HYCOS: A NOVEL CLASS OF ANTI-INFLAMMATORY AGENTS

A new class of hybrid compounds with dual biological activity acting as Nrf2 activators and CO-releasing molecule (CO-RMs).

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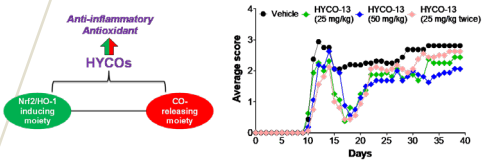
PRESENTATION

Heme oxygenase-1 (HO-1), an inducible enzyme that degrades heme to carbon monoxide (CO) and which expression is controlled by the transcription factor Nrf2, is an essential protective system against oxidative stress and inflammation. Developing strategies that target or mimic the Nrf2/HO-1/CO axis may offer new therapeutic avenues in the treatment of a variety of diseases. Our technology consists of a novel class of anti-inflammatory hybrid compounds termed HYCOs that are able to activate Nrf2/HO-1 and simultaneously liberate CO *in vitro* and *in vivo*. HYCOs have shown significant anti-inflammatory effects in different cell types (macrophages, monocytes, keratinocytes, microglia) and efficacy in pre-clinical models of psoriasis, endotoxin-induced inflammation as well as multiple sclerosis.



HYCOs exert a dual biological activity by activating Nrf2/HO-1 and simultaneously releasing CO in vitro and in vivo (left panel). Effect of HYCO-13 on the clinical progression of multiple sclerosis in a mouse model of experimental allergic encephalitis (EAE). HYCO-13 was administered orally once or twice a day at the doses indicated (right panel).

Nrf2 - CO-releasing molecules (CO-RMs) - Small molecules - Anti-inflammatory - Cardiovascular - Psoriasis - Multiple Sclerosis

COMPETITIVE ADVANTAGES

- Novel class of anti-inflammatory chemical entities
- Novel therapeutic approach with a dual biological activity
- Comparable efficacy with DMF, an orally approved drug for the treatment of multiple sclerosis

APPLICATIONS

- Treatment of inflammatory diseases, multiple sclerosis, psoriasis
- Cardiovascular protection

INTELLECTUAL PROPERTY

International patent application WO2015140337
Priority patent application filed on sept. 2015

PUBLICATIONS

Motterlini R. & Otterbein LE, Nature Review Drug Discovery 2010
Wilson JL & al., Chemistry 2014
Motterlini, R. & Foresti, R. Antioxydants & Redox sSignaling 2014
Nikam A. & al., Journal of Medicinal Chemistry 2016
Motterlini R. & al., Redox Biology 2019
Ollivier A. & al., ChemMedChem 2019

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DEVELOPMENT PHASE

- ☑ Hit to lead optimization on in vitro human cell line models and in vivo murine models of LPS-induced inflammation, psoriasis and multiple sclerosis
- ☑ Ongoing in vivo efficacy in mice disease models