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Synthesis of 1, 2, 3-triazole-linked salicylamide analogs as potent aurora kinase inhibitors

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The Aurora family is a member of the Ser/Thr protein kinases regulating mitosis. They includes Aurora A, B and C possessing individual function and different cellular localization during cell cycle. An overexpression of Aurora A and B, which has been observed in various tumor types, is known to connect to chromosomal instability, oncogenic transformation, and tumor progression. Although Aurora kinase is considered as a promising therapeutic target in cancer and several Aurora inhibitors have currently reached the clinical evaluation stage, Aurora-selective drug is not yet approved by FDA. Previously, we identified a potent antiproliferative substance by constructing a small molecule library that mimics lavendustin, a natural kinase inhibitor, using a rapid 'click-fragment assembly' and screening method. Based on this lead compound, various 1,2,3-triazolylsalicylamide analogs were designed, synthesized via Cu(I)-catalyzed azide–alkyne 1,3-dipolar cycloaddition (CuAAC) and evaluated biochemically for the Aurora kinase inhibitory activities. Among twenty-four membered 1,2,3-triazole library, compound **8a** exhibited much lower IC_{50} values against Aurora A kinase than the lead compound, and compound **8m** showed a nanomolar IC_{50} value against Aurora B. In this presentation, we describe the design, synthesis, and biochemical evaluation of 1,2,3-Triazole-linked Salicylamide Analogs.

Biography

Jae-Sang Ryu has completed his PhD from Northwestern University, IL, USA and postdoctoral studies from Memorial Sloan-Kettering Cancer Center, NY, USA. He is a profssor of college of Pharmacy & Graduate School of Pharmaceutical Sciences, Ewha Womans University, Seoul, Korea. He has been searching for new drug candidates based on disease mechanisms and combinatorial approaches. His lab is currently working on the development of allergic/anticancer drugs using peptide libraries and natural compound-like compound libraries. He has published many papers in SCI international journals and applied for patents related to the development of antiallergic drugs and anti-cancer drugs.

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