

RTEF Therapy for Ocular Neovascular Disease

Therapeutics that target angiogenesis are well accepted for treating human ocular neovascular diseases such as AMD. Commercially successful drugs include Lucentis, which targets the vascular endothelial growth factor (VEGF) receptor. However, drawbacks associated with antibodies targeting VEGF include mode and frequency of administration as well as undesirous side-effects including stroke.

In developing more specific and potent therapies, Dr. Tim Stout and his team have demonstrated that related transcriptional enhancer factor-1 (RTEF-1) is expressed in retinal vascular endothelial cells and is a key regulator of VEGF expression under hypoxic conditions. While RTEF-1 itself promotes VEGF expression, and is thus pro-angiogenic, Dr. Stout and his team have isolated isoforms produced by alternative splicing of the RTEF mRNA that positively or negatively regulate VEGF gene transcription. Notably, one of these isoforms, human RTEF-651, potently and competitively inhibits VEGF activity. The Stout team has also identified RTEF transcripts in uterine, colon, breast and renal tumor cells, suggesting a role for RTEF expression and perhaps splicing in cancer or cancer cell proliferation.

Applications

- *RTEF-651 gene therapy* for ocular neovascular diseases
- *RTEF-651 polypeptide therapeutic* for various solid tumor cancers
- Assay to screen for small molecule therapeutics to inhibit angiogenesis

Development stage

- Proof of concept using lentiviral vectors in ocular neovascularization animal models
- Animal studies with RTEF polypeptide are currently being conducted

Advantages

- One-time administration rather than monthly injections
- Potential greater potency as RTEF targets both the VEGF and FGF pathways.

References & Intellectual Property

Appukuttan et al, *Investigative Ophthalmology & Visual Science*, August 2007, Vol. 48, No. 8, pp 3775-3782

World-wide intellectual property protection for this technology:
US Pub. No. 2009/0117119 & corresponding applications in Australia, Canada, China, Europe, Japan and Israel ; US13/089687, PCT/US2011/032994

Available for licensing or partnering

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