



Corrigendum: Metabolic Dependencies in Pancreatic Cancer

Ali Vaziri-Gohar¹, Mahsa Zarei^{2,3}, Jonathan R. Brody⁴ and Jordan M. Winter^{1,5*}

¹ School of Medicine, Case Western Reserve University, Cleveland, OH, United States, ² Department of Veterinary Physiology and Pharmacology, Texas A&M University, College Station, TX, United States, ³ Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, United States, ⁴ Division of Surgical Research, Department of Surgery, Jefferson Pancreas, Biliary and Related Cancer Center, Jefferson Medical College, Thomas Jefferson University, Philadelphia, PA, United States, ⁵ Department of Surgery and Division of Surgical Oncology, University Hospitals Cleveland Medical Center, Cleveland, OH, United States

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A Corrigendum on

Metabolic Dependencies in Pancreatic Cancer

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In the original article, all references for in **Tables 1, 2** were incorrectly listed. The corrected references for both **Table 1** and **Table 2** have been corrected and provided below.

In the original article, references in **Table 2** were not provided in the reference list. The references have now been inserted.

The authors apologize for these errors and state that they do not change the scientific conclusions of the article in any way. The original article has been updated.

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*Correspondence:

Jordan M. Winter
jordan.winter@UHhospitals.org

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TABLE 1 | Metabolic dependencies in PDA.

Event	Mediated by	References
MITOCHONDRIAL METABOLISM		
Increased oxidative phosphorylation	Down regulation of Drp1 HuR	(61) (50)
Increased biogenesis	HuR	Unpublished
NUTRIENT ACQUISITION		
Autophagy	Oncogenic KRAS	(74)
NAD ⁺ salvage pathway	miR-206	(78, 79)
Macropinocytosis	Oncogenic KRAS	(35)
Increased alanine uptake	Oncogenic KRAS	(85)
REDOX HOMEOSTASIS		
Upregulation of ME1	Oncogenic KRAS	(57)
Upregulation of NRF2	Oncogenic KRAS	(97)
Upregulation of IDH1	HuR	(50)

TABLE 2 | Clinical trials targeting key steps of PDA metabolism.

Target	Agent	Phase and status	NCT No.	References
MITOCHONDRIAL OXPHOS				
ETC	Metformin + gemcitabine + ertotinib	II; Completed	NCT01210911	(63)
	Metformin + paclitaxel	II; Completed	NCT01971034	(103)
	Metformin + gemcitabine/nab-paclitaxel	I; Recruiting	NCT02336087	
	Metformin + mFOLFIRINOX	II; Active	NCT01666730	
	Metformin + rapamycin	Ib; Active	NCT02048384	
	Metformin + radiosurgery	I; Active	NCT02153450	
TCA cycle	CPI-613	I; Completed	NCT01839981	
	CPI-613 + mFOLFIRINOX	I; Active	NCT01835041	(67)
	CPI-613 + gemcitabine/nab-paclitaxel	I; Active	NCT03435289	
NUTRIENT ACQUISITION				
Autophagy	HQC	II; Completed	NCT01273805	(104)
	HQC + gemcitabine	I/II; Active	NCT01128296	
	HQC + gemcitabine + abraxane	I/II; Active	NCT01506973	
	CQ + gemcitabine	I; Completed	NCT01777477	(105, 106)
REDOX HOMEOSTASIS				
Glutaminase	CB-839	I; Active	NCT02071862	

HQC, hydroxychloroquine; CQ, chloroquine; mFOLFIRINOX, modified FOLFIRINOX.

REFERENCES

- Commisso C, Davidson SM, Soydaner-Azeloglu RG, Parker SJ, Kamphorst JJ, Hackett S, et al. Macropinocytosis of protein is an amino acid supply route in Ras-transformed cells. *Nature* (2013) 497:633–7. doi: 10.1038/nature12138
- Zarei M, Lal S, Parker SJ, Nevler A, Vaziri-Gohar A, Dukleska K, et al. Posttranscriptional upregulation of IDH1 by HuR establishes a powerful survival phenotype in pancreatic cancer cells. *Cancer Res.* (2017) 77:4460–71. doi: 10.1158/0008-5472.CAN-17-0015
- Son J, Lyssiotis CA, Ying H, Wang X, Hua S, Ligorio M, et al. Glutamine supports pancreatic cancer growth through a KRAS-regulated metabolic pathway. *Nature* (2013) 496:101–5. doi: 10.1038/nature12040
- Rambold AS, Kostecky B, Elia N, Lippincott-Schwartz J. Tubular network formation protects mitochondria from autophagosomal degradation during nutrient starvation. *Proc Natl Acad Sci USA.* (2011) 108:10190–5. doi: 10.1073/pnas.1107402108
- Kordes S, Pollak MN, Zwinderman AH, Mathot RA, Weterman MJ, Beeker A, et al. Metformin in patients with advanced pancreatic cancer: a double-blind, randomised, placebo-controlled phase 2 trial. *Lancet Oncol.* (2015) 16:839–47. doi: 10.1016/S1470-2045(15)00027-3
- Alistar A, Morris BB, Desnoyer R, Klepin HD, Hosseinzadeh K, Clark C, et al. Safety and tolerability of the first-in-class agent CPI-613 in combination with modified FOLFIRINOX in patients with metastatic pancreatic cancer: a single-centre, open-label, dose-escalation, phase 1 trial. *Lancet Oncol.* (2017) 18:770–8. doi: 10.1016/S1470-2045(17)30314-5
- Yang S, Wang X, Contino G, Liesa M, Sahin E, Ying H, et al. Pancreatic cancers require autophagy for tumor growth. *Genes Dev.* (2011) 25:717–29. doi: 10.1101/gad.2016111
- Ju HQ, Zhuang ZN, Li H, Tian T, Lu YX, Fan XQ, et al. Regulation of the Nampt-mediated NAD salvage pathway and its therapeutic implications in pancreatic cancer. *Cancer Lett.* (2016) 379:1–11. doi: 10.1016/j.canlet.2016.05.024
- Chini CC, Guerrico AM, Nin V, Camacho-Pereira J, Escande C, Barbosa MT, et al. Targeting of NAD metabolism in pancreatic cancer cells: potential novel therapy for pancreatic tumors. *Clin Cancer Res.* (2014) 20:120–30. doi: 10.1158/1078-0432.CCR-13-0150
- Sousa CM, Biancur DE, Wang X, Halbrook CJ, Sherman MH, Zhang L, et al. Pancreatic stellate cells support tumour metabolism through autophagic alanine secretion. *Nature* (2016) 536:479–83. doi: 10.1038/nature19084
- DeNicola GM, Karreth FA, Humpton TJ, Gopinathan A, Wei C, Frese K, et al. Oncogene-induced Nrf2 transcription promotes ROS detoxification and tumorigenesis. *Nature* (2011) 475:106–9. doi: 10.1038/nature10189
- Braghiroli MI, de Celis Ferrari AC, Pfiffer TE, Alex AK, Nebuloni D, Carneiro AS, et al. Phase II trial of metformin and paclitaxel for patients with gemcitabine-refractory advanced adenocarcinoma of the pancreas. *Ecancermedicalscience* (2015) 9:563. doi: 10.3332/ecancer.2015.563
- Wolpin BM, Rubinson DA, Wang X, Chan JA, Cleary JM, Enzinger PC, et al. Phase II and pharmacodynamic study of autophagy inhibition using hydroxychloroquine in patients with metastatic pancreatic adenocarcinoma. *Oncologist* (2014) 19:637–8. doi: 10.1634/theoncologist.2014-0086
- Balic A, Sørensen MD, Trabulo SM, Sainz B, Cioffi M, Vieira CR, et al. Chloroquine targets pancreatic cancer stem cells via inhibition of CXCR4 and hedgehog signaling. *Mol Cancer Ther.* (2014) 13:1758–71. doi: 10.1158/1535-7163.MCT-13-0948
- Samaras P, Tusup M, Nguyen-Kim TDL, Seifert B, Bachmann H, von Moos R, et al. Phase I study of a chloroquine-gemcitabine combination in patients with metastatic or unresectable pancreatic cancer. *Cancer Chemother Pharmacol.* (2017) 80:1005–12. doi: 10.1007/s00280-0173446-y

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