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: $K_d = 0.036 \mu M$; $S_{0.5} = 8.87 \mu g/mL$

OCR6558-333 analog has desirable plasma exposure

**Novel/Improved Assays for SAR**

- OCR6558-326 Drug-like properties
  - Eurofins CerebHitProfile + CYP450s: 35 assays – no hits
  - Human & Rat Liver Microsomes: $t_{1/2} > 60$ min; $C_L < 115 \mu L/min/mg$

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