Background

The healthy cornea lacks both blood and lymphatic vessels. However, a variety of inflammatory conditions can lead to a breakdown of this “angiogenic privilege”. This leads to the outgrowth of blood as well as lymphatic vessels from the limbus into the avascular cornea, reducing transparency and visual acuity. Furthermore, corneal neovascularization is also the most important risk factor for graft rejection after corneal transplantation, and especially lymphangiogenesis has been shown to be essential in mediating immune reactions after corneal grafting.

Topical administration of GS-101 eye drops significantly reduces inflammatory corneal hemangiogenesis.

GS-101 is an antisense oligonucleotide that inhibits the expression of the scaffold protein insulin receptor substrate-1 (IRS-1). GS-101 was shown to be a potent anti-angiogenic compound in vivo, and further results of a phase II study demonstrate that topical application of GS-101 eye drops specifically inhibit and regress corneal neovascularization.

So far, it is not known whether GS-101 eye drops are also able to inhibit murine corneal hemangiogenesis. Additionally, there are no data whether GS-101 eye drops can inhibit corneal lymphangiogenesis.

Results

Topical application of GS-101 eye drops significantly reduces inflammatory corneal hemangiogenesis.

At a dose of 0.43 mg/ml and 0.86 mg/ml, GS-101 eye drops showed not yet a significant inhibition of corneal hemangiogenesis. When used at a dose of 1.72 mg/ml, corneal hemangiogenesis was significantly inhibited by 17% in comparison to control animals (p<0.01).

Purpose

Aim of this study was to analyze whether GS-101 eye drops are able to inhibit murine corneal hem- and lymphangiogenesis.

Materials and Methods

Inflammatory corneal neovascularization was induced by placing three interrupted 1-0 nylon sutures in the corneal stroma of 6 week old BALB/c mice. Prior to suture placement, the central cornea was marked with a 2.0-mm diameter trephine and deepithelialized. Four groups were treated with different concentrations of GS-101 eye drops (2x/day for one week; 0.43, 0.86 and 1.72 mg/ml) or saline solution (18 mice per group). Afterwards, whole mounts of the corneas were prepared and stained with CD31 as a panendothelial marker and LYVE-1 as a lymphatic endothelial specific marker. The area covered with pathologic blood and lymphatic vessels was detected on digitized fluorescence pictures with an algorithm established in the image analyzing program cell^F (Soft Imaging System, Münster, Germany).

Conclusions

GS101 eye drops are able to inhibit murine corneal hem- and lymphangiogenesis in a dose dependent manner, and could be used for the treatment of corneal neovascularization, a major risk factor for graft rejection after corneal transplantation.

References


Support

Interdisciplinary Center for Clinical Research (IZKF) Erlangen (A9); German Research Foundation (DFG): SFB 643 (B10)