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

- OCR6558-336: \( K_d = 0.043 \, \mu M \)
- OCR6558-333: \( K_d = 0.036 \, \mu M \); \( S = 867 \, \mu g/mL \)

- OCR6558-333 analog has desirable plasma exposure

**Novel/Improved Assays for SAR**

- OCR6558-326 Drug-like properties
  - Eurofins Cereb HitProfile + CYP450s: 35 assays – no hits
  - Human & Rat Liver Microsomes: \( t_1/2 > 60 \, \text{min}; \text{CLint} < 115 \, \mu L/\text{min}/\text{mg} \)

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