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Author Name: Ito, Masahiro; Tanaka, Toshio; Toita, Akinori; Uchiyama, Noriko; Kokubo, Hironori; Morishita, Nao; Klein, Michael G.; Zou, Hua; Murakami, Morio; Kondo, Mitsuyo; Sameshima, Tomoya; Araki, Shinsuke; Endo, Satoshi; Kawamoto, Tomohiro; Morin, Gregg B.; Aparicio, Samuel A.; Nakanishi, Atsushi; Maezaki, Hironobu; Imaeda, Yasuhiro

Accession Number: 2018:1418364 CAPLUS

Source: Journal of Medicinal Chemistry (2018), 61(17), 7710-7728 CODEN: JMCMAR; ISSN: 0022-2675

Digital Object Identifier: 10.1021/acs.jmedchem.8b00683

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Abstract: Cyclin-dependent kinase 12 (CDK12) plays a key role in the coordination of transcription with elongation and mRNA processing. CDK12 mutations found in tumors and CDK12 inhibition sensitize cancer cells to DNA-damaging reagents and DNA-repair inhibitors. This suggests that CDK12 inhibitors are potential therapeutics for cancer that may cause synthetic lethality. Here, we report the discovery of 3-benzyl-1-(trans-4-((5-cyanopyridin-2-yl)amino)cyclohexyl)-1-arylurea derivatives as novel and selective CDK12 inhibitors. Structure-activity relationship studies of a HTS hit, structure-based drug design...

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DOI: 10.1021/acs.jmedchem.8b00683

Journal title: Journal of Medicinal Chemistry

ISSN: 0022-2623 CODEN: jmcmar Year: 2018

Volume: 61 Issue: 17 Page(s): 7710

Author(s): Ito, Masahiro

Article title: Discovery of 3-Benzyl-1-(trans-4-((5-cyanopyridin-2-yl)amino)cyclohexyl)-1-aryurea Derivatives as Novel and Selective Cyclin-Dependent Kinase 12 (CDK12) Inhibitors

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Vol: 61 Issue: 17 Page(s): 7710-7728

Author(s): Michael G. Klein, Masahiro Ito, Toshio Tanaka, Akinori Toita, Noniko Uchiyama, Hironori Kokubo, Nao Morishita, Michael G Klein, Hua Zou, Morio Murakami, Mitsuyo Kondo, Tomoya Sameshima, Shinsuke Araki, Satoshi Endo, Tomohiro Kawamoto, Gregg B. Morin, Samuel A. Aparicio, Atsushi Nakanishi, Hironobu Maezaki, Yasuhiro Imaeda

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