

## Accepted Manuscript

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PII: S0005-2728(18)30055-0  
DOI: doi:[10.1016/j.bbabbio.2018.03.012](https://doi.org/10.1016/j.bbabbio.2018.03.012)  
Reference: BBABIO 47892

To appear in:

Received date: 17 January 2018  
Accepted date: 19 March 2018

Please cite this article as: Roberto E. Flores, Ashley K. Brown, Luke Taus, Julianna Khoury, Frank Glover, Kenjiro Kami, Rangaprasad Sarangarajan, Tony Walshe, Niven R. Narain, Michael A. Kiebish, Laura Shelton, Christos Chinopoulos, Thomas N. Seyfried , Mycoplasma infection and hypoxia initiate succinate accumulation and release in the VM-M3 cancer cells. The address for the corresponding author was captured as affiliation for all authors. Please check if appropriate. Bbabbio(2018), doi:[10.1016/j.bbabbio.2018.03.012](https://doi.org/10.1016/j.bbabbio.2018.03.012)

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# Mycoplasma infection and hypoxia initiate succinate accumulation and release in the VM-M3 cancer cells

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## Abstract

Succinate is known to act as an inflammatory signal in classically activated macrophages through stabilization of HIF-1 $\alpha$  leading to IL-1 $\beta$  production. Relevant to this, hypoxia is known to drive succinate accumulation and release into the extracellular milieu. The metabolic alterations associated with succinate release during inflammation and under hypoxia are poorly understood. Data are presented showing that *Mycoplasma arginini* infection of VM-M3 cancer cells enhances the Warburg effect associated with succinate production in mitochondria and eventual release into the extracellular milieu. We investigated how succinate production and release was related to the changes of other soluble metabolites, including itaconate and 2-HG. Furthermore, we found that hypoxia alone could induce succinate release from the VM-M3 cells and that this could occur in the absence of glucose-driven lactate production. Our results elucidate metabolic pathways responsible for succinate accumulation and release in cancer cells, thus identifying potential targets involved in both inflammation and hypoxia.

Abbreviations: succinate, Warburg effect, hypoxia, itaconate, lactate, fermentation, Crabtree effect, inflammation, cancer, macrophage, immunometabolism

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