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Identification of novel hit against mutant influenza A virus

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Although amantadine derivatives are the only M2 drugs for influenza virus A, their use is limited in the U.S. because of drug resistance. We initially identified multiple M2 inhibitors that were rapidly generated through focused screening of a small primary amine library that was designed using a scaffold-hopping strategy based on amantadine. Though these compounds are novel M2 inhibitors and are as active as amantadine, they have no any effect against adamantane-insensitive A/M2 mutants. We further explored the hit and made a series of Pinanamine derivatives, fortunately some of the new compounds were capable of inhibiting WT A/M2 and selected adamantane-resistant M2 mutants. Several imidazole and guanazole derivatives of pinanamine were found to inhibit WT A/M2 well and one of these compounds exhibits inhibition of A/M2-S31N mutan (IC50 = 28.7 μM). Our study may provide a new insight into the structural nature of drugs required to inhibit WT A/M2 and its mutants.

Biography

Dr. Hu completed his Ph.D. in Medicinal Chemistry from the Institute of Materia Medica, Chinese Academy of Medical Sciences in 2002. During 2003-2006, He did the post-doctoral research at the Center for drug discovery and chemical biology, Northwestern University Medical School in the US. He is the Principal Investigator of Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences where he is running multiple drug discovery projects, including anti-diabetic drug discovery, anti-alzheimer's disease drug discovery (anti-neuroinflammatory inhibitors) and anti-influenza A drug discovery (M2 inhibitors). He is the owner of several drug candidates and more than 20 publications in high level journals along with 10 PCT patents.

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