QM111 and QM107 inhibit sprout formation to a comparable level (>50%). However, the inhibitory affects are enhanced when used in combination (COM) and the response is considerably less variable.

Lead Inventor

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Publications

De Rossi, G & Whiteford J.R. “Syndecans in angiogenesis and endothelial cell biology” Biochem Soc Trans. 42 (2014):1643-46.

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De Rossi, G., Evans, A.R., Kay, E., Woodfin, A., McKay, T.R., Nourshargh, S. & Whiteford J.R. “Shed syndecan-2 inhibits angiogenesis.” J Cell Sci. 127 (2014): 4788-99.

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