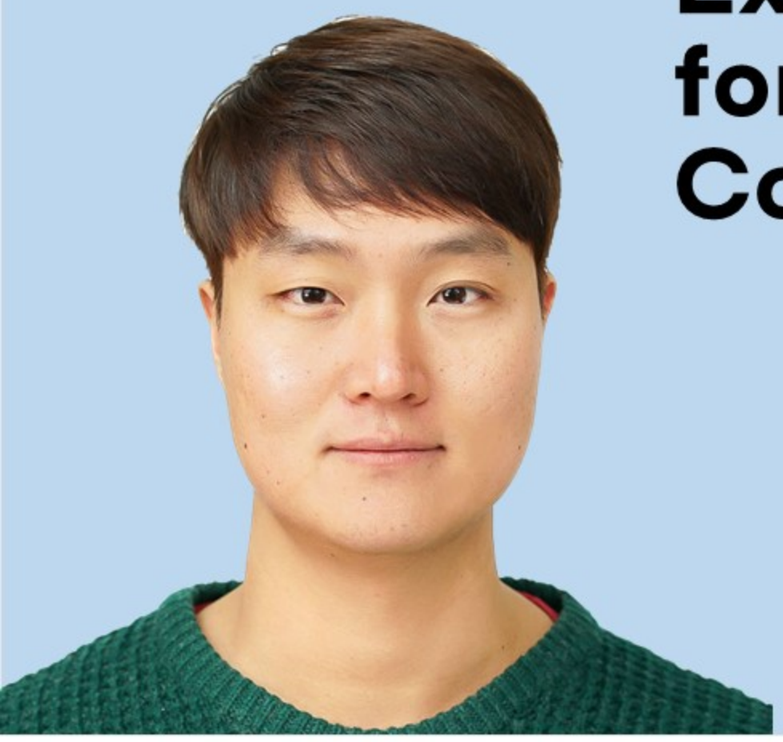
No. 2020-04

School of Life Sciences
Seminar Series

Thursday
4:00 PM

2 July

Jukhyun Bio Auditorium(RM.121)



Exploration of Alternative Scaffolds for P2Y14 Receptor Antagonists Containing a Biaryl Core

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언어: English

학력

2017 지스트 생명과학부 박사
2013 지스트 생명과학부 석사
2011 동국대학교 생명화학공학과 학사

경력

2018.2 – 현 재 미국국립보건원 방문연구원
2017.9 –2018.1 지스트 생명과학부 박사후연구원

Abstract

Various heteroaryl and bicyclo-aliphatic analogues of zwitterionic biaryl P2Y14 receptor (P2Y14R) antagonists were synthesized and affinity measured in P2Y14R-expressing CHO cells by flow cytometry. Given this series' low water solubility, various polyethylene glycol derivatives of distally binding piperidin-4-yl moiety of moderate affinity were synthesized. Reversal of a previously identified 1,2,3-triazole attached to the central m-benzoic acid core (25) provided moderate affinity, but not indole and benzimidazole substitution of the aryl-triazole moiety. The corresponding region of P2Y14R is predicted by homology modeling as a deep and sterically-limited hydrophobic pocket, with the outward pointing piperidine moiety being the most flexible. Bicyclic substituted piperidine ring derivatives of naphthalene antagonist 1, e.g. quinuclidine 17 (MRS4608, IC_{50} ~20 nM at hP2Y14R and mP2Y14R), or of triazole 2, preserved affinity. Potent antagonists 1, 7a, 17 and 23 (10 mg/kg) protected in an ovalbumin/Aspergillus mouse asthma model. Thus, we expanded P2Y14R antagonist SAR, introducing diverse physical-chemical properties.