Author’s response to reviews

Title: The adipokine vaspin reduces apoptosis in human hepatocellular carcinoma (Hep-3B) cells, associated with lower levels of NO and superoxide anion

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Author’s response to reviews:

Dr. Magdalena Skonieczna
Gliwice, 13.10.2018
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Dear Editor,

Mainul Haque, MBBS, MPhil, MSc, CIDTT
BMC Pharmacology and Toxicology

Thank you very much for all critical marks, we are grateful for all comments. Followed by Reviewers comments, we have corrected our manuscript (PHAT-D-18-00156; titled “The adipokine vaspin reduces apoptosis in human hepatocellular carcinoma (Hep-3B) cells,
associated with lower levels of NO and superoxide anion.” By Magdalena Skonieczna, Ph.d.; Dorota Hudy; Tomasz Hejmo; Rafal J Buldak; Malgorzata Adamiec; Michal Kukla). We did not impact a substantive content of the manuscript, however we have added some technical and cosmetic changes, which in our opinion make the manuscript clear and more readable. All changes are pointed bellow and are highlighted in core of the re-submitted manuscript.

We are looking forward for editorial decision.

Yours sincerely
Magdalena Skonieczna

Page 1

Line 11-13: the e-mail addresses for all authors were added;

"Magdalena Skonieczna1,2*(magdalena.skonieczna@polsl.pl), Dorota Hudy1,2(dorota@hudy.pl), Tomasz Hejmo3 (tomekhejmo@gmail.com), Rafal J. Buldak3 (rbuldak@gmail.com), Malgorzata Adamiec1,2 (malgosiaa93@gmail.com), Michal Kukla4 (kuklamich@poczta.onet.pl)";

Page 2

Line 12: “hepatocarcinoma” changed to “hepatocellular carcinoma (HCC)”; 

Line 32: “p<0.050.” changed to “p<0.05).”;

Line 38: “hepatocellular cancer line” changed to “HCC”;

Line 47: “hepatomas” changed to “cancer”;

Page 3

Line 8: “Introduction” changed to “Background”;

Line 11: “termed adipokines or adipocytokines” was added;

Line 28-33: “An adipose tissue delivers a set of adipokines, which are regulators (growth factors, cytokines) of different signaling pathways.” was removed;

Line 33: “stimulation” changed to “regulation”;

Line 35: “metastasis” changed to “metastases”;

"Magdalena Skonieczna1,2*(magdalena.skonieczna@polsl.pl), Dorota Hudy1,2(dorota@hudy.pl), Tomasz Hejmo3 (tomekhejmo@gmail.com), Rafal J. Buldak3 (rbuldak@gmail.com), Malgorzata Adamiec1,2 (malgosiaa93@gmail.com), Michal Kukla4 (kuklamich@poczta.onet.pl)";
Line 50: “(NF-kB)” was added;

Line 50: “tumor necrosis factor α (TNF-α)” was added;

Page 4

Line 5: “Kukla et al., 2010” was added;

Line 14: “metabolic syndrome with insulin resistance” and (Derra et al. 2018) were added;

Line 20: “hepatocellular carcinoma” changed to “HCC”;

Line 37: „apoptosis” changed to “apoptotic”;

Line 47: “In the present study” was changed to “Aim of presented work, was to study”

Page 6

Line 15: “and at 5 ng/ml the level decreased.” was changed to “while at 5 ng/ml its level decreased.”

Line 35: “on” was added;

Page 7

Line 10: “free radicals” was added;

Page 8

Line 1: “adipose tissues play” was changed to “adipose tissue plays”;

Line 22: “tissues” changed to “tissue”;

Line 47: “supressed” was changed to “suppressed”;

Line 55: “Adipokines” was changed to “Some adipokines”;

Page 9

Line 2: “Only a few studies suggest a stimulatory effect of vaspin on proliferation of cancer cells (Booth at al., 2015; Erdogan et al., 2011; Fazeli et al., 2013) an elevated level was reported in colorectal cancers (Harwood et al., 2013) but a lower level in endometrial cancers (McCullough et al., 2008) and vaspin increased the proliferation of rat insulinoma cells (Liu et al., 2017) and stimulated angiogenesis after liver injuries and hepatocellular carcinoma (Waluga et al., 2017).” was changed to “Only a few studies suggest a stimulatory effect of vaspin on proliferation of cancer cells (Booth at al., 2015; Erdogan et al., 2011; Fazeli et al., 2013). An elevated vaspin level was reported in colorectal cancer (Harwood et al., 2013) but a lower level in endometrial
cancer (McCullough et al., 2008). Vaspin also increased the proliferation of rat insulinoma cells (Liu et al., 2017). Angiogenesis, new blood vessels formation, seems to be essential in cancer development and progression. Vaspin was positively related to intensity of angiogenesis in chronic hepatitis (Kukla et al., 2011) via association of adipokines with angiogenesis. The main risk factor of HCC in chronic liver diseases is advanced fibrosis/cirrhosis, which is strictly associated with angiogenesis intensity (Gabriel et al., 2009, Kukla et al. 2010). Vaspin serum levels and mRNA liver expression were found to be increased in patients with advanced fibrosis or cirrhosis in the course of chronic hepatitis (Kukla et a. 2012, Waluga et al. 2017). Pointing to these results, vaspin plays pivotal role in HCC development. Increased vaspin levels and expression in advanced liver disease may protect cancer cells against apoptosis and facilitate their proliferation.”

Line 55: “liver hepatocellular carcinoma cells showed connections” was changed to HCC cells showed association”;

Page 10

Line 10: “Although in Hep-3B cells we observed no significant elevation of global ROS level during 24 h of vaspin treatment” was changed to “Although in Hep-3B cells no significant elevation of global ROS level during 24 h of vaspin treatment was observed in our study”;

Line 37: “in our study” was added;

Line 40: “molecule; modulation” was changed to “molecule. Modulation”;

Line 44: “An adipose tissue produced set of adipocytes, which could be normal or damaged cells. Consequence for that could be also elevated pro-inflammatory cytokines production and vaspin inhibited that inflammatory process” was changed to “Consequence for that could be also elevated pro-inflammatory cytokines production and vaspin inhibited that inflammatory process”; 

Page 11

Line 28: “suppresed” was changed to “suppressed”;

Line 33: “liver hepatocellular carcinoma” was changed to “HCC”;

Line 38: “nuclear factor-kappaB (NF-κB)” was changed to “NF-κB”;

Line 45: “this adipokine” was changed to „ vaspin”; 

Line 48: “observed; although” was changed to “observed. Although”;
Moreover, vaspin levels increased in definite nonalcoholic steatohepatitis when compared to simple steatosis and in patients with hepatocyte ballooning, which may reflect oxidative stress and mitochondrial dysfunction in hepatocytes (Kukla et al. 2010)."

Page 13

Line 8: “Dr” was changed to “Dr.”

Page 19


Page 20


Page 21

Line 28:
