Inflammatory Disease Therapeutics

OCR Number: OCR 6558

Description:

**Structure-based design of MIF Antagonists**

Macrophage migration inhibitory factor (MIF) is a pro-inflammatory cytokine released by T-cells and macrophages. Key role in a wide range of diseases including rheumatoid arthritis, sepsis, atherosclerosis, asthma, and ARDS.

Highly potent (<100nM) MIF antagonists with drug-like properties and economical synthesis routes discovered using structure-based drug design.

- OCR6558-333 analog has desirable plasma exposure

![](image)

- OCR6558-326 Drug-like properties
  - Eurofins Cereb HitProfile + CYP450s: 35 assays – no hits
  - Human & Rat Liver Microsomes: t½ > 60 min; CLint < 115 µL/min/mg

**Novel/Improved Assays for SAR**

3 x 3 DBA/2 male mice were dosed at 10 mg/kg = 50 mg/kg OCR6558-333

**B**

- OCR6558-316 Kd = 0.181 µM
- OCR6558-334 Kd = 0.056 µM

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