Letter to the Editor

Cancer Research

Targeting Taspase1 for Cancer Therapy—Letter

Roland H. Stauber[1], Carolin Bier[1], and Shirley K. Knauer[2]

To the Editor

We read with interest the article by Chen and colleagues (1), identifying a potential Taspase1 inhibitor by using a cellular translocation assay similar to the one described by Bier and colleagues (2). These results impressively underline the power of cell-based screening, as previous attempts to identify effective small-molecule Taspase1 inhibitors by *in silico* or *in vitro* assays failed. However, one is wondering why screening was conducted in HEK293T cells, which do not express measurable levels of Taspase1 (3). Also, the results of the Ala-scan mutagenesis question the previously published Taspase1 consensus motif (2). The authors claim the critical importance of isoleucine at position P5, although the Taspase1 target USF2 contains an aspartate at P5 (2). Collectively, these factors might have contributed to the fact that only one chemical inhibitor, NSC48300, was identified, showing Taspase1 specificity in *in vitro* assays. Albeit the authors show that NSC48300 inhibited the growth of breast and brain tumors in murine models, the question of high interest remains that whether this activity is causally based on the inhibition of Taspase1 alone? Notably, besides its reported growth inhibition of numerous tumor cell lines, NSC48300 interfered with cell migration and invasion (4) and was patented as an antiangiogenic compound (5). This activity of the arsenic compound is further underlined by the results of the tail vein injection experiments, which might indicate potential limitations in the clinical use of NSC48300.

Although we appreciate the importance of the work for the relevance of Taspase1 in solid tumors, future works need to define the molecular mechanism how NSC48300 inhibits Taspase1 and whether Taspase1-independent effects of NSC48300 contribute to its antitumoral activity. Hence, the direct targets of Taspase1 responsible for its tumor-promoting activity need to be identified before the (pre)clinical exploitation of NSC48300 or related compounds by industry and academia.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Received January 23, 2012; accepted February 27, 2012; published OnlineFirst May 16, 2012.

Authors' Affiliations: [1]Molecular and Cellular Oncology, Mainz Screening Center, University Medical School Mainz, Mainz; and [2]Centre for Medical Biotechnology ZMB, Department of Molecular Biology II, University of Duisburg-Essen, Essen, Germany

Corresponding Author: Roland H. Stauber, Medical University of Mainz, Langenbeckstr. 1, Mainz D-55131, Germany. Phone: 496131177002; Fax: 496131176671; E-mail: rstauber@uni-mainz.de

doi: 10.1158/0008-5472.CAN-12-0150

References

1. Chen DY, Lee Y, Van Tine BA, Searleman AC, Westergard TD, Liu H, et al. A pharmacological inhibitor of the protease Taspase1 effectively inhibits breast and brain tumor growth. Cancer Res 2011;72:736–46.
2. Bier C, Knauer SK, Klapthor A, Schweitzer A, Rekik A, Krämer OH, et al. Cell-based analysis of structure-function activity of threonine aspartase 1. J Biol Chem 2011;286:3007–17.
3. Knauer SK, Fetz V, Rabenstein J, Friedl S, Hofmann B, Sabiani S, et al. Bioassays to monitor Taspase1 function for the identification of pharmacogenetic inhibitors. PLoS One 2011;6:e18253.
4. Saunders LP, Ouellette A, Bandle R, Chang WC, Zhou H, Misra RN, et al. Identification of small-molecule inhibitors of autotaxin that inhibit melanoma cell migration and invasion. Mol Cancer Ther 2008;7:3352–62.
5. Zudaire E, Aparicio M, Cuttitta F, inventors; The United States of America, as represented by The Secretary, Department of Health and Human Services (National Institutes Of Health, Office Of Technology Transfer6011 Executive Blvd., Suite 325,MSC 766, Bethesda MD, 20892-7660, US). Antiangiogenic small molecule and methods of use. United States patent US WO2011/014825 A2. 2011 Feb 3.