EuroSciCon

Annual Congress on
Medicinal Chemistry, Pharmacology and toxicology

July 30-31, 2018
Amsterdam, Netherlands

Song Feng et al., J Org Inorg Chem 2018, Volume 4
DOI: 10.21767/2472-1123-C3-009

DISCOVERY OF METHYLSULFONYL INDAZOLES AS POTENT AND ORALLY ACTIVE RESPIRATORY SYNCYTIAL VIRUS (RSV) FUSION INHIBITORS

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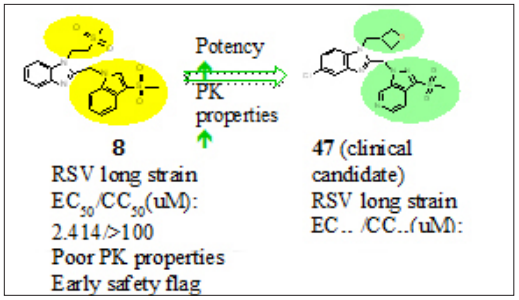
Recently we described a novel class of imidazopyridine compounds that showed exceptional anti-RSV potency in cell culture. However, unfavorable pharmacokinetic (PK) properties and glutathione (GSH) adduct liabilities impeded their further development. In a bid to address the PK and early safety concerns, a small compound library consisting of dozens of scaffold-hopping analogues was designed and synthesized for RSV CPE assay screening, which led to the identification of a new chemical starting point: methylsulfonyl indole compound 8. In this poster, we present the discovery and optimization of a series of methylsulfonyl indazoles as potent RSV fusion inhibitors. In particular, compound 47 was orally efficacious in a RSV mouse model, with 1.6 log unit viral load reduction at 25 mg/kg BID upon oral dosing. The results may have broad implications for the design of new RSV fusion inhibitors, and demonstrate the potential for developing novel therapies for RSV infection.

Image



Biography

Song Feng has obtained his PhD in 2004 from Shanghai Institue of Materia Medica(SIMM), Chinese Academy of Sciences(ACS), and completed his Postdoctoral studies in Arizonal Statie University and Ohio State Univerisity from 2004 to 2006. Now he is a Principal Scientist in Roche Inovation Center Shagnhai (RICS). He has published more than 25 papers in reputed journals and more than 10 patents in Cardiovascular and Metabolism (CVM) and infectious disease research area.

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