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A company of the LifeScience Foundation

REFERENCE NUMBER TO 03-00248

MAS-G-PROTEIN-COUPLED RECEPTOR AGONISTS FOR THE TREATMENT OF THE METABOLIC SYNDROME

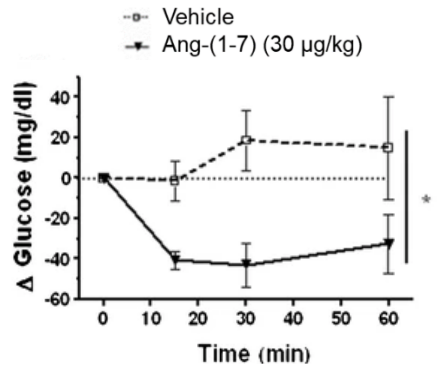
Keywords: metabolic syndrome, obesity, Angiotensin-(1-7), MAS receptor agonist

INVENTION NOVELTY

The metabolic syndrome is a combination of medical disorders in the fields of obesity, hyperinsulinemia, dyslipidemia, and hypertension that increases the risk of developing cardiovascular disease and diabetes. The MAS-G-Protein-coupled receptor (GPCR) and its agonist Angiotensin-1-7 (Ang-(1-7)) play a key role in the emergence of hypertension and cardiovascular diseases. The inventors discovered a new molecular function of MAS-GPCR. Activation of MAS-GPCR by its agonist Ang-(1-7) modulates health parameters (e.g., blood triglyceride and glucose level) in a highly desirable manner and thus is a promising approach to prevent and treat the metabolic syndrome and related diseases.

VALUE PROPOSITION

Despite its high occurrence, pathogenesis and underlying molecular mechanisms of the metabolic syndrome are poorly understood. Current therapy requires a multiple approach, including diet, weight control, and a combination of pharmaceuticals against high cholesterol, hypertension, and diabetes leading low adherence. Strikingly, targeted activation of MAS-GPCR by agonists collectively ameliorates key health parameters responsible for the manifestation of the metabolic syndrome and related diseases. MAS-GPCR agonists offer a new promising therapeutic strategy to partly replace time- and cost-intensive multiple approaches leading to higher compliance and thus to health improvement of patients suffering from the metabolic syndrome.



Oral administration of Ang-(1-7) leads to a decrease in blood glucose concentration and an improvement of insulin sensitivity (shown) in rats. (Santos et al., 2014)

TECHNOLOGY DESCRIPTION

The proposed technology focuses on the use of known or identification of new MAS-GPCR peptide or small molecule agonists such as Ang-(1-7) peptide and its analogs for the prevention, treatment, and modulation of the metabolic syndrome. Interestingly, MAS-GPCR receptor knock-out mice show a marked alteration in lipid and glycemic metabolism. In a recently developed rat model of inducible diabetes mellitus type 2, a novel oral formulation of Ang-(1-7) showed remarkable effects during onset and progression of disease. Strikingly, in both a prevention and a therapeutic study, oral administration of Ang-(1-7) led to a significant decrease in blood glucose level and to an improvement in insulin sensitivity. Furthermore, a reduction in fibrosis in the kidney medulla points to decrease in diabetic nephropathy. A phase I clinical study with Ang-(1-7) including the oral formulation has been completed.

COMMERCIAL OPPORTUNITY

The technology is offered for in-licensing and/or co-development as prognostic or therapeutic tool.

DEVELOPMENT STATUS

In vitro and animal *in vivo* proof of concept data available.

PATENT SITUATION

Patents are granted in Europe (EP2018185B1), USA (US8586054B2) and Brazil (BRPI0602366B1) with priority of 2007.

FURTHER READING

MAS deficiency in FVB/N mice produces marked changes in lipid and glycemic metabolism. Santos SH et al., Diabetes. 2008.
Oral administration of angiotensin-(1-7) ameliorates type 2 diabetes in rats. Santos SH et al., J Mol Med, 2014.
Angiotensin-(1-7) induces beige fat thermogenesis through the MAS receptor. Vargas-Castillo A et al., Metabolism, 2020.

Last updated February 2022

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