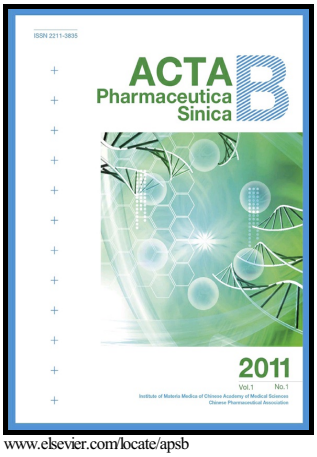
Arenobufagin is a novel isoform-specific probe for sensing human sulfotransferase 2A1

Xiangge Tian, Chao Wang, Peipei Dong, Yue An, Xinyu Zhao, Weiru Jiang, Gang Wang, Jie Hou, Lei Feng, Yan Wang, Guangbo Ge, Xiaokui Huo, Jing Ning, Xiaochi Ma



www.elsevier.com/locate/apsb

PII: S2211-3835(18)30208-9
DOI: https://doi.org/10.1016/j.apsb.2018.07.007
Reference: APSB571

To appear in: *Acta Pharmaceutica Sinica B*

Received date: 25 March 2018
Revised date: 20 May 2018
Accepted date: 18 July 2018

Cite this article as: Xiangge Tian, Chao Wang, Peipei Dong, Yue An, Xinyu Zhao, Weiru Jiang, Gang Wang, Jie Hou, Lei Feng, Yan Wang, Guangbo Ge, Xiaokui Huo, Jing Ning and Xiaochi Ma, Arenobufagin is a novel isoform-specific probe for sensing human sulfotransferase 2A1, *Acta Pharmaceutica Sinica B,* https://doi.org/10.1016/j.apsb.2018.07.007

Arenobufagin is a novel isoform-specific probe for sensing human sulfotransferase 2A1

Xiangge Tian[a,b,†], Chao Wang[a,†], Peipei Dong[a,†], Yue An[a], Xinyu Zhao[a], Weiru Jiang[a], Gang Wang[a], Jie Hou[b], Lei Feng[a,b], Yan Wang[a], Guangbo Ge[c], Xiaokui Huo[a], Jing Ning[a,*], Xiaochi Ma[a,b,*]

[a]*Academy of Integrative Medicine, College of Pharmacy, College of Basic Medical Science, Second Affliated Hospital, Dalian Medical University, Dalian 116044, China*

[b]*Institute of Functional Materials and Molecular Imaging, College of Emergency and Trauma, Hainan Medical University, Haikou 571199, China*

[c]*Shanghai University of Traditional Chinese Medicine, Shanghai 201210, China*

Received 25 March 2018; received in revised form 20 May 2018; accepted 1 June 2018

*Corresponding authors. Tel./fax: +86 411 86110419.

E-mail addresses: ningjing0626@163.com (Jing Ning), maxc1978@163.com (Xiaochi Ma).

[†]These authors made equal contributions to this work.

Abstract Human cytosolic sulfotransferase 2A1 (SULT2A1) is an important phase II metabolic enzyme. The detection of SULT2A1 is helpful for the functional characterization of SULT2A1 and diagnosis of its related diseases. However, due to the overlapping substrate specificity among members of the sulfotransferase family, it is difficult to develop a probe substrate for selective detection of SULT2A1. In the present study, through characterization of the sulfation of series of bufadienolides, arenobufagin (AB) was proved as a potential probe substrate for SULT2A1 with high sensitivity and specificity. Subsequently, the sulfation of AB was characterized by experimental and molecular docking studies. The sulfate-conjugated metabolite was identified as AB-3-sulfate. The sulfation of AB displayed a high selectivity for SULT2A1 which was confirmed by *in vitro* reaction phenotyping assays. The sulfation of AB by human liver cytosols and recombinant SULT2A1 both obeyed Michaelis-Menten kinetics, with similar kinetic parameters. Molecular docking was performed to understand the interaction between AB and SULT2A1, in which the lack of interaction with Met-137 and Tyr-238 of SULT2A1 made it possible to eliminate substrate inhibition of AB sulfation. Finally, the probe was successfully used to