World J Surg (2016) 40:1023
DOI 10.1007/s00268-015-3309-9

REPLY, LETTER TO THE EDITOR

# Upregulation of Neutrophil Gelatinase-Associated Lipocalin in Colorectal Cancer Predicts Poor Patient Survival: Reply

**Herbert Maier**[1] · **Felix Aigner**[2]

Published online: 6 November 2015


To the Editor

The findings by Cristobal et al. [1] help getting further insights into signaling pathways influencing Lcn-2 expression. The mechanism of Lcn-2 expression in cancerogenesis and metastasis is not well understood; however, activation of the phosphatidylinositol 3-kinase/Akt pathway as well as nuclear factor-κB activation to promote Lcn-2-dependent proliferation of tumor cells is still under debate. Lee et al. [2] showed a correlation between miR-138 and Lcn-2 in an in vitro model, although the paper lacks information on how miR-138 effects on the Lcn-2 gene itself or via other proteins. This is of importance as miR-138 is described to target various oncogenes like CCND1, p53, cyclins, MAP kinases, and others [3–5]. This might be an explanation for the interesting finding that miR-138 is downregulated in the metastatic tissue of liver but not lung metastases. To exclude bias due to small cohorts of patients (12 patients with liver metastasis, five patients with lung metastasis), confirmation of results in a larger patient series will be necessary, as stated by the authors in their conclusion. To summarize, miR-138 is identified as one target for the molecular regulatory mechanism of Lcn-2 that gives support to our descriptive data [6].

✉ Felix Aigner
felix.aigner@charite.de

[1] Department of Visceral, Transplant and Thoracic Surgery, Innsbruck Medical University, Innsbruck, Austria

[2] General, Visceral and Transplantation Surgery, Charité Universitätsmedizin Berlin, Campus Virchow-Klinikum, Berlin, Germany

## References

1. Cristóbal I, Torrejón B, González-Alonso P, Manso R, Rojo F, García-Foncillas J (2015) Downregulation of miR-138 as a contributing mechanism to Lcn-2 overexpression in colorectal cancer with liver metastasis. World J Surg. doi:10.1007/s00268-015-3241-z
2. Lee YC, Tzeng WF, Chiou TJ, Chu ST (2012) MicroRNA-138 suppresses neutrophil gelatinase-associated lipocalin expression and inhibits tumorigenicity. PLoS ONE 7(12):e52979. doi:10.1371/journal.pone.0052979
3. Wang Q, Tang H, Yin S, Dong C (2013) Downregulation of microRNA-138 enhances the proliferation, migration and invasion of cholangiocarcinoma cells through the upregulation of RhoC/p-ERK/MMP-2/MMP-9. Oncol Rep 29(5):2046–2052. doi:10.3892/or.2013.2304
4. Liu X, Lv XB, Wang XP, Sang Y, Xu S, Hu K et al (2012) MiR-138 suppressed nasopharyngeal carcinoma growth and tumorigenesis by targeting the CCND1 oncogene. Cell Cycle 11(13):2495–2506. doi:10.4161/cc.20898
5. Ye D, Wang G, Liu Y, Huang W, Wu M, Zhu S et al (2012) MiR-138 promotes induced pluripotent stem cell generation through the regulation of the p53 signaling. Stem Cells 30(8):1645–1654. doi:10.1002/stem.1149
6. Maier HT, Aigner F, Trenkwalder B, Zitt M, Vallant N, Perathoner A et al (2014) Up-regulation of neutrophil gelatinase-associated lipocalin in colorectal cancer predicts poor patient survival. World J Surg 38(8):2160–2167. doi:10.1007/s00268-014-2499-x