From: Tamara Maes
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To: JoVE

Dear Dr. Meyers,

Please receive our manuscript:

"Direct Measurement of KDM1A Target Engagement Using Chemoprobe-based Immunoassays", by Mascaró et al.

A number of years back, we selected KDM1A, an enzyme involved in the control of histone methylation status and transcription, as a potential target for treatment of oncological and neurodegenerative disease. It was a bold choice, and we soon found how challenging it can be to perform drug development when no proper tools are available. Although we identified potent tool compounds quite early, the biology was a challenge and more than once, potential partners voiced disbelieve on our statements related to the potency of the compounds we had been designing. Our compounds were good, our evidence needed to be improved.

The relevance of proper assessment of the drug-target engagement to drug development can't be sufficiently underscored; and the use of the right assays is key. The desired biological effect should go hand in hand with the target engagement. This simple fact is ignored all too often by academic researchers, who have both reported biological effects in absence of any target engagement, or vice versa, have reported biological effects that were produced only at doses hundreds of time above target saturation. The error has also been committed by industrial promoters who admittedly finalized clinical trials without having a clue on whether their drug actually hit the target.

This manuscript provides a protocol to assess engagement to KDM1A, a hot target being explored in multiple indications including oncology and neurodegenerative disease. But it also reflects a general strategy and the reminder that robust assays are indispensible to move forward on solid ground in basic biology and drug development. We would be honored if our manuscript would be considered for publication in JoVE.

Best regards,

Tamara Maes. PhD
CSO Oryzon Genomics S.A.