

MicroRNA Therapeutics for Augmenting Blood Vessel Growth

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BACKGROUND

This invention provides microRNA therapeutics that augment blood vessel growth, which may have application for indications where it is desired to reduce or stimulate angiogenesis. Reducing or inhibiting angiogenesis may be useful for indications such as degenerative eye diseases and cancer. Stimulating blood vessel growth may be useful for treating indications such as cardiovascular, thrombotic or ischemic diseases. Cells lining blood vessels are usually among the least proliferative cell types, but this desired quiescence may be interrupted in response to growth factors during pathological neovascularization manifested in disease states such as macular degeneration and cancer. MicroRNAs are known to be key regulators of angiogenesis and specific miRNAs have been found to be effective toward these indications.

TECHNOLOGY DESCRIPTION

UCSD inventors used differential screens of HUVEC cells to identify specific miRNAs that are significantly altered in response to genotoxic stresses (radiation, doxorubicin, cisplatin and hydrogen peroxide). In vitro experiments with primary endothelial cells have confirmed a specific microRNA is able to modulate endothelial function in response to genotoxic stress. Therefore, manipulating levels of this microRNA offers avenues to sensitize the endothelium to several DNA damaging agents or protect the endothelium from stress induced injury.

APPLICATIONS

Increasing levels of this miRNA blocks angiogenesis, which may treat disease, such as cancer, retinal age-related macular degeneration, diabetic retinopathy and inflammatory diseases, including rheumatoid arthritis, psoriasis, and fibrosis. This technology may be particularly suited for ocular disorders where route of administration is favorable.

Conversely, blocking the activity of this miRNA encourages blood vessel growth, which may treat cardiovascular, thrombotic and ischemic diseases, including stroke and myocardial infarction.

ADVANTAGES

Agents that enhance the expression of this miRNA may allow the treatment of diseases with excessive neovascularization and agents that inhibit this miRNA expression may be used to treat diseases with insufficient neovascularization.

The specific mode of action is particularly well-suited for combination therapy with standard genotoxic chemotherapies or radiation to improve outcome for cancer and by enhanced killing of endothelial cells and decrease tumor angiogenesis.

STATE OF DEVELOPMENT

Gain and loss of function experiments with this miRNA demonstrates strong efficacy in, respectively, sensitizing endothelial cells to DNA damaging agents or protecting them from DNA damage. Specific target proteins of this miRNA that play a critical role in DNA maintenance in cells have been identified. Manipulation of these targets has shown the role of this pathway in modulating endothelial genotoxic stress response.

In addition, intravenous delivery of this microrna mimic sensitizes tumor xenografts to radiation, decreases angiogenesis and tumor burden in a mouse model of colorectal cancer.

INTELLECTUAL PROPERTY INFO

US rights available for licensure.

PATENT STATUS

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OTHER INFORMATION

KEYWORDS

Angiogenesis, miRNA, retinal age related macular degeneration, diabetic retinopathy, cancer, inflammatory disease, rheumatoid arthritis, psoriasis, fibrosis, retinal age related macular degeneration, diabetic retinopathy, cancer and inflammatory diseases

CATEGORIZED AS

- **Biotechnology**
 - Health
- **Medical**
 - Disease: Autoimmune and Inflammation
 - Disease: Blood and Lymphatic System
 - Disease: Cardiovascular and Circulatory System
 - Disease: Ophthalmology and Optometry
 - Therapeutics

RELATED CASES

2012-122-0

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	9,242,000	01/26/2016	2012-122

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