Reply to Struys: Role of biomarker of 2-hydroxyglutarate in acute myeloid leukemia

We agree with E. A. Struys’ point (1) that 2-hydroxyglutarate (2-HG) consists of two distinct forms, L-2-hydroxyglutarate (L2HG) and D-2-hydroxyglutarate (D2HG), and that these two endogenous metabolites should be differentiated in characterizing their association with isocitrate dehydrogenase1/2 (IDH1/2) mutations and with clinical consequences in acute myeloid leukemia (AML). In fact, in our report (2) we discuss that there are two different 2-HG enantiomers, D2HG and L2HG, previous experiments showed only D2HG was increased in IDH1/2 mutations, and that the determination of the D2HG/L2HG ratio as a more sensitive and specific clinical test may be developed in the future.

Recent studies have shown that either D2HG or L2HG, when increased, is implicated in tumorigenesis (3, 4). Although elevated serum D2HG can be oncogenic in IDH-mutated AML compared with IDH-mutated AML patients with IDH1-R132H and IDH2-R140Q mutations.

Although the measurement of 2-HG may be more practically feasible, an analytical method that quantifies D2HG and L2HG, respectively, is needed—as Struys suggests—to fine-tune such a measurement. We are in the process of evaluating a more accurate analytical method to quantify the two molecules and obtain the ratio of D2HG/L2HG, and compare the two methods (combined or separated D2HG and L2HG) for AML patient stratification and prognosis.

Yang Shen, Jing-Han Wang, Wen-Lian Chen, Wei Jia, Sai-Juan Chen1, and Zhu Chen

State Key Laboratory of Medical Genomics, Department of Hematology, Shanghai Institute of Hematology, Rui Jin Hospital affiliated with Shanghai Jiao Tong University School of Medicine and Key Laboratory of Systems Biomedicine of Ministry of Education, Shanghai Center for Systems Biomedicine, Shanghai 200025, People’s Republic of China


Author affiliations: 1State Key Laboratory of Medical Genomics, Department of Hematology, Shanghai Institute of Hematology, Rui Jin Hospital affiliated with Shanghai Jiao Tong University School of Medicine and Key Laboratory of Systems Biomedicine of Ministry of Education, Shanghai Center for Systems Biomedicine, Shanghai 200025, People’s Republic of China

Acknowledgments:

1To whom correspondence may be addressed. E-mail: sjchen@stn.sh.cn or zchen@stn.sh.cn.

Financial support: This work was supported by the National Natural Science Foundation of China (30970910, 30930041, 81021063, 31100960, and 30921063).

Editorial support: Biomedical Publishing Services provided editorial assistance.


The authors declare no conflict of interest.