Print Close

From: **Clinical Epigenetics Editorial Office** (em@editorialmanager.com)
Sent: Sat 2/27/16 1:19 PM
To: Shicheng Guo (shicheng.guo@hotmail.com)

CLEP-D-15-00211
MiR-34a-5p promotes multi-chemoresistance of osteosarcoma through the down-regulation of the DLL1 gene
Youguang Pu; Fangfang Zhao; Haiyan Wang; Wenjing Cai; Jin Gao; Shanbao Cai
Clinical Epigenetics

Dear Dr. Guo,

I would like to invite you to review the manuscript above which has been submitted to Clinical Epigenetics. Further details including the full abstract can be found at the end of this email.

If you are able to review this submission please click on this link:

http://clep.edmgr.com/l.asp?i=8527&l=HY5RE76P

If you are unable to review this submission please click on this link:

http://clep.edmgr.com/l.asp?i=8528&l=HEMOI4S4

We ask reviewers to return their report within 14 days of agreeing to review, however if you need more time please do let us know as we may be able to arrange an alternative deadline.

You are requested to submit your review online by using the Editorial Manager system which can be found at:

http://clep.edmgr.com/

Your username is: shicheng.guo@hotmail.com
Your password is: available at this link http://clep.edmgr.com/Default.aspx?pg=accountFinder.aspx&firstname=Shicheng&lastname=Guo&email_address=shicheng.guo@

In order to keep delays to a minimum, please accept or decline this invitation online within the next three days. If you are unable to review the manuscript, we would be most grateful if you could suggest alternative reviewers.

Thank you for your time, and I look forward to hearing from you.

Best wishes,

Carmen Jeronimo, PhD
Clinical Epigenetics
http://www.clinicalepigeneticsjournal.com/

CLEP-D-15-00211
Research
MiR-34a-5p promotes multi-chemoresistance of osteosarcoma through the down-regulation of the DLL1 gene
Clinical Epigenetics

Abstract: Abstract
Background: MicroRNAs have been identified as key players in the development and progression of osteosarcoma (OS). The molecular mechanisms that lead to OS development and metastasis are poorly understood. MiR-34a-5p has been implicated in the tumorigenesis and progression of several types of cancer, however, its role in OS remains elusive.
Results: We found that miR-34a-5p promotes multi-chemoresistance in OS cells. Using a systematic analysis of two multi-chemosensitive (G-292 and MG63.2) and two resistant (SJSA-1 and MNNG/HOS) OS cell lines, we showed that miR-34a-5p promotes OS multi-drug resistance via its repression of the Delta-like ligand 1 (DLL1) gene, the ligand of the Notch pathway, and thus negatively correlates with OS chemoresistance. siRNA-mediated repression of the DLL1 gene suppressed cell apoptosis and de-sensitized G-292 and MG63.2 cells, while overexpression of DLL1 sensitized SJSA-1 and MNNG/HOS cells to drug-induced cell death. Parallel to the changes in the drug-induced cell death, the activity of the ATF2/ATF3/ATF4 signaling pathway was drastically altered by a forced reversal of miR-34a-5p or DLL1 levels in OS cells.
Conclusions: We demonstrated that DLL1 is a direct target of miR-34a-5p and negatively regulates the multi-chemoresistance of OS through the activation of the ATF2/ATF3/ATF4 signaling pathway. This study also provided a new set of genes in this newly identified miR-34a-5p/DLL1/ATF axis as diagnostic targets for guided anti-OS chemotherapy, including the level of the miR-34a-5p gene, DLL1 gene and the ATF2/ATF3/ATF4 signaling pathway-associated genes.